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USG MUSCULOSKELETAL COURSE
USG Musculoskeletal Course: Introduction

APLAR-0516

Image acquisition and ultrasound technique

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In general, sonography is considered as the most operator dependent imaging technique. However, if operator is equipped with correct and precise ultrasound knowledge and understand well the importance of machine set-up for optimal image acquisition and operator can manipulate aspects of US equipment to obtain optimal image, it is not so difficulty thing to get good images avoiding intra- and inter observer variation.

Before you start you ultrasound examination, it needs to check the ergonomics of ultrasound systems and the operating environment. Appropriate lightening is necessary to view the US equipment monitor. The operator must be comfortable during the examination to prevent musculoskeletal pain and strain. A higher frequency probe which has more than 10 MHz is preferable for the assessment of superficial lying structures such as hand metacarpophalangeal joint. While examining patients, operator should check the number of focus and its position.

Anisotropy is one that displays different properties depending on the direction of ultrasound beam. Musculoskeletal ultrasound involves imaging of strongly anisotrophic reflectors such as tendons, muscles and ligaments. Thus, even minimal changes of the position of the probe can significantly affect the final sonographic image.

The position in which a joint is scanned for synovitis appears to significantly influence the ultrasound assessment of synovitis. The pressure of the probe on the skin may result in a marked reduction of the Doppler signal to the almost total disappearance. Pulse Repetition Frequency (PRF) is the Doppler sampling frequency of the transducer reported in Hz. The sensitivity of both colour Doppler and power Doppler is affected by PRF adjustments.

USG Musculoskeletal Course: The Knee

APLAR-0511

Standard scans, sonographic anatomy, and basic sonographic pathology

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Anatomy; The knee joint is a synovial joint that consists of hyaline cartilage articulations between the femur, the tibia and patella. A prominent joint recess, the suprapatellar recess, extends superiorly from the knee joint between the patella and the femur and extends over the medial and lateral aspects of the femoral condyle. In the sagittal plane, the quadriceps fat pad is located anteriorly between the suprapatellar recess and quadriceps tendon. Various bursa exist about the anterior knee joint, including the prepatellar bursa, the superficial infrapatellar bursa, and the deep infrapatellar bursa. The knee joint is stabilized by a number of ligaments. Medially, the medial collateral ligament extends from the medial femoral condyle to the tibia. The lateral or fibular collateral ligament originates from the lateral femur and extends over the popliteus tendon to insert on the lateral aspect of the fibula with biceps femoris tendon.

Standard Scan; The primary structures evaluated from the anterior approach of ultrasound are the quadriceps tendon, the patellar tendon, suprapatellar recess and the bursa about the anterior knee. The structures of interest medially include the medial collateral ligament, the anterior horn of medial meniscus and the pes anserinus. Structures of interest laterally include the iliotibial band, the lateral collateral ligament and the biceps femoris tendon. The structures and pathology of interest posteriorly include a Baker's cyst.

Basic ultrasonographic pathology; Knee joint effusion is characterized by anechoic or hypoechoic distension of the suprapatellar recess. Synovial proliferation is found in most inflamed knees. It may exhibit power Doppler signals in correlation with the inflammatory activity. Synovial proliferation can best be detected in the lateral area of the suprapatellar recess. Prepatellar and infrapatellar bursitis can be depicted by ultrasound. Commonly used urate lowering therapy in gout. It is generally well tolerated but rarely is associated with the potentially fatal allopurinol hypersensitivity syndrome (AHS). Risk factors for development of AHS include female sex, age, renal impairment, diuretic use, recent commencement of allopurinol therapy and in some ethnic groups, the HLA-B*5801 genotype.

The relationship between allopurinol dose and AHS is controversial. Dose reduction in renal impairment is based on a reported relationship between 'full dose' allopurinol (≥300 mg/d) in patients with renal impairment and development of AHS. This observation, along with recognition that excretion of the active metabolite oxypurinol is significantly reduced in patients with impaired renal function, led to the suggestion that allopurinol should be dosed according to creatinine clearance. However, such dosing is frequently association with failure to reach target serum urate. The relationship between allopurinol starting dose and AHS is unknown. Furthermore, once established on allopurinol the maintenance dose may not be associated with AHS.

In a retrospective case-control study of patients with gout who developed AHS we have shown that allopurinol starting dose is associated with AHS. For the highest quintile of starting dose/eGFR, the odds ratio was 23.2 ($P < 0.01$). ROC analysis indicated that 91% of AHS cases and 36% of controls started on a dose of allopurinol at ≥1.5 mg allopurinol per unit eGFR (mg/mL/min). In another intervention study we have shown that, in patients who tolerate allopurinol the dose can be up-titrated to achieve target serum urate, even in patients with renal impairment.

APLAR REVIEW COURSE ABSTRACTS
ARC01 – APLAR review course

Rheumatoid arthritis: treatment of severe RA

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Abstract not available.

APLAR-0494

Review and update of ankylosing spondylitis

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SPA consists of a lot of diseases in this family, which includes AS, ReA, PsA, etc. They shared some clinical features RF(−), B27(+), sacroiliiitis, mucotaneous lesions. The most common and important prototype is ankylosing spondylitis. Recently, in order to recognize early and treat SpA early, to determine the pre-axial SpA is becoming an important issue.

In AS, the primary target lesion is enthesis. Enthesitis starts first and then spreads from center area to the surrounding tissues or organs, for example, the synovial tissues to induce synovitis, the cartilage to cause chondritis, the subchondral bone to cause osteitis and tendon-synovial part to cause tenosynovitis or dactylitis.

The destination of AS is variable in each patient. It can start from acute inflammation and then chronic inflammation in the synovium, cartilage, tendon and bone. At this stage, many inflammatory cells infiltration which is shown in the pathologic pictures. The bone inflammation can present osteitis or Romaneus sign which may accompany with SI joint or bone erosion. After inflammation, activated osteoblasts may promote later new bone formation and syndesmophyte formation. Eventually, some patients get ankylosis and bamboo spine on x-ray.

For treatment of AS, until now, we are still follow the 2006 ASAS/EULAR recommendations. For only axial involvement, NSAIDs are the 1st line drugs and 70–80% got improvement. If fail, biologic therapy is indicated. In case with peripheral joint involvement, salazopyrin 2–3 gm/day is added with NSAIDs and if fail, anti-TNF-a therapy is recommended.

The new therapy that we are looking forward to use in AS including the anti-IL17, Tocilizumab (anti-IL6R), Usterkinumab (anti-P40), and JAK inhibitor, etc.

Psoriasis and cutaneous manifestations of rheumatic diseases, what is new?

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Abstract not available.

APLAR-0498

Crystal-induced arthritis: diagnosis and management

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Gout, CPPD deposition disease, and BPC deposition disease are probable the three most common crystal-induced arthritis (CIA) in man. If left untreated, this CIA can become chronic, and lead to progressive joint destruction. The diagnosis of CIA requires demonstration of pathologic crystals in synvovial fluid (SF) or body tissue. SF analysis using light and compensated polarized light microscopy is the most convenient and cheapest method for identifying crystals; unfortunately, many physicians ignore the importance of SF analysis. Treatment of acute CIA should be initiated as soon as the arthritis starts, in order to stop the acute inflammatory process as early as possible. NSAIDs are the main anti-inflammatory therapy. Colchicine is also effective if started very early in the course of arthritis. Corticosteroids, intra-articular corticosteroids, and adrenocorticotropic hormone can be used in patients who are contra-indicate to NSAIDs and colchicine. Recently, interleukin-1β blockades have been shown as very effective in treating difficult-to-treat acute gout, however, they have not been approved yet for this condition. In those with frequent, recurrent attacks, a prophylaxis should be considered. Except for gout, there has been no medication that can remove crystals from the body so far. In gout, uricosuric agents should be considered in patients with hypoexcretor and no renal calculi. Xanthine oxidase inhibitors should be considered in patients with advanced disease, presence of tophi or renal calculi, and renal impairment. A recent FDA approved urate oxidase, pegloticase, has been shown as effective in reducing serum uric acid in patients with severe gout, allopurinol intolerance or refractoriness to conventional hypouricemic agents. In addition, physicians should search for co-morbidities, and underlying metabolic or endocrine diseases, which commonly co-exist, and treat them properly. The education of patients also is important for obtaining good compliance, which in turn achieves the highest benefit from the treatment.

APLAR-0527

Measurement, management and new target therapy in SLE

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Systemic lupus erythematosus is a chronic autoimmune disease characterized, especially in Asian patients, by severe multi-organ damage and loss of life expectancy. Assessment of disease activity in a multisystem disease is highly complex, and agreement on the optimum method for this has not been reached. Current treatments are incompletely effective, and assessment of treatment responses is made difficult by these complexities. New ways to assess treatment responses in SLE are needed in order to facilitate the evaluation of novel targeted therapies.

In this presentation, current methods of measurement of disease activity in SLE, and methods of measuring treatment responses, will be examined. A proposal for a novel measurement of treatment success in SLE, which is the subject of a current multinational Asian study, will be discussed. Finally, progress on the identification and study of new therapeutic targets will be reviewed.

APLAR-0529

The uses of imaging in musculoskeletal diseases

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Musculoskeletal imaging has been revolutionised, the standard was x-ray which is insensitive and only measures radio-opaque features. It is good at measuring boney erosions in late disease but it is poor at measuring small erosions early. The ability of MRI and ultrasound to simultaneously visualise soft tissue and boney changes has completely changed assessments.

MRI: MRI has the ability to do what x-ray does, but better. It measures erosions early and in addition measures synovitis which can predict erosions. It has been validated with biopsies. It is ideal for proof of concept studies and has been used to show the evidence of bisphosphonates and recently correctly predict x-ray progression with new agents. Furthermore it can do *what x-ray cannot do* which is measure synovitis as a predictor of erosions, can measure enthesitis in the spondyloarthropathies and has allowed a diagnosis based on pathogenesis (recently confirmed by the IL-23R spondylo arthroprogenic cell). It has allowed an understanding of the basic features of psoriatic arthritis including nail disease. It can also measure a cartilage and has been shown to demonstrate differences in cartilage loss with new agents. It can be used in osteoarthritis to show both boney and ligamentous changes. Finally it is capable of measuring tenosynovitis, an area which is becoming increasingly important particularly in early disease and pre-clinical disesase.

Ultrasound: Ultrasound can do nearly all the things that MRI can with the exception of bone oedema. It has a particular use in assessing the patients at presentation. Perhaps its greatest use currently is assessing patients in stable state/remission. It is now clear that Power Doppler in patients in apparent clinical remission is a good predictor of subsequent x-ray progression. Furthermore it has been demonstrated that prolonged therapy is required to reduce Power Doppler. To this end an international group has been established, the targeted ultrasound initiative (TUI) which aims to make ultrasound a standardised part of ultrasound assessment and has produced a series of recommendations. These have recently been endorsed by the EULAR recommendations for imaging.

APLAR-0491

Systemic sclerosis, macro and microvascular problem and its management

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Systemic sclerosis (SSc) is an autoimmune condition that is characterised by RaynaudsÕ phenomenon, sclerodermatous skin changes and internal organ fibrosis. Endothelial dysfunction, immune hyperactivity and fibroblast hyperproliferation are believed to play important role in the underlying pathogenesis. SSc predominantly presents with microvascular involvement such as nailbed capillary abnormality and vasospastic and occlusive small vessel changes in RaynaudÕs phenomenon. Repetitive ischaemia-reperfusion injury is believed to contribute to endothelial injury in SSc with resultant production of reactive oxygen species and free radicals from oxidative stress. Endothelial injury leads to reduction in bioavailability of endothelial derived nitric oxide resulting in loss of regulation of vasomotor tone and procoagulant phenotype of the endothelium. Production of various cytokines in the process contributes to inflammatory reaction and the occlusive small vessel changes leading to organ ischaemia and malfunction.

As endothelial dysfunction is central to pathogenesis of SSc and is shared by the atherogenic process in early development of generalised atherosclerosis andin addition to the underlying inflammation, SSc patients are likely at risk of developing atherosclerosis and macrovascular disease. Indeed, coronary and cerebrovascular diseases have been increasing reported in these patients. Using flow-mediated dilatation of peripheral arteries and CT coronary calcium scoring respectively, SScpatients with endothelial dysfunction and subclinical vascular disease as well as those with macrovascular disease can be identified. As cardiovascular burden plays a significantrole in the long term prognosis of SSc, identification of high-risk patients using these investigative means with early intervention and prevention may hopefully reduce the impact of atherosclerosis and vascular diseases in these patients.

PLENARY LECTURE ABSTRACTS
Plenary lecture 1

PL01

Future therapy for rheumatoid arthritis

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Future management will largely be an extension of present day practice combined with new innovations.

Presentation: As the optimal management of RA is the central activity for rheumatologists and early diagnosis is essential; much better networks will be established for referring patients early. Patients will be referred for one stop assessment which will include imaging. This will focus on synovial inflammation; boney damage will be a thing of the past.

Prediction: Part of the initial assessment will be an accurate prediction of the outcome and algorithms will be developed for patients such that early remission will be the aim for all. Imaging will again be an important part of this. Predictors of response to methotrexate will be included to avoid unnecessary periods of time without effective therapy. Knowledge of B-cell responses related to B-cell levels will also be included in the initial assessment.

Remission and stopping therapy and maintaining response: Remission will be induced as rapidly as possible. The minimum acceptable remission rate will in future be >50% would be obtained by using methotrexate where they are likely to be responsive and a combination of biologics and those that are not.

A proportion of patients having reached remission can successfully stop therapy. This is particularly true for patients who have remission induced by combination biologic and methotrexate. Assessment will take place during remission allowing a prediction of whether it is possible to stop or just reduce therapy.

Prevention: Pre-clinical disease is now much better defined and pre-clinical clinics are now established in several centres. Patients will be seen when they are at risk of inflammatory arthritis, particularly those with systemic autoimmune disease. There is already evidence that assessing these patients by imaging, immunological biomarkers and evidence of systemic inflammation can predict the rapid progression to clinical disease, and in these patients intervention will take place probably with methotrexate. The aim as always will be to normalise patients as rapidly as possible from an immunological and imaging point of view.

Therapeutic strategy based on pathogenesis – It is now clear that RA can be viewed as a palindrome with early changes in imaging and immunology preceding other abnormalities. Based on this understanding there will be targeted therapies. Overall in the future the aim will be to make rheumatoid arthritis an acute rather than a chronic condition.

Plenary lecture 2

PL02

Treatment strategies in patients with rheumatoid arthritis for whom methotrexate has failed

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The current treatment strategy of patients with RA should focus on the following aspects:

- early diagnosis
- early use of synthetic disease modifying therapies (MTX)
- identify a treatment target (remission or low disease activity)
- monitor (tight control) and adjust disease-modifying therapy according to the target
- add biological DMARD if target is not achieved
- continue to monitor and adjust therapy as long as the target is not achieved

As the management of RA continues to advance, the scope of what rheumatologists need to consider for the optimal management of their patient is evolving. This scope currently includes pertinent topics such as the unmet need of patients with moderately active RA, the importance of registry data when considering drug survival, effectiveness and safety of the TNF inhibitors and the cost-effectiveness of various regimens.

Patients who fail therapy with MTX monotherapy (with or without corticolsteroids) will usually have three options: Change to another synthetic DMARD (e.g. leflunomide), add on other synthetic DMARDs (e.g. triple therapy with sulfasalazine and hydrochloroquine) or add on a biological DMARD (usually a TNF inhibitor). The 2013 update of the EULAR recommendation for the management of RA with synthetic and biological DMARDs addresses these issues in detail, and recommend that prognostic factors should be taken into account when the clinician will either start another regimen with synthetic DMARDs (absence of poor prognostic factors) or start a biological DMARD regimen (presence of poor prognostic factors). When such second therapies are started, the general principles listed above should be followed, i.e. a treatment target should be determined and a tight control follow-up regimen should be established with options to modify or again switch therapy if the target is not achieved.

Plenary lecture 3

PL03

The new insight in pathogenesis of systemic sclerosis

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Abstract not available.

Plenary lecture 4

PL04

How to treat osteoarthritis: international consensus

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Over 53 treatments are available for osteoarthritis (OA). Clinical practice guidelines recommend non-pharmacological treatment first, followed by or added with pharmacological treatments if needed. Surgical treatments are only provided to patients with severer OA who do not respond to the conservation therapy.

Although non-pharmacological treatment has limited benefit, it is safer and suitable for long-term management. Exercise, for example, is a core therapy recommended by all guidelines for OA. The long-term application may lead to both symptomatic and disease modification effects. Current research shows that mind-body exercise such as Taiqimay be more effective than body only exercise. This observation has led to the further understanding of pain due to OA and suggests that the treatment of OA should not only target on the joint, but also brain where the pain is centred. However, adherence to exercise ispoor. Further research to increase adherence is required.

Pharmacological treatment is often limited by side effects. Unlike acute pain, OA is a chronic painful arthritis which requires long-term management. Unfortunately except for nutraceuticals (vitamin supplements, glucosamine and chondroitin products, avocado soybean unsaponifiables), all other drugs have serious side effects. Paracetamol is no longer safe according to the current evidence. Topical non-steroidal anti-inflammatory drugs are the only oneanalgesic which has preferable safety profile but it is not applicable for multiple join OA. Intra-articular corticosteroid is useful but only suitable for single joint OA and ina short-term period. The efficacy of intra-articular hyaluronic acidremains controversial.

Surgical treatment is required if the conventional therapy is ineffective at the late stage of the disease. Lavage and debridement are no better than placebo. Osteotomy, patellar resurfacing or unicompartment knee arthroplastymay be considered prior to the total joint replacement.

New agents targeting on inflammation biomarkers (e.g. cytokines), and neuropathic pathways (e.g. nerve growth factors) are currently developed. Stem cells and joint distraction have been investigated to treat OA. However, side effects of these treatments remain unknown and it is still too early to recommend. Current management of OA largely relies on the optimisation of the available treatments. Research is heading towards the identification of clinical subgroups of OA, predictors of response and contextual care to enhance the treatment benefits. It is anticipated that in the next 5 years, the OA therapy will change substantially.

Plenary lecture 5

PL05

The challenges of rheumatic treatment in developing country

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Rheumatologists in developing countries face many challenges in providing the best treatment for their patients. Prevention measures have also been proven a challenge by many rheumatologists. Even though our discussion is mainly based on condition in Indonesia (as one of the world's biggest developing countries with population of 240 million), many studies conducted in other developing countries have concluded similar conditions. First and foremost challenge is the socio-economic factor; poverty, education and the society's lack of awareness towards health and well-being in general.

As the result of increase aging population and economic growth, developing countries are currently facing the so-called "epidemiological transition"; in which life-threatening communicable diseases such as tuberculosis, malaria, hepatitis and diarrhea are still endemic, and at the same time non-communicable diseases such as cardiovascular disease, hypertension, diabetes and rheumatic are also increasingly widespread. Thus, the priority of health professionals in these countries is currently divided (albeit infectious diseases take precedence) with the growing number of patients in both categories. The countries continuous fight against infectious diseases cause a non-infectious disease such as rheumatic not becoming a main priority for government policy and funding – thus the inadequacy of treatment facility, as well as the unavailability of affordable rheumatic medication. In Indonesia, many patients of low socio-economic status often simply cannot afford the best rheumatic treatment.

The second challenge faced by rheumatologists in developing countries is the lack of awareness and understanding of cause and symptoms of rheumatic disease. Individuals suffering from rheumatic diseases often try to self-medicate and after sometime without any significant improvements they seek the help of health professionals – often when it is already too late. Rheumatologists frequently discover the incorrect use of NSAIDs by self-medicating individuals as well as the excessive use of herbal and other natural products. In Indonesia, it is common to switch and see a number of doctors or known as physician window shopping – and patients often end up with a number of conflicting drugs and different advice. Additionally, the general perception towards rheumatic drugs is that long-term use can cause renal damage and individuals suffering this disease are better off taking traditional or herbal medicine.

The third challenge is the small number of available rheumatologists in proportion of the countries' population. GPs and nurses often treat rheumatic patients in which sometimes inappropriate drugs and treatment have been prescribed due to their lack of expertise – often in the case of autoimmune rheumatic diseases. Some of these individuals are eventually referred to a rheumatologist when it is often too late. Another challenge faced by rheumatologists in developing countries is the differing clinical manifestation of the disease such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and Gout in comparison to the developed countries. In developing countries, the clinical manifestation found in SLE patients is often more severe – impacts on kidneys, progressive disease activity and infections which ultimately result in shorter life expectancy. In the case of RA, even though it was reported that extra articular manifestations is rare in developing countries, RA is reported more progressive in some patients. It is suggested that the different is related to a number of factors such as racial, low socio-economy and lack of education. Gout is also increasingly common in developing countries, with more severe clinical manifestation often due to treatment failure.

A different manifestation of rheumatism can also be found as the result of certain infectous diseases endemic in developing countries. Chikunguya is an example of infectious disease found in developing countries with rheumatic symptoms. Formerly Chikunguya reported to be associated with polyarthalgia only, however some recent cases have developed into chronic arthritis mimicking RA. Another example is the much higher prevalence Leprosy and HIV infection in developing countries which also show a significant manifestation of arthritis. The association between infection and rheumatic diseases has show us the importance of tropical rheumatology, at least for rheumatologists in developing countries.

The prevalance of tuberculosis, hepatitis B&C and HIV in developing countries has proven to be a challenge in relation to the use of DMARDs and biological agents on RA. To prevent recurrence of these diseases, tighter screening needs to be applied before administering DMARDs and biological agents. There is a need for a guideline to resolve related problems, such as the criteria and methods to determine latent TB and their prevention measures. These guidelines should also explain the vaccination procedure to individuals with autoimmune rheumatic disease such as RA.

In facing these challenges rheumatologists are urged to be more proactive in their approach to the disease in developing countries. This can done through extensive data findingon the prevalence and severity of rheumatic disease in their own country and presenting these facts to their respective government. The results of epidemiological studies in developing countries show that rheumatism/musculoskeletal symptoms are one of the most common diseases within the society. With the improved government and general population's awareness against rheumatic disease, policy and funding for treatment may be brought out and made available. Additionally, a broader understanding of the disease both in general population and health professionals: GPs and nurses should be reinstated. Lastly, new medical graduates should be made aware of the prevalence of rheumatic disease, in the hope of attracting their interest in the field to further overcome the rheumatologist shortage.

Biologics are highly effective in the treatment of rheumatoid arthritis (RA), but they are very expensive. The costs of biologics should limit their usage in patients with RA, especially in the developing countries. Therefore, it is necessary to develop suitable strategies for treating RA patients in these countries. Several studies showed that with tight control strategy the use of DMARDs may give better outcome for patients with rheumatoid arthritis. The high costs problem of biologic agents for patients with RA in developing countries will soon be overcome with the development of biosimilar agents. However, major issues regarding their safety and efficacy should be solved before these agents can routinely substitute previous biologic agents.

Plenary lecture 6

PL06

Standards of care for rheumatoid arthritis: NICE or nasty?

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Abstract not available.

SYMPOSIA ABSTRACTS
SS01 – Updates on osteoporosis and vitamin D

APLAR-0493

Vitamin D levels: its relationship to bone mineral density response and disease activity in systemic lupus erythematosus patients on corticosteroids

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Vitamin D is a fat-soluble steroid hormone which is responsible for maintaining the concentration of serum calcium and phosphate and promoting the healthy mineralization, growth and remodeling of bone. This is mediated through its active metabolite 1,25 dihydroxyvitamin D3 [1,25(OH)D3]. In addition, T cells, B cells and dendritic cells are capable of producing hydroxylase enzymes that convert vitamin D into 1,25(OH)D3 locally in a paracrine manner. This locally produced 1,25(OH)D3 has been shown to modulate both the innate and adaptive immune responses.

Patients with systemic lupus erythematosus (SLE) generally have low levels of 25(OH)D, a marker of vitamin D stores in the body. Sunlight is a major source of vitamin D; however, SLE patients are advised to avoid sunlight due to photosensitivity and to reduce the chances of a disease flare.

Higher levels of 25(OH)D have been linked to higher BMD. However, in SLE patients, low levels of 25(OH)D have not been consistently associated with low BMD. The presence of osteoporosis in SLE patients has been shown to be between 4% and 42%, and osteopenia in another 11–74%. In addition, a high incidence of asymptomatic vertebral fractures has been shown in both pre- and post-menopausal SLE patients. The influence of glucocorticoids (GC) on BMD in SLE patients remains uncertain; studies that have shown a positive association between GC with reduced BMD are balanced by almost an equal number those that do not. Low levels of 25(OH)D have also been shown in the larger cross-sectional studies to have an inverse relationship with SLE disease activity.

In conclusion, physicians caring for SLE patients need to be aware of potential vitamin D insufficiency/deficiency and should try to maintain a level of 25(OH)D of above 30 ng/mL.

APLAR-0479

Understanding osteoporosis in rheumatic diseases beyond bone density – bone quality and strength

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Previous cross-sectional and longitudinal studies offer epidemiologic evidence for reduced bone mineral density (BMD) and increased fracture risk in rheumatic disease patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Recent studies have demonstrated that prevalent vertebral fractures occur in SLE patients is independent of bone mineral density (BMD). Apart from the traditional risk factors, increased inflammatory mediators and cytokines, and the use of corticosteroids are associated with lower BMD, and both higher cumulative and daily dosages of corticosteroids appear to be predictive of reduced BMD in longitudinal studies.

The factors contribute to bone strength include BMD and bone quality, which encompasses important factors such as the rate of remodeling (bone turnover), mineralization, microarchitecture, and bone size and geometry. Areal BMD (aBMD) measurement with dual-energy X-ray absorptiometry (DXA) is the current gold standard for clinical assessment of bone fracture risk, and it is clear that fracture risk generally increases with decreasing BMD. However, a normal BMD T-score in an individual patient does not exclude the possibility of osteoporosis. Advances in technology have allowed non-invasive assessment of bone microarchitecture in vivo. The high-resolution peripheral quantitative computed tomography (HR-pQCT) system yields 3D images with an isotropic voxel size of 82 μm. It has potential to measure volumetric BMD and to visualize bone microarchitecture that previously could be assessed only on bone biopsy samples. HR-pQCT provides measurement analogues to those obtained by 2D histomorphometry and 3D μCT of biopsy specimens, including trabecular bone volume to tissue volume, number of trabeculae, trabecular separation. Studies using this technique have provided unique insights into sex-specific and compartment-specific bone loss in the appendicular skeleton.

We applied the HR-pQCT system onto the patients with SLE and RA to investigate the role of this new technology in determining fracture risk and monitoring anti-resorptive treatment in SLE.

APLAR-0540

Mythbusters – busting the myths of the 10 areas of most controversy in osteoporosis management

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The last decade has seen an explosion in Osteoporosis therapies, predominantly anti-resorptive agents, just as the next decade will be that of novel anabolic agents. The biggest challenge to therapy, however, is that of adherence to and persistence with therapy so that in particular with the available oral agents <50% of patients remain on treatment for more than 12 months.

A number of controversial issues contribute to poor compliance and they will be highlighted in this brief review, time permitting, including issues such as:

1. We are doing a good job treating Osteoporosis.
2. We dont see Vitamin D deficiency.
3. Osteonecrosis of the Jaw.
4. Sub-trochanteric fracture.
5. Calcium and Vitamin D and cardiovascular disease.
6. Bisphosphonates and atrial fibrillation.
7. Bisphosphonates and oesophageal cancer.
8. How long to treat.
9. 'Too old to treat'.
10. Progress densitometry.

SS02 – New insight in immunology

APLAR-0532

Circulating follicular helper T memory cells, from immuno monitoring to immuno modulation

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Follicular B helper T (Tfh) cells support high affinity and long-term antibody responses. Assessment of Tfh activity in vivo is important to monitor protective antibody responses during infection or vaccination and pathogenic antibody responses in autoimmune diseases. Here we demonstrate two major subsets within circulating $CXCR5^+$ CD4 T cells in both humans and mice: the $CCR7^{lo}PD\text{-}1^{hi}$ subset with a partial Tfh effector phenotype and the $CCR7^{hi}PD\text{-}1^{lo}$ subset with a resting phenotype. $CCR7^{lo}PD\text{-}1^{hi}$ $CXCR5^+$ CD4 T cells in blood was indicative of active Tfh differentiation and correlated with clinical indices in patients with autoimmune disease, thus establishing the $CCR7^{lo}PD\text{-}1^{hi}$ subset as an important cellular biomarker. Differentiation of both $CCR7^{hi}PD\text{-}1^{lo}$ and $CCR7^{lo}PD\text{-}1^{hi}$ subsets is dependent on ICOS and BCL6, but not SAP, suggesting that circulating $CXCR5^+$ helper T cells are primarily generated before germinal centres. Upon antigen re-encounter, $CCR7^{lo}PD\text{-}1^{hi}$ $CXCR5^+$ precursors rapidly differentiate into mature Tfh cells, accelerate germinal centre formation and promote antibody production.

APLAR-0488

RNA-seq reveals activation of both common and cytokine-specific pathways following neutrophil priming

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Background: Neutrophils play key roles in initiation, progression and resolution of inflammatory diseases such as rheumatoid arthritis (RA), regulating both innate and adaptive immune response via *de novo* expression of multiple cytokines/chemokines and cell surface molecules. The aim of this study was to use RNA-Seq to develop amodel of inflammatory neutrophil gene expression and identify molecular biomarkers to predict response to TNF inhibition therapy (TNFi) in RA.

Methods: RNA was isolated from healthy neutrophils incubated for 1 hour with priming agents and RA neutrophils obtained pre- and 12-weeks post-TNFi. RNA was sequenced by Illumina HiSeq2000 and reads mapped to the human genome using Tophat. Expression analysis was carried out using edgeR (5% false discovery rate) and signalling pathway analysis by Ingenuity software (IPA).

Results: Healthy neutrophils expressed genes regulating specific neutrophil functions: ROS production, phagocytosis and more general functions: RNA processing, ubiquitination. TNF stimulation activated NF-κB signalling, death receptor signalling and production of chemokines. GM-CSF treatment activated JAK/STAT signalling and down-regulated anti-apoptotic genes. IPA predicted activation of IFN signalling in RA neutrophils, specifically that expression of 178 ÒIFN-responseÓ genes was regulated by IFN-α, IFN-β or IFN-γ ($P < 0.01$). IPA also predicted activation of STAT transcription factors in RA neutrophils ($P < 0.01$), which was confirmed by Western blotting. Heterogeneous expression of IFN-response genes segregated patients into ÒIFN-highÓ or ÒIFN-lowÓ. IFN-high patients achieved a better response to TNFi therapy (?DAS28, $P = 0.03$). Anti-TNF therapy mediated up-regulation of IFN-response genes in non-responders.

Conclusion: Our in vitro model of inflammation indentified cytokine-specific changes in gene expression in human neutrophils and an IFN signature in RA neutrophils. The IFN signature was more evident in patients who achieved a good response to TNFi, and was significantly up-regulated in TNFi non-responders. Expression of IFN genes may be a useful predictive marker of good response to TNFi therapy in RA.

APLAR-0514

Aberrant expression of CD247 in systemic lupus erythematosus patients

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The prototype autoimmune disease, systemic lupus erythematosus (SLE), has been known to be associated with a deficiency in cluster of differentiation 247 (CD247, also known as CD3zeta), a component of the T-cell receptor*CD3 complex. Comprehensive analysis showed that in more than half of SLE patients tested CD247 expression was either attenuated or absent. Recent evidence suggests that these variations in expression profiles may be, at least in part to polymorphism in the *CD247* gene. Aberrant *CD247* transcripts variants displaying either spliced exon 7 or short 3′-untranslated region, have been detected in SLE T cells. By investigating the molecules expressed in the cell lines transfected with these two variant CD247, we identified syndecan-1, TXK and beta 7 integrins as up-regulated molecules. Furthermore, a recent genome-wide association study reported the existence of new CD247 single-nucleotide polymorphisms in SLE patients. In this lecture, the authors will review these unique and significant features of defective CD247 observed in SLE and other autoimmune diseases. Given the evidences obtained from SKG autoimmune arthritis model with ZAP70 mutation and autoimmunity developed in mice carrying a scalable signaling defects in ITAMs of TCR-CD3 complex, a possible role of CD247 defect in autoimmunity is discussed.

SS03 – Solution in rheumatoid arthritis therapy

Update on the safety of biologics in the treatment of rheumatoid arthritis

ZG LI

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Abstract not available.

Treat to target therapy in RA

J SMOLEN

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Abstract not available.

APLAR-0490

Monitoring of tuberculosis for rheumatic disease patients with biologic agents

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Biologic agents especially anti-TNF agents made a great progress of the treatment of rheumatoid arthritis, and spondyloarthropathy. However, the introduction of anti-TNF agents induced increased incidence of infection, especially reactivation of tuberculosis. Screening of latent tuberculosis infection (LTBI), and country specific prophylactic treatment significantly decreased the incidence of tuberculosis.

Currently detection of LTBI is dependent to history taking, chest radiograph, PPD skin test, or interferon-g release assay (IGRA) by Quantiferon-TB gold test, or ELISPOT assay. Because of the limitation of detecting LTBI, there must be some undetected LTBI patients depending on the tuberculosis burden of each country. Asia Pacific area has many countries with various TB burden from very low area to very high area. Therefore, many LTBI patients undetected by screening procedures may receive biologic agents in the absence of tuberculosis prophylaxis, and may face increased risk for developing tuberculosis.

Monitoring of tuberculosis is recommended when patients are at increased risk of tuberculosis, or annually in the area with low risk of TB. However, the rheumatic diseases patients under biologic agent trial may have higher risk of developing tuberculosis, especially in high TB burden area. In counties with high or intermediate TB burden, monitoring must include careful history taking, physical examination and also certain marker of tuberculosis infection including PPD skin test, or IGRA. However, a reliable guideline for monitoring of IGRA after starting biologic agents has not been established yet.

Here, we can discuss the reported data, and data of serial follow up IGRA by QTF-TB-Gold IT assay among patients receiving biologic agents from various TB burden areas.

SS04 – The role of imaging musculoskeletal disease

APLAR-0517

The evolution of ultrasound in Rheumatology

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Musculoskeletal ultrasound in rheumatology has been considered as an important diagnostic tool for a variety of rheumatologic diseases for more than 30 years. However, its use has increased dramatically over the past decade. Moreover, ultrasound in rheumatology has been rapidly evolving towards earlier detection of arthritis, more precise assessment of joint inflammation. Education and standardization of rheumatology ultrasound have mainly been led by OMERACT-EULAR Ultrasound working group.

A lot of advances were made during the past decade. Power Doppler has emerged as the most important imaging modality to assess inflammation and remission in rheumatoid arthritis. The use of ultrasound in the evaluation of enthesitis in spondyloarthropathies has increased. Ultrasound is regarded as a valuable tool for the diagnostic workup for vasculitis. The three/four dimensional (3D/4D) ultrasound and fusion imaging started to be studied in rheumatologic diseases and expected to grow further in the future. Furthermore, ultrasound has emerged as a promising modality to be able to replace invasive test for the diagnosis of Sj*gren syndrome. These evolutions will be more accelerated in the future as consensus based evidences regarding its standardization accumulate.

APLAR-0528

A decade experience of a bedside MSK Ultrasound by a clinician - was it worth it?

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Introduction: Of the many advances that have come into the field of rheumatology today is the art of musculoskeletal ultrasonography (MSUS). We procured a Philips Envisor machine with Doppler in 2003 for the department of Rheumatology at Referral and Research Hospital New Delhi India. As there was paucity of literature on use of MSUS for inflammatory rheumatic diseases at that time, I embarked on a journey of self learning in MSUS.

Authors Experience: At our centre we found Baker's cyst to be more common in osteoarthritis (OA) than rheumatoid arthritis (RA). Using MSUS we preferred to decompress Bakers'cyst from the posterior aspect, after identifying the popliteal artery by Doppler. We found the utility of MSUS in differentiating arthralgia and arthritis, erosive and non-erosive RA, synovial effusion and hypertrophy. Joint injections were possible with more confidence in difficult joints e.g. hip joint, sacro-iliac joint, and small joints of hands and feet, especially first metatarsophalangeal joint. The author also got the opportunity to scan many patients of gout, where the crystals appear as hyperechoic or mixed echogenicity which sit on superficial articular surface. The author also learned various tissues characteristic appearance on MSUS- A tendon wpould appear hyperechoic and fibrillar; Muscle appears relatively hypoechoic with fine hyperechoic fibres; bone appears very hyperechoic; Nerves appear speckled.

Conclusion: In the authors decade long experience, MSUS aids in achieving a correct diagnosis in undifferentiated arthritis, facilitates correct placement of needle in intra articular injections.

APLAR-0489

The benefits of imaging in rheumatology

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The rheumatologist is the ultimate medical detective, using carefully collected pieces of clinical information to fill in a tapestry that defines, with clarity, the diagnosis and leads finally to a well-honed therapeutic approach to an oftentimes complex presentation.

It is said that 80% of the diagnosis is based on the Òclinical equationÓ that derives mostly from the history and an illuminating bit from the physical examination. The history and physical examination are the most powerful Òbiomarkers, Ó especially in the hands of a master clinician. Although a smaller percentage of the final diagnosis is based on and guided by laboratory tests and imaging studies, these play a critically important role in further refining and clarifying the diagnosis, the extent of disease, type, character and amount of visceral damage, and importantly, the response to treatment. The latter is key because our clinical microscope can only ÒseeÓ just so far and thus we need other more sensitive tools to define with greater precision what is going on in the tissues that we are trying to protect. The perfect example of this is the fact that while we feel comfortable in defining remission and therapeutic victory in the treatment of rheumatoid arthritis with the use of validated scores such as the DAS28, a significant proportion of patients so classified have active inflammation on ultrasound and power Doppler. Stopping the development of erosions is the holy grail of the treatment of rheumatoid arthritis, one of the rheumatologistÕs most common foes, but while we employ all kinds of clinical proxies to augur their presence, we are in the dark without the use of imaging.

The number, sensitivity, specificity, accuracy, and diagnostic power of imaging modalities have grown exponentially over the past 30 years and with them have grown our use of and reliance on them. This has occurred because of the excellent clinical radiologic correlations that have been made by the many rheumatologists who now have cerebral Òhard drivesÓ that contain expertise in both areas.

SS05 – Basic science in systemic lupus erythematosus

APLAR-0520

MicroRNAs-novel regulators of systemic lupus erythematosus pathogenesis

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The disorder of fine regulation of gene expression can cause complex diseasesÕ phenotypes. Recently microRNAs have emerged as a major class of gene expression regulators linked to most biological functions. They post-transcriptionally regulate gene expression by imperfectly base pairing with the 3¢ untranslated regions (3¢-UTR) of target mRNAs, preventing protein accumulation by repressing their translation or by accelerating mRNA degradation. MicroRNAs have been implicated as fine-tuning regulators controlling the development of immune cells and in modulating innate and adaptive immune responses. Dysregulation of miRNAs has been described in various disease states, including several autoimmune diseases. We hypothesize that some miRNAs expression is altered in SLE and may have unknown impacts on the some key lupus disease pathways. The roles of dysregulated miRNAs in SLE pathogenesis are just beginning to be uncovered. First, miRNA expression profiling studies based on lupus patientsÕ blood cells, body fluid and target tissues have revealed unique miRNA signatures as well as their associations with disease activity and major organ involvements, suggesting miRNAs as potential biomarkers for the disease assessment of lupus patients. Moreover, a series of in vitro studies has recently unveiled novel cellular and molecular mechanisms underlying roles of miRNAs in SLE disease processes including their functions in control of IFN pathway activation, inflammatory mediator production and DNA methylation state of T cells as well as their interaction with disease relevant genetic variants. More importantly, During the past several years, we have demonstrated that manipulation of lupus-related miRNAs (such as miR-146a, miR-125a and miR-23b) can lead to coordinate activation of the type I IFN pathway, reduction in inflammatory chemokine RANTES expression, restoration of normal DNA methylation state of lupus T cells, correction of lupus T cell mediated IL-2 production deficiency and attenuation of local tissue inflammation respectively, suggesting that miRNAs may have therapeutic potential for lupus.

APLAR-0535

Baff and immune system

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B activating factor (BAFF) orB lymphocyte stimulator (BLyS) is a member of TNF ligand super family which is mainly produced by cells of innate and adaptive immune system.

BAFF expression is increased in presence of IL-2, IL10, TNF-α, Granulocyte-colony stimulating factor, IFN-γ, and IFN-α or by TLR activation, particularly TLR4 and TLR9.

The most important biologic effect of BAFF on B cells is to drive B2 cell survival, particularly after the transitional stage 1 (T1), thus promoting the survival of transitional stage 2 (T2) B cells, marginal zone B cells which mediate T cell independent response, and follicular B cells which mediate T cell dependent response.

Transition from T1 to T2 B cells is a crucial step in B cell development because during this stage B cells undergo a critical selection process for the elimination of autoreactive B cells. In the presence of BAFF excess, as in SLE patients, low-affinity self-reactive B cells can be positively selected.

IFN-α produced by plasmocytoid dendritic cells stimulates myeloid dendritic cells to produce BAFF which can upregulate TLR on B cells, promote B cell survival and, in collaboration with cytokines and co-stimulatory signals or TLR signals, promote Ig class switching.BAFF supports the survival and differentiation of monocytes and enhances cytokine and chemokine production by macrophages; BAFFcan also be produced by cytokine-activated neutrophils or immune complex-activated basophils and eosinophils.

The relevance of BAFFto human SLE is supported by a number of observations: SLE patients have elevated levels of BAFF in their serum as well as in cerebrospinal fluid; high serum levels of BAFF are correlated with anti-dsDNA antibody levels and disease activity.

The importance of BAFF is rapidly increasing since Belimumab, a fully human monoclonal antibodywhich selectively targets and inhibits soluble BAFF, was approved for SLE by FDA and EMA.

APLAR-0533

The role of follicular helper T cell in systemic lupus erythematosus

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Follicular helper T (Tfh) cells select mutated B cells in germinal centres, which can then differentiate into long-lived high affinity memory B cells and plasma cells. Tfh cells are regulated by a unique molecular program orchestrated by the transcriptional repressor Bcl6. This transcription factor turns down expression of multiple genes, including transcriptional regulators of other T helper lineages and a vast amount of microRNAs. This enables Tfh cells to express a suite of chemokine receptors, stimulatory ligands and cytokines that enable migration into B-cell follicles, and provision of effective help to B cells. Growing evidence of the important role of Tfh cells in maintaining germinal centre tolerance and demonstration that autoimmunity can arise when Tfh cells are dysregulated have placed this helper T cell subset in the limelight of the pathogenesis of autoantibody-driven autoimmune diseases. Indeed, aberrant accumulation of Tfh cells has been linked with systemic lupus erythematosus, SjogrenÕs disease and autoimmune arthritis. Multiple checkpoints that operate throughout Tfh cell development and maturation to maintain immunological tolerance whilst mounting robust and long-lasting antibody responses will be discussed.

SS06 – The bend to bench of spondyloarthropathy

APLAR-0495

Managing in inflammatory back pain—to treat or to refer

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SPA consists of a lot of diseases in this family, which includes AS, ReA, PsA, etc. They shared some clinical features RF(−), B27(+), sacroiliitis, mucotaneous lesions. The most common and important prototype is ankylosing spondylitis. Recently, in order to recognize early and treat SpA early, to determine the pre-axial SpA is becoming an important issue. The axial SpA has been defined by 2009 new classification criteria.

In the General population, virtually the prevalence of USPA is more common when compare to AS. The prevalence of AS in Chinese (0.21–0.3%) is similar to the western people but both are much higher when compared to Japanese.

The clinical course for AS patients is entirely different or individualized. Some patients may present LBP and sacroiliitis. Some patients may progress rapidly to bamboo spine or ankylosis. When patient comes to the stage of bamboo spine, some of them have no any symptom (silent) few may get spinal fractures after trauma and in fact, many of them still have very active symptoms with elevated ESR & CRP.

The primary goal to treat AS or inflammatory back pain is to manage inflammation, structure damage, mobility and function.

For treatment of AS or axial SpA, until now, we are still follow the 2006 ASAS/EULAR recommendations. For only axial involvement, NSAIDs are the 1st line drugs and 70–80% got improvement. If fail, biologic therapy is indicated.

In 2010 EULAR Guideline, anti-TNFα therapy has been suggested for intractable axial SpA.

APLAR-0537

ImmunoGenetic study in Chinese population with Ankylosing Spondylitis: are ther specific genes recently disclosed?

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Ankylosing spondylitis (AS) is a chronic inflammation disease resulting in the destruction of affected joints. In the past 40 years, genetic factors have been proved to play an important role in the pathogenesis of AS. HLA-B27 has been established to be associated tightly with AS and is being widely used as a diagnostic test in the clinical practice. However, the genetic risk from HLA-B27 was no more than one-third in AS, Over the past 5 years, The development of genomic technologies such as GWAS and candidate gene studies has helped to understand the involvement of some genes in the etiology of AS. Several new genes or genetic regions associated with AS have been identified in Chinese population. The new susceptibility SNP loci between EDIL3 and HAPLN1 at 5q14.3 (rs4552569) and within AN06 at 12q12 (rs17095830) are associated with AS in Han Chinese. The other SNPs (rs13202464 and rs10865331) are also identified in association with AS. These findings strongly proved the presence of non-MHC genes involved in AS which was consistent with the prior results. These new findings provide a useful platform for hypothesis-driven research into AS pathogenesis and make it possible to develop new makers to inhibit damage to bone structure and radiographic progression in AS which relate with HLA-B27 and differenciated expression of microRNA in AS patients.

Experiences of Ankylosing spondilitis management in Indonesia?

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Indonesia

Abstract not available.

SS07 – The problem and solution of treating gout

APLAR-0539

Gout and comorbidities

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Gout is a common disease and has increased prevalence worldwide. In the United States, the National Health and Nutrition Examination Survey (NHANES) documented a prevalence of gout in 2007–2008 of approximately 3.9%, which has increased by roughly 45% compared to in 1988–1994. Besides, gout also has elevated mortality. Our study showed the all-cause standardized mortality ratio (95% confidence interval) was 1.29 (1.21–1.37) for men and 1.70 (1.53–1.89) for women in gout as compared with the national population of Taiwan in 2000, which is accounted for by increased kidney, metabolic, endocrine and cardiovascular disease.

Patients with gout frequently have multiple comorbidities. Keeman et al reported a median number of 3–4 comorbidities among gout patients cared for in a Veteran Affairs system. The most common comorbidities include hypertension, cardiovascular disease, renal impairment, diabetes, obesity, hyperlipidaemia and in combination known as the metabolic syndrome. Nephrolithiasis, myocardial infarction, congestive heart failure, stroke, fatty liver and even increased risk of cancer have also been reported to be associated with gout.

The cause and effect relationship between gout, hyperuricemia, and comorbidities remains unclear. Impaired renal uric acid excretion is the dominant mechanism in most hyperuricemic individuals and renal impairment itself may play a contributory role in the development of gouty arthritis. Conversely, comorbidities can be consequence of hyperuicemia and gout. The prevalence of some comorbidities was also noted to increase with the degree of hyperuricemia. Co-morbidities increase with gout progression, negatively impact long-term prognosis and quality of life.

The management of gout includes effective therapy of acute attacks and long-term preventive therapy through adequate urate lowering. It is particularly challenging in those with comorbidities because of contraindications, the need for dosage adjustments, and polypharmacy. The patients' comorbidities, particularly renal function, need to be considered when choosing the most appropriate therapy. Some studies did show beneficial effect to comorbidities with urate-lowering, such as significantly decreased cardiovascular and stroke mortality; preservation or even improvement of renal function.

APLAR-0499

Treatment approach to refractory gout

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Refractory gout refers to patients who have ongoing symptoms of active arthritis and cannot maintain a hypouricemic state [serum uric acid (SUA) < 6.0 mg/dL]. Such patients usually have very severe active ongoing arthritis. This results in progressive joint destruction, functional impairment, and reduced quality of life. Poor compliance, or intolerance, or fail to achieve SUA < 6.0 mg/dL despite taking appropriate dosage of urate lowering drugs (ULDs) by patients, and delay in prescribing ULDs or titrate their doses to achieve SUA < 6.0 mg/dL by physicians are among the common causes of refractory gout. Furthermore, many patients with refractory gout has chronic kidney disease (CKD) that prohibits the use of NSAIDs, colchicine, and ULDs, or the use of these agents is ineffective. Recently, IL-1β and TNF-α have been implicated in the development of acute arthritis in gout. This leads to the use of IL-1β and TNF-α inhibitors treating acute gout. Although these agents have been shown as very effective in abolishing acute inflammation in refractory gout, they have not been approved yet for this condition. Managing hyperuricemia in refractory gout also is a clinical challenge. Dose adjustment of allopurinol according to creatinine clearance rarely achieves SUA < 6.0 mg/dL. Febuxostat can be another option for patients with allopurinol intolerance. A recently approved urate oxidase, pegloticase, has been shown as effective in reducing SUA, and it could be another hypouricemic agent choice in refractory gout. In addition, physicians should be instructed to initiate hypouricemic agents early in order to avoid late complications of hyperuricemia. Diet therapy and use of losartan and fenofibrate should be considered in patients with co-morbidities such as obesity, hypertension and dyslipidemia. Alcohol consumption should be discontinued. Patients should be encouraged to comply with the therapy in order to obtain the highest benefit from the treatment.

APLAR-0484

Starting dose is a risk factor for allopurinol hypersensitivity syndrome: a proposed safe starting dose of allopurinol

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Successful long term management of gout requires a sustained reduction in serum urate. Allopurinol is the most commonly used urate lowering therapy in gout. It is generally well tolerated but rarely is associated with the potentially fatal allopurinol hypersensitivity syndrome (AHS). Risk factors for development of AHS include female sex, age, renal impairment, diuretic use, recent commencement of allopurinol therapy and in some ethnic groups, the HLA-B*5801 genotype.

The relationship between allopurinol dose and AHS is controversial. Dose reduction in renal impairment is based on a reported relationship between "full dose" allopurinol (≥300 mg/day) in patients with renal impairment and development of AHS. This observation, along with recognition that excretion of the active metabolite oxypurinol is significantly reduced in patients with impaired renal function, led to the suggestion that allopurinol should be dosed according to creatinine clearance. However, such dosing is frequently association with failure to reach target serum urate. The relationship between allopurinol starting dose and AHS is unknown. Furthermore, once established on allopurinol the maintenance dose may not be associated with AHS.

In a retrospective case-control study of patients with gout who developed AHS we have shown that allopurinol starting dose is associated with AHS. For the highest quintile of starting dose/eGFR, the odds ratio was 23.2 ($P < 0.01$). ROC analysis indicated that 91% of AHS cases and 36% of controls started on a dose of allopurinol at ≥1.5 mg allopurinol per unit eGFR (mg/mL/min). In another intervention study we have shown that, in patients who tolerate allopurinol the dose can be up-titrated to achieve target serum urate, even in patients with renal impairment.

SS08 – New insight of anti phospholipid syndrome

APLAR-0531

Inter-relationship between pregnancy and autoimmune rheumatic diseases

C LAU

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Autoimmune rheumatic disorders commonly affect young to middle-aged persons. In addition, there is a female preponderance in a number of these conditions, the most notably of which is systemic lupus erythematosus (SLE). Questions concerning fertility and management of these conditions during pregnancy are commonly asked. Hormonal and neuroendocrine changes that occur during pregnancy may modify the activity of the immune system and potentially alter the clinical presentation of the underlying rheumatic condition. Conversely, the underlying disease and its treatment may induce the development of pregnancy complications, adversely affect pregnancy outcome and cause foetal complications. In this lecture, I will provide a summary of the inter-relationship between pregnancy and various autoimmune rheumaticdiseases such as rheumatoid arthritis, ankylosing spondylitis, systemic sclerosis and necrotizing vasculitis. Particular emphasis on pregnancies in SLE will be made. Thus, the effects of pregnancy on SLE manifestations will be discussed. In addition, the effects of SLE on pregnancy and foetal outcome, particularly the association between recurrent spontaneous abortion and anti-phospholipid antibodies, and neonatal lupus syndrome will be discussed. The use of immunosuppressive drugs during pregnancy will also be highlighted.

APLAR-0519

Clinical spectrum of anti-phospholipid syndrome in Asia

A LATEEF

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Antiphospholipid syndrome (APS) was first described in early 80s as a subgroup of Systemic Lupus Erythematous (SLE) patients, presenting with thrombosis and pregnancy morbidity in association with antiphospholipid antibodies. Three decades later, APS is an established entity, with both secondary and primary formsand a wide clinical spectrum. Prospective follow up of large cohorts of patients have expanded our knowledge about APS. However, Asian patients are mostly under-represented in these cohorts and the question remains if they share the same characteristics and clinical spectrum of the disease.

Thrombosis remains the predominant presentation and forms part of classification criteria for APS. Any part of vascular tree can be affected although most prevalent is deep vein thrombosis. Obstetric presentations remain an important feature, including pregnancy loss, prematurity, pre-eclampsia, and eclampsia. Lupus anticoagulant has been noted to be most reliable predictor of poor outcomes.

Non criteria manifestations are features that occur in a large fraction of APS patients in association with aPLs. However, they were not included in the classification criteria because of low specificity or weak evidence. Most common are thrombocytopenia, hemolytic anemia, cardiac valve lesion and cutaneous manifestations such as livedo reticularis.

Catastrophic APS, characterized by clots in multiple small vascular beds leading to multiorgan failure with high mortality, is a rare but severe form of APS. About 60% has an identifiable precipitating event, most commonly infections. Another subgroup of patients has positive aPLs but no clinical features. The risk of thrombosis in these carriers depends on the type of the antibody, and co-morbidities. The term sero-negative APS has been suggested for another subgroup of patients with clinical features suggestive of APS but persistently negative serologies. The limited data from Asia suggests that our patients generally exhibit similar features but with some differences.

Management of antiphospholipid syndrome

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Abstract not available.

SS09 – Updated treatment of lupus

APLAR-0507

Treatment of lupus nephritis – an update

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Lupus nephritis is an important cause of renal failure in Asia. The outcome of patients with lupus nephritis has improved considerably over the past few decades because of advances in immunosuppressive treatment and overall improvements in general medical care. Various options of effective immunosuppressive treatment are now available, so that the efficacy-to-risk ratio can be better optimized to suit the needs and cater for the risk profiles of individual patients. Experience continues to accumulate on the use of mycophenolic acid and calcineurin inhibitors, while the role of novel immune-modulatory medications is still being investigated. Although various clinical or histological parameters have been demonstrated to confer prognostic significance, the prediction of treatment response and its sustainability at the level of individual patients remains a challenge. The impact of racial and ethnic variations with regard to disease manifestations, natural history and response to treatment within Asia deserves further investigation. More collaborative effort is required to address this and other knowledge gaps.

APLAR-0525

Advances in SLE therapy

S NAVARRA

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A better understanding of the molecular pathomechanisms of systemic lupus erythematosus (SLE) has led to the development of drugs targeted towards specific cells, molecules or pathways – including B cells, T cells, complement, cytokines and the innate immune system.

The B-cell targeted therapies have the most robust clinical trial data to date. These agents include rituximab (chimeric anti-CD20), ocrelizumab (humanized anti-CD20), epratuzumab (anti-CD22), belimumab (anti-BLymphocyte stimulator or BLyS), and atacicept (anti-BLyS and anti-APRIL [a proliferation-inducing ligand]).

Although EXPLORER trial on rituximabin non-renal lupus did not meet its primary or secondary outcome measures, the placebo group had more nonresponders than the treatment groupamongAfrican American and Hispanic patients. Similarly, LUNAR trial among patients with lupus nephritis showed actually more responders in the rituximab than in placebo among African American patients., laying the ground for development into phase 3 trials.

Two large phase 3 trials on belimumab: BLISS-52 and BLISS-76 trials met the primary endpoint utilizing the novel SLE Responder Index (SRI) plus progressive restrictions on background therapies, leading to the drugOs approval for use in active SLE. The phase 2 EMBLEMtrial on epratuzumab showed an impressive rapid response in 3 months over placebo.

There are currently ongoing trials on T-cell inhibitors abataceptand Lupuzor, and agents that target interferon alpha and gamma. Trials on anti-cytokines particularly interleukin (IL)-6, as well as small oral molecules that target toll-like receptors 7 and 9 are in clinical development. Sirolimus, an agent that blocks the mTOR (mammalian target of rapamycin) surface receptor pathway is currently in a phase 2 trial.

SLE is an extremely heterogenous disease, and drug development will continually be faced with the challenge to choose the most appropriate clinical trial design on the right kind of patients * as in clinical practice.

APLAR-0534

Standard care for SLE is not working: the need to do better

CC MOK

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Systemic lupus erythematosus (SLE) is a systemic autoimmune disease associated with significant morbidity and mortality, especially in the younger population. Up to 30% of SLE patients with major organ manifestations do not respond optimally to conventional immune-modulatory therapies. Persistent inflammation and therapies themselves may cause damage to organ functions. The treatment of refractory lupus manifestations should balance between medical evidence and adverse effects of additional treatment modalities. Intravenous immunoglobulin, apheresis, more aggressive use of cyclophosphamide, and the introduction of novel biological agents on top of standard therapies are options for SLE manifestations that fail to respond to conventional therapies. This talk will summarize the evidence of various modalities in the treatment of refractory SLE, with special focus on the novel biological agents.

SS10 – Progress of progressive systemic sclerosis

APLAR-0504

Clinical profile of PSS in Asia Pacific region

C FOOCHAROEN

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The incidence and the prevalence of progressive systemic sclerosis (PSS) in the Asia Pacific region during 1950–2002 was 1.96–22.8/million/year and 30–233/million, respectively. The highest incidence and prevalence reported was in South Australia. The incidence of PSS trended to be stable. Age of disease-onset is primarily in the fourth decade of life: it is younger among Chinese and Indian populations. The limited cutaneous systemic sclerosis subset (lcSSc) is more frequently found than the diffuse cutaneous systemic sclerosis subset (dcSSc); as in Western countries except isolated reports from China and Thailand. HLA-DR was the most commonly encountered gene particular HLA-DRB1*1502 that was associated with dcSSc and anti-topoisomerase I (ATA). Raynaud's phenomenon was the most common clinical characteristic in PSS (80%). The renal crisis was the least common clinical manifestation among all Asia Pacific patients (<10%). CardiopulmonaryComplicationsNparticularly pulmonary arterial hypertension (PAH) Nranges broadly 3.5–59%; possibly related to the definition of PAH diagnosis by echocardiogram. The prevalence of pulmonary fibrosis (PF) was around 40–60% and higher after detection by chest radiography or a pulmonary function test. Specific serology for PSSN i.e., ATA and anti-centromere (ACA) Nwas between 20–35% and 10–40%, respectively. The rate of ATA positive was high among Thais and Koreans (40–70%) and the rate of ACA positive was low among Thais (<5%); in contrast to Western countries. The mortality rate of PSS is higher than for the general population (standardized mortality rate 1.46–9.11). The overall mortality rate in PSS is around 5–38%. The 5-,10- and 20-year survival rate is approximate 90%, 80% and 60%, respectively. Men, old age at onset, dcSSC, high modified Rodnan skin score, cardiopulmonary involvement, renal crisis, and ATA are predictors of death in Asia Pacific PSS patients. Complications caused by PSS itself is the most common cause of death in most series (viz., for PF, PAH or renal crisis).

The role of Capillaroscopy in patients with SSc

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Abstract not available.

Updated management of progressive systemic sclerosis

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Abstract not available.

SS11 – New insight in osteoarthritis

APLAR-0506

Impact of the context in the management of osteoarthritis

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Over 250 million people (3.6%) have osteoarthritis (OA) of the knee globally, accounting for a quarter of the primary are consultations and resulting in a huge economic burdens for both patients and care providers. The burden of the disease keeps rising due to aging, increasing prevalence of obesity and poor treatments. Over 53 treatments have been developed so far. However, the benefits of these treatments are just slightly better than placebo and majority have serious side effects. Treatment of OA hits on the break wall and many people with OA continue to have pain and poor quality of life.

Is there any magic bullet for OA? Instead of developinganother molecule which may give a little bit of benefits but serious side effects, we simply examined the benefit from placebo in randomised controlled trials for OA. We foundthat placebo was effective and its effect size was moderate, 0.51 for OA pain. This effect size was much larger than most OA therapies including non-steroidal anti-inflammatory drugs (0.35). Placebo was also effective to improve function and stiffness due to OA. The study suggests that placebo is a powerful treatment for OA. The findings are in line with the literature where placebo is effective in many chronic conditions such as depression and irritable bowel syndrome.

Can we use placebos outside the clinical trials? It is unethical to prescribe placebo. We have therefore reconceptualised treatment in order to ethically use placebo in clinical practice. We consider that any treatment consists of specific and non-specific components. The treatment effect may also be separated into two parts (1) specific effect, and (2) contextual effect (placebo effect or non-specific effect). When we deliver a treatment, we always deliver both, not one or another. Large amount of literature have found that many contextual elements have therapeutic effect such as empathy, physician and patient relationship, and environment. We recently found that for example in OA, 60% of treatment benefit wasobtained from the contextual effect. Even for opioids, a strong analgesic, the contextual effect was 35%. By contrast, the contextual effect from vitamins and joint lavage was 100%.

What are the key messages to take homefrom this lecture? Placebo is effective for OA. It is always part of agiven treatment, which can be ethically delivered in clinical practice. The treatment outcome may be enhanced if we are aware of the key contextual elements and deliver them with a specific treatment. We should treat a patient with OA, not OA that a patient has!

APLAR-0523

Osteoarthritis and osteoporosis: what is the relationship?

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There has been considerable interest in the relationship between osteoarthritis (OA) and osteoporosis (OP) since the 60s. This first arose when surgeons noticed the gen-eral absence of osteoarthritic changes in the fractured hips of subjects with osteoporo-sis. Osteoarthritis was also found to be protective against hip fractures and com-pressive vertebral fractures. In clinical practice, the coexistence of the two disorders in individual patients has been considered to be rare by several authors. However, the extent of the inverse relationship between OA and OP has long been debated.

Osteoarthritis and osteoporosis are both diseases with high prevalence. Especially among the ageing female population. They may represent, though, anthropometrically distinct populations. A woman with OA are more obese have more fat, muscle girth and strength (mesomorph), while osteoporotic women are shorter, more slender, and have less fat, muscle girth and strength (ectomorph).

An association between higher BMD and radiographic OA of knees and hips undoubt-edly exists from the published studies. The relationship at other sites is less clear prob-ably reflecting different mechanisms involved in the pathogenesis of OA. The presence and severity of osteophytes is strongly related to higher bone mass. Subjects with OA do not appear to be at lower risk of fractures, suggesting that the extra bone is not mechanically useful. The recently published longitudinal studies confirmed the rela-tionship by showing that a higher baseline bone density increases the risk of incident radiographic knee OA. These studies also suggested that mechanisms affecting pro-gression might be different.

APLAR-0503

Stem cells therapy for OA: the role of rheumatologist?

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Osteoarthritis is a degenerative joint disease characterized by the destruction of joint cartilage. Classically it was thought to be a ÒWear and TearÓ disease. Modern pathophysiology showed that until the superficial layer of the cartilage remains normal, the joint cartilage resist any hard work, without any derangement. Mesenchymal Stem Cells (MSC) are found in low number in the cartilage, mainly in the superficial layer. In the superficial layer of OA cartilage, MSCs are seen in a larger number, but act chaotic and unable to repair the cartilage. Adult bone marrow MSCs (obtained by culture and transplanted in the joint) may redirect them to their normal function. OA is no more seen as a mechanical disease. Synovial membrane interacts with the cartilage, and nowadays, many look at osteoarthritis as an inflammatory disease. Transplanted MSCs have the ability to normalize the lymphocytic reaction and down regulate the inflammation which causes chondrocytes to produce metalloproteinases and inflammatory cytokines.

Animal studies showed that MSCs could repair and slow down the experimental osteoarthritis. The labeled injected MSCs are found in synovial membrane and medial meniscus, but not in degenerated cartilage. They prevent cartilage destruction, thickening of the lining synovial membrane, production of metalloproteinases and TNF-α by chondrocytes, and inhibit the expression of MMP-1 and TNF-α by synovial membrane.

Human study of transplantation of bone marrow MSC for OA was first done by Centeno on one patient and then Davatchi et al. on four patients. Both studies showed a beneficial effect at 6 months after the therapy.

Adipose Stem Cells (ASC) extracted from knee fat pad was also used as MSC. They were used in combination with hyaluronic acid (HA) or with Platelet Rich Plasma (PRP) injection. They too report good results, but none of them were done exclusively with ASCs.

SS12 – What is new in vasculitides?

APLAR-0492

Current diagnosis and management of IgG 4 related disease

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IgG4-related disease is an increasingly recognized condition characterized by fibrosing and inflammatory infiltration of organs. In fact, many previously identified medical conditions such as Mikulicz syndrome are now identified as part of the IgG4-related disease spectrum. This disease can affect the pancreas, hepato-biliary system, lacrimal and salivary glands, kidneys, lungs, lymph nodes, meninges, aorta and retroperitoneum. The disease typically has an indolent presentation over months or years and may not be easy to recognise as constitutional symptoms are usually subtle or absent. IgG4-related disease tends to develop pseudotumours in organs including lacrimal or salivary glands, and may also cause diffuse infiltrative lesions such as in the meningitis or aorta. Serum IgG4 concentration is elevated in most patients but can be normal in 20–40% of patients with biopsy*provendisease. Thus, serum IgG4 levelis not sufficient tohelp make a diagnosis of the condition. Histopathology and immunostaining studies are the essence of diagnosis of this disease. Major histopathological features of this disease include dense lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis. The diagnosis of IgG4-related disease requires both appropriate histological appearance and increased numbers of IgG4+ plasma cells (or an elevatedIgG4/IgG ratio) in tissue.

Assessing of Takayasu vasculitis

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Abstract not available.

APLAR-0518

The experience of treatment of vasculitis in Bangladesh

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Objective: To gain an idea of response to and complications of treatment of vascultitis patients in Bangladesh.

Methods: Review of patients who received treatment and came for follow up in a rheumatology clinic during May 16 to July, 2013.

Results: Six Takayasu's arteritis (TA), seven gralulomatous with polyangiitis (GPA), two eosinophilic granulomatosis with polyangiitis (EGPA), two polyarteritis nodosa (PAN), one giant cell arteritis, one microscopic polyangiitis, five rheumatoid vascultitis (RV) and one lupus vasculitis (LV) patients reported for follow up. Mean age at onset was 39 ± 9.2 years, duration of follow up 32.7 ± 21.0 months. Patients with RV, PAN and LV presented with gangrene. Four had otitis.

Treatment was initiated with high dose glucocorticoid (HFDGC). Patients with gangrene were initially treated with debridement, antibiotics and amputation, those with OM with antibiotics. Glucocorticoid sparing agents (GSA) were added (six GPA, two EGPA, one MPA, three RV), MTX (four TA, one cutaneous GPA) and MMF (one TA). Cyclophosphamide was replaced by azathioprine (one GPA, one EGPA), MTX (three GPA, one EGPA) and MMF (one GPA). Twenty-two underwent remission, it was induced in one refractory GPA patient with IVIg. Two RV cases are having new ischemia. TA claudication improved in none.

Seven patients completed 2-year follow up. Prednisolone was withdrawn within 1–2 years. One GPA and one TA patients are enjoying drug-free remission for last seven and 4 years after 4 years of treatment. Others are on GSA because of relapses (3) or grumbling activity (2). Relapses occurred in two GPA, both EGPA, and one TA cases. Second relapse in an EGPA patient proved refractory and treated with rituximab.

Adverse effects were Cushing syndrome, proximal myopathy (2), hypertension (2), diabetes, osteoporosis, AZT cytopenia, AZT hepatotoxicity each in one. Infections occurred in nine.

Conclusions: Progressive digital ischemia in RV and limb claudication in TA are more refractory than other manifestations.

SS13 – The roles of complimentary alternative medicine in rheumatology

Ubiquinol-10 Suplementation in Juvenile fibromyalgia

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Abstract not available.

APLAR-0496

Alternative therapies: what role do they have in the management of lupus?

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Systemic lupus erythematosus (SLE) is an autoimmune disease with higher morbidity and mortality among ethnic Chinese patients than Whites. Corticosteroid and other immunosuppressive drugs, including cyclophosphamide, azathioprine, and hydroxychloroquine are traditional therapies for this disease. Since the year 2000, mycophenolate mofetil and rituximab have been widely used in refractory SLE or severe lupus nephritis. Because the high disease activity remains, even after active therapy, and serious side effects from Western medicines may develop, more than 40% of SLE patients in Western countries are pursuing complementary and alternative therapies (CATs). CAT remedies are multiplex, and include herbal medicines, diets and vitamins, acupuncture, chiropractice, folk medicine, massage, spiritual healing, etc. Many herbal formulas have been used but in general their efficacy in treating lupus is doubted because of the lack of strong evidence. Tripterygium (T2) has demonstrated good efficacy in rheumatoid arthritis (RA) and SLE, but widespread use is limited due to the side effects. Through randomized clinical trials, we hope in the future that some Chinese medicines may be found helpful as CATs for SLE.

APLAR-0522

Past, present and future of herb medicine in rheumatology

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All people need a good health in their life. Last time when no drug was already discovered, people used the traditional medicine especially the herbs medicine. They did not have any scientific evidence of the herbs medicine they used. They used the herbs medicine empirically for some diseases including the rheumatic diseases, until they have some empirically evidences of herbs medicine.

In the present time not only the quantity but also the quality of scientific evidences of herbs medicine are significantly increase. More than 6000 species of plants are used for herbs medicine. More than 380 medicinal florain Asia Pacific reported have some fantastic potent because content some active ingredient for the treatment of inflammation in chronic diseases especially in rheumatic diseases. Using herbs medicine in Asia Pacific has two dimensional aspects, medical aspect and economical aspect. The herbs market in developing countries is significantly improve.

In the next future, the strategic of using the herbs medicine are: integration of herbs medicine to the National Health Care System, increase the safety, efficacy and quality with increase the knowledge, regulation and standard of herbs medicine, increase the availability especially for the poor population and promotion of using the herbs medicine. Understanding the risk and benefit of using the herbs medicine in rheumatology is the main priority of the doctor. Next researches should able to find the new molecular target which able to explain the efficacy, drugs interaction and side effect of herbs medicine in rheumatology.

Free paper Oral Case Report: The very interesting cases in Rheumatology

APLAR-0502

Oncogenic hypophosphataemia presenting with progressive joint and back pain, chest deformity, weakness, height and weight loss in a young man

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We present a rare case of oncogenic phophosphataemic rickets.

Mr T A S, a 25-year-old man, experienced mechanical pain over both upper tibiae in mid-2007 followed by progressive low back pain. He had mechanical hip pains in March 2009, difficulty getting up from sitting or squatting in July, and in October, a height loss of over 6 cm. In 2010, his chest wall became deformed. He was wheelchair bound by early 2012. He lost 20 kg between 2010 and 2012. He was treated for ankylosing spondylitis when MRI in June 2010 was reported as showing ankylosed sacroiliac joints and hip arthritis. ESR was 45 mm/1 hour but CRP was repeatedly normal. He remained unwell and in Oct 2011 he underwent right hip hemiarthroplasty. Another rheumatologist he consulted found no evidence of inflammatory arthritis but osteoporosis on BMD. Serum alkaline phosphatase was 156 U/L (NR 38–126), calcium, iPTH and thyroid function normal, phosphate 1.2 mg/dL (NR 2.7–4.5), and compression fractures of thoracic vertebrae on X-Rays. Strontium ranelate, calcium and vitamin D were prescribed.

He was referred to our hospital in June 2012. Examination revealed pectus carinatum, kyphosis, wasted quadriceps muscles, proximal limb muscle weakness, normal heart, lungs and abdomen. There was no palpable lymph node or soft tissue mass. Repeat serum phosphate was low, 24-hour urinary phosphate inappropriately normal, vitamin D and muscle enzymes normal. A diagnosis of hypophosphataemic rickets was made. He returned to Indonesia where FDG-PET scan (to exclude mesenchymal tumour) was normal. He returned to Singapore in 2013. Careful examination revealed a non-tender, lobulated, soft tissue mass 2 by 2.5 cm on his left sole. Ga 68-Dotate PET/CT hybrid fusion scan showed this to be the only "hot" spot and MRI left foot confirmed the tumour. He underwent excision biopsy. Histology revealed plexiform fibrohistiocytic tumour. Serum FGF-23 which was elevated normalized by 4-hour post-surgery. He experienced severe re-mineralisation bone pains day 11 post-surgery which resolved on day 44. Muscle power gradually improved and 2 months post-surgery he walked without aid. Serum phosphate remained normal.

APLAR-0232

Difficult lupus nephritis in pregnancy

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease that occurs frequently in women of childbearing age. Although fertility is not compromised, pregnancies among SLE patients are commonly associated with complications. Studies have suggested that renal involvement and the presence and degree of proteinuria at the time of conception may contribute to adverse maternal and fetal outcomes. We describe a case of a 30 year old Filipino female who had an unplanned pregnancy during active lupus nephritis (Type IV). She was treated with monthly Methylprednisolone pulse therapy but eventually delivered via caesarian section (C- section) due to intrauterine growth retardation (IUGR) at 35 weeks AOG.

Case report: A 30 year-old female (G3P3) was diagnosed with Type IV Lupus Nephritis in 2005. She received induction treatment with IV Cyclophosphamide for 6 months followed by Mycophenolate mofetil at 2 gms/day for maintenance treatment. She continued to have active disease and subsequently received 2 doses of Rituximab 1 gm IV with 500 mg/m2 IV Cyclophosphamide. She achieved clinical remission for 3 months but had an unplanned pregnancy during recurrent active kidney disease. Proteinuria with active urinary sediments were observed despite IV pulse methylprednisolone therapy. At 35 weeks AOG, abdominal ultrasound showed asymmetric IUGR requiring C- section.

Discussion and Conclusion: Pregnancy in women with lupus nephritis is associated with an increased risk of fetal loss and lupus flares. Several risk factors associated with poor pregnancy outcomes include a serum creatinine of >2.8mg/dl, active lupus nephritis, hypertension during the first trimester, and presence of anti-phospholipid antibodies. Since treatment options for active lupus during pregnancy are limited, this case emphasizes the importance of planned pregnancies during lupus disease quiescence to provide the best maternal and fetal outcome.

APLAR-0270

An autopsy case report: IgG4-related disease with dysautonomia and nonocculusive mesenteric ischemia

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IgG4-relaterd disease (IgG4RD) is increasingly recognized syndrome of unknown etiology comprised of a collection of disorders. We have experienced an autopsy case of IgG4RD with dysautonomia and nonocculusive mesenteric ischemia(NOMI).A 77-year-old man was admitted with orthostatic hypotension, dysuria and appetite loss. Laboratory findings include hyponatremia, eosinophilia, hyperproteinemia, and elevated serum IgG, IgG4 and IgE. Computed tomography (CT) and Magnetic resonance imaging showed hypophysitis, retroperitoneal fibrosis and sclerosing cholangitis. The diagnosis was confirmed by reevaluating histopathology of the tumor of submandibular gland that is surgically excised four years before. He had three times of syncopal attacks and dysuria requiring withdrawing urine. The lower uptake of MIBG scintigraphy suggests these dysautonomia was developed by pure autonomic failure. The day before starting glucocorticoids treatment the patient complained severe abdominal pain followed by a fall in blood pressure with severe metabolic acidosis. The contrast-enhanced CT scan suggested that extensive intestine was affected by NOMI. The endoscopic findings also confirmed the necrosis of rectum. Although necrotic intestinal resection was tried, extensive necrosis of intestinal tract was found. The patient died 21 hours after the onset of abdominal pain. The autopsy found that.

IgG4-positive plasma cells (IgG4-PPC) were disseminated all over his body including aorta, retroperitonium, liver, bile duct, lung, kidney, bladder, prostate, heart, lymph node and colon. The infiltration was also observed into AuerbachÕs plexus of mesocolon and colon muscularis propria. As far as we know, this is the first report to prove the direct invasion of IgG4-PPC into nerve tissues. Although the association between dysautonomia and IgG4RD are suspected, conclusive evidences could not be found. However, distribution of IgG4-PPC was dominant at peripheral nerve sites around abdominal aorta, left internal iliac artery and prostate. Regarding the cause of NOMI, there was no direct invasion of IgG4-PPC into the feeding vessels of intestine.

APLAR-0382

Presenile dementia with multiple fractures in distal of appendicular skeleton due to cystic lesions: Nasu-Hakola syndrome

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Progressive dementia in conjunction with multiple bone fractures in a previous healthy young man led to the investigation for the underlying reason. Basal ganglion calcification in the brain CT scan born in mind limited differential diagnosis, firstly hypoparathyroidism. This patient also complained about recurrent episodes of ankle pain and swelling over the past three years. Radiologic findings included multiple cystic lesions in ankle and wrist. Due to normal related parameters and presenile dementia non-relevant to any known psychiatric diagnosis an electronic search with the key words: ÒBasal ganglion calcificationÓ and ÒosteoporosisÓ and ÒdementiaÓ was conducted which was found a rare condition with the name of Nasu*Hakola disease (NHD) or Ópolycystic lipomembranous osteodysplasia and sclerosing leukoencephalopathyÓ or ÒPLOSLÓ. This very rare and potentially fatal autosomal recessive disease is characterized by pathologic fractures, multiple cyctic bone lesions, and pre-senile dementia. Symptoms and signs of PLOSL can occur in some other diseases separately or sometimes in conjunction. For example, brain calcification may be found in hypoparathyroidism, pseudohypoparathyroidism, infections like syphilis or HIV, systemic lupus erythematosus and FahrÕs syndrome. Some of these diseases like FahrÕs syndrome, lupus, and hypoparathyroidism may also follow demential presentations. Parathyroid disorder and systemic lupus erythematosus may present with mood disorder, brain calcification, and osteoporosis. Importantly, when laboratory parameters are normal brain calcifications may be due to idiopathic calcifications, Cockayne syndrome, tuberous sclerosis and Down syndrome. Wilson disease can also present with those calcifications, neurologic symptoms, and osteoporosis. Finally, Nasu-Hakola disease is an inborn error without any special treatment, therefore conservative treatment is recommended only. What is important will be the adequate diagnosis, because of various not related symptoms and rarity of the disease, and genetic consulting before marriage for these patients.

SS14 – Contemporary concepts in rheumatoid arthritis

APLAR-0508

From genetics to functional insights into rheumatoid arthritis

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The etiology of autoimmune diseases including rheumatoid arthritis (RA) is still unknown. In order to identify diseases-associated genes, genome-wide association study (GWAS) is a promising strategy. Several laboratories including us have identified RA association polymorphisms. However, identification of such genes does not suggest the end of the story. We should further examine the functional relevance of these polymorphisms to RA pathogeneses, leading to the findings of new therapeutic targets as well as personalized medicine.

Through a preliminary method of GWAS, we reported functional haplotypes of PADI4, encoding citrullinating enzyme peptidylargimine deiminase 4, are associated with RA (Nat Genet 34:395, 2003). The susceptible mRNA was found to be more stable than non-susceptible mRNA. Our results imply that the RA susceptible PADI4 haplotype increases production of citrullinated peptides acting as autoantigens, resulting in heightened risk of developing the disease. The function of PADI4 in inflammatory arthritis has been studied using knock-out mice.

We have also identified a polymorphism in the chemokine (C-C motif) receptor 6 (CCR6) gene that was associated with RA susceptibility (Nat Genet 42: 515, 2010). The association was validated in two independent replication cohorts in Japanese. A tri-allelic dinucleotide polymorphism of CCR6 (CCR6DNP) in strong linkage disequilibrium with the original SNP was identified. The CCR6DNP genotype was correlated with the expression level of CCR6 and associated with the presence of interleukin-17 (IL-17) in the sera of RA patients. Moreover, CCR6DNP was significantly associated with susceptibility to GravesÕ and CrohnÕs diseases. Since CCR6 is a surface marker for Th17 cells, these results suggest that CCR6 is critically involved in IL-17-driven autoimmunity in human diseases.

APLAR-0543

Cytokines Interplay in the Pathogenesis of Rheumatoid Arthritis

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Rheumatoid arthritis (RA) is known as the most devastating autoimmune rheumatic disease that characterized by chronic inflammation at the synovium and leading to joint destruction.

The pathogenesis of RA is not clear enough as we can see a lot of factors plays an important role on it, such as the genetic susceptibility, environmental factors that trigger the autoimmunity processes and various kinds of molecules known as cytokines produced by several actors in the immune system.

The cellular interaction amongst macrophages, T and B cells and other cells i.e. fibroblast, synoviocytes, is believed to be of important in the pathogenesis of RA. All of that cells will communicate each other using their own language namely cytokines. In RA, there will be relatively reduced expression of several inhibitory cytokines that creates an imbalance between pro-inflammatory and the anti-inflammatory cytokines in the joints. The imbalance favors to joint destruction.Unfortunately, how cytokines are organized within the network is remains unclear and still we cannot stop them interact each other as one of the best target for clinical intervention nowadays. Failure to biologic agents is common. What make it happens?Even we do not have the exact explanation, but a better understanding on the cytokines interplay will bring us closer to the best therapy approach. Determination which cytokines is pivotal in the pathogenesis of RA is crucial. To date TNF alpha and IL-1 are believed as predominant cytokines. Then we found IL-6 as another important cytokine also. TNF alpha could induce release of other pro-inflammatory cytokines (IL-1, IL-6, IL-23, and GM-CSF), chemokine release, endothelial cell activation, hepcidin induction, leukocytes accumulation, angiogenesis, PGE2 production, chondrocytes activation and also osteoclast activation.To know which of cytokines is most important needed a clear measurement and should be validated. Further, the pathway that one cytokines interact with another and its consequences and which cells act as a conductor in the autoimmune orchestration should be taking into consideration.

Key words: RA, cytokines, pathogenesis.

APLAR-0509

Premature atherosclerosis in rheumatoid arthritis

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Atherosclerosis is now considered an immuno-inflammatory disease. Autoimmune rheumatic diseases like rheumatoid arthritis (RA) provide a fertile ground for accelerated atherosclerosis due to convergence of both traditional and novel risk factors. Patients with RA have increased mortality compared to the general population. Most of the excess mortality is attributable to cardiovascular (CV) causes. The problem of atherosclerosis in RA is overshadowed by articular symptoms which dominate the clinical picture. Cardiovascular disease in RA has some distinctive features that need reiteration: silent coronary artery disease is common, the disease burden is more, mortality rates are higher and the risk begins early, it may even precede the ACR (American College of Rheumatology) criteria based diagnosis of RA.

Different authors have utilized different techniques to detect atherosclerosis in RA. Flow mediated dilatation (FMD) and carotid intimo-medial thickness (IMT) have been widely used as surrogate markers of atherosclerosis. Several authors including our own group have demonstrated increased dyslipidemia, impaired flow mediated vasodilatation and increased carotid IMT in RA compared to age and sex matched controls.

Physicians caring for patients with RA should have a high index of suspicion for accelerated atherosclerosis. Cardiovascular risk reduction should be considered an integral part of management. Advice about cessation of smoking, exercise and optimization of body weight should be offered to all patients. Treatable risk factors like dyslipidemia and hypertension should be diligently sought and appropriately managed. Tight disease control of RA is likely to have a beneficial effect on CV risk reduction. Issues like which modality to use for screening and the cost effectiveness of different strategies to detect atherosclerotic CV disease in different population groups need further studies.

SS15 – Last updates of systemic lupus erythematosus

APLAR-0536

How early diagnose of SLE

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In around 1980 antinuclear antibody (ANA) testing became widely used in routine laboratory practice leading to a decreasing in the lag time between SLE onset and diagnosis. In our cohort of 487 SLE patients, recruited between 1970 and 2008, the mean lag time between the onset and the diagnosis was 59 months in patients diagnosed before 1980, 28 months in those diagnosed between 1980 and 1989, 15 months in those diagnosed between 1990 and 1999, and 9 months after 2000. Notably, the difference was significant between the first and the second group and between the second and the third group, but not between the third and fourth group, which means that since 1990 until now nothing relevant has been introduced which could have improved our diagnostic potential.

Early diagnosis and treatment could increase SLE remission rate and improve patient prognosis. This concept is also supported by animal models, which represent suitable models from this point of view due to the possibility of manipulating them before disease occurrence. All successful interventions in lupus mouse models are most effective when they are introduced before the development of full-blown clinical lupus; only a few of them are also effective after the disease has established.

Although it has been shown that autoantibodies appear before clinical manifestations in SLE patients, currently we cannot predict which autoantibody positive subjects will eventually develop the disease. Thus, great effort should be made in order to identify new biomarkers able to improve our diagnostic potential. B lymphocyte stimulator (BLyS), anti-ribosomal P protein and anti-C1q antibodies are among the most promising.

In recent years, some therapeutic options have emerged as appropriate interventions for early SLE treatment including antimalarials and vitamin D. All these immune modulators seem to be particularly useful when introduced in an early stage of the disease.

APLAR-0526

Unmet need and how to measure success of SLE therapy

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Systemic lupus erythematosus is a chronic autoimmune disease characterized, especially in Asian patients, by severe multi-organ damage and loss of life expectancy. Assessment of how well patients are currently being managed is made complex by the difficulties of assessment of disease activity in a multisystem disease. Current treatments are incompletely effective, and while assessment of treatment responses is made difficult by these complexities it is clear to those involved in managing SLE that new ways to assess treatment responses in SLE are needed in order to facilitate the evaluation of novel targeted therapies.

In this presentation, data on the state of SLE management and outcomes will be examined. A proposal for a novel measurement of treatment success in SLE, which is the subject of a current multinational Asian study, will be discussed.

APLAR-0510

Functional tests for complement and application in rheumatology

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Complement is an important part of the innate immune system comprising around 40 different proteins. It is a pattern recognition system ready at all times to fight infections, clear waste products like immune complexes and damaged cells. Disturbances of the complement system may lead to infections and contribute to tissue damage in inflammatory diseases. It is increasingly recognized that aberrant activity of complement is a major player in the pathogenic immune responses that underlie the development and progression of various inflammatory and autoimmune diseases, including rheumatic diseases.

The complement system is composed of three parts; the classical pathway, the lectin pathway and the alternative pathway. The classical pathway is activated by immunoglobulins bound to antigen, the lectin pathway by carbohydrate surfaces and the alternative pathway with LPS and foreign surfaces. Activation of each of these pathways leads to cleavage and activation of C3 into a small C3a fragment and a large C3b fragment that can opsonize pathogen cells and immune complexes. The three pathways then converge into a common pathway to form the membrane attack complex inserting itself into the lipid bilayer of cell membranes and killing the cell.

There are three major reasons to study complement function.

1. Complement deficiencies are associated with susceptibility to infections and autoimmune diseases. Deficiencies of the classical pathway are often associated with SLE, glomerulonephritis and susceptibility to infections. Deficiencies of the alternative pathway often leads to Neisseria infections, meningococcal diseases etc. An excellent way to screen for deficiencies is to study the function of the three pathways of the system.

2. Activation of the complement system is seen in active autoimmune diseases and may therefore reflect ongoing disease processes. Activation of the classical pathway has long been recognized in immune complex mediated diseases such as cryoglobulinemic vasculitis and systemic lupus erythematosus. Therefore in SLE it is important to follow activity of disease since complement activation follows disease activity and can detect flares. In anti-neutrophil cytoplasmic antibody ANCA) associated vasculitis the complement system was considered not to be involved however recent studies demonstrates that activation via the alternative pathway can be a major pathogenic mechanism.

3. A third reason is new therapies aiming at stopping or increasing complement activity and therefore complement function is important to follow. An example is the anti-C5 monoclonal antibody therapy, where it is important to follow the effect of the drug on the complement function.

Complement function has traditionally been measured by hemolytic assays using sheep or rabbit erythrocytes. Now ELISA's are available for measuring the functional activity of the three pathways. They are based on surfaces coated with binding ligands specific for the individual pathways, diluents especially prepared to allow only one pathway to be active and a common detection system, the MAC complex. These assays are excellent for screening of complement deficiencies and to follow disease activity in immune complex mediated diseases like SLE.

SS16 – New insight of Sjogren's Syndrome

APLAR-0512

Clinical and pathological features of Sjogrens syndrome: Japanese experiences

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Sjogren's syndrome is characterized by xero-stomia and kerato-conjunctivitis sicca clinically. Although the exact epidemiology for patients with Sjogren's syndrome (SjS) in Japan is await to be explored, the prevalence of the patients with primary SjS in 2002 is estimated to be 78 000 in Japan. It is diagnosed based on the criteria proposed by Japanese Ministry of Health, Labor and Welfare (MHLW) study group in 1999. I will discuss the issues for diagnosis of SjS, comparing Japanese criteria, America-European Consensus Group criteria (2002), and most recent ACR criteria (2012). Recently, the awareness of the disease not only in medical professionals, but also in society is increasing so that the prevalence is thought to be much higher up to some 200 000 patients in Japan.

The sign and symptom of this disease include not only dry mouth and dry eye, but include a variety manifestation such as dry skin, dry cough, fatigue, anxiety and arthralgia. Although the dryness stem from impaired exocrine gland function is central, more than half of the patients may exhibit arthritis/arthralgia (22%), leucocytopenia (12%), fever (5%), skin rush (3%), interstitial pneumonitis (2%), interstitial nephritis (2%), AV-block (1%) and so on in the our cohort.

Much effort has been made on the pathogenesis of the disease, focusing on the lymphocytic infiltration into the salivary and lacrimal glands in SjS patients. These lymphocytes are predominantly CD4+T cells. In addition, small numbers of CD8+T cells are found around the acinar epithelial cells, and the germinal center formation is seen in the advanced diseases. The molecular understanding of the pathogenesis such as adhesion molecules such as Fas-FasL, and aEb7 (CD103)-E-cadherin, cytokines such as IL-6 and BAFF is accumulating. Finally, molecular intervention focusing on these new targets is now exploring to clinical development.

APLAR-0538

The new insight in the pathogenesis of Sjogrens syndrome

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Sjogren's syndrome (SS) is a systemic autoimmune disease which is characterized by chronic inflammation of exocrine glands (especially lacrimal and salivary glands) and B-cell hyperactivity. Similar to other autoimmune diseases, the etiology of SS remains unknown. Data from animal-model studies and human researches point out that the pathogenesis should be the interactions between genetic, epigenetic, environmental, hormonal and neuropsychological factors. Hypothetically, the development of SS might be divided into three stages. Firstly, some environmental factors (eg. viruses) trigger the autoimmunity in a genetic susceptible individual. Secondly, there is an activation of both innate and adaptive immune response and finally there are tissue damages from local lymphocytic infiltration, cytokines, inflammatory mediators, autoantibody and immune-complex mediated mechanism. The innate-immune response might be important at the early stage through activation of type I interferon (IFN) pathway. Epithelial cells are important players not only as a target of the disease but also promote overactivation of the immune system. Activation of the autoreactive B cells is mediated by B-cell-activating factor (BAFF). Both type I and II IFN can induce BAFF release from monocytes, dendritic cells (DCs), T cells, B cells including salivary epithelial cells. Ectopic germinal center (GC)-like structures and follicular helper T(TFH) cells are important for chronic B-cell activation in salivary glands. In some patients this continuous B-cell activation and NFκB pathway dysfunction might cause lymphomatogenesis. Dysfunction of neuroendocrine systems (eg. hypothalamic-pituitary-adrenal axis) can also be demonstrated in SS patients. The increase in understanding of the pathogenesis of SS has led to the development of promising novel therapeutic strategies.

APLAR-0542

Treatment challenge of Sjogren's syndrome

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Sjogren's syndrome is an autoimmune inflammatory disorder of exocrine glands. It particularly affects the lacrimal and salivary glands. dry eyes and dry mouth eyes are frequently proffered as presenting symptoms. These symptoms are frequently accompanied by nonspecific symptoms, such as malaise and fatigue. In addition, extraglandular manifestations, such as purpura, polyneuropathy, and arthritis, can be present, even as presenting signs of the disease. Lymphomas develop in 5-100% in patients with Sjogren's syndrome. Sjogren's syndrome affects mainly women with a female/male ratio of 9: 1 and can occur at all ages. In-vitro and in-vivo experimental data have pointed to new immunopathogenic mechanisms in primary Sjogren's syndrome (PSS). The availability of targeted treatment modalities has opened new ways to selectively target these mechanistic pathways in vivo. A problem of all studies assessing the efficacy of these new modalities is the large variety of outcome parameters used in the various studies which makes a proper comparison of results between studies difficult if even possible. Therefore, this presentation reviews the current views and future challenges with regard to measuring disease activity and disease progression in Siogren's syndrome.

SS17 – Updated of pediatric rheumatology

APLAR-0521

Juvenile idiopathic arthritis: how different is it from adults?

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Juvenile idiopathic arthritis (JIA) and Rheumatoid arthritis (RA) in adults share similar clinical and pathological characteristics (both present as a chronic destructive arthropathy), genetic susceptibility (linkage with HLA genetic markers) and treatment options. But they also have a number of differences: JIA are more heterogeneous having different subtypes while the population of RA is more homogeneous, JIA has been more associated with chronic inflammatory eye disease which is not common in RA, JIA has low RF positivity compared to RA which somehow affects the outcome of the disease. These differences are proof that JIA and RA are two different clinical entities and that RA is not a continuum of JIA.

APLAR-0541

Systemic inflammation in pediatric rheumatic diseases: inflammatory cytokines and anti-cytokine therapy

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Inflammation has been considered to be a non specific reaction against exogenous and endogenous stimuli, and to play only a bridging role in the activation of immune system. However, it was recently clarified that inflammation is a unique defense system to be generated by the innate immune mechanism though it was closely linked to the adaptive immune system. The key players of inflammation have been suggested to be the inflammatory cytokines in multiple lines of both in vitro and in vivo evidence. Due to the crucial role of inflammatory cytokines in the pathogenesis of autoimmune disorders, anti-cytokine treatment has been developed as a therapy for rheumatoid arthritis, juvenile idiopathic arthritis (JIA), and inflammatory bowel disease. We recently completed several clinical trials of anti-cytokine treatment for children with systemic inflammatory diseases: anti-IL-6 receptor monoclonal antibody (tocilizumab) for children with 2 subtypes of JIA (poly-JIA and systemic JIA), anti-TNF-alpha monoclonal antibody (infliximab) for children with Kawasaki disease, and anti-IL-1-beta monoclonal antibody (canakinumab) for children with cryopyrin-associated periodic syndrome. In this presentation, I am trying to summarize the basis of inflammation of these systemic inflammatory diseases in terms of innate immunity and adaptive immunity, clinical efficacy and tolerability of these biologic agents, and to mention about the roles of individual inflammatory cytokines in inflammatory pathogenesis.

How to treat JIA – important clinical management issues to remember

T ARKACHAISRI

Abstract not available.

FREE PAPER ORAL SESSIONS ABSTRACTS
FP01 –Systemic lupus erythematosus and infection in rheumatic disease

APLAR-0487

Consensus definition of a low disease activity state in systemic lupus erythematosus

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Background: In systemic lupus erythematosus (SLE), organ damage, morbidity and mortality are the result of acute or sustained disease activity. The diversity of clinical features of active SLE makes quantification of disease activity problematic. The definition of a low disease activity state in rheumatoid arthritis has resulted in it being widely applied in research and clinical practice, but in SLE there is currently no such definition and thus no related outcome data. In contrast, clinicians often intuitively recognize a state of low SLE disease activity, wherein patientOs disease activity is low and treatment burden acceptable. No empirical definition of a low disease activity state in SLE has been described.

Objectives: To define a lupus low disease activity state (LLDAS), for subsequent validation using prospective cohort data.

Methods: Firstly, we defined LLDAS conceptually as follows: A state which, if sustained, is associated with a low likelihood of adverse outcome, considering both disease activity and medication safety. Next, a panel of experts from Hong Kong, China, Philippines, Thailand, Singapore, Indonesia and Australia individually generated items for potential inclusion in a definition of LLDAS. These items were scored on a 5-point scale, then reduced using the Delphi method. Six experts participated in the first round of Delphi, and items with a mean score >3 were retained. Eleven experts then participated in a consensus meeting using the nominal group technique and in a second round of Delphi, in which items with a mean score >4 were retained.

Results: Fifty-six unique items were initially generated. These fell into two domains: (i) descriptions of disease activity, and (ii) descriptions of medication use. Following two rounds of Delphi, unanimous agreement on the preliminary definition of LLDAS was reached. The final list of five items defining LLDAS comprised:

1 SLEDAI-2K ≤ 4, with *no* SLEDAI activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, hemolytic anemia, fever) and no gastrointestinal activity;
2 No *new* features of lupus disease activity compared to the previous assessment;
3 SELENA-SLEDAI physician global assessment (PGA, scale 0–3) ≤ 1;
4 Current prednisolone (or equivalent) dose ≤7.5 mg daily; and
5 Well-tolerated standard maintenance doses of immunosuppressive drugs and/or approved biologic agents, excluding investigational drugs

Conclusions: We have generated a definition of LLDAS. The definition of LLDAS will be validated in a large prospective multicentre Asian-Pacific lupus cohort, using outcomes including organ damage and death, and refined in response to subsequent findings. Once validated, LLDAS may serve alone, or in combination with variables such as patient reported outcomes, as a treatment target in SLE clinical practice, research, and clinical trials.

APLAR-0008

Anxiety and depression in Filipino patients with SLE using the validated Filipino version of the hospital anxiety and depression score

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Rationale: Identifying both overt and subclinical anxiety and depression in SLE patients may help identify additional points of care.

Objectives: To determine the presence of anxiety and depression in Filipino SLE patients compared to healthy controls using the validated Filipino version of Hospital Anxiety and Depression Scale (HADS-P) and to correlate this with patients' disease activity using Mexican-SLEDAI.

Design: This cross-sectional study recruited a non-probability sample of Filipino-speaking patients aged 19 years and above diagnosed with SLE (ACR 1982 Classification criteria) in the Philippine General Hospital Arthritis Clinic, matched by age and sex with healthy controls. Written informed consent was obtained. Rheumatologists independently assessed patients' disease activity using Mexican-SLEDAI. After giving written consent, subjects answered HADS-P, a self-administered questionnaire with subscales for anxiety and depression. Scores ³ 8 suggest presence of depression or anxiety. Chi-square or Fisher's exact tests compared nominal data and determined association between HADS-P and Mex-SLEDAI.

Results: One hundred fifty-five SLE patients were matched with controls. Mean age of patients with SLE was 35.7 years. Majority were females (97.4%), with college education (41.9%), dependents (61.9%), non-smokers (81.3%), and non-alcohol drinkers (74.2%). Patients with SLE and controls were comparable for most demographic characteristics, except that significantly more controls were not married (P = 0.022), self-supporting (P = 0.002), and with annual family income of more than PhP 100 000. (P = 0.041). There were significantly (P ≤ 0.0001) more SLE patients with high HADS-P depression and anxiety subscale scores (21% and 49%, respectively) compared to healthy controls (3% and 20%, respectively). Mex-SLEDAI scores and HADS-P did not show any correlation (P = 0.63 for depression, P = 0.998 for anxiety).

Conclusion: More Filipino SLE patients regardless of disease activity are found to have depression and anxiety over healthy controls. HADS-P could facilitate early detection of these conditions and prompt proper management.

APLAR-0076

The effect of autoantibodies on salivary gland function in patients with Sjögrens syndrome

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Objective: To examine the effect of autoantibodies on salivary gland function in patients with Sjögren's syndrome (SS), by using quantitative measures of salivary gland scintigraphy (Nishiyama S et al. J Rheumatol 2006;33:2470–4).

Methods: Patients who underwent salivary gland scintigraphy were classified into 94 with SS and 53 without SS according to ACR criteria. Patients with at least one of autoantibodies (anti-centromere, RNP, SS-A or SS-B) were named Ab+, and those without autoantibodies were named Ab-.

Results: Compared with non-SS, SS patients were young and had low amount of saliva by the Saxon test, high grade of salivary echogram and high focus scores of labial glands. All quantitative measures of scintigraphy but excretion fraction were significantly lower in SS patients than non-SS. The clinical features and quantitative measures did not differ between primary and secondary SS. Patients were divided into four groups: 88 with Ab+SS (A), six with Ab-SS (B), 18 with Ab+non-SS (C) and 35 with Ab-non-SS (D). Group A had lower peak count, uptake speed and excretion speed than group D. Group C had high uptake speed compared with group A and low excretion speed compared with group D. Among all patients, 17 with anti-centromere had significantly lower excretion fraction than 47 Ab- patients. There was a negative correlation between the titers of anti-RNP and quantitative measures of peak count and excretion speed. Among SS patients, six with anti-centromere + SS-A and/or SS-B had lower excretion fraction than 68 with SS-A and/or SS-B.

Conclusions: Patients with SS showed impaired salivary gland function. Anti-centromere and anti-RNP affected salivary gland function.

APLAR-0366

Premature atherosclerosis of Apoe−/−FasL−/− C57BL/6 mice was mediated by dysfunction of bone marrow derived endothelial progenitor cells

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with premature atherosclerosis. To establish a mouse model of accelerated atherosclerosis in lupus, apolipoprotein E-deficient [apoE(−/−)] and Fas ligand-deficient [FasL(−/−)] C57BL/6 mice were generated, and found that this mice had severe proteinuria, increased circulating autoantibody levels, and increased atherosclerotic lesions compared with single knockout mice, which remind us the existence of a common pathway between lupus and atherosclerosis, which needs further research. Preliminary data suggest that endothelial progenitor cells (EPCs) are decreased in SLE, which might contribute to its premature atherosclerosis.

Objectives: To detect whether premature atherosclerosis of Apoe−/−FasL−/− C57BL/6 mice was mediated by dysfunction of EPCs.

Methods: Monocytes were isolated from peripherial blood and bone marrow of ApoE+/+FasL+/+, ApoE+/+FasL−/−, ApoE−/−FasL+/+, ApoE−/−FasL−/− C57BL/6 mice, The percentage of EPCs was analyzed by FACS as CD11b-Sca-1+CD309+ cells. EPCs were stained with Dil-ac-LDL and FITC-UEA-1 double dyeing to determine their swallow function. Adherent function of EPCs was determined by counting the number of recultured EPCs. Capacity of EPCs to form the cavity structure was detected by counting the number of formed vascular-like structure.

Results: The percentage of circulating EPCs and bone marrow derived EPCs was significantly decreased in ApoE−/−FasL−/− group compared to single knockout mice. Compared with the other three group respectively, the percentage of Di-lac-LDL and FITC-UEA-1 double positive cell, adherent function of EPCs and the capacity of EPCs to form the cavity structure were markedly decreased in ApoE−/−FasL−/− group.

Conclusions: Premature atherosclerosis of Apoe−/−FasL−/− C57BL/6 mice was associated with decreased number and dysfunction of EPCs.

APLAR-0371

Down-regulation of LILRA4 expression on peripheral plasmacytoid dendritic cells in systemic lupus erythematosus

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Objective: Leukocyte immunoglobulin like receptor A4(LILRA4), a receptor specifically expressed on plasmacytoid dendritic cells (pDCs), negatively regulates the interferon α(IFNα)-secreting function of pDCs, which is known to play the key role in the pathogenesis of systemic lupus erythematosus (SLE) and lupus nephritis (LN). Thus in this study, we examined the surface expression of LILRA4 and other LILR family receptors known to be expressed on peripheral dendritic cells in both SLE patients and healthy donors, and also investigated the relationship between LILRA4 expression and disease characteristics.

Methods: PBMCs freshly isolated from whole blood samples of 11 SLE patients and 10 healthy donors were stained with antibodies against lin, HLA-DR, CD11c, CD123 and a panel of antibodies recognizing LILRA2, LILRA4, LILRB1 and LILRB2. Afterward, cells were washed, fixed, and analyzed by flow cytometry. Both mean fluorescence intensity (MFI) of LILR and the proportion of LILR-expressing cells were analyzed in pDCs and myeloid dendritic cells (mDCs). SLE disease activity index (SLEDAI), titer of anti-dsDNA antibody, kidney involvement were evaluated. Relationship between LILR expression and clinical characteristics were investigated.

Results: A significant down-regulation of LILRA4 expression on pDCs was seen in SLE patients compared to healthy donors both on single cell level and expressing proportion (MFI: 1351 ± 423 versus 1147 ± 363, P = 0.0014; proportion: 64.87 ± 7.77 versus 93 ± 1.91, P = 0.0035) while no significant differences were seen in the expression of LILRA2, LILRB1 and LILRB2 on pDCs or mDCs. Both MFI of LILRA4 on single pDC and proportion of LILRA4 (+) pDCs were negatively correlated with SLEDAI (MFI: P = 0.0422, R^2 = 0.3834; LILRA4(+) proportion: P = 0.0321, R^2 = 0.4161) or 24 hours urine protein levels in LN patients (MFI: P = 0.0377, R^2 = 0.5404; LILRA4(+) proportion: P = 0.0143, R^2 = 0.6594). However, no correlation were seen between LILRA4 expression and the tilter of anti-dsDNA.

Conclusion: Down-regulation of LILRA4 expression on peripheral plasmacytoid dendritic cells was seen in systemic lupus erythematosus, implicated the breach of LILRA4-mediated controlling function of pDCs might involved in the pathogenesis of SLE and LN.

APLAR-0184

Elevated level of circulating cell-free DNA and increased percentage of low-density granulocytes are associated with active lupus nephritis

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Objective: Neutrophil extracellular traps (NETs) are important source of autoantigens in systemic lupus erythematosus (SLE). Low-density granulocytes (LDGs) could form NETs spontaneously and excessively than normal neutrophils, and DNase1 was responsible for degrading NETs. If excessively formed-NETs could not be degraded in time, they can serve as autoantigens and cause increase of circulating cell-free DNA (cfDNA) level. However, whether elevated level of cfDNA could be attributed to LDGs and DNase1 is still unknown in SLE. This study was undertaken to address the question and to explore whether cfDNA could be a biomarker for organ involvement related to abnormal formation and degradation of NETs in SLE.

Methods: Fifty four patients with SLE and 43 age-and sex-matched healthy controls were included in the study. DNase1 activity was measured by radial enzyme-diffusion method, and cfDNA concentration was measured with Picogreen Kit. Percentage of LDGs in PBMC was tested by flow cytometer. SLE disease activity index (SLEDAI) was assessed for every patients. These parameters were compared in patents group and healthy control group respectively. Linear correlation analysis were performed between these three, SLDAI and other serological parameters.

Results: cfDNA in SLE group was 239.76 ± 57.15 ng/mL, significantly higher than that in healthy control group (187.96 ± 40.55 ng/mL, P < 0.0001). DNase1 activity in SLE group was 0.26 ± 0.17 U/mL, significantly lower than that in healthy control group (0.43 ± 0.26 U/mL, P < 0.0001). Percentage of LDGs in PBMCs of SLE group was 8.29 ± 12.86%, significantly higher than that in healthy controls group (1.15 ± 0.71%, P = 0.0036). In SLE group, cfDNA positively correlated with percentage of LDGs in PBMCs (r = 0.651, P = 0.002), ESR (r = 0.364, P = 0.007), CRP (r = 0.291, P = 0.032) and urine protein (r = 0.350, P = 0.013) and reversely correlated with albumin (r = −0.500, P < 0.0001).

Conclusion: The elevated level of cfDNA may indicate renal involvement in SLE patients. Patients with higher percentage of LDGs in PBMCs tend to suffer higher rate of lupus nephritis.

FP02 – Systemic lupus erythematosus

APLAR-0148

Familial Mediterranean fever gene mutations as a risk factor for early coronary artery disease

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Objective: Cardiovascular diseases (CVD) are very common in general population. Atherosclerosis is responsible for main pathogenesis. Familial Mediterranean fever (FMF) is an autosomal recessive disease. The gene causing FMF, designated MEFV, encodes a protein called pyrin or marenostrin that is expressed mainly in myeloid bone marrow precursors, neutrophils, and monocytes. We herein aimed to determine the prevalence of MEFV mutations (all exon 2, 10 mutations) in patients with early coronary heart disease (early CHD) and coronary heart disease (CHD) carrying with multiple risk factors and among the healthy subjects as controls.

Methods: A total of 197 patients and 119 healthy subjects were recruited and enrolled into three groups in terms of inclusion criteria. Ninety-one patients diagnosed with early CHD enrolled into group one (men <45 years of age, women <40 years of age), 106 patients with CHD (men >50 years of age) to group two and 119 healthy controls enrolled into group three. None of patients was diagnosed with FMF. The diagnosis of CHD was established on electrocardiographic changes, echocardiography and coronary angiography.

Results: Thirty-eight patients (41.8%) with early CVD, 17 patients (16%) with CVD, 24 healthy controls (20.2%) carried at least one mutated MEFV allele. Young patients with CHD have different risk factor profiles, clinical presentations, and prognoses than older patients. Young patients with CHD usually have multiple risk factors.

Conclusion: This study suggests that MEFV mutations with early CHD patients had significantly increased in contrast to CHD patients and healthy controls.

APLAR-0326

Correlation of anti C1q antibodies with disease activity in Pakistani patients with systemic lupus erythematosus

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Objectives: To study the correlation of anti C1q antibodies with disease activity in Pakistani patients with systemic lupus erythematosus.

Material and Methods: The study was conducted at the Department of Immunology, Armed Forces Institute of Pathology, Rawalpindi (Pakistan) from January 2012 to December 2012. Patients with a clinical diagnosis of SLE were included in the study on fulfilling revised ACR criteria (1997). Main outcome measures were SLEDAI scores and anti C1q antibody levels in serum. Anti C1q antibody levels in the serum were determined by ELISA and correlated with the SLEDAI scores. The cutoff value for anti C1q antibody positivity in the serum was determined by evaluating the serum levels of anti C1q antibodies in 30 healthy subjects and was 12 U/mL.

Results: Six male and forty-nine female SLE patients with an age range of 16–47 years (mean 34.5 years) and 8–70 years (mean 31.7 years) respectively were studied. The correlation between anti C1q levels and SLEDAI scores in all patients was demonstrated by calculating the correlation coefficient and was not significant ($r = 0.19$, $P = 0.14$). However, there was an inverse correlation between anti C1q levels and SLEDAI scores in patients with severe disease and this was statistically significant ($r = *0.448$, $P = 0.037$). The difference in anti C1q antibody positivity between patients with and without nephritis was not significant. The anti C1q antibody levels correlated poorly with anti dsDNA antibody positivity. A significantly higher percentage of patients with evidence of consumption of complement component C3 was found to be positive for anti C1q antibodies ($P = 0.01$).

Conclusion: A significant inverse correlation was found between SLEDAI scores in patients with severe SLE and serum anti C1q antibody levels. The anti C1q antibody positivity is significantly higher in patients with reduced C3 levels.

APLAR-0451

Sweet potatoes decreases Th17 cells and regulatory T cells persentage also increases regulatory T cells/Th17 cells ratio

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Background: Systemic lupus erythematosus (SLE) is autoimmune disorder affecting various organs. SLE patients show decreasing T regulatory cells and increasing Th17 cells. It lowers Treg cell/Th17 cell ratio and inflammation.

Subjects and Methods: Here we purposed to find effect of sweet potato on naive CD4 T cells differentiation from SLE patients. Naive CD4 T cells were performed in vitro in medium containing TGF-β dan IL-6 that naive CD4 T cells can differentiate into Th17 cell. Crude extract of sweet potato was added to medium of treatment group while control group wasnÕt. Administration of sweet potato was to increase T regulatory cells, decrease Th17 cells so that it could increase regulatory T cell/Th17cell ratio.

Results: Here we showed that sweet potatoe exert differentiation of Th0 into both Th17 cells ($CD4^+IL\text{-}23R^+$) ($P > 0.05$) and regulatory T cells ($CD4^+CD25^+$) ($P > 0.05$). However, a decrease in Th17 cells was lower than the decrease in Treg cells. The decrease in Treg cells thought to be a compensatory mechanism to decrease in Th17 cells. Sweetpotatoe also increased the ratio of Treg cells/Th17 cells ($P < 0.05$).

Conclusion: Thus, sweetpotatoes can inhibit inflammation and potentially improve condition of SLE patient by lowering Th17 cells and increasing the ratio of Treg cells/Th17 cells.

Key words: SLE, Treg cell, Th17 cell, sweet potato

APLAR-0402

Serum values of cathelicidin (LL37) in lupus patients and healthy controls, a comparison with lupus markers too

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Background: Neutrophil extracellular traps (NETs) are important defense mechanisms against microorganisms. Clearance of NETs is impaired in patients with systemic lupus erythematosus and NETosis is increased in neutrophils of lupus patients. Cathelicidin (LL37) is one of the NETsÕ component that acts as a natural antibiotic and is a part of the innate immune defense in human. Over expression of LL37 has been detected in skin lesions of lupus patients. This abstract points to the difference between serum values of LL37 in healthy controls and SLE patients. Besides, association of lupus markers and LL37 will be discussed.

Method and material: Serum of 50 female SLE patients who fulfilled the American College of Rheumatology (ACR) criteria and 20 age- and sex-matched healthy controls were collected. All patients with DLE, recent trauma or surgery, infectious or antibiotic therapy over recent 3 months were excluded. All patients received lower than 10 mg prednisolone or samples was obtained before pulse therapy. LL37 levels were measured using a commercial ELISA kit.

Results: The mean age of the patientsÕ was 31.3 ± 9 years. LL37 showed no statistical difference between patients and controls ($P = 0.1$, $t = 1.6$). LL37 did not correlate with disease duration ($P = 0.5$, $r = 0.08$). C3 ($P = 0.07$, $r = -0.26$), C4 ($P = 0.8$, $r = 0.02$), anti-dsDNA ($P = 0.8$, $r = -0.02$), prednisone dosage ($P = 0.8$, $r = -0.02$) and the amount of proteinuria ($P = 0.1$, $r = 0.2$). However, only patients with low C3 levels presented higher LL37 serum values ($P = 0.02$).

In brief, although imbalance in Netosis pathway like apoptosis imbalance plays an important role in the pathogenesis of systemic lupus erythematosus, the current study demonstrated that in a point of time its serum values is not a good marker of disease development and does not correlate with laboratory parameters on SLE.

APLAR-0091

Histopathological classification of ANCA associated glomerulonephritis and its impact on outcome

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ANCA associated vasculitis involves variety of organs, of which renal involvement is a common and severe manifestation. The morphologic changes in the renal biopsy are the gold standard for establishing a diagnosis. The new histopathological classification for ANCA associated glomerulonephritis was developed by an international working group of renal pathologists in 2010 and includes four categories, viz. Focal, crescentic, sclerotic and mixed. There are very few studies in relation to this classification and its implication on prognosis. This study was aimed to classify these patients according to the new classification and assess its impact on outcome. A total of 86 patients were included. The mean age was 42.5 ± 15.23 years with 51.2% females. Clinical diagnosis was GPA in 34 (39.53%), MPA in 36 (41.86%); CSS in one patient and the rest were unclassified. Among the patients of GPA, 24 patients (70.59%) had renal manifestations compared to 32 patients (88.89%) in MPA and 15 patients (100%) in unclassified group. Thirteen patients (15.5%) were classified as focal, 43 (51.2%) as crescentic, 12 (14.3%) as sclerotic and 16 (19%) as mixed group. The mean serum creatinine at baseline was 3.17 mg/dL in focal, 7.46 mg/dL in crescentic, 6.49 mg/dL in sclerotic and 6.14 mg/dL in mixed group. Intravenous methylprednisolone, IV cyclophosphamide and oral cyclophosphamide were given in 53.5%, 50% and 24.4% of patients respectively. Plasmapheresis was given in 12 patients; haemodialysis at onset was given in 50%, while 23.3% of the patients went on to require RRT for life. The probability of improvement in renal function at 6 months was seen with decreasing frequency from focal to crescentic to mixed to sclerotic group. The probability of death was highest in sclerotic group followed by mixed group. The mean BVAS score of the patients was 18.15 and among patients with BVAS <20, 14.81% of patients expired at 6 months as compared to 25% among patients with score >20. In our study, the most common histological class was crescentic group irrespective of the clinical diagnosis. This study has shown that the new histopathological classification can be used to predict the severity of initial renal dysfunction.

APLAR-0405

Prevalence of positive autoantibody biomarkers in brucellosis

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Aim: Brucellosis is a chronic infectious disease with articular involvement. Sometimes differentiation between brucellosis and rheumatologic disorders is difficult in endemic region for brucellosis. Autoantibodies are a biomarker in rheumatologic disorders, but there are a few studies about the rate of positive biomarkers in brucellosis and the prevalence is variable. Evaluation of prevalence of positive rheumatic factor (RF), anti-nuclear antibodies (ANA), anti-cyclic citrullinated peptide (anti-CCP) in brucellosis was the aim of this study.

Methods: All patients with brucella infection in two referral academic center in Tehran, Iran were enrolled in this study during 2011. Diagnosis of brucellosis was made based on clinical symptoms and positive serology for brucellosis (wright, coombs wright and 2-Mercaptoethanol [2ME]). Rheumatic factor and ANA were evaluated in all patients. Anti-CCP and anti-dsDNA were checked if patient was RF positive or ANA positive, respectively.

Findings: Out of 39 patients (26 male and 13 female) with mean age of 35.4 (2–75 years) 13 patients (33.3%) was RF positive and two patients (0.5%) was ANA positive. Anti-dsDNA was positive in one patient with ANA positive but anti-CCP titer was positive in 8/13 (61.5%) of the RF positive patients (20.5% of total patients). Any patients with positive autoantibody biomarkers didnÖt fulfilled rheumatoid arthritis, juvenile idiopathic arthritis or lupus criteria and all patients were symptom free after 4 months of brucellosis treatment. Fifty percent of the patients with RF positive and 75% with positive Anti CCP had skeletal involvement ($P < 0.05$). There is no significant relation between biomarkers positivity and serology titer of brucellosis.

Conclusion: Autoantibody biomarkers can be positive in brucellosis. Rheumatologists should be aware of the brucellosis in patients with musculoskeletal involvement and positive autoantibody biomarkers in endemic regions.

Key words: Brucellosis; Anti CCP, Rheumatic Factor; Anti nuclear Anti body; Chronic Arthritis

FP03 – Rheumatoid arthritis I

APLAR-0199

CD3+CD154+ change may be a predict factorof efficacy by TNF-ainhibitor treatment in axial SpA patients

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Objective: To detect the association the expression of the subtype of T lymphocytes between healthy controls and axial SpA, and evaluated if the precentage some subtypes of T lymphocytes could be as a index for predicting clinical efficacy before and after TNF-αinhibitor (Infliximab and Etanercept) treatment 12 weeks in active axial SpA patients.

Methods: Fifty-eight healthy controls crowd and 74 active axial SpA patients (47 AS and 27 non-radiographic axial SpA) were Included. Defination of active axial SpA patients was that BASDAI ≥ 40 mm (VAS=100 mm) in patients. We collected the data of all subjects, which include gender, age, disease duration, onset age, family history, HLA-B27, arthritis (baseline), hip involved (baseline) and CRP (baseline). Thirty-five patients received 5 mg/kg of infliximab by intravenous injection at weeks 0, 2, 6, 12, and 39 patients received 50 mg once a week of etanercept by hypodermic injection during 12 weeks. At weeks 12, ASAS20 was used to evaluate the effect of the treatment. During this period, at baseline, 6 mL peripheral blood was obtained from patients to detected the percentage of CD3+CD4+, CD3+CD8+, CD3+CD19+, CD3+CD28+ and CD3+CD154+. Nonparametric test was used to analyze the association between healthy controls and axial SpA patients. In addition, we evaluated if the percentage of above subtype of T lymphocytes could predict clinical efficacy with ROC curve analysis.

Result: Mean age was 26.28 ± 9.08 years and 26.95 ± 8.13 years in healthy controls and axial SpA patients, respectively (P = 0.013). Mean disease duration and onset age were 2.18 ± 3.30 years and 20.06 ± 12.03 years, respectively. 89.19% (n = 66) patients were HLA-B27(+), 14.86% (n = 11) patients had positive family history, 34.43% (n = 24) had arthritis, 12.16% (n = 9) had hip involvement. The percentage of CD3+CD19+ on peripheral blood T-lymphocytes were detected significantly more higher in axial patients than in healthy controls (13.04 ± 12.99% versus 8.26 ± 2.59%, P = 0.013). Analogously, the percentage of CD3+CD154+ on peripheral blood T-lymphocytes were detected significantly more higher in axial patients than in healthy controls (1.62 ± 1.89% versus 0.79 ± 0.52%, P = 0.000). At baseline, the percentage of CD3+CD154+ was significant high-expression in HLA-B27(+) patients (HLA-B27- versus HLA-B27+:1.77 ± 1.95% versus 0.41 ± 0.27%, P = 0.005). In addition, we detected that high-expression of CD3+CD154+ was an index to predict satisfactory response for clinical efficacy after ROC curve analysis (AUC=0.83, P = 0.014; Figure 1).

Conclusion: High-expression of CD3+CD19+ and CD3+CD154+ in active axial SpA patients than healthy controls. In addition, high-expression of CD3+CD154+, which was associated with HLA-B27(+) axial SpA patients, may be an predictive factor of clinical efficacy of infliximab treatment.

APLAR-0216

Incidence of tuberculosis, serious bacterial infection, and lymphoma in patients with rheumatoid arthritis receiving biologic and non-biologic treatment in Taiwan

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Introduction: Our study assesses the incidence of TB, serious bacterial infection (SBI) and lymphoma in rheumatoid arthritis (RA) patients who received anti-TNF therapy and non-biologic treatment in Taiwan, as limited data exists.

Methods: National Health Insurance Research Database data (1999–2009, covering 99.9% of the Taiwan population) were analyzed.[1] Eligible patients (≥18 years) were required to have: ≥2 recorded RA diagnostic codes (ICD-9 "714.0x"), a catastrophic illness card and had received traditional Disease Modifying Anti-Rheumatic Drugs (tDMARDs) or biologic DMARDs (bDMARDs). Patients with prior TB/SBI/lymphoma were excluded. Propensity scoring matched patients received tDMARDs and bDMARDs 2:1, adjusting for age, gender, disease severity, and co-morbidities. Incidence rates (IR) of TB, SBI and lymphoma were defined: (number of events/total patient exposure years); ratios (IRRs) were calculated across therapies.

Results: Of 34 947 eligible patients (mean age 60.6 years, 79% female, mean RA duration 7.6 years), the bDMARDs group had higher incidence of TB, SBI and lymphoma than the tDMARDs only group (Table). Within the bDMARDs group 3109 patients (77.1%) were treated solely with ETN and 865 patients (21.4%) solely with ADA. Patients receiving ADA had higher rates of TB, SBI and lymphoma, which also occurred earlier, than those receiving ETN. All stated differences were statistically significant, except bMARDs versus tMARDs SBI and ADA versus ETN lymphoma incidence (Table).

Conclusions: bDMARDs increase the risk of TB, SBI and lymphoma, risks to differing extents: risk was lower with ETN than ADA.

Reference: 1. National Health Insurance Research Database, Taiwan. http://www.nhri.org.tw/nhird/en/index.htm

Table Incidence of Infection during RA Therapy

	bDMARD IRR (95% CI)	Referent
TB	2.67* (2.12–3.34)	tDMARD
Lymphoma	3.24* (1.37–7.06)	tDMARD
SBI	1.04 (0.89–1.19)	tDMARD
ADA compared with ETN		
TB	2.35* (1.29–4.15)	ETN
Lymphoma	1.49 (0.03–18.66)	ETN
SBI	1.83* (1.19–2.77)	ETN

*P < 0.05.

APLAR-0284

Societal costs of rheumatoid arthritis in China: a hospital-based cross-sectional study

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Objective: To determine the annual direct and indirect costs of rheumatoid arthritis (RA) in China, and identify the predictors for cost-of-illness.

Methods: A cross-sectional study of cost-of-illness was conducted on 829 patients with RA in 21 tertiary care hospitals in China between July 2009 and December 2010 from the societal perspective. Data on demographics, clinical variables, and components of costs were collected by physician interview. Costs were represented in 2009 US dollars ($). Univariate and multivariate regression analysis were performed to identify the predictors for cost-of-illness.

Results: The mean (SD) total costs of RA were $1980 (2929) (2009 US dollars) per patient-year in China, given the individual GDP of $3678 in China in 2009. Direct costs and indirect costs comprised 90.0% and 10.0% of the total costs, respectively. Drug expense represented approximately half of total costs, dominated by biologics (48.2%) and DMARDs (23.6%). Besides, the costs of extracted herbal drugs and traditional Chinese medicine were about 17.6% of drug expense. Both univariate and multivariate linear regression analysis showed uninsured residents, higher education level, longer disease duration, more extra-articular manifestations and higher HAQ score were independent predictors for high cost-of-illness.

Conclusion: Our results provide first study of costs of RA in China. This study not only demonstrates the substantial economic burden of RA, but also identifies the predictors that could be interventional factors to reduce the societal costs of RA in China.

APLAR-0464

Prevalence and predictor factors of atherosclerosis in rheumatoid arthritis patients at Cipto Mangunkusumo Hospital Jakarta Indonesia

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Objective: To study prevalence and predictor factors of atherosclerosis among rheumatoid arthritis (RA) patients at Cipto Mangunkusuma Hospital Jakarta Indonesia.

Method: A cross-sectional study was conducted at Rheumatology Clinic at Faculty of Medicine/Cipto Mangunkusumo Hospital Jakarta Indonesia. Intima media thickness (IMT) of carotid artery as a surrogate marker of atherosclerosis was measured at common carotid artery (CCA), internal carotid artery (ICA) and bulbous (carotid sinus) by using ultrasonography at both sides. We define atherosclerosis if we found IMT ≥ 1.0 mm at CCA, or ICA or bulbous, or if evidence of plaque formations was found. We analyze clinical parameters (sex, age, duration of illness), comorbidities (DMT2, hypertension, obesity, dyslipidemia), anti CCP antibody, anti Oxidized-LDL antibody level and Sharp's van der Heijde score. Anti CCP and anti Oxidize-LDL antibody level were measured by Eliza kit.

Result: We analyzed 86 subjects patient with RA who fulfill EULAR/ACR 2010 criteria (age 21–69 years old; eight men, 78 women). Atherosclerosis was found in 50% of patients. Median IMT was 0.683 mm (min 0.39–max 1.94), 0.705 mm (0.45–2.04), and 0.850 mm (0.38–4.34) at CCA, ICA and bulbous respectively. Plaque formation was found in 29.1% of patients. Age (≥40 years old), duration of illness (≥24 months), hypertension, DMT2, were associated with atherosclerosis in bivariate analysis. Sex, anti CCP antibody, anti Oxidized-LDL antibody level and Sharp's van der Heijde score were found not significant associated with atherosclerosis. In multivariate analysis age and duration of illness were associated with atherosclerosis. Relative risk was 7.90 (95%CI 2.50–24.91) and 4.39 (95%CI 1.41–13.73) respectively.

Conclusion: Atherosclerosis was found in 50% of RA patients at Cipto Mangunkusumo Hospilatal. Age ≥ 40 years old and duration of illness ≥24 months were predictor factors for atherosclerosis.

APLAR-0048

Identification of potential serum biomarkers for rheumatoid arthritis by high resolution quantitative proteomic analysis

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Objective: To find serum biomarkers of rheumatoid arthritis (RA) by high resolution quantitative proteomic analysis.

Methods: Low-abundance proteins from the serum of 20 RA patients and 20 healthy controls were enriched using ProteominerTM enrichment kits. Subsequently, the enriched proteins were eluted from the column and separated on 1D SDS-PAGE. The gel bands were excised, reduced and dried, followed by in-gel trypsin digestion. The digested products were labeled with the TMT 6-plex reagents. The labeled products were desalted by a C18 stage tip column and analyzed by LC-MS/MS with nano-LC combined with orbitrap velos. Differential expressed proteins were screened by fold change (RA/HC ≥ 1.5or ≤0.66). Enzyme-Linked Immunosorbent Assays (ELISA) were performed in order to confirm these differentially expressed proteins identified by quantitative proteomic analysis.

Results: We identified 22 proteins differentially expressed between RA patients and healthy controls. Levels of Thrombospondin-1, Ficolin-2, Apolipoprotein E, Isoform 1 of Clusterin, Antithrombin-III, were much higher in the sera of the RA patients than those in healthy controls (RA/HC ≥ 1.5), while Angiotensinogen, serum Paraoxonase/arylesterase 1 and Plasminogen were significantly lower in RA patients (RA/HC ≤ 0.5). Levels of Thrombospondin-1 and Ficolin-2 were further examined by ELISA in 98 RA patients and 58 healthy controls. The result showed that these two proteins were potential biomarkers to distinguish the two populations from each other. The Thrombospondin-1 level was positively correlated with swollen joint number and DAS28. The Ficolin-2 level was positively correlated with swollen joint number, DAS28, rheumatoid factor and total IgM.

Conclusion: High resolution quantitative proteomic analysis coupled with validation using a complementary low-throughput experimental technique may be a reliable and accurate method to explore new biomarkers of autoimmune disease. Thrombospondin-1 and Ficolin-2 may play important roles in the development of RA and may be a potential biomarker to assess RA disease activity.

Key words: rheumatoid arthritis; quantitative proteomic analysis; biomarker; Thrombospondin-1; Ficolin-2

APLAR-0308

Apremilast, an oral phosphodiesterase-4 Inhibitor, in psoriatic arthritis: results from two phase III clinical trials

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Background: Apremilast (APR), a small molecule oral phosphodiesterase-4 inhibitor, is under investigation for psoriasis, ankylosing spondylitis, and PsA.

Methods: The phase III PALACE-1 and PALACE-3 studies enrolled active PsA patients despite previous oral and/or biologic and/or current oral DMARDs. Patients were randomized to placebo, APR 20 mg BID (APR20), or APR 30 mg BID (APR30) for 24 weeks. At week 16, patients without ≥20% improvement in both SJC/TJC were required to rescue: placebo patients were randomized to APR20 or APR30; APR patients continued current therapy. Efficacy analyses used pre-defined per-protocol populations. Missing data for ACR response at week 16 used NRI methodology.

Results: Five hundred and 504 (PALACE-1) and 505 (PALACE-3) patients were randomized: 60%-65% taking baseline DMARDs (majority, MTX), 23.6%-27.9% biologic experienced, and ≤9.3% biologic failures.

In both studies, significantly more patients receiving APR20 and APR30 achieved ACR20 (the primary endpoint) at week 16 vs placebo (table). APR monotherapy sometimes yielded higher responses. Secondary endpoints, including improvement in HAQ and PASI, demonstrated greater efficacy for APR.

AEs occurring in ≥5% of any group were diarrhea, nausea, headache, and URTI. Of APR-treated patients with AEs, most (>92%) were mild or moderate. Discontinuations due to AEs were low across arms (5%-8%). SAEs occurred in 7 (PALACE-1) and 9 (PALACE-3) placebo, 8 and 3 APR20, and 9 and 6 APR30 patients. Serious/opportunistic infections and cardiovascular events were balanced between groups; no lymphoma was observed.

Palace-1	Placebo (n = 165)	APR20 (n = 163)	APR30 (n = 161)
ACR20 at week 16,%	19	31*	40**
APR monotherapy (n = 172)	11	32*	48**
Palace-3	**Placebo (n = 164)**	**APR20 (n = 163)**	**APR30 (n = 159)**
ACR20 at week 16,%	19	29*	43**
APR monotherapy (n = 184)	14	25	45‡

*$P < 0.5$, **$P \leq 0.0001$, ‡$P \leq 0.005$.

Conclusions: APR significantly improved PsA signs and symptoms, including joint and skin symptoms. APR was well tolerated with no new safety or laboratory signals detected.

FP04 – Rheumatoid arthritis II

APLAR-0436

The role of arsenic trioxide on survivin expression in rheumatoid arthritis fibroblast-like synovial cells

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Object: Survivin is the the smallest molecule of the inhibitor of apoptosis proteins (IAPs) with dramatic anti-apoptotic ability and complex functions including angiogenesis. Recent investigations confirmed overexpression of survivin in rheumatoid arthritis (RA) patients. High levels of survivin predicted joint destruction, and correlated with failure of treatment with biological agents. As the most important cells of RA synovial tissue, fibroblast-like synovial cells (FLS) are potential sources of extracellular survivin. Our previous studies have shown positive effect of arsenic trioxide (ATO) on RA treatment through anti-inflammation and apoptosis induction. This research detected basement survivin protein level of RA FLS and actions of ATO on survivin secretion. We intend to further clarify the mechanism of ATO and search for new treatments for refractory RA.

Methods: RA FLS were cultured in vitro with or without 10 ng/mL TNF-α, and then treated with different concentrations of ATO (2 or 4 μmol/L) for 24 h. Survivin protein level of cell culture supernatant was measured by ELISA.

Results: A certain concentration of survivin protein could be detected in RA FLS supernatant (111.3 ± 3.9 pg/mL). ATO treatment notably down-regulated protein levels of survivin (2 μmol/L: 75.0 ± 3.9 pg/mL; 4 μmol/L: 63.1 ± 15.4 pg/mL). Significant elevated level of survivin was found after TNF-α induction (162.2 ± 1.3 pg/mL). Treatment with ATO inhibited TNF-α-induced extracellular secretion of survivin to control level (2 μmol/L: 106.8 ± 2.6 pg/mL, 4 μmol/L: 104.1 ± 3.9 pg/mL).

Conclusion: RA FLS secreted a certain amount of survivin. TNF-α intervention significantly elevated protein level of survivin. ATO treatment effectively inhibited survivin expression in RA FLS, as well as TNF-α-induced augmentation of survivin protein.

APLAR-0089

An OPG polymorphism is a genetic risk factor for hip fracture in Japanese patients with rheumatoid arthritis

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Background/Purpose: Patients with rheumatoid arthritis (RA) have a higher prevalence of osteoporosis and hip fracture than do healthy individuals. Bone mineral density is the major predictor of osteoporotic fracture, and several clinical risk factors for hip fracture have been reported thus far. Recently, multiple genetic loci for bone mineral density and osteoporotic fracture were identified in a meta-analysis of genome-wide association studies in people of European descent. The purpose of our study was to identify genetic variants associated with the occurrence of hip fracture in Japanese patients with RA.

Methods: DNA samples of 2068 Japanese patients with RA were obtained from the Institute of Rheumatology Rheumatoid Arthritis cohort study (IORRA) DNA collection. Six single nucleotide polymorphisms (SNPs) were selected and genotyped in the DNA samples: rs6993813, in *OPG*; rs6696981, in *ZBTB40*; rs3130340, in *MHC*; rs3018362, in *RANK*; rs1189505, in *SPTBN1*; and rs2306033, in *LRP4*. The occurrence of hip fractures was determined from the responses to a patient questionnaire and confirmed by review of medical records and radiographs. Finally, 39 hip fractures in 39 patients were identified and included in this study. Prediction analyses for the occurrence of hip fractures were performed by using a multivariate Cox proportional hazards regression model in 1957 Japanese patients with RA.

Results/Conclusions: Prediction analyses revealed that patients who are homozygous for the major allele of SNP rs6993813, in *OPG*, had a higher risk of hip fracture compared with other patients in the recessive model [HR (95% CI): 3.12 (1.48–5.63); P = 0.002 (α = 0.008 after Bonferroni correction)]. No associations were found with the other SNPs. Although these results might be affected by the presence of genetic heterogeneity in bone metabolism among different ethnic populations, they indicate that an *OPG* genetic variant is a risk factor for hip fracture in Japanese patients with RA.

APLAR-0340

Association of LILRA3 gene with bone destruction of early rheumatoid arthritis in Chinese Han population

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Objective: Leukocyte immunoglobulin (Ig)-like receptors (LILRs) are a family of HLA class I-recognizing receptors comprising activating and inhibitory forms. Previous studies have illustrated that a 6.7 Kb deletion in LILRA3 gene was associated with MS and pSS in European. However, the distribution of LILRA3 deletion and the association between this gene and autoimmune diseases in Chinese population were unknown. The aims of this study are to examine the geographical distribution of variations in the LILRA3 region for the Chinese and to investigate the association between LILRA3 gene and RA.

Methods: An LILRA3-deletion polymorphism was genotyped by the PCR-SSP typing method in two independent cohorts of Chinese subjects (North China subjects1623 cases and 1658 controls, South China subjects 574 cases and 549 controls). To seek whether LILRA3 gene influence bone erosive in RA patients, x-rays were scored using Sharp-van der Heijde (SHSs) on hands.

Results: Different from European, LILRA3-deletion are very common in Chinese population, the frequency of deletion allele is up to 70%. Compared with controls, the frequency of LILRA3-non deletion are higher in two cohorts and associated with RA especially with ACPA positive RA. (OR 1.13, 95%CI 1.04–1.30, $P = 7.16 \times 10^{-3}$ and OR 1.40, 95%CI 1.16–1.68, $P = 3.65 \times 10^{-4}$); LILRA3 gene contribute risk to RA in a recessive model (OR 1.92 95%CI 1.41–2.62, $P = 4.01 \times 10^{-5}$ and OR 1.67, 95%CI 1.03–2.71, $P = 3.93 \times 10^{-2}$); Moreover, this association is stronger in male than in female. (OR 1.47, 95%CI 1.10–1.96, $P = 8.96 \times 10^{-3}$ and OR 4.49, 95%CI 2.46–8.19, $P = 1.04 \times 10^{-6}$); Finally, RA risk non-deletion/non-deletion genotype exhibit a significant increase in sharp scores among patients with RA with a disease duration <2 years (P = 0.0098), but not among patients with a longer disease duration.

Conclusions: Our data provide evidence for association between LILRA3 gene and RA in Chinese populations and illustrate that LILRA3 gene influence bone erosive in RA patients with early durations.

APLAR-0023

Serum chemokines in patients with rheumatoid arthritis treated with recombinant human IL-1 receptor antagonist

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Objective: To investigate serum expressions of CCL2 and CCL3 in patients with early or established rheumatoid arthritis (RA) treated with recombinant human IL-1 receptor antagonist (IL-1Ra).

Methods: Seventy-six patients with RA and 36 healthy controls were enrolled in the study. Early RA was defined for patients with disease course of <1 year who had no radiological bone erosions. Patients with active RA refractory to methotrexate were randomized to receive daily subcutaneous injections of IL-1Ra (80 mg) or placebo in a 3:1 ratio for 24 weeks. Clinical outcomes were assessed by using the criteria of the American College of Rheumatology. Serum expressions of CCL2 and CCL3 were determined by means of ELISA before and after IL-1Ra treatment.

Results: (1) Serum expressions of CCL2 in patients with early or established RA were significantly higher than that in healthy controls (P < 0.001), while higher serum CCL3 was shown in early RA patients compared with established RA patients or controls (P < 0.01). Neither serum CCL2 or CCL3 correlated with 28 joints of disease activity scores (DAS28) in 61 patients with early or established RA (P > 0.05). (2) In 54 active RA patients treated with IL-1Ra or placebo, serum CCL2 or CCL3 before and after treatment were both significantly higher than healthy controls (P < 0.05). However, a significant decrease in the mean changes in serum CCL2 or CCL3 from baseline at the last injection was shown in patients who had good response to IL-1Ra treatment, as compared with the non-responders to IL-1Ra (P < 0.01).

Conclusions: CCL2 and CCL3 may play a pivotal role in early stage of RA. However no correlation of serum CCL2 or CCL3 with clinical activity was shown in RA patients, these chemokines might be useful efficacy markers in IL-1Ra treatment.

APLAR-0431

Sonic hedgehog promotes survival and suppresses apoptosis through Smoothened protein in human umbilical vein endothelial cell

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Introduction: Rheumatoid arthritis (RA) is characterized by chronic synovitis and pannus formation. Sonic hedgehog (Shh) acts as a morphogen in embryonic development. The aberrant activation of Shh signaling pathway in post-embryonic development has been implicated in tumor angiogenesis. Endothelial cell apoptosis may play a major regulatory role in neovascularization. The current study aims to investigate the pathogenic role of Shh signaling in RA.

Methods: The expression of Smoothened (Smo) in synovial tissues was examined by immunohistochemistry. Expressions of Shh signaling pathway components in EA.hy926 cells exposed to TNFα with or without Smo antagonist (cyclopamine) were measured by real time PCR and western blot analysis. The effects of cyclopamine and Smo gene knockdown mediated by siRNA on cell apoptosis induced by TNFα and actinomycin D (ActD) were also investigated.

Results: Smo was highly expressed in synovial tissues in RA, especially in endothelial cells than that in control group. TNFα significantly increased the expression of Shh pathway components in EA.hy926 cells, while the expression was decreased in the presence of cyclopamine. EA.hy926 cells treated with different concentrations of cyclopamine (2, 4 and 8 μmol/L) showed a significant decrease in cell viability, with cell survival rates (56.72 ± 5.79)%, (44.40 ± 7.78)% and (31.66 ± 5.45)% compared with that of TNFα/ActD group (64.50 ± 6.45)% ($P < 0.05$) and cell apoptosis rates (12.36 ± 3.28)%, (14.49 ± 2.73)% and (15.74 ± 2.41)% compared with that of TNFα/ActD group (7.05 ± 1.26)% ($P < 0.05$). EA.hy926 cells transfected with Smo-siRNA also showed a lower cell survival rate (24.30 ± 0.45)%, and higher apoptotic rate (48.00 ± 1.96)%, compared with those of the negative control group (36.86 ± 0.62)% and (31.70 ± 0.82)%, respectively ($P < 0.05$).

Conclusion: Shh signaling pathway may play a role in the regulatory of apoptosis in endothelial cells in RA synovium and promote angiogenesis.

APLAR-0363

Umbilical cord mesenchymal stem cells inhibit the generation of T follicular helper cell in rheumatoid arthritis

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Background: The immune suppressive properties of mesenchymal stem cells (MSCs) have garnered increasing attention over the past decades. Rheumatoid arthritis (RA) is characterized by persistent synovitis and systemic inflammation, leading to cartilage and bone destruction. Previous studies showed that MSCs transplantation had effect in an animal model of RA. However, the mechanism remains largely unknown.

Objective: The purpose of this study was to confirm the hypothesis that umbilical cord (UC) MSCs might suppress the generation of T follicular helper (Tfh) cells in RA patients.

Methods: The percentages of CXCR5+PD-1+CD4+ cells were analyzed by flow cytometry in peripheral blood mononuclear cells (PBMC) from RA patients and healthy controls. PBMC from RA patients stimulated with or without phytoagglutinin (PHA) were cultured with UC-MSCs supernatant or UC-MSCs at a ratio of 1 to 1, 1 to 10 or 1 to 100 in a cell-to-cell contact or in a transwell system for 3 days. Na•ve T cells were isolated from PBMC of RA patients and then co-cultured with UC-MSC in the presence of anti-CD3, anti-CD28, anti-IFNg, anti-IL-4, anti-TGFb, IL-6, IL-21 and IL-12 for 4 days. The percentages of CXCR5+PD-1+CD4+ cells were tested by means of flow cytometry.

Results: The results showed that the circulating percentages of CXCR5+PD-1+CD4+ cells were significantly higher than that of healthy controls. UC-MSCs did not inhibit non-activated Tfh cells but dose-dependently inhibited the generation of Tfh cells when stimulated with PHA whether in a cell-to-cell contact or in a transwell system. The differentiation of Tfh cells were also blocked by UC-MSCs significantly. However, UC-MSCs supernatant was not able to suppress the generation of Tfh cells in RA.

Conclusions: These results suggest an inhibitory effect of UC-MSCs on the generation of Tfh cells via soluble factors secreted from UC-MSCs, which may be one the mechanism of UC-MSCs treatment in RA.

FP05 – Osteoarthritis and metabolic bone disease

APLAR-0338

The effect of hydroxychloroquine on symptoms of knee osteoarthritis: a double blind randomized controlled clinical trial

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Background: Osteoarthritis is a degenerative joint disorder of articular cartilage and is the most common type of arthritis in elderly persons. There are few reports regarding the use of hydroxychloroquine in the treatment of osteoarthritis.

Methods: To investigate the effects of hydroxychloroquine on symptoms of mild to moderate knee osteoarthritis (Kellgren & Lawrence grade II and III), we performed a double-blinded, placebo-controlled study in 44 patients. The patients were randomly assigned to two groups: one group used hydroxychloroquine pills (200 mg twice daily) and the other group used placebo pills. Symptoms were assessed by Western Ontario and McMaster Universities (WOMAC) osteoarthritis index at baseline and at the end of weeks 4, 8, 12, 16, 20 and 24.

Results: Approximately 98% of patients were women with an average age of 47 years. There was no significant difference in baseline characteristics between the two groups. In Placebo group maximum improvement occurred at the 4th week and during the remaining time, there was no significant improvement. In Hydroxychloroquine group maximum improvement occurred at the 8th week and maintained over the entire remaining follow-up period. There were significant differences between two groups regarding the degree of reduction in WOMAC total score and WOMAC subscales scores of pain, stiffness, and function at the end of weeks 4, 8, 12, 16, 20 and 24.

Conclusion: Hydroxychloroquine resulted in significant improvement in symptoms of mild to moderate knee osteoarthritis and may be useful in their treatment.

APLAR-0459

Anti-inflammatory activities and the safety of curcuminoid compared to diclofenac sodium for the treatment of osteoarthritis

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Aims: To learn the anti-inflammatory activities and safety of Curcuminoid compared to diclofenac sodium for osteoarthritis.

Method: P*rospective randomized open end blinded evaluation*. Thirty-nine patients got 3 × 30 mg of curcuminoid from *Curcuma domestica* Val. extract and 41 patients got 3 × 25 mg of diclofenac sodium for 28 days. The severity of pain was assessed by visual analogue scale (VAS). Synovial fluid analysis was done. Adverse events during the study were noted.

Results: The reduction of COX-2 and ROI secretion by synovial fluid monocytes in curcuminoid versus diclofenac treatments were 0.70 ± 0.51 versus 0.67 ± 0.45 (P = 0.89) and 1.48 ± 0.44 versus 1.46 ± 0.42 (P = 0.92). The reduction of synovial fluid leucocytes count, MDA level and VAS score in curcuminoid versus diclofenac treatments were 174.27 ± 78.93 versus 164.10 ± 50.91 (P = 0.52), 0.63 ± 0.43 versus 0.44 ± 0.87 (P = 0.29) and 33.76 ± 21.73 versus 29.54 ± 21.57 (P = 0.23). There was no significant differences of adverse events during the study in both groups,

Conclusion: Curcuminoid and diclofenac sodium are comparable in efficacy and safety for the treatment of osteoarthritis.

APLAR-0161

Common dysfunctional variants of ABCG2 cause renal overload hyperuricemia

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ATP-binding cassette transporter, sub-family G, member 2 (ABCG2, also known as BCRP) is a high-capacity urate exporter and its dysfunction has an association with serum uric acid (SUA) levels and gout/hyperuricemia risk. Hyperuricemia causes gout and kidney stones, and accelerates development of chronic kidney disease. Generally, hyperuricemia has been classified into urate "overproduction type," "underexcretion type," and "combined type" based on only renal urate excretion, without considering extra-renal pathway. Here we show that decreased extra-renal urate excretion caused by ABCG2 dysfunction is a novel common mechanism of hyperuricemia. Clinical parameters, including urinary urate excretion (UUE) were examined in 644 Japanese male outpatients with hyperuricemia. The severity of their ABCG2 dysfunction was estimated by genotype combination of two common *ABCG2* variants, non-functional Q126X (rs72552713) and half-functional Q141K (rs2231142). Contrary to the general understanding that ABCG2 dysfunction leads to decreased renal urate excretion, UUE was significantly increased by ABCG2 dysfunction ($P = 3.60 \times 10^{-10}$). Mild, moderate and severe ABCG2 dysfunctions significantly raised the risk of "overproduction" hyperuricemia including overproduction type and combined type, conferring risk ratios of 1.36 (95% confidence interval [CI] 1.09–1.71; $P = 4.55 \times 10^{-3}$), 1.66 (95% CI 1.32–2.10; $P = 8.58 \times 10^{-6}$) and 2.35 (95% CI 1.86–2.97; $P = 3.32 \times 10^{-7}$), respectively. *Abcg2*-knockout mice show that SUA and renal urate excretion were increased, while intestinal urate excretion was decreased, compared to those of wild-type mice. Together with high ABCG2 expression in extra-renal tissues, present results suggest that common dysfunctional variants of *ABCG2* decrease extra-renal urate excretion, especially in intestines, and cause hyperuricemia. This novel mechanism would have been mistaken for urate "overproduction." Thus, "overproduction type" in the current concept of hyperuricemia should be renamed "renal overload type," which is caused by two different mechanisms, "extra-renal urate underexcretion" and genuine "urate overproduction." This new concept will provide a more accurate diagnosis and more effective treatment for hyperuricemia and gout.

APLAR-0257

Clinical analysis of gout outpatient database from a tertiary Medical Center

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Objective: To analyse the clinical characteristics of Chinese gout patients from a tertiary. Medical Center.

Methods: Questionnaire survey and clinical analysis were conducted to collect data regarding demographic features, arthritic calculus, lifestyle, precipitating factors, kidney store and other comorbidities in 358 gout outpatients in this medical center.

Results: Among the 358 patients aged 46 ± 13 years the proportions of males and females were 97.8% and 2.2% respectively. Average course was 99 months and mean serum uric acid (sUA) level was 586 ± 123 μmol/L. Multi-joints affected patients accounted for 78.4%. Tophus was found in 77 (21.5%) paitents, which commonly affected hands, metatarsophalangealjoints and auricle. Logistic regression showed the incidence of tophus was associated with serum uric acid level and disease course. Two hundred and fifty-six cases (71.5%) had comorbidities which was higher in patients with older age ($P < 0.001$). Divided into two groups at age 45, the younger group (<45 years) had a shorter course of disease than that of the older group ($P < 0.01$), but had a higher sUA ($P < 0.05$). Rank-sum test showed no statistical significance in the number of affected joints and incidence of tophus between the two groups ($P > 0.05$). The proportion of kidney injury (GFR<60 mL/min) in the older age group (38.4%) was higher than the younger group (4.3%).

Conclusion: Gout patients who experience longer course of disease and more incidence of arthritic calculus are more diversified and complicated in clinical features. Most patients have multi-joints affected with a high rate of underlying disorder coexisting. Earlier and more aggressive control of reversible risk factors such as obesity, excessive alcohol consumption, high purine diet and use of drugs may be beneficial for ameliorating the quality of life by reducing the possibility of refractory gout, joint mutilation and gout nephropathy. In the

recent years, the incidence of gout has been increasing in younger population, which calls for our special attention.

Key words: gout, hyperuricemia, diet, tophus

APLAR-0192

Monosodium urate crystal enhanced osteoclastogenesis through TRAF6 signaling pathway in RAW264.7 macrophage cells

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Objective: Gout is an inflammatory arthritis characterized by metabolic disorder of monosodium urate (MSU) crystals, resulting in bone destruction in affected joints. MSU crystals induce secretion of interleukin-1β (IL-1β) that can enhance osteoclast differentiation and bone resorption. This study is to investigate action mechanisms by MSU crystals for the regulation of osteoclastogenic activity through tumor necrosis factor receptor-associated factor 6 (TRAF-6) signal pathways in RAW 264.7 macrophage cells.

Methods: Cell viability in RAW 264.7 macrophage cells were determined using a MTT assay after MSU crystal treatment. We examined the effects of MSU crystals on mitogen activated protein kinases (MAPK), their signaling cascade genes, and osteoclast differentiation markers were measured using real-time polymerase chain reaction and western blotting. Effects of TRAF6 knockdown using siRNA for TRAF6 on osteoclastic transcription factors and IL-1β expression were measured by western blotting. We performed tartrate-resistant acid phosphatase (TRAP) staining to identify formation of osteoclasts.

Results: MSU crystals induced expressions of IL-1β and MAPK signaling molecules. MSU, in the presence of RNAKL, also resulted in significantly enhanced expressions of osteoclatogenesis related genes including cathepsin K, MMP9, and carbonic anhydrase II, and TRAP activity. Furthermore, inhibition of TRAF6 decreased expressions of IL-1β and its transcription factors such as c-Jun and NFATc1. These results showed that the expression of tumor necrosis factor receptor-associated factor 6 (TRAF-6) signal pathways are active in monosodium urate (MSU) crystals induced in the presence of RANKL and that these stages can lead to mediated by the expression of inflammatory osteoclastogenesis.

Conclusions: These results suggest that MSU crystal enhances osteoclast differentiation through TRAF6 signaling pathway.

APLAR-0036

Association study of the candidate gene for knee osteoarthritis in Koreans

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Objective: The aim of this study was to examine a single-nucleotide polymorphism (SNP) rs7639618 of double von Willebrand factor (DVWA) gene for the association with osteoarthritis (OA) susceptibility in Korean cohort.

Methods: The study was a part of the Korean cohort study.Two thousand four hundred sixty-two subjects aged 50 years and older who were derived from the cohort and who were assessed for OA at the knee were genotyped. The anteroposterior extended-view weight-bearing radiographs of the knees were obtained. Of the subjects, 725 subjects had radiographic OA. Genomic DNA was extracted from peripheral blood using a QIAamp DNA Blood Mini Kit (Qiagen, Valencia, CA). Genotyping was performed using High Resolution Melt or the Taq-Man allelic discrimination assay and the Rotor-Gene 6000 (Corbett Research, Sydney, Australia). Associations were tested by calculating the odds ratios (ORs) and 95% confidence intervals (95% CIs), using logistic regression analysis with adjustments for age, gender and body mass index (BMI).

Results: The mean age of the OA patients (Females: 554 subjects, 76.4%) was 67.4 (7.9) years.

The intraobserver agreement was high for the identification of osteophytes (kappa: 0.80) and joint space narrowing (kappa: 0.70). There was no significant difference (all P-values > 0.05) in the genotype or allele frequencies between the patients with OA and healthy controls. There was also no significant difference when the cases were adjusted by age, gender, BMI.

Conclusions: The associations of DVWA SNPs with OA were noted in previous studies, were not found in the Korean OA cohort.

FP06 – Basic science in rheumatic disease

APLAR-0178

Tumor necrosis factor-alpha gene promoter region single nucleotide polymorphism change the susceptibility to psoriasis vulgaris and psoriatic arthritis: a meta-analysis

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Background: As a pro-inflammatory cytokine, tumor necrosis factor-alpha (TNFα) plays a crucial role in the pathogenesis of psoriasis disease. In contrast, the reported association of TNFα promoter region SNPs and psoriasis disease susceptibility has remained controversial. Accordingly, we performed a meta-analysis to provide new evidence that SNPs in the TNFα promoter region alter not only the risk of psoriatic arthritis (PsA) or psoriasis vulgaris (PsV) but also of psoriasis disease, which includes both PsA and PsV.

Methods: We searched the PubMed, ScienceDirect, and SpringerLink databases for papers published up to October 2012. The number of the genotypes and/or alleles for the TNFα promoter polymorphisms in the case and control subjects was obtained. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated the risk of PsA and/or PsV with TNFα promoterpolymorphisms using a fixed-effects or random-effects model according to heterogeneity analysis.

Results: A total of 26 papers of 2360 for PsA (2997 normal controls) and 2159 for PsV (2129 normal controls) were included in meta-analysis. The results showed that the variant genotype and allele of TNFα −308A/G was protective in pooled groups of psoriasis disease (OR=0.682, 0.750; 95% CI, 0.596–0.779, 0.653–0.861). However, the variant genotypes and alleles of TNFα −238A/G and −857T/C had an increased risk of psoriasis disease (OR=2.493, 2.228, 1.536, 1.486, 95% CI, 1.777–3.498, 1.628–3.049, 1.336–1.767, 1.309–1.685). Moreover, the meta-analysis revealed a significant association between TNFα −238A/G and −857T/C polymorphism and PsA susceptibility (OR=2.242, 2.052, 1.419, 1.465; 95% CI, 1.710–2.941, 1.614–2.610, 1.214–1.658, 1.277–1.681). In contrast, the variant genotypes and alleles of TNFα −308A/G proved to be protective against PsV (OR=0.574, 0.650, 95% CI, 0.478–0.690, 0.556–0.759), whereas TNFα −238A/G was found to have a risk association (OR=2.636, 2.223, 95% CI, 1.523–4.561, 1.317–3.751).

Conclusions: SNPs in the TNFα promoter region alter the risk of PsA and/or PsV.

APLAR-0051

Effect of the combination of methotrexate and 1,25-dihydroxyvitamin D3 on the balance of Treg and Th17 in collagen-induced arthritis

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Objective: In this study, we aimed to determine the effect of methotrexate (MTX) and 1,25-(OH)2D3, used alone or in combination, in the balance of Tregs and Th17, in a rat model of collagen induced arthritis (CIA).

Methods: Arthritis was induced in 50 female Sprague-Dawley rats. After the clinical onset of CIA, rats were assigned to treatment with MTX (1 mg/kg/week), 1,25-(OH)2D3 (5 mg/kg twice weekly), both treatments at the same regimens, or vehicle. Arthritis score and paw thickness were recorded twice weekly.At termination of the experiment (day 56), bone mineral density (BMD) was analyzed by densitometry, and hind paws were removed for radiographic, histological and immunohistochemical analysis. mRNA expression of transcription factor and proinflammatory mediators was determined by reverse transcriptase*polymerase chain reaction (RT-PCR), and purified T cell proliferation was assessed using [3H]-thymidine incorporated assay, and T-cell phenotypes and activation were assessed by fluorescence-activated cell sorting analysis and T helper (Th) 17/Th1/Th2/Tregs type cytokine production from supernatants from spleen, lymph node and paw cultures was examined by ELISA.

Results: The combination of 1,25-(OH)2D3 with MTX was more effective than MTX alone for reducing the incidence and severity of CIA, and inhibited the production of IL-1β, TNF-α and IL-6, IL-2, IFN-γ, and MMP-3 and up-regulated anti-inflammatory cytokines IL-4, IL-10. Cytokine analysis indicated that the combination of 1,25-(OH)2D3 with MTX not only modulated the T-helper cell balance from Th1 to Th2 effector function but also associated with the upregulation Tregs, downregulation of Th17 differentiation. Correspondingly, the mRNA expression of IL-17A and RORrt was also reduced.

Conclusions: A combination of MTX and 1,25-(OH)2D3 had beneficial effects on CIA by regulating the balance of Tregs and Th17. These two different mechanisms of action provide support for the use of a combination of these two drugs to improve the prevention of structural joint damage in RA.

APLAR-0442

Immunologic characteristics of CD21-23- B lymphocyte

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder of an unknown ethology. Rheumatoid factor and anticyclic-citrillunated peptide (anti-CCP) autoantibodies are well established indicators of disease and disease severity. The contribution of B cells to the pathogenesis of autoimmune disorders has been recognized, especially in the production of autoantibodies and number of B cell directed therapeutic options have become available. Antibody diversity occurs as B cells recombine their immunoglobulin (Ig) heavy and light chain genes during development. $CD21^{-}23^{-}$ B cells have been reported to increase in surrogate light chain (SLC) −/− mice. In a previous study, we have found that the proportion of $CD21^{-}23^{-}$ B cells was significantly higher in the RA patients compared with that in control subjects. Therefore, we investigated the character of $CD21^{-}23^{-}$ B cells and whether producing autoantibodies.

Methods: We stimulated B cells with anti-CD40 antibody and interleukine 21 (IL-21), and evaluated the production of various cytokines including IL-10, IL-2, IL-4, IL-6, TNF-alpha and IFNr, and the production of autoantibodies including antinuclear antibodies (ANAs), anti-ds DNA antibody, rheumatoid factor (RF) and anticyclic-citrillunated peptide (anti-CCP) antibodies.

Results: The number of $CD21^{-}23^{-}$ B cells increased after simulation with anti-CD40 antibody and IL-21, and developed into $CD27^{+}$ $CD38^{+}$ plasma cell. In contrast, $CD21^{+}23^{+}$ B cells developed into $CD27^{+}$ $CD38^{-}$ memory cell eventhough autoantibodies were not produced. The level of IL-6 was significantly higher in $CD21^{-}23^{-}$ B cells compared to $CD21^{+}23^{+}$ B cells and $CD21^{+}23^{-}$ B cells.

Conclusion: Simulated $CD21^{-}23^{-}$ B cell developed into plasma cell and produced IL-6 which plays a crucial role in the pathogenesis of RA.

APLAR-0073

T helper 17 cytokine profile in psoriatic arthritis and their relations with clinical findings

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Objectives: In this study, we evaluated Th17 group cytokine profile which is supposed to play an important role in inflammatory diseases, the Wnt pathway which is essential for bone formation and destruction and parameters of osteoclastogenesis in psoriatic arthritis (PsA) patients.

Methods: We included 48 PsA patients, 20 psoriasis patients and 19 healthy controls into the study. The clinical features of the patients were recorded down from hospital records. A dermatologist evaluated PASI scores. ESR, CRP were determined. ELISA was used to determine Th17 group cytokine (IL-17, IL-22, IL-23), Wnt pathway inhibitor DKK-1, and osteoclastogenesis marker soluble RANKL levels.

Results: Mean ages and sex distributions of PsA, psoriasis and control subjects were similar. Nail involvement (72.9% versus 36.8%), methotrexate usage (74.5% versus 24%), and systemic steroid usage (31.9% versus 5%) of PsA patients were significantly higher than in psoriasis patients (P values, respectively, 0.006, <0.001, 0.014). The general features of PsA, psoriasis, and control group subjects are seen in Table 1. Although the duration of disease in PsA patients was longer than that of psoriasis patients, the difference between the groups was not significant (P = 0.085).

PsA, psoriasis patients and control subjects had similar leucocyte counts, hemoglobin, and CRP levels. PsA group had significantly higher ESR than the healthy control group (P = 0.018). IL-17 levels in the PsA group was significantly lower than the values in psoriasis and control groups (P values, respectively, <0.001 and P = 0.005). The comparison of whole blood count, acute phase parameters, and biochemical data are seen in Table 2. In the PsA group, IL-22 levels were significantly lower than in the healthy control group (P = 0.001). Psoriasis group was not significantly different from PsA and healthy control groups in their IL-22 levels. Both PsA and psoriasis groups had lower IL-23 levels than the control group (P values, respectively, P < 0.001, P = 0.014; Table 2). Soluble RANKL levels in both PsA and psoriasis groups were significantly lower than in healthy controls (both P values<0.001). There was no significant difference between psoriasis and PsA groups in their sRANKL levels (P = 0.344). Serum DKK-1 levels were similar in all three groups (Table 2).

The number of tender joints in PsA patients correlated with IL-17 (r = 0.534, P < 0.001), DKK-1 (r = 0.296, P = 0.041) and PASI scores (r = 0.284, P = 0.049). In addition, DKK-1 levels in PsA correlated with CRP levels (r = 0.332, P = 0.026). In the PsA group, IL-22 levels and sRANKL were correlated (r = 0.668, P < 0.001). In the psoriasis group, the only correlation was between IL-22 and DKK-1 (r = 0.873, P < 0.001).

Of all PsA patients included into the study, 37 had oligoarthritis and 11 had polyarthritis. The evaluated parameters were compared between these two groups. It was observed that

despite higher IL-22 levels in the PsA group with polyarthritis, the difference was not significant (P = 0.08).

Conclusions: As a conclusion, interestingly, we found significantly lower Th17 group cytokines in PsA. Another substantial result was the correlation of IL-17 with PsA activity and number of tender joints, and the correlation of IL-22 with sRANKL which is associated with osteoclastogenesis. In spite of the suppressed levels of Th17 cytokines in PsA, their partially association with disease activation makes one think their contribution to the pathogenesis in some way. However, our current knowledge seems not to be at a level to solve myths of the complex interactions in PsA. The Wnt pathway inhibitor DKK-1, which is attributed a role in the response to anti-TNF therapy in AS, was not significantly altered in PsA. We assume the mechanism of new bone formation in PsA is somewhat different from AS, and that the Wnt pathway is not primarily responsible in PsA.

APLAR-0350

Inhibitory effect of curcumol on Jak2-STAT signal pathway molecules of fibroblast-like synoviocytes in patients with rheumatoid arthritis

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Purpose: Synovial membrane hyperplasia of rheumatoid arthritis (RA) is a critical pathological foundation for inducing articular injury. The janus kinase and Signal Transducer and Activator of Transcription (Jak-STAT) pathway plays a critical role in synovial membrane proliferation induced by platelet-derived growth factor (PDGF). To explore the anti-cell proliferation mechanism of curcumol, a pure monomer extracted from Chinese medical plant zedoary rhizome, the changes of Jak2-STAT1/3 signal pathway related molecules in synoviocytes were observed *in vitro*.

Methods: In the study, the fibroblast-like synoviocytes (FLS) in patients with RA were collected and cultured. The following parameters were measured: cell proliferation (WST-1 assay), cell cycles (fluorescence-activated cell sorting, FACS), the mRNA expression of STAT1, STAT3, SOCS1 and SOCS3 (fluorescent quantitative-polymerase chain reaction, FQ-PCR), STAT1 and STAT3 activities (electrophoretic mobility shift assay, EMSA), the protein expressions of phosphorylated Jak2, STAT1 and STAT3 (Western Blotting).

Results: It was shown that certain concentration curcumol including 25, 50 and 100 mg/mL could inhibit the RA synoviocyte proliferation and DNA synthesis induced by PDGF-BB though it had no effect on the mRNA expression of STAT1, STAT3, SOCS1 and SOCS3 *in vitro*. The transcription factors activities and protien expression of STAT1 and STAT3 were obviously elevated after PDGF-BB stimulation, meanwhile, the different concentraion curcumol could down-regulated the DNA binding activities of STAT1 and STAT3. The curcumol at the concentration of 100 mg/mL could inhibit the phosphorylation of JAK2 and the expression of STAT1 protein while it had no effect on the protein expressions of STAT3, SOCS1 and SOCS3.

Conclusion: The curcumol might suppress the FLS proliferation and DNA synthesis induced by PDGF-BB through attenuating Jak2 phosphorylation, down-regulating STAT1 and STAT3 DNA binding activities, which provide theoretical foundation for clinical RA treatment of curcumol.

Key words: rheumatoid arthritis; curcumol; synoviocytes; JAK2-STAT1/3; mechanism.

APLAR-0380

Interleukin – 18 in rheumatoid arthritis as a marker for endothelial dysfunction

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Aims: Cardiovascular disease (CVD) has emerged to be the major cause of mortality among Rheumatoid Arthritis (RA) patients. Endothelial dysfunction is a hallmark for vascular disease, and it is a sign of a very early atherosclerosis. Several proinflammatory cytokines has been identified to be potential angiogenesis markers in CVD. The aim of this study was to evaluate endothelial dysfunction by assessing with flow mediated vasodilatation (FMD) in RA patients who are in remission and do not have clinical evident of cardiovascular disease (CVD). Serum Interleukin-18 (IL-18) was also measured to determine their correlation with endothelial dysfunction in RA patients.

Methods: A cross-sectional study was carried out with 25 RA patients who were in remission or with low disease activity (DAS28 < 3.2), and 25 matched age and sex healthy control participants who underwent assessments of brachial FMD and serum interleukin-18 level. Both groups had no clinical evident of CVD and CVD risk factors.

Results: Majority of RA patient in this study falls within the 0–5 year's duration category of diagnosis of RA which is 64%. Median duration of RA was 4 years with IQR of 6.0.The median DAS28-CRP score was 2.10 (0.88). There was no difference in the FMD and serum IL-18 level between RA and control patients [FMD: 27.27(23.17) versus 32.4(24.51), $P = 0.58$], [IL-18: 143.42(251.79) versus 125.81(159.42), $P = 0.304$]. BMI ($P = 0.44$) and FBS ($P = 0.017$) were statistically significant between RA and control patients. Significant negative correlation was noted between FMD and age of RA patients ($r = -0.606$, $P = 0.001$); and positive correlation between level of IL-18 with RA duration ($r = 0.505$, $P = 0.01$).

Conclusion: There was no increased prevalence of endothelial dysfunction among well controlled and low CVD risk RA patients. However, there were significant negative correlation between FMD and age and postive correlation between level of IL * 18 and RA duration.

FP07 – Systemic sclerosis and spondyloarthritis

APLAR-0057

Semi-quantitative nailfold capillaroscopy for assessing patients presenting with Raynauds phenomenon: a new diagnostic and prognostic tool?

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Aims: To assess the ability of a semi quantitative nailfold capillaroscopy (NVC) score to differenitiate between benign RaynaudOs phenomenon (RP) and RP presenting as part of a connective tissue disorder.

Methods: Sequential patients attending Dunedin Hospital, New Zealand with RP were consented for the study and 52 underwent NVC between 2009 and 2012 using a DS Medica Videocap portable capillaroscope and image capture programme. NVC was used to assess patients with a pre-existing diagnosis of scleroderma spectrum disorder (SSc) and new patients presenting with RaynaudOs phenomenon (RP). Using criteria adapted from those of Cutolo et al., NVC scores were used to assess five capillary morphological changes, each on a scale from 0 to 3. The total NVC score is out of 15. Appearnences in SSc are also graded as OearlyO, OactiveO or OlateO pattern. NVC was completed in 10–12 min for each patient.

Results: Patients mean age was 54.1 years, 41 female and 11 male. Diagnoses were: 11 diffuse cutaneous systemic sclerosis (DcSSc), 17 limited cutaneous systemic sclerosiş (LcSSc), seven mixed connective tissue disease, three myositis, nine primary RP and four OotherO conditions.

The NVC score accurately differentiated between patients with a connective tissue disease (Mean 8.9 ± SD 3.4) and those with benign RP (2.9 ± 1.8), $P < 0.001$.

The NVC pattern correlated with the NVC score in SSc. Mean scores were: late pattern 10.8, active pattern 8.6, early pattern 4.3, and normal pattern 2.4. NVC scores differed significantly between active and normal pattern ($P < 0.01$), and late pattern compared with normal pattern ($P < 0.001$), but not between the early pattern and normal, likely to be due to low numbers in this group.

Conclusion: The NVC score is a reproducible, feasible and clinically useful assessment in patients presenting with RP and SSc, and could form part of the routine assessment of patients presenting with RP.

APLAR-0119

Association between Rho-kinase 2 gene polymorphisms and systemic sclerosis

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Objective: Systemic sclerosis (SSc, scleroderma) is a devastating multisystem inflammatory disease characterized by widespread vascular injury and progressive fibrosis of the skin and internal organs. Rho-kinase may contribute to endothelial dysfunction, vascular reactivity, remodeling, inflammation, and fibrosis. Thus, it might be hypothesized that Rho-kinase might be involved in SSc. The aim of this study was to investigate a possible association between *Rho-kinase 2 (ROCK2)* gene polymorphisms and SSc patients in a Turkish population.

Material and Methods: A total of 284 patients fulfilling the American College of Rheumatology criteria on SSc and 284 healthy control subjects with similar age and sex were enrolled to this study. Genomic DNA from the participants was analyzed by a BioMark HD dynamic array system (Fluidigm, CA, USA). For calculation of the significance of differences in genotype and allele frequencies, the chi-square test (with YatesÖ correction) or FisherOs exact test was used. The haplotype analysis was performed by using online program, SHEsis (http://analysis.bio-x.cn/myAnalysis.php).

Results: There was an increase in TT genotype frequencies (73.1% in SSc versus 65.4% in control) and decrease in GG genotype frequencies (1.1% in SSc versus 10.6% in control, $P < 0.0001$) of the *ROCK2* gene rs10178332 polymorphism. Additionally, T allele frequency was high (86.0% in SSc versus 77.4%, in control), and G allele frequency was low (14.0% in SSc versus 22.6% in control, $P = 0.0002$) in the patients group. AG genotype and G allele of the rs10929732 polymorphism were not detected in the SSc group. However, AG genotype and G allele were found in low frequencies the control group (AG, 2.7%, G, 1.3%). In the haplotype analysis based on these two polymorphisms, two haplotypes (GA and TA) were found to be markedly associated with SSc. GA haplotype frequency (15.5%) was low, but TA haplotype frequency was high (84.5%) in the SSc group when compared to the controls (GA, 21.7%, TA, 76.9%, $P = 0.0094$). Additionally, no marked association was found between rs2230774, rs35768389, rs726843, rs2290156, rs965665, and rs6755196 polymorphisms and SSc.

Conclusions: To the best of our knowledge, this is the first study to examine the potential involvement of *ROCK2* gene variation in the risk of developing SSc. Our data demonstrated that genetic polymorphisms in *ROCK2* gene may modify individual susceptibility to SSc in the Turkish population.

Acknowledgement: This study has been funded by a project (BAP TF.12.16) from the University of Gaziantep.

APLAR-0280

Utility of BAL fluid cytology and cytokine levels in predicting active ILD in systemic sclerosis patients

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Though the presence of ground-glass opacities on HRCT chest suggest the presence of alveolitis but it is a very soft marker which is also present in infections and other conditions resulting in alveolar exudation. This study was done to assess the utility of BAL fluid cytology and IL-6 and IL-7 levels as a marker of activity of ILD in SSc.

Method: Twenty cases of SSc- ILD and 20 controls with healthy lung (undergoing bronchoscopy for indications other than lung disease) were recruited. Ethical clearance obtained and informed consent taken. Patients having overlap syndromes, smokers, taken immunomodulatory drugs, having lung infection, pulmonary hypertension and pregnant/lactating women were excluded.

Detailed baseline evaluation including

1. Severity of dyspnea
2. PFT
3. HRCT chest to assess ILD severity and activity using semiquantitative methods
4. BAL fluid cytology and IL-6 & IL-7 estimation
5. Echocardiography

Controls were evaluated only once and BAL fluid analysis was done for cytology and cytokine (IL-6 and IL-7) levels.

Follow up evaluation of cases was done at 6–9 months post treatment.

Results: Twenty SSc-ILD patients (18 females; two males) had mean age 36.2 ± 10.2 years and median disease duration 33 months (IQR 24–54). At baseline all patients had neutrophilia and seven patients had eosinophilia in BAL fluid cytology. IL-6 and IL-7 levels at baseline were significantly elevated in cases than controls ($P < 0.0001$). Posttreatment only mean IL-7 levels decreased which correlated with clinical improvement as suggested by increase in 6MWD.

No correlation was found between HRCT activity scores and BAL fluid cytology, IL-6 level, and IL-7 levels.

Conclusion: Higher baseline BAL neutrophil count, IL-6 and IL-7 levels predicted active ILD.

No correlation between BAL fluid IL-7 levels and HRCT scores but positive correlation with clinical parameters suggest their possible role in assessing ILD activity.

APLAR-0159

Thalidomide reduces recurrence of ankylosing spondylitis in patients following discontinuation of etanercept

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Objectives: Previous study showed most ankylosing spondylitis (AS) patients relapsed within 6 months after discontinuation of etanercept. How to maintain low disease activity following discontinuation of etanercept or other anti-TNF agents should be further studied.

Methods: In this study, 111 ankylosing spondylitis patients who met the Assessment of SpondyloArthritis international Society 20% response (ASAS20) criteria after 12-week administration of etanercept were randomized into three groups: Group I, 150 mg thalidomide once/day; Group II, 1 g sulfasalazine, twice/day; Group III, NSAIDs for the maintenance treatment. The patients were regularly followed once a month, and efficacy and safety profiles were evaluated and spinal pain, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the patient global assessment (PGA) were assessed at the same time. The follow-up lasted for 1 year, and AS relapse was defined as the end of a visit.

Results: One hundred patients completed the follow-up study, of whom 30 were in Group I, 33 in Group II, and 37 in Group III. The average follow-up period was 5.1 ± 3.9 months and the longest lasted for 12 months. At the end of the follow-up study, the recurrence rates in Groups I, II, and III were, respectively, 60.0% (18/30), 84.8% (28/33), and 89.2% (33/37). The recurrence rates of Group I were statistically significantly lower than that of Group II and III ($P = 0.0265$; $P = 0.0053$), while there was no significant difference between Group II and Group III. In addition, we found that PGA, C-reactive protein (CRP), and spina linflammation could be regarded as predictive factors for AS recurrence by analysis with the Cox proportional hazard model.

Conclusion: This study points provided new medicine for AS disease control following etanercept discontinuation and provide useful indicators for prediction of AS recurrence.

APLAR-0145

microRNA-146a, TRAF6 gene and IRAK1 gene expressions in patients with ankylosing spondylitis

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Objective: To investigate the expression of microRNA-146a(miR-146a), TNF receptor-associated factor 6(TRAF6) gene and IL-1 receptor-associated kinase 1(IRAK1) genen in PBMCs of patients with ankylosing spondylitis (AS) and as well as their relationship with the disease activity. Explore miR-146a, TRAF6, IRAK1 in pathogenesis of AS.

Methods: Expression of miR-146a, TRAF-6 and IRAK-1 in PBMCs was studied using qRT-PCR in 45 AS patients and 22 healthy controls. The indicators of disease activity were BASDAI, ESR, CRP, Ig.

Results: The relative expression level of miR-146a observed in PBMCs of ASpatients was significantly higher than that in normal acontrol group [1.46 (0.39, 4.79) and 0.81 (0.17, 1.90), $P < 0.05$],? There was significantly difference in the relative expression level of IRAK-1 between ASpatients and the normal acontrol group. IRAK1 was significantly higher in ASpatients than that in normal acontrol group (1.44 ± 0.72, 1.13 ± 0.43, $P < 0.05$); ? TRAF6 expression was obviously lower in AS patients than that in normal acontrol group (1.27 ± 0.61, 1.68 ± 0.81, $P < 0.05$), and that was also significantly lower in untreated group and active group than that in normal acontrol group (1.10 ± 0.72, 1.68 ± 0.81; 1.09 ± 0.53, 1.68 ± 0.81, $P < 0.05$). ?Significantly postitive correlation was observed between the miR-146a level and BASDAI, Duration of morning stiffness ($r = 0.557$, $P = 0.000$; $r = 0.363$, $P = 0.018$).

Conclusion: miR-146a expression was upregulated in patients with AS, and it may be a potentially useful marker of disease activity in AS patients; ?The abnormal expression of IRAK1, TRAF6 may play a role in the pathogenesis of AS.

APLAR-0147

Plasma DNase I with impaired activity fails to degrade Neutrophil extracellular traps in patients with polymyositis and dermatomyositis

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Objective: Neutrophil extracellular traps (NETs) acting as effectors of the innate immune system are closely related to autoimmune disease. DNase1 is responsible for degradation of NETs and if DNase1 with impaired activity fails to degrade NETs, NETs could be one source of circulating cell-free DNA (cfDNA). Previously, it was unknown whether DNase1 activity * and, consequently, NETs degradation and cfDNA concentration * was normal in patients with polymyositis (PM) and dermatomyositis (DM). This study was undertaken to address this question and to explore the possible mechanisms for the impairment of DNase1 activity.

Methods: Sixty one patients with PM/DM and 48 age- and sex-matched healthy controls were included in a retrospective, cross-sectional study. DNase1 activity was measured by the radial enzyme-diffusion method. Degree of NETs degradation was assessed by confocal microscopy. And cfDNA concentration was measured by using the PicoGreen Kit. Possible mechanisms for the impairment of DNase1 activity were further analyzed.

Results: DNase1 activity in PM/DM group was 0.3353 ± 0.1894 UI/mL, significantly lower than that in the healthy control group (0.5441 ± 0.2536 UI/mL, $P < 0.0001$). Specific DNase1 inhibitors were found in 11 PM/DM patients with severely reduced DNase1 activity. The plasma of patients with remarkably reduced DNase1 activity incompletely degraded NETs in vitro. Plasma cfDNA in the PM/DM group was 247.1 ± 61.09 ng/mL, significantly higher than that in the healthy control group (197.1 ± 31.36 ng/mL, $P < 0.0001$).

Conclusion: Impaired DNase1 activity, abnormal NETs degradation and elevated levels of cfDNA may affect each other in a vicious cycle in PM/DM patients, implying that the production of NETs-associated nuclear autoantigens may directly contribute to the initiation or progression of PM/DM.

FP08 – Pediatric rheumatology

APLAR-0393

Sensitivity and specificity of adenosine deaminase in diagnosis of juvenile idiopathic arthritis

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Objective: Juvenile Rheumatoid Arthritis (JIA) is one of the most common rheumatoid diseases in children with unknown etiology and pathogenesis. It also has no diagnostic test and its clinical diagnosis is made through ruling out other types of arthritis. The aim of this study was to evaluate the level of ADA in the serum of JIA patients and to compare it with that of patients with Reactive Arthritis (RA). Evaluation of sensitivity and specificity of serum ADA level in JIA was another objective.

Patients and Methods: The study included 120 children with JIA (mean age = 7.6 ± 4.3 years) and 40 children with RA (mean age = 5.5 ± 3.1 years). The ADA was measured in the active phase of both diseases.

Results: The mean ADA serum level was obtained as 15.8 ± 11.8 U/L in JIA patients and 14.3 ± 7.5 U/L in RA patients. The difference was statistically insignificant (P = 0.4). The mean of serum ADA level was higher in systemic onset JIA patients than pauciarticular and polyarticular JIA patients (25.6 ± 21.3 U/L versus 14.2 ± 6.7 U/L in pauciarthicular and 13.7 ± 7.3 U/L in polyarticular). These differences was significant (P = 0.009). There is a significant difference between Systemic JIA and polyarticular JIA (P = 0.027), but serum ADA level didnÕt have significant difference in poly and pauciarticular JIA (P = 0.9). Another finding of this study was the significant specificity (77.5%) of this laboratory parameter for JIA in comparison with its low sensitivity (36.7%). Positive predictive value was 83% and negative predictive value 29%.

Conclusion: ADA serum levels is as noninvasive biomarker, reliable and easy for diagnosis of JIA and it can be used as alternative parameters representing disease activity.

Key words: Juvenile Idiopathic Arthritis, Reactive Aarthritis, Adenosine Deaminase, Chronic Arthritis, Children.

APLAR-0001

Familial juvenile idiopathic arthritis: clinical features and localization to chromosome 13q

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Objective: To delineate the clinical features of familial juvenile idiopathic arthritis (JIA) in Saudi patients and to localize the underlying gene.

Methods: All included patients fulfilled the ILAR criteria for JIA. We defined familial JIA patients as belonging to a family with more than one sibling diagnosed with JIA. All patients were assessed with respect to: age of onset of JIA, disease activity, disease damage and laboratory variables. DNA was obtained from all patients and a whole genome scan was performed using the Affymetrix Gene Chip Mapping 10 K 2.0 Array for linkage analysis.

Results: Eleven affected siblings (nine females/three males) with JIA belonged to four apparently unrelated families. All patients were from the same geographical area. The mean age at onset was 2.4 years, and mean age at diagnosis was 3.5 years. The mean duration of follow up was 6.4 years. All patients presented with multiple joint involvement at diagnosis. One third of the patients had a poly-articular onset subtype, and the remainder had a systemic onset subtype. All patients had elevated inflammatory markers and rheumatoid factor was positive in 38% of them. Radiological evaluation revealed significant osteopenia, joint space narrowing and erosions. Genome-wide parametric linkage analysis of the four families using an autosomal recessive model of inheritance localized the disease to a ~4 cM region of chromosome 13q with a combined multipoint LOD score of 9.87.

Conclusion: Familial JIA has similar clinical features to the more common sporadic JIA. Localization of familial JIA to chromosome 13q and subsequently cloning of the underlying gene may provide further insight into the immunopathology of JIA. Thereby, opportunities for earlier diagnosis and detection of carrier status may provide the basis for reduced morbidity and disease prevention.

APLAR-0173

25(OH) vitamin D plasma concentration decreased in autoimmune/ inflammatory rheumatic diseases in children

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Objectives: Recent reports suggest a role of hypovitaminosis D in the pathogenesis of inflammatory autoimmune diseases (ARD) in adult. We investigated 25(OH) vitamin D (VITD) plasma level in autoimmune/inflammatory rheumatic disease (ARD) in children.

Methods: Data from 32 ARD children (including juvenile idiopathic arthritis, henoch-schonlein purpura, Juvenile dermatomyositis) and 106 subjects with acute low respiratory infection (ALRI) attending at ChildrenOs Hospital Zhejiang University from Dec 2012 to Feb 2013 were collected. After exclusion of patients with renal failure, primary hyperparathyroidism and hypercalcaemia, plasma VITD, PTH, calcium and phosphate concentrations were compared between these two groups.

Results: Plasma VITD concentrations were <25?nmol/L in 7 (including three ARD and four ALRI) of all 138 patients (severe deficit, 9.4% and 3.8% respectively), ≥25?nmol/L but <75?nmol/L in 86 of all 138 patients (mild deficit, 62.3%), including ARD in 28 of 32 patients (87.5%) and ALRI in 58 of 106 patients (54.7%) and? ≥?75?nmol/L in 207 (normal, 18.4%) ≥75 nmol/L (normal) in 45 of all138 patients (32.3%), including ARD in one and ALRI in 44 patients (normal, 3.1% and 41.5% respectively). Despite no difference in PTH, calcium and phosphate concentrations, plasma VITD was lower in ARD (38.95 ± 14.99 nmol/L) than in ALRI (66.85 ± 25.46 nmol/L, P?<?0.05).

Conclusions: Lower VITD plasma concentration existed in ALRI, especially in ARD, suggesting an impaired vitamin D metabolism may be involved in the mechanism of ARD in children. Vitamin D supplementation to ARD patients may be helpful.

APLAR-0099

Nine cases of juvenile idiopathic arthritis (JIA) treated with adalimumab (ADA)

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Introduction: We report efficacy of ADA in 9 JIA cases who had not responded to other therapy.

Methods: We investigated sex, age of onset, disease duration, subtype, autoantibodies and medication before ADA initiation on our patients. All patients were followed up to 24 weeks. We examined serum matrix metalloproteinase-3 (MMP-3) and DAS28 before and after dosage, and ACR pedi 30 and ACR pedi 50 at 8, 12, 16 and 24 week.

Results: Three boys (one carryover case included) and six girls are enrolled. Age of onset: 2.6 to 11.8 years old. Disease duration: 4 month to 29 years (mean 8.6 ± 1.2). JIA subtype: six polyarticular type, two oligoarticular type and one enthesis related type. Autoantibodies: 7 (77.8%) are rheumatoid factor positive, 3(33.3 %)are antinuclear antibody positive(>160 ×) and 6(66.7 %)are anti cyclic citrullinated peptide antibody positive. Six cases were given 20 mg and three cases were given 40 mg of ADA once 2 weeks respectively. All cases were treated with methotrexate(6.8 ± 2.2 mg/m^2/week)before ADA adoption and they were continued. Other medication before ADA initiation were prednisolone in eight cases, (4.5 ± 2.6 mg/day),naproxen in five cases, and ibuprofen, etodolac, tacrolimus, salazosulfapyridine in one case for each. MMP-3 mean value changed from 102 ± 59.9 ng/mL to 85.5 ± 99.7 ng/mL.DAS28-ESR changes from 4.41 ± 0.95 to 2.27 ± 0.87, DAS28-CRP changed from 3.48 ± 0.80 to 1.75 ± 0.74. ACRpedi30 was 50% at 8 week, 75% at 12 week, 66.7 % at 16 week and 100% at 24 week. ACRpedi50 was 50% at 8 week, 62.5% at 12 week, 33.3% at 16 week and 50% at 24 week. Active uveitis in one case improved prominently.

Conclusion: ADA is valid in JIA.

APLAR-0321

Prevalence of Group A b-hemolytic streptococcus and clinical-functional funcational peculiarities assessment of rheumatic fever in the Kyrgyz republic

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Objective: To evaluate high prevalence of A Group b-hemolytic streptococci (GAS) and clinical-functional manifestations of rheumatic fever (RF) in the Kyrgyz Republic.

Material and Methods: Screening of 389 inhabitants has been carried out by rapid antigen detection test, including 259 children (80 of which with RF) from 3 to 17 years of age (average age 12.9 ± 4.0) in the I Group, and 130 adults (15 with RF) at the ages of 18–45 years (31.0 ± 10.0) in the II Group. Total of 200 patients with acute RF (27 patients) and with reoccurring (173 patients) RF have been studied in the age group of 15–45 (average age 25.6 ± 8 years). The following studied were conducted: clinic diagnosis, rapid antigen detection test of GAS, smear from throats, ECG, Doppler EchoCG, Holter ECG-monitoring.

Results: Results have indicated that the use of highly technological express-methods of antigen detection tests of GAS and bacterial seeding smears from throats demonstrated that there is a high prevalence of GAS among patients with tonsillopharyngitis, RFand among relatively healthy people. The specificity of the diagnostic express-method reached 85%, sensitivity* 67.5%, which contributed to rapid diagnostic (within 5–10 min) of the etiology of tonsillopharyngitis and development of treatment methodology. In determining the GAS sensitivity to antibiotics, a high resistance to unprotected Penicillin (87.5%), Cephalosporins (61.3%), and macrolides (73.8%) was detected in patients with RF and tonsillopharyngitis. At that, RF clinical manifestations in the Kyrgyz Republic were characterized by latent beginning, predominance of minimal and moderate activity, the first rheumatic fever episode was frequently followed by formation of post inflammatory mitral valve prolapse (MVP), rheumatic heart disease of predominantly aortal valves in males, and high probability of combined heart diseases in females. It was demonstrated that tonsillopharyngitis or other lasting chronic epipharyngeal infections and syndrome of dysplasia of heart connective tissues mostly affected the ARF prevalence.

APLAR-0477

Review of maternal and fetal outcomes in pregnancy among Filipinos with SLE

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Objective: To describe the outcomes of pregnancy among Filipino patients with systemic lupus erythematosus (SLE).

Design: Descriptive retrospective study.

Results: A total of 86 SLE patients with 184 recorded pregnancies occurring during the course of SLE were included in the study. The mean age at pregnancy was 30.02 ± 5.02 years (range 19–42). Among the pregnancy outcomes (n = 184), normal term deliveries were recorded in 104 (56.5%), abnormal pregnancy outcomes recorded as miscarriages in 54 (29.3%), preterm deliveries in 17 (9.2%), intra-uterine fetal death (IUFD) in 4 (2.2%) including congenital heart block reported in 3 and 1 due to cord coil, and blighted ovum in 5 (2.7%). After birth, glucose-6-phosphate dehydrogenase (G6PD) deficiency, meningocoele and thyroid abnormality were reported in 1 infant each. Among those with miscarriages, associated conditions included lupus nephritis (LN) in 9, hypertension (HPN) in 8, pre-eclampsia in 7, tuberculosis (TB) in 3, varicella zoster infection in 2, gestational diabetes mellitus (GDM) in 1, hyperthyroidism in 1 and urinary tract infection (UTI) in 1. Patients with pre-term deliveries had concomitant pre-eclampsia in 8, HPN in 2, LN in 2 and TB in 2. Five patients with blighted ovum had LN in 4 and recent chickenpox in 1. The 4 patients with IUFD outcomes had HPN and LN in 2 patients each. Anemia, leucopenia, thrombocytopenia, active urine sediments and presence of anti-cardiolipin antibodies were associated with poor pregnancy outcomes. Post-pregnancy complications included 3 (1.6%) patients who developed dilated cardiomyopathy, pericarditis, pericardial effusion and 1 (0.55%) post-partum depression. There were no recorded maternal deaths.

Conclusion: Successful term pregnancies were observed in the majority of SLE patients although miscarriages, pre-term deliveries and infant deaths remain a concern.

FP09 – Alternative medicine, epidemiology, osteoporosis

APLAR-0333

Innovative therapies of endothelial dysfunction in rats with experimentally induced arthritis

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Chronic pain, a devastating, widespread problem, is a syndrome that cuts across traditionally defined disciplinary boundaries within the health sciences. The present study explored the effects of a Quercetin on pain, inflammation and endothelial dysfunction in a rat model of adjuvant-induced arthritis (AIA). Tibio-tarsian arthritis was induced in white Wistar rats by subcutaneous injections with Freund adjuvant in the left hind paw.

Four groups were compared: a non-arthritis control group and three AIA groups treated orally with saline solution, Indomethacin and Quercetin.

After 21 days the change in the paw volume was measured and nociception was evaluated. Four weeks later we measured the plasmatic levels of MDA and carbonylated proteins (CP) as markers of oxidative stress, and the activities of the antioxidant enzymes catalase, and SOD, as well as the serum NO.

A large increase was observed in the hind paw volume of untreated arthritic rats compared with non-arthritic rats. Our results showed that Indomethacin (2 mg/kg/day) and Quercetin (20 mg/kg/day) treatments significantly decreased the edema and mechanical hyperalgia both in the AIA rats. Quercetin effectively lowered the pain score of AIA rats from day 21 after the induction of arthritis, its efficiency being similar to that of Indomethacin. The study confirms the analgesic effect and the anti-inflammatory efficiency of Quercetin.

Freund adjuvant administration induced significant increases in plasma MDA and CP concentration, and decreased SOD and catalase activities. Quercetin treatment significantly decreased the elevated MDA and CP ($P < 0.05$), while increasing the antioxidant enzyme activities ($P < 0.05$). The activation of NOOs increased degradation was also observed in the treated AIA rats. Al these effects were abolished by Quercetin. From the present study, it can be concluded that Quercetin administration to AIA rats restores vascular function.

APLAR-0014

High mortality in patients with older onset systemic lupus erythematosus

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Objective: To explore whether clinical features and prognosis were affected by the age of onset in patients with systemic lupus erythematosus (SLE) in a large, multicenter cohort.

Methods: Medical records of 1 956 SLE inpatients from 15 hospitals, followed up in January 2010 for investigating the influential factors related to poor prognosis (1), were reviewed. Those with known onset age were enrolled and classified into three groups according to their age of onset: childhood onset (≤18 years), younger onset (>18 and ≤45 years) and older onset (>45 years). Chi-square test was applied to analyze potentially associated factors among three groups.

Results: One thousand eight hundred and ninety-eight SLE patients were studied, including 259 childhood, 1444 younger and 195 older onset patients. Whenever disease occurred, most patients were diagnosed within 2 years. Childhood onset patients were more likely to have mucocutaneous manifestations ($P < 0.0001$), while less frequent to have musculoskeletal symptoms ($P = 0.01$) and leucopenia ($P < 0.05$). Neuropsychiatric, cardiopulmonary, renal and gastrointestinal involvements were similar among three groups, while older onset patients tended to have a higher disease activity, measured by SLEDAI, on admission and a lower activity at discharge as compared to the others. There was no difference of autoantibody profiles among three groups except that fewer older onset patients had positive anti-Sm antibodies ($P = 0.01$). Steroids and immunosuppressive treatments were identical for the three groups. However, anti-malaria drugs were most likely given to childhood onset patients ($P < 0.0001$). Mortality was elevated in older onset SLE group, in which half of them died of infections that was much higher than those in the other two groups ($P < 0.05$).

Conclusion: Infection contributes to the high mortality in patients with older onset SLE. A less intensive treatment should be considered when dealing with these patients.

Reference: 1. Feng X, Zou Y, Pan W, Wang X, Wu M, Zhang M et al. Prognostic indicators of hospitalized patients with systemic lupus erythematosus: a large retrospective multicenter study in China. J Rheumatol 2011; 38(7):1289–95.

APLAR-0127

Trabecular bone score in women with rheumatoid arthritis

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The aim of this study is evaluating trabecular bone score (TBS) in womenwith rheumatoid arthritis depending on their age.

Participants were 185 women with RA who fulfilled the American Collegeof Rheumatology criteria. Clinicalassessment included demographic data: age, height, weight, and BMI (kg/m^2). Disease duration was defined as the time elapsed between the onset of firstdisease-related symptoms and enrollment. We have included 76 women aged 42–76 years (mean age * 60.2 ± 1.1 years; mean height * 161.5 ± 0.7 cm; mean weight * 73.0 ± 1.8 kg), who weredivided into the groups depending on their age: 40–49 years (n = 11), 50–59 years (n = 24), 60–69 years (n = 24), 70–79 years (n = 17). BMD of wholebody, PA lumbar spine and proximal femur were measured by DXA method (Prodigy, GEHC Lunar, Madison, WI, USA) and PA spine TBS were assessed by TBS iNsight® software package installed on our DXA machine (Med-Imaps, Pessac, France).

We have observed a non-significant decrease of TBS in ageing women with rheumatoidarthritis (40–49 years * 1.270 ± 0.06, 50–59 years * 1.262 ± 0.03; 60–69 years * 1.214 ± 0.03; 70–79 years * 1.139 ± 0.03; $F = 2.09$; $P = 0.11$). TBS valuesof women with rheumatoid arthritis were significantly lower than those ofhealthy women of the corresponding age groups. Significant difference in TBS as a function of BMD WHO criteria werealso observed (group withnormal BMD * 1.236 ± 0.04; group with osteopenia * 1.253 ± 0.03; group withosteoporosis * 1.098 ± 0.05 ($F = 4.43$; $P = 0.02$).

In conclusion, accordingto the TBS values, the bone status of women with rheumatoid arthritis was muchlower than that of healthy women. TBS of women with rheumatoid arthritis decreasedwith ageing but in our sample without reaching the significance while whenusing BMD WHO categories TBS values were significantly different.

APLAR-0170

Quantitave impact of low bone mass on hip fracture incidence in Asia Pacific and Middle East

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Background: As part of the Global Burden of Diseases Study 2010 the Musculoskeletal Expert Group estimated the influence of low bone mineral density (BMD) on the hip fracture incidence by world region [1]. Estimates for 2005 in Asia Pacific regions and North Africa-Middle East are discussed here.

Methods: A systematic review was done through MEDLINE, EMBASE, CINAHL, CAB abstract, WHOLIS, and SIGLE for population based studies with BMD at femoral neck (FNBMD) mea-

sured with Dual-X-Ray-Absorptiometry. Age- and sex-specific values (mean and SD) in g/cm^2 were extracted, standardized and pooled using a Bayesian meta-regression tool for population aged 50 years and over. Comparative Risk Assessment Methodology was used to estimate the proportion of fractures attributable to sub-optimal FNBMD evaluated as a continuous variable, using the Potential Impact Fraction (PIF). Relative Risks were derived from a meta-analysis [2] of population-based studies and converted into absolute RR/0.1 g/cm^2 values for each sex-age group. Three different theoretical maximum risk distributions of FNBMD obtained from non-Hispanic whites in NHANES III were used: the young female reference (YFR), the sex-specific young reference (SSYR), and the sex- and age-specific 90th percentile (SASR).

Results: High inter-region variability was observed. PIFs were lower in men when YFR was used. PIFs for population 65–69 years old are shown in the table.

Conclusions: BMD has a potential influence on hip fracture incidence in the studied regions.

References: 1. Lim S et al. Lancet 2012.
2 Johnell O et al. J Bone Miner Res 2005.

Asia high income	Asia Southeast	Australasia	Asia East	North Africa-Middle East
0.620 *0.816*	0.652 *0.832*	0.402 *0.735*	0.609 *0.820*	0.599 *0.812*
0.764 *0.816*	0.785 *0.832*	0.622 *0.735*	0.758 *0.820*	0.751 *0.812*
0.773 *0.739*	0.794 *0.761*	0.636 *0.625*	0.768 *0.744*	0.761 *0.734*

PIF values in 0–1 scale. Females in *italics*. Use of YFR, SSYR, and SASR in vertical order.

APLAR-0182

Nutraceuticals: hope, hype and reality

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The commonest prevalent the world over, Osteoarthritis (OA) has humbled we rheumatologists making us apologetic, as no worthwhile medical treatment is available. In free arthritis camps that this author conducted, OA cases were highest at 36%. OA afflicts ten percent of world population over age 65.

With no new drug on the anvil unlike for inflammatory arthritis, nutraceuticals are not unpopular with patients, even if prescribed grudgingly by doctors. NSAIDs used over decades are poor pain relievers with no effect on disease progression, prone to serious adverse effects gastro-intestinal (GI) and cardiovascular complications, at times dubbed "plain killers" rather than "pain killers". Glucosamine (GlcN) is a natural physiological molecule resident in the cartilage (building block) reportedly depleted in OA cartilage studies. Like vitamins, substitution supplement with GlcN seems logical.

Open, and randomised clinical trials (RCTs) are carefully reviewed. Cochrane reported studies have used several indices. Such outcome measures and their applicability, utility with pros and cons are debated. Sharp scores, WOMAC, Lequesne Index the basis of statistical tools in assessing prognosis of OA. Their equivocal results are analysed.

On balance, meta-analysis shows symptomatic relief and delayed progression of knee OA. Confounding factors in these trials are taken into account. EULAR recommendations for management of knee OA state glucosamine and chondroitin as "systematic slow acting drugs for OA which may improve the structure of cartilage". Further evidence suggests that salts of GlcN may have little bearing with variable brand bioavailability. Combination of glucosamine and chondroitin is slightly more effective in short term studies, long term studies awaited.

Let's face it, over a decade nutraceuticals such as glucosamine have come to stay till convincing treatments are invented.

POSTER SESSION I ABSTRACTS
Clinical rheumathology: T01 – rheumatoid arthritis – prognosis, predictors and outcome

APLAR-0081

Predictors of long-term mortality in lupus and non-lupus patients undergoing maintenance dialysis: a comparative study

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Background: To compare the prognosis of patients with systemic lupus erythematosus (SLE) receiving dialysis and non-SLE patients receiving dialysis and determine the factors that affect survival after dialysis.

Method: We used the National Health Insurance Research Database and collected data on patients who started maintenance dialysis from 2001 to 2003. The patients were followed from initiation of dialysis until death, discontinuing dialysis, or the end of 2008. We performed a Kaplan-Meier analysis of the cohort and used multivariate Cox regression analysis to identify significant predictors of survival.

Results: Of the 22 394 dialysis patients studied, 303 (1.35%) had SLE. Hypertension and diabetes were the two most common comorbidities associated with dialysis for lupus and non-lupus patients. After adjusting for age, gender, dialysis modality, and comorbidities, we did not find a significant survival difference between the two patient groups after 8 years of follow-up. Multivariate analysis showed that older age (≥45), male gender, initial choice of hemodialysis, diabetes mellitus, heart failure, coronary artery disease, cerebrovascular disease, and malignancy were associated with increased mortality in the non-SLE patient group ($P < 0.05$). For SLE patients, older age (≥65), male gender, and the presence of diabetes were independent predictors of mortality ($P < 0.05$).

Conclusions: The long-term survival outcome was similar between the SLE and non-SLE patients undergoing dialysis. The factors affecting patient mortality were not all identical in these two groups.

APLAR-0082

BMP gene polymorphism associated with ankylosing spondylitis in Taiwanese

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Background: Previous study demonstrated serum BMP levels were significantly increased in Ankylosing Spondylitis (AS) patients. BMP was also overexpressed in enthesitis of AS patients. This study is to deterrmine whether BMP gene polymorphism is associated with AS, especially in patients with spinal fusion.

Methods: We enrolled 90 patients with spinal fusion (Group 1), 49 AS patients without spinal fusion (Group 2) and 41 healthy subjects as control (Group 3). Nine SNPs of BMP were used to measure gene polymorphism (BMP2, 4, 7).

Results: For BMP2 and 7, there was no significant difference to detect gene polymorphism between different groups. Only BMP4 rs 17863 showed a significant difference (Group 1 versus 2 versus 3, $P = 0.026$), between 1 versus 2 ($P = 0.034$) and between 2 versus 3 ($P = 0.040$).

Conclusion: The BMP gene polymorphism in AS has not been reported. In spite of the limited number of patients, the preliminary results suggest BMP gene polymorphism may play a role in AS, particularly in AS with spinal fusion or bamboo spine.

APLAR-0093

Evaluation of radiograph and function of rheumatoid arthritis patients in remission of CDAI

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Background and Objective: Management of RA has evolved radically because of the development of aggressive therapies for early stages of the disease and advent of biologics. The treatment goal of rheumatoid arthritis (RA) has been clinical remission. Some patients in remission progress radiographically and become worth functionally. The aim of the present study was to evaluate radiograph and function of RA patients in remission of CDAI.

Method: In the present study, 56 RA patients (12 males and 44 females; mean age 52.1 ± 11.1 years) were included in which monthly examination showed in remission of CDAI more than six times during the past year. We classified patients by region of swollen and/or tender joint or not. We evaluated the radiographic change by scoring erosion and joint space, and the functional disability difference by using HAQDI and DASH score between groups.

Result: In radiographic scores, only no swollen/tender joint group improved and hand joint group was deteriorated significantly faster compared with other groups. Some patients in hand joint and elbow joint groups were not in functional remission by HAQDI. DASH score of hand joint and elbow joint groups were higher significantly compared with other groups.

Conclusion: We expect we might improve RA patients in remission who has swollen/tender joint of wrist or elbow by additional treatment.

APLAR-0163

Prevalence and prognostic factors of clinical remission in rheumatoid arthritis

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Objective: To identify the prevalence and prognostic factors of clinical remission in patients with rheumatoid arthritis (RA) in Phramongkutklao hospital.

Methods: We conducted a retrospective review of RA patients who regularly followed up at rheumatology clinic during January to December 2012. The baseline characteristics, clinical data, serology including rheumatoid factors (RF) and anti-cyclic citrullinated protein antibody (ACPA) levels, previous and current treatments, 28-joint counts, patient global assessments and erythrocyte sedimentation rates (ESR) were collected. Clinical remission was defined as DAS28 scores < 2.6 in two last consecutive visits, at least 3 months apart.

Results: Three hundred and thirty-five patients were enrolled, 89.9% were female. Mean (SD) age was 61 (11.4) years, mean disease duration was 145.9 (93.7) months. RF and ACPA were positive in 69.9% and 67.8%, respectively. Eighty-nine percent of patients were treated with synthetic DMARDs, of which 29% received monotherapy. The combination of biologic and synthetic DMARDs was used in 10.4% of the patients. Clinical remission was observed in 49 patients (14.6%). Early diagnosis and treatment within 12 months of onset (OR 1.95, 95%CI 1.02–3.74, $P = 0.04$), rheumatoid factor negativity (OR 2.10, 95%CI 1.04–4.21, $P = 0.04$) and good EULAR response at 1st year of treatment (OR 2.75, 95%CI 1.08–6.99, $P = 0.03$) were associated with clinical remission in univariate analysis. In multivariate regression analysis, only good EULAR response at 1st year was significantly correlated with clinical remission in this study (OR 3.1, 95%CI 1.15–8.36, $P = 0.03$).

Conclusion: Although remission is currently a treatment goal in patients with RA, only one-seventh of patients achieved clinical remission in our clinical practice. The good EULAR response at 1st year was an independent predictive factor of clinical remission. Higher rate of remission could be achievable by implementation of the early and aggressive treatment strategies in daily clinical practice.

APLAR-0179

Decoy receptor 3 increases the expression of IL-12B in rheumatoid synovial fibroblasts

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Background: Decoy receptor 3 (DcR3) is a secreted decoy tumor necrosis factor receptor and competitively binds and inhibits the TNF family including FasL, LIGHT, and TL1A. We previously reported that DcR3 overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNF-α protects the cells from Fas-induced apoptosis. Meanwhile, we recently reported that DcR3 induces VLA-4 expression in THP-1 macrophages to inhibit cycloheximide-induced apoptosis, and that DcR3 binds to TL1A expressed on RA-FLS resulting in the negative regulation of cell proliferation induced by inflammatory cytokines. Therefore, DcR3 may regulate gene expressions in RA-FLS by binding to TL1A on RA-FLS as a ligand.

Objectives: In the present study, we studied the genes expression profiles in RA-FLS regulated by DcR3 to identify key molecules in DcR3-TL1A signaling.

Methods: Four cell lines of RA-FLS were incubated with recombinant human DcR3-Fc or control IgG1 for 12 hours and gene expressions in RA-RLS were detected by microarray assay. The relative expression levels of mRNA were quantified by real-time PCR. The expression of protein was investigated by western blotting.

Results: Microarray data analysis revealed that DcR3 up-regulates 45 genes and down-regulates 55 genes expression in RA-FLS among the most significantly regulated 100 genes by DcR3. The profile indicated that shared p40 subunit (IL-12B) of IL-12 and IL-23 was up-regulated by DcR3-Fc. Real-time PCR revealed that IL-12B mRNA in RA-FLS was significantly increased in a dose dependent manner when stimulated with DcR3-Fc. Western blotting confirmed that IL-12B p40 protein in RA-FLS was increased when stimulated with DcR3-Fc.

Conclusions: IL-12 consisting of IL-12A (p35) and IL-12B induces Th1 immune responses. Meanwhile, IL-23 consisting of IL-23A (p19) and IL-12B is involved in the inflammatory pathway via IL-17. DcR3 may up-regulate the expression of IL-12B in RA-FLS by binding to membrane-bound TL1A as a ligand to affect the pathogenesis of RA.

APLAR-0190

Decoy receptor 3 regulates the expression of tryptophan hydroxylase TPH1 in rheumatoid synovial fibroblasts

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Background: Tryptophan hydroxylase (TPH) is the rate-limiting enzyme involved in the synthesis of serotonin. We previously reported that decoy receptor 3 (DcR3), a member of TNF receptor superfamily, overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated with TNFα inhibits Fas-induced apoptosis. We recently reported that DcR3 induced VLA-4 expression in THP-1 macrophages to inhibit cycloheximide-induced apoptosis, and that DcR3 inhibited cell proliferation induced by TNFα or IL-1β via TL1A expressed on RA-FLS, and that the concentration of DcR3 in RA was significantly higher than in osteoarthritis (OA). Further, by using comprehensive genetic analysis using microarrays, we newly identified TPH1 as one of the genes of which expression in RA-FLS was suppressed by DcR3.

Objectives: In this study, we investigated the expression of TPH1 in RA and OA-FLS stimulated with DcR3 and inflammatory cytokines.

Methods: Primary cultured RA or OA-FLS were incubated with 1.0 μg/mL recombinant human DcR3-Fc protein or 1.0 μg/mL control IgG1 for 12 hours, or 1.0 ng/mL recombinant human TNFα or 1.0 ng/mL IL-1β for 24 hours, then the relative expression levels of TPH1 mRNA were quantified by real-time PCR. Serotonin expressed in RA-FLS was detected by immunohistochemistry.

Results: TPH1 mRNA was expressed in both RA and OA-FLS. TPH1 mRNA expression was decreased significantly by DcR3 in RA-FLS, but not in OA-FLS. Meanwhile, TPH1 mRNA expression was significantly decreased by TNFα or IL-1β both in RA and OA-FLS. Immunohistochemistry confirmed that serotonin was present in RA-FLS.

Conclusions: In this study, we first revealed that TPH1 in RA-FLS was suppressed by DcR3 in a disease-specific fashion. Therefore, TPH1 in RA-FLS regulated by DcR3 may affect serotonin expression to be involved in the pathogenesis of RA, such as modulating inflammatory pain and bone remodeling. Both DcR3 and TPH1 could be a possible therapeutic target of RA.

APLAR-0214

Relationship between clinical response and radiographic outcomes in patients with moderate rheumatoid arthritis

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Introduction: Early, intensive rheumatoid arthritis (RA) treatment decreases disease activity and prevents joint damage.[1] Our objective is to examine the relationships between disease activity and inhibition of radiographic progression after moderate RA etanercept (ETN) + methotrexate (MTX) therapy, in the PRESERVE trial.

Methods: Patients (DAS28 3.2*5.1 after stable MTX for ≥3 months), received open-label ETN 50 mg + MTX (QW) for 36 weeks. Relationships between final mTSS [baseline mTSS + mTSS progression rate (units/year)] and disease activity (CDAI and DAS28) were analyzed.

Results: Of 704 patients, 28% achieved CDAI remission and 87% low disease activity (LDA); 69% achieved DAS28 remission (88% LDA). Radiographic progression (units/year) was lower in CDAI and DAS28 remitters than non-remitters ($P < 0.05$; Table); Proportions of patients achieving radiographic non-progression (mTSS $\Delta \leq 0.5$) were similar (~80*87%) across CDAI and DAS28 response categories. Baseline mTSS was significantly associated with week 36 mTSS, and both were significantly associated with CDAI response categories ($P < 0.05$; Table).

Conclusion: ETN+MTX treatment was associated with CDAI and DAS28 remission. Improved clinical response by week 36 was associated with better radiographic response. Less radiographic progression was observed in the remission group versus LDA or no response (NR) groups. Achievement of clinical goals has implications for structural benefits in moderate RA.

Reference: 1. Combe B. *Best Pract Res Clin Rheumatol.* 2007;21:27*42.

Descriptive Statistics for mTSS by Week 36 Disease Activity Category

Week 36	ETN + MTXmTSS (units), mean (median)			
	n	Baseline	Final†	Progression Rate, Units/Year‡
CDAI Remission (≤2.8)	195	36.5 (14.5)*	36.6 (14.5)*	0.1 (*0.1, 0.4)*
CDAI LDA (>2.8 ≤ 10)	415	39.3 (17.5)	39.7 (19.5)	0.4 (0.2, 0.6)
CDAI NR (>10)	94	44.4 (22.3)	45.0 (22.3)	0.6 (*0.3, 1.4)
DAS28 Remission (≤2.6)	487	37.9 (16.5)	38.2 (18.0)	0.3 (0.2, 0.5)*
DAS28 LDA (>2.6 ≤ 3.2)	135	41.9 (19.4)	42.1 (19.5)	0.2 (*0.1, 0.6)
DAS28 NR (>3.2)	82	42.6 (16.0)	43.3 (17.0)	0.7 (*0.2, 1.6)

*$P < 0.05$, Kruskal-Wallis test; †Baseline+progression rate; ‡mean (95% CI). DAS28 = 28-joint Disease Activity Score; CDAI=Clinical Disease Activity Index; LDA=low disease activity; NR=no response.

APLAR-0246

Positive and negative magnetic separation of peripheral blood lymphocytes in Rheumatoid patients as a potential method for atypical T-cells detection

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Objectives: Previously it was shown, that peripheral blood lymphocytes (PBL) in RA patients had increased adhesion to human thymic epithelial cells forming rosette-like structures. Significant imbalance of CD3+4+ and CD3+8+ T-cells in RA also takes place So the presence of T-cells with atypical phenotype is supposed for systemic autoimmunity. The aim of work is test different variants of T-cells magnetic separation methods for T-cells with atypical phenotype detection.

Methods: The research was performed in isolated mononuclear cells suspension and after magnetic separation of T-cells in 12 Rheumatoid patients and seven healthy donors. We used the "negative separation" provided by magnetic particles with anti-CD3 antibodies, "positive separation" with magnetic particles, loaded by anti-CD4. and Onegative separationÓ with ÒuntouchedÓ human CD4+ T-cells magnetic particles. T-cells phenothype was investigated cytometrically using double monoclonal antibodies scanning.

Results: The more prospective method of magnetic separation for T-cells with atypical phenotype detection was the use of ÒuntouchedÓ human CD4+ T-cells magnetic particles which allowed to investigate ÒuntouchedÓ CD4+T-cells population. So in three patients with low level of CD3+4+T-cells we found significant percentage of CD3+4-8- ÒdoubleÓ negativeÓ thymocyte-like T-cells (from 5% to 12%). After the separation the level of these cells rose till 20–39%.

Conclusion: T-cells phenotype abnormalitiesare common for systemic autoimmunity. In human SLE activated CD3 4–8- cells can augment the production of pathogenic anti-DNA-

antibodies by 30-fold. So the presence of such T-cells in RA peripheral blood needs to pay attention on as a potential target for biological therapy.

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APLAR-0251

Recent thymic emigrants investigation as an approach of in vivothymus gland function study in rheumatoid arthritis

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Objectives: T-regs and Th17 cells are the new generations of CD4+T-cells which play crucial role in autoimmunity. Both of subsets can influence each other and probably have common precursor: so called Recent thymic emigrants (RTE). Thymic output of T lymphocytes can also be estimated by accounting of episomal products of the TCR rearrangement, TCR rearrangement excision circles (TREC), which can be detected in RTE populating.

The aim of work was to test different variants of T-cells magnetic separation methods for Recent thymic emigrants study in peripheral blood of Rheumatoid patients.

Methods: The research was performed in isolated mononuclear cells suspension and after magnetic separation of T-cells in 10 Rheumatoid patients and five healthy donors. We used the "negative separation" provided by magnetic particles with anti-CD3 antibodies, "positive separation" with magnetic particles, loaded by anti-CD4. and Ònegative separationÓ with ÒuntouchedÓ human CD4+ T-cells magnetic particles. T-cells phenothype was investigated cytometrically using double monoclonal antibodies scanning. We also studied CD31 as RTE marker and CD127 as T-regs marker.

Results: We found that CD31+ cells are present in donors and patients peripheral blood. Their percentage in the total lymphocyte pool was small enough (from 025% to 1, 3%). Among these cells were found CD4+CD31+ cells, and CD4-CD31+.cells After removal of CD3+ lymphocyte percentage of CD4-CD31+ cells tended to increase, which is probably indicative of their lack of CD3 receptor. At the same time, the use of "negative" separation of CD3+ cells and "positive separation" of CD4+ cells allowed us to study other T-cell populations probably belonged to thymic migrants. The more prospective method of magnetic separation for T-cells with atypical phenotype detection was the use of ÒuntouchedÓ human CD4+ T-cells magnetic separation which allowed to investigate ÒuntouchedÓ CD4+T-cells population. In three patients we found definite enrichment of CD4+CD31+ cells till 7–8.5%. All RTE were CD127 negative.

Conclusion: T-cells magnetic separation could be prospective method of Òin vivoÓ thymic output study and future estimation of T-regs defect in RA.

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APLAR-0260

Methylenetetrahydrofolate reductase gene polymorphisms and response to methotrexate in Pakistani patients with rheumatoid arthritis

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Objective: Methotrexate (MTX) is the drug of choice in the treatment of rheumatoid arthritis (RA). However, tolerability and efficacy of this drug varies from one population to another. Methylenetetrahydrofolate reductase (MTHFR) gene polymorphism has been found to be associated with response to MTX. The objective of this study was to find out whether there is any relationship of single nucleotide polymorphisms (SNPs) * *MTHFR* C677T and *MTHFR* A1298C with response to MTX in a Pakistani population of RA patients.

Method: Allele frequencies of 677C>T and 1298 A>C polymorphisms were determined in 67 RA patients (nine males and 58 females; mean age 42.87 ± 13.5 years) who had previously participated in a prospective clinical trial. Fifty one patients had received MTX and were followed up for response up to 6 months. Genotyping of the two polymorphisms was done using PCR-RFLP based assays. Fasting levels of plasma homocysteine were determined using a kit method.

Results: Twenty-eight RA patients were found to be Ògood respondersÓ to MTX, while 23 were classified as Òpoor respondersÓ. Frequencies of *MTHFR* 1298C and *MTHFR* 677T alleles in RA patients were not significantly different from their frequencies in general population in Karachi[1] (0.553 versus 0.55; P = 0.977) and 0.194 versus 0.15; P = 0.338, respectively). Plasma homocysteine levels in female RA patients were significantly higher compared to levels in females in general population in Karachi (13.1 ± 6.7 versus 11.4 ± 5.3 µmol/L; P = 0.02). *MTHFR* 1298C allele frequency in good responders to MTX was not significantly different from bad responders (0.574 versus 0.521; P = 0.6). Similarly, 677 C>T polymorphism also had no significant influence on response to MTX (P = 0.744).

Conclusion: Results indicate lack of association between *MTHFR* polymorphisms and response to MTX in a population of Pakistani RA patients.

Reference: 1. Yakub et al. (2012). PLoS One 7(2): e33222

APLAR-0279

The performance of new and old classification criteria for rheumatoid arthritis in a Turkish cohort with early-undifferentiated inflammatory arthritis

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Background-Aim: Given the fact that early initiation of therapy can ameliorate the disease course, it is important to diagnose RA patients as early as possible. In parallel with this purpose, new classification criteria were published in August 2010. Although the diagnostic performance of these new criteria compared with the ACR 1987 criteria were investigated in several cohorts from different populations, no such study was performed among patients from Turkey. We therefore evaluate the sensitivity of ACR/EULAR 2010 criteria and ACR 1987 revised criteria in an early arthritis cohort from Turkey.

Methods: From May 2009 to April 2010, patients who first visited university hospital outpatient clinic with arthritis and who does not fulfill the classification criteria of a specific diagnosis (n = 90) were included to the study Attending physicians were asked to classify patients either as RA or undifferentiated arthritis. All patients were reassessed at 12th month and were re-classified. Proportions of patients fulfilling the aforementioned criteria were determined and compared with clinicians' diagnoses.

Results: At the beginning of the cohort, none of the patients were fulfilling the ACR-1987 revised criteria, while 16 (17.8%) of them were fulfilling the 2010 classification criteria for RA. On the other hand, 43 patients were diagnosed as RA by their attending physicians, which make the sensitivity of the new criteria as 37% at the beginning of the cohort. At the end of the 12-month follow-up period, rates of fulfilling old and new criteria were 31%, and 50%, respectively. The sensitivities of the old and new criteria were 58% and 94%, respectively.

Conclusion: Our results have confirmed the high sensitivity of new RA classification criteria for patients with early arthritis in a country where the diseases such as FMF and BD are prevalent.

APLAR-0310

Clinical profile and outcomes of filipino patients with early rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is the most common inflammatory arthritis worldwide. It leads to joint damage, which occurs at a high rate early in the disease course.

Objective: To describe the clinical profile and outcome of Filipino patients with early RA included in the Rheumatoid Arthritis Database and Registry (RADAR) of the Philippine General Hospital.

Design: This is a retrospective study of adult patients diagnosed with RA, whose symptoms are ≤2 years. We described their clinical profile, and radiographic findings at baseline, disease activity, and treatment regimen at 3–6 months and 1 year of follow-up.

Results: Data of 95 patients with early RA included in the RADAR were reviewed. Female to maleratio is 9:1 and the mean age at diagnosis is 47.9 years. Majority (85%) werenon-smokers and most patients (83%) had current or previous employment.

At baseline, 99% presented with polyarthritis and 97% showed hand-joint involvement. Radiographic changes were seen in 61% of patients, with erosions detected in 27%. Among patients with radiographic changes, 58% were RF positive. Initial mean DAS-28 score was 5.78, indicating high activity. Prednisone and NSAIDs were the most commonly used medications, while only 47% received methotrexate. At 3–6 months of treatment, the average DAS 28 score was 4.53, indicating moderate disease activity. At 1 year of follow-up, disease activity remained moderate, with a mean DAS-28 of 4.63. Most (87%) were maintained on methotrexate, but prednisone use decreased to 40%.

Conclusion: Joint damage is seen early in the course of RA. Disease activity remains poorly controlled even after 1 year of standard treatment. We recommend a more aggressive approach in the management of RA to prevent joint damage progression, and further studies to characterize factors unique to the Filipino RA patient that may predict outcomes.

APLAR-0327

Investigation of the relationship between ultrasound findings and physical examination in the MTP joint in patients with rheumatoid arthritis

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Purpose: To evaluate the accuracy of physical examination, we investigate the concordance rate of ultrasound (US) findings and physical examination findings with MTP joint of rheumatoid arthritis patients.

Materials and Methods: Fifty rheumatoid arthritis patients within 1 year from on-set of arthritis were examined (10 males, 40 females, mean age 57.9 years). There was no patient using biologics in this series. Thirty-eight joints consisting of 10 MTP joints and 28 joints used in the DAS28 evaluation were assessed by joint survey of swelling and tenderness and were followed by the evaluation of gray scale (GSUS) and power doppler ultrasonography (PDUS) by another specialist. In the assessment of GSUS and PDUS, grade2 or higher of semi-quantitative grade (grade 0–3) was evaluated as positive value. Concordance rate between the assessment of US findings and physical examinations of joint swelling or tenderness in MTP joints was calculated.

Results: Moderate disease activity was observed as 4.50 on an average of DAS28ESR and 20.1 on an average of SDAI. Concordance rate of GSUS findings and swollen joint or tenderness joint assessment in MTP joint ($n = 500$) were $\kappa = 0.12$ and $\kappa = 0.07$ respectively and the rate of PDUS findings and swollen or tenderness joint assessment were $\kappa = 0.11$ and $\kappa = 0.10$ respectively. The sensitivity in diagnosis of swollen joint assessment with GSUS as "gold standard" was 18.5%, specificity 91.4%, positive predictive value 48.3%, negative predictive value 72.2%. And also sensitivity analysis with PDUS as standard was resulted in 20% sensitivity, 91.7% specificity, 13.3% positive predictive value, and 94.7% negative predictive value.

Conclusion: The concordance rate of physical examination and US assessment is very poor in MTP joints. The anatomical features of the MTP joint may affect the results but aggressive US indication might helpful for better precise management of arthritis.

APLAR-0341

Analysis of fecal Lactobacillus community structure in patients with early rheumatoid arthritis

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The objective of this study was to analyze human Fecal Lactobacillus community and its relationship with rheumatoid arthritis. Samples taken from rheumatoid arthritis (RA) patients and healthy individuals were analyzed by quantitative real-time PCR. Bacterial DNA was extracted from feces, and amplicons of the Lactobacillus-specific regions of 16S r RNA were analyzed by denaturing gradient gel electrophoresis (DGGE). The richness, Shannon-Wiener index and evenness of gut microbiota of both groups were analyzed to compare fecal Lactobacillus community structures. Results of this study demonstrated that fecal microbiota of RA patients contained significantly more Lactobacillus (10.62 ± 1.72 copies/g) than the control group (8.93 ± 1.60 copies/g). Significant increases were observed in RA patients in terms of the richness, Shannon-Wiener and evenness measures, indicating more bacterial species, and increased bacterial diversity and abundance. These results suggest a potential relationship between Lactobacillus communities and the development and progression of rheumatoid arthritis.

APLAR-0342

The objective research on 322 rheumatoid arthritis patients with damp-heat impeding and cold-damp impeding medical pattern of Traditional Chinese Medicine

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Objective: To analyze the objective regularity between damp-heat impeding and cold-damp impeding medical pattern of rheumatoid arthritis (RA) with Traditional Chinese Medicine (TCM).

Methods: TheDAS28 (ESR) scores and laboratory indexes including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin (ALB), globulin (GLB) and blood count level of 322 patients with RA were tested by conventional approach, and the level of TNF-a and IL-1β from serum were detected by ELISA, all of which were tend to find the discrepancies between the two TCM medical patterns with RA.

Results: The levels of DAS28 scores, ESR, CRP, white blood cell counts (WBC) and platelet (PLT) of RA patients with dampness-heat impeding pattern were significantly higher than that of cold-dampness impeding pattern ($P < 0.01$). The level of serum GLB of RA with dampness-heat impeding pattern was obviously higher than that of cold-dampness impeding pattern and normal control group ($P < 0.01$), while ALB showed opposite tendency. Compared with dampness-heat impeding pattern, the sequences below ROC curve were ranked as DAS28 score > ESR > CRP > GLB > PLT > WBC. ALB was the only index that was of diagnostic value for cold-dampness impeding pattern and the area below the curve was 0.636 ($P = 0.000$), when cold-dampness impeding pattern was selected as positive control.

Conclusion: These seven indicators DAS28 score, CRP, WBC, ESR, PLT, GLB and ALB might be used as objective criterion to identify the differences between damp-heat impeding and cold-damp impeding medical pattern of RA.

Key words: damp-heat impeding medical pattern; cold-damp impeding medical pattern; rheumatoid arthritis; Chinese medical pattern; objective.

APLAR-0361

Metabolic syndrome prevalence in rheumatoid arthritis pacients

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Background: Inflammation in rheumatoid arthritis (RA) pacients plays an important role in developing metabolic syndrome (MetS). The autoimmune systemic inflammatory response, along with the presence of MetS, doubles the risk for fatal or non-fatal cardiovascular disease (CVD) and coronary atherosclerosis, regardless of age and sex.

Objectives: The aim of this study was to evaluate the prevalence of vascular risk factors and the metabolic syndrome (MetS) in RA pacients.

Methods: The subjects were 64 RA patients and 63 healthy controls, frequency matched by age and sex. Waist and hip circumferences, body weight, body height and blood pressure were measured. Fasting blood was taken for glucose and lipid levels. The MetS was defined by the criteria proposed by the new International Diabetes Federation (IDF) worldwide definition using the European criteria for central obesity: increased waist circumference to ≥94 cm in men or ≥80 cm in women plus two of: (1) elevated blood pressure to ≥130/85 mmHg or requiring drug therapy, (2) elevated serum triglyceride level to ≥1.7 mmol/L or specific treatment; (3) reduced serum high density lipoprotein (HDL)-cholesterol to ≤1.0 mmol/L in men and ≤1.3 mmol/L in women or specific treatment (4) elevated fasting glucose level to 5.6 mmol/L or previously diagnosed type 2 diabetes. Medications being received by patients were also reviewed. RA disease activity (DAS 28) was performed.

Results: The criteria for MetS were met by 41% RA patients versus 21.5% in the control group ($P < 0.001$). By multiple logistic regression analysis (adjusted for age, sex) the risk of having MetS was significantly higher for RA patients than for controls [odds ratio (OR) 1.85, 93% confidence interval (CI) 1.14–2.85.00, $P = 0.009$]. The DAS28 was significantly higher in RA patients with MetS than in those without MetS (3.61 ± 1.28 versus 3.18 ± 1.49; $P = 0.01$). One-way ANOVA test revealed a significantly higher body mass index (BMI) in patients with RA than the control group (25.2 ± 3.3 versus 23.3 ± 4.4 kg/m^2; $P = 0.02$ post-hoc test).

Conclusion: MetS is increased in RA pacients and is correlated with disease activity. The higher prevalence of cardiovascular risk factors in RA suggests that tight control of systemic inflammatory activity should be recommended.

APLAR-0392

Study efficacy of stress management skill training upon reduction anxiety and depression among women with rheumatoid arthritis

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Background: The anxiety and depression effect on patients with chronic diseases. Rheumatoid arthritis (RA) is auto-immune and chronic disease that observe high prevalence of anxiety and depression on patients with rheumatoid arthritis.

Aim: The purpose of this research was consider the efficacy of stress management skill training based on cognitive-behavior upon reduction anxiety and depression among women with rheumatoid arthritis.

Method: This study was a quasi -experimental research with pre-test, post-test, follow up and control group design. Through 100 women with RA were who had referred to rheumatology clinic 40 women with rheumatoid arthritis randomly selected and assigned to experimental ($n = 20$) and control group ($n = 20$). stress management skill training based on cognitive-behavior was received experimental group in eight session and compared with control group. Datas were collected by beck depression inventory (BDI-II), speilberger state-trait anxiety inventory and rheumatoid arthritis disease activity index.

Results: The result of this research showed that stress management skill training based on cognitive-behavior has significantly decreased scores means of anxiety ($P < 0/01$), depression ($P < 0/001$) on experimental group in comparison with the control group also, after the final of intervention rheumatoid arthritis disease activity in the experimental decreased in comparison with the control group ($P < 0/05$). follow up test was performance in three time interval and the result showed management skill training based on cognitive-behavior upon decrease anxiety and depression women with rheumatoid arthritis have persistence effects in 3 months of follow? up ($P < 0/01$).

Conclusions: Outcomes indicated ?in besides medical treatments, psychology intervention stress management skill training based on cognitive-behavior cause has been decreased anxiety and depression on women with RA.

Key words: anxiety, cognitive-behavior, depression, rheumatoid arthritis, stress management, rheumatoid arthritis disease activity index.

APLAR-0399

Peripheral circulating anti-cyclic citrullinated peptide antibody in the patients with rheumatoid arthritis and chronic obstructive pulmonary disease

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Objectives: Anti-cyclic cirullinated peptide (anti-CCP) antibody is used to diagnose rheumatoid arthritis (RA) with high specificity. Different environmental factors including smoking can trigger the production of anti-CCP. Chronic obstructive pulmonary disease (COPD) is a chronic lung disease with highly associated with smoking. We aimed to evaluate levels of anti-CCP antibody and rheumatoid factor (RF) in patients with RA or COPD.

Methods: The study sample included 41 subjects with RA, and 70 subjects with COPD. We checked the levels of anti-CCP antibody and RF.

Results: Higher positive anti-CCP antibody was found in the patients with RA (58.5%), and no positive anti-CCP antibody was found in the patients with COPD. Positive RF was observed in RA (90.2%) and COPD (40.3%). Among the patients with RA, we could find that the smoking patients had higher level of anti-CCP antibody when compared with non-smoking patients.

Conclusions: RF was not specific for diagnosis of RA, and was easily positive in COPD. Anti-CCP antibody was specific in RA, and was reliable serological markers to diagnose RA.

APLAR-0404

Laboratory characteristics of a prospective of patients with rheumatoid arthritis: biomarkers

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Background: Rheumatoid Arthritis (RA); an inflammatory disease is the health problem in all human societies around the world. Despite all efforts to diagnosis, up to know; there is no punctual laboratory method. Currently the origin of inflammatory diseases is rolled by microbial antigens and Superantigens are undeniable. Thus, the aim of this study was to find staphylococcal enterotoxins in synovial fluid of Rheumatoid Arthritis patients.

Materials and Methods: In this study, sixty synovial fluid samples from patients with rheumatoid arthritis were studied. All samples were processed, SDS- PAGE analysis was performed continue to purifying stage. Then, the results were confirmed by western blot test.

Using specific antibodies to Staphylococcus aureus enterotoxins A and B separate ELISA plates were designed and the samples assayed. The results were subject to statistical analysis by SPSS ver. 16.

Results: The results indicated that, the synovial fluids electrophoresis of product centrifugal tubes Amicon-Ultra -15; Ultracel – 10, 30 and 50 KDa showed the presence of *Staphylococcus aureus* enterotoxin proteins in the molecular weight range indicated. Immunoblotting also confirmed their existence. The ELISA results showed that in 45% of samples were found in synovial fluid of patients with Staphylococcus aureus enterotoxima. ANOVA and Chi-Square analysis results showed a significant level ($P < 0.06$) and ($P < 0.05$).

Conclusion: The survey results showed that almost half of the synovial fluid samples have staphylococcal enterotoxins A or B accommodation. However, the main hypothesis of this study was confirmed. Given that there are over 20 different types of staphylococcal enterotoxins. To determine the relationship between the disease and these staphylococcal superantiges further researches are necessary.

APLAR-0446

Correlation between Vitamin D, TNF-a, and disease severity in rheumatoid arthritis patients

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Background: Vitamin D, in addition to its primary function as a regulator in calcium homeostasis, also had immunomodulator effect that affects the immune system. Rheumatoid arthritis is an autoimmune disease characterized by the presence of symmetric erosive synovitis, Formly by antigen-dependent T cell activation that will trigger an immune response, especially Th1. Tumor necrosis factor (TNF-α) is a central cytokine in the pathogenesis of RA. Vitamin D deficiency was associated with exacerbation of Th1 immune response. Vitamin D and its prohormones have been the focus of a growing number of studies in past years, demonstrating their function not only in calcium metabolism and bone formation, but also their interaction with the immune system. Vitamin D insufficiency is emerging as a clinical problem of global proportions and epidemiology has linked vitamin D status with autoimmune disease susceptibility and severity such as rheumatoid arthritis. The aim of this study was to know the correlation between vitamin D levels with the level of TNF-α, and clinical manifestation in rheumatoid arthritis patients.

Research Methods: This is an observasional study with cross sectional design. 24 rheumatoid arthritis patients was recruited. Serum vitamin D level was measured using ELISA method. Rheumatoid Arthritis (RA) diagnostic criteria assessed ACR/EULAR 2010 criteria, TNF-α was measured using ELISA method, the clinical manifestations of RA was assessed by DAS28 score, VAS, and functional status.

Result: The average age of the patient was 51 years, and the majority was menopause (66.7%), with the average duration of illness was 51.29 months. The average Disease Activity Score [DAS 28 (CRP)] was 3.29, with high disease activity was affect 37.5% patients. 45.8% patients were vitamin D deficiency, and the average levels of vitamin D was 36.13 ng/mL. There was a significant correlation between vitamin D with patient age ($P = 0.005$, $r = -0.553$), with a duration of illness [$P = 0.009$, $r = -0.522$)], the DAS 28 (CRP; $P = 0.001$, $r = -0.615$), VAS patients ($P = 0.004$, $r = -0.567$) and the levels of TNF-α ($P = 0.048$, $r = -0.408$) and patients functional status ($P = 0.039$, $r = -0.424$).

Conclusion: There is significant correlation between the levels of vitamin D with TNF-α levels and clinical manifestation in rheumatoid arthritis patients.

Key words: Rheumatoid arthritis, TNF-α, DAS28 (CRP), vitamin D, VAS, functional status.

APLAR-0452

The correlations between interleukin-6 level and disease activity in rheumatoid arthritis patients

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Background: Rheumatoid arthritis is a chronic inflammation disorder which is involved various cytokines in its pathogenesis. Among various cytokines that responsible in its inflammatory process, several investigations have suggested the important role of IL-6 in pathophysiology of rheumatoid arthritis (RA) and itOs level correlates with disease activity and the joint destruction . This study was aimed to find out the correlation between IL-6 cytokine level and disease activity in RA.

Materials and Methods: Thirty one RA patients with minimally 3 months treatment with MTX were involved in this study. We examined several variables such as: RA disease activity using DAS28; high sensitivity C-reactive protein levels and IL-6 serum level using ELISA methods. The correlation between variables were determined using PearsonOs correlation test if the data distributed normally, and using Spearman correlation test if the data didnOt distribute normally. All statistic analysis were calculated using SPSS version 17 and P value < 0.05 was considered significant.

Results: Based on the disease activity, we found that 35.5% patiens were in remission state ($DAS28 \leq 2.6$), 48.4% in mild activity ($2.6 < DAS28 \leq 3.2$), 9.7% in moderate activity ($3.2 < DAS28 \leq 5.1$), and 6.5% in severe activity ($5.1 < DAS28$). Among RA patients who have been received minimally 3 month standard RA therapy with MTX, we found there was significant positive correlation between IL-6 and DAS28 ($r = 0.770$, $P < 0.05$), but no correlation between IL-6 levels and hs-CRP levels ($r = 0.009$, $P < 0.05$).

Conclusion: These findings suggest a possible role of IL-6 cytokine in the pathogenesis of RA. IL-6 can be considered as an additional marker in the evaluation of treatment response in RA patients, particularly when usual markers like ESR and hsCRP show discordant results compared with the clinical features.

Key words: Rheumatoid arthritis, interleukin-6, high sensitivity C-reactive protein (hsCRP), DAS28.

APLAR-0453

Traditional risk factor for atherosclerosis in rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic systemic inflammation which can cause inflammation and bone destruction. Atherosclerotic is one of extraarticular manifestation that can cause the increase of cardiovascular and cerebrovaskular event and this is the major cause of mortality in RA patient. Traditional risk factor as a predictor of atherosclerotic was frequently found in patient with RA.

Objective: To determine the different traditional risk factor such as total cholesterol, HDL, LDL, Triglycerides, blood pressure, body mass index (BMI) between atherosclerotic and non atherosclerotic patient with rheumatoid arthritis and to correlate it with carotid intima media thickness (CIMT) as a marker of atherosclerotic.

Method: This was cross sectional study in rheumatoid arthritis patient, diagnose was established according to ACR/EULAR 2010. All subjectOs traditional risk factors and carotid intima media thickness were measured.

Result: From 28 patients, there were 14 patients with atherosclerotic and 14 patients with non atherosclerotic. Mean age atherosclerotic versus non atherosclerotic (58.1 ± 8.5 versus 40.9 ± 12.6). Mean total cholesterol atherosclerotic versus non atherosclerotic (239.6 ± 39.2 versus 199.1 ± 43.1). Mean LDL atherosclerotic versus non atherosclerotic (158 ± 29.8 versus 114.8 ± 35.8). Mean HDL atherosclerotic versus non atherosclerotic (59.8 ± 19.9 versus 63 ± 20.1). Mean triglycerides atherosclerotic versus non atherosclerotic (118.9 ± 35.7 versus 106.4 ± 50). Mean BMI atherosclerotic versus non atherosclerotic (22.2 ± 4.9 versus $22,.1 \pm 5.7$). Mean systolic blood pressure (SBP) atherosclerotic versus non atherosclerotic (147.1 ± 13.9 versus 115 ± 10.2). Mean diastolic blood pressure (DBP) atherosclerotic ver-

sus non atherosclerotic (87.9 ± 6.9 versus 76.4 ± 4.9). Age (r = 0.671), SBP (r = 0.859), DBP (r = 0.739) correlate with CIMT in atherosclerotic patient ($P < 0.05$).

Conclusion: Age, Total cholesterol, LDL, blood pressure as traditional risk factor in RA with atherosclerotic were significantly higher than RA non atherosclerotic patient. Only age and blood pressure correlated significantly with CIMT in atherosclerotic patient.

Key words: RA, Traditional risk factor, atherosclerosis, CIMT.

APLAR-0454

The correlation of CTX-1 serum and disease activity in rheumatoid arthritis patients

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic and progressive systemic inflammation which can cause cartilage and bone destruction. The inflammation activity in RA patients can be measured Disease Activity Score 28 (DAS 28). RA patients were receive DMARDS and corticosteroid as a standard therapy. The use of corticosteroid caused imbalance of bone metabolism and increased risk of bone reabsorption. Carboxy terminal crosslink telopeptide type 1 (CTX-1) has been known as marker of bone reabsorption.

Objective: To determine a correlation between Disease Activity Score 28 (DAS 28) and steroid dose with serum level of CTX-1 in RA patients.

Methods: All subject were measured serum level of CTX-1, doses of steroid and disease activity by DAS 28 score. Level of CTX-1 determined by electrochemiluminescence immunoassay (ELISA).

Results: There was 31 participants of RA participated in this study. Mean serum level of CTX-1 is 0.91 ng/mL. Mean of DAS-28 is 3.12. Mean of steroid doses is 8 mg per day. There was no correlation of CTX-1 serum and disease activity ($P = 0.301$ and $r = -0.097$). A positive correlation was found between serum level of CTX-1 and doses of steroid r = 0.590, $P = 0.001$.

Conclusion: In this study, there is no significant correlation between serum level of CTX-1 and disease activity, while there is significant correlation between serum level CTX-1 and doses of steroid.

Key words: rheumatoid arthritis, CTX-1, DAS 28, steroid.

APLAR-0458

Increased soluble CD4 in serum of rheumatoid arthritis patients is generated by matrix metalloproteinase (MMP)-like proteinases

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Higher soluble CD4 (sCD4) levels in serum have been detected in patients of infectious and chronic inflammatory diseases. However, how and why sCD4 is produced remains poorly understood. We establish sensitive ELISA and WB assays for sCD4 detection in conditioned medium of *in vitro* cell culture system and serum of chronic inflammatory patients. Serum samples from patients with systemic lupus erythematosus (SLE) (n = 79), rheumatoid arthritis (RA) (n = 59), ankylosing spondylitis (AS) (n = 25), gout (n = 31), and normal controls (n = 99) were analyzed using ELISA for sCD4 detection. Results from each assay were analyzed by the Kruskal-Wallis test. DunnOs multiple comparison post-test was then applied between groups. We confirm that cells expressing exogenous CD4 produce sCD4 in a constitutive and PMA-induced manner. Importantly, sCD4 production in a heterologous expression system is inhibited by GM6001 and TAPI-0, suggesting receptor shedding by matrix metalloproteinase (MMP)-like proteinases. Moreover, similar findings are recapitulated in human primary $CD4^+$ T cells. Finally, we show that serum sCD4 levels are increased in patients of chronic inflammatory diseases including RA and SLE, but not in those with gout. Intriguingly, sCD4 levels in RA patients are correlated positively with the disease activities and higher sCD4 levels seem to associate with poor prognosis. Taken together, we conclude that CD4 is shed from cell surface by a MMP-like sheddase and sCD4 level is closely related with the inflammatory condition in certain chronic diseases. Hence, sCD4 might be considered an important parameter for RA disease progression with potential diagnostic importance.

APLAR-0322

Pure water intake and risk of rheumatoid arthritis: result from Korean National Health and Nutrition Examination Survey (2007–2010)

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Purpose: The objective of this study was to reveal the association between pure water intake and risk of rheumatoid arthritis (RA) in Korean population using a representative sample.

Methods: A cross-sectional study was used to evaluate the association between pure water intake and risk of RA. Participants were 19851, aged from 20 to 64 years from 4th Korean National Health and Nutrition Examination Survey (KNHANES IV, 2007*2010) who underwent a health interview and 24-h dietary recall and a food frequency questionnaire.

Results: The prevalence of RA in KNHANES IV was 2.1% (425 of 19 342) and mean pure water intake was 6.04 ± 36.7 cup (200 mL) per day. Pure water intake of RA group were lower than that of non-RA group (670.8 ± 20.5 g versus 767.9 ± 3.24 g). Before adjust, there was no significant relationship between pure water intake and risk of RA (P value from *t*-test ±0.501), while after adjust age, sex, education and house income, pure water intake was significantly related to risk of RA (odds ratio 1.05, 95% CI 1.01–1.10).

Conclusion: These results suggest that water intake related to risk of RA in normal population.

APLAR-0095

Serum levels of osteopontin does not indicate the disease activity and responsiveness to therapeutic treatments in patients with rheumatoid arthritis

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Objective: Osteopontin (OPN) is known to be significantly involved in the pathogenesis of RA. This study was aimed to evaluate if serum concentrations of OPN in patients with rheumatoid arthritis (RA) before and after therapeutic treatments is correlated to disease activity and response to therapy.

Methods: Blood samples from 40 patients with RA were collected at baseline and six months after starting treatment with disease-modifying antirheumatic drugs (DMARDs) and/or tumor necrosis factor (TNF)-α blocker. Serum levels of OPN were measured by ELISA.

Results: At baseline, the serum OPN level in RA patients was significantly higher than that of the healthy group. The OPN level at baseline in RA patients with severe disease activity on the basis of DAS28 was slightly higher than that of those with moderate disease activity. The serum OPN level in RA patients was not significantly correlated with DAS28 level. The serum OPN level in both responders and nonresponders after therapy was significantly decreased regardless of responsiveness to therapy. Also, the OPN level at baseline did not affect the responsiveness to therapeutic treatments.

Conclusions: Serum OPN level was not correlated to disease activity and responsiveness of RA patients by therapeutic treatments. This result may partly explain why humanized monoclonal antibody against OPN did not produce any apparent clinical response in RA patients. Thus, targeting OPN in RA may not be clinically effective.

APLAR-0403

Expression of RICTOR in rheumatoid arthritis fibroblast-like synoviocytes

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Background: RICTOR (rapamycin-insensitive companion of mTOR) is a key component of mTORC2 (mammalian target of rapamycin complex 2), which can regulate the organization of actin cytoskeleton and phosphorylate/activate Akt. Aktsignaling is activated in rheumatoid arthritis fibroblast-like synoviocytes (RA-FLS) and plays an important role in the pathogenesis of RA. We hypothesized that RICTOR might be involved in the long-lasting changed phenotype of RA-FLS.

Objectives: To investigate the expression of RICTOR in RA-FLS.

Methods: FLS were isolated from the primary synovial tissues, which were obtained during joint replacement surgery or arthroscopy from seven patients with RA, four patients with osteoarthritis (OA), and four patients with joint trauma (Trauma group). The expression of RICTOR in FLS from the three groups was evaluated at the protein level by western blotting and at the mRNA level by Real-time PCR. Three of the RA-FLS samples were selected randomly for being treated with 10 ng/mL TNF-alpha, 4 nmol/L Akt pathway blocker MK-2206 with or without 10 ng/mL TNF-alpha. The expression of RICTOR was detected by western blotting after 24 h.

Results: (i) Western blotting and Realtime-PCR showed that the expression of RICTOR was elevated in RA-FLS compared with that in Trauma-FLS (both $P < 0.05$) at protein and mRNA

level. But no difference was found between RA-FLS and OA-FLS. (ii) Compared with the control group, treatment with MK-2206 (with or without TNF-alpha) for 24 h decreased the expression of RICTOR protein (both $P < 0.01$), while the expression of RICTOR in RA-FLS was not influenced by stimulation with TNF-alpha.

Conclusions: Expression of RICTOR is elevated in RA-FLS in vitro. The increase is due to the activation of Aktsignaling. The results suggest that RICTOR may contribute to the stable activation of RA-FLS.

APLAR-0417

Diagnostic value and significane of the anti-Sa antibodyanti-CCP antibody,GPI antigen and rheumatoid factor with rheumatoid arthritis (RA)

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Objective: To analyze and detect the diagnostic significance of the anti-Sa antibody, anti-CCP antibody, GPI antigen and rheumatoid factor in patient with RA.

Methods: (i) The methods of Enzyme-linked immunosorbentassay (ELISA) was used to determine the anti-Sa antibody, anti-CCP antibody, GPI antigen and rheumatoid factor in 97 RA patients? Sixty-seven other autoimmune diseases and 49 healthy controls from the hospital of Xinjiang Uygur Autonomous Region, RF were detected by immunoturbidimetric assay. (ii) Collect the clinical data and laboratory index of 97 RA: age of onset, sex, morning stiffness, the pain number of joints, the swell number of joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antinuclear antibody (ANA) and calculated the DAS28 scores.

Results: (i) The specificitiy and sensitivity of anti-Sa antibody, anti-CCP antibody, GPI antigen, RF, RF-IgA, RF-IgG, RF-IgM were 95.69% and 59.79%, 98.28% and 90.72%,76.14% and 78.35%, 67.24% and 91.75%, 89.66% and 58.76%, 90.52% and 68.04%, 79.31% and 79.38%. (ii) In Patient with RA whose RF is negative, the rate of male of anti-Sa antibody, anti-CCP antibody, GPI antigen were 25.0%, 50.0%, 50.0%. (iii) Specificitiy and sensitivity were 92.24–100% and 47.42–86.60% as two index turned out to be positive; were 99.14–100% and 46.39–71.13% as three index, were 100% and 46.39% as four index. (iv) The RA patients with anti-Sa were statistically different from the patients without this antibody in C-reactive protein. (v) GPI in active RA patients was higher than stable patients ($P < 0.05$).

Conclusion: Dictation of anti-Sa antibody, anti-CCP, GPI and rheumatoid factor can greatly improve the specificity for diagnosis of early-stage RA.

APLAR-0418

To compare diagnostic value and significance of the anti-Sa antibody and anti-CCP antibody with rheumatoid arthritis (RA)

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Objective: To compare the anti-Sa antibody, anti-CCP antibody and analyze and detect the diagnostic significance of the anti-Sa antibody, anti-CCP antibody in patient with RA.

Methods: The methods of Enzyme-linked immunosorbent assay (ELISA) was used to anti-Sa antibody, anti-CCP antibody in 89 RA patients? Seventy-three non-RA patients from the hospital of Xinjiang Uygur Autonomous Region. Collect the clinical data and laboratory index of 89 RA: the pain number of joints, the swell number of joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antinuclear antibody (ANA).

Results:

1 The specificity and sensitivity of anti-Sa antibody, anti-CCP antibody were 97.26% and 60.67%, 98.63% and 92.13%.
2 Specificity and sensitivity were 100% and 60.67% as two index turned out to be positive. The sensitivity of anti-CCP antibody were Higher than anti-Sa antibody.
3 The RA patients with anti-Sa were statistically different from the patients without this antibody in counts of joints with pain and swelling; The RA patients with anti-CCP were statistically different from the patients without this antibody in counts of joints with pain and swelling, and in male of antinuclear antibody.

Conclusion: The sensitivity of anti-CCP antibody were higher than anti-Sa antibody.

APLAR-0219

The correlation of ACR recommended clinical disease activity measures with grading of histological synovitis in rheumatoid arthritis

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Objectives: To explore the correlation of 2012 updated ACR recommended RA disease activity measures (DAS28, CDAI, SDAI, PAS) with grading of histological synovitis in RA.

Methods: Synovial tissue was obtained by closed needle biopsy from inflamed knees of 152 consecutive patients with active RA and stained with H&E. Grading of Lining hyperplasia, inflammatory cell infiltration or stroma activation was each performed on a scale from 0 to 3, yielding a final Krenn'ssynovitis score (KSS) from 0 to 9.

Results: (i) Among 152 RA patients, 128 (84%) were female, median age was 52 years (range 23–80) and median disease duration was 42 months (range 3–480). The median of KSS was 3.5 (range 0.5–6.5). (ii) DAS28-crp and CRP in high-grade synovitis group (KSS > 4, n = 50) were significantly higher than that in no synovitis group (KSS ≤ 1, n = 15) (DAS28-crp: $\chi^2 = 5.973$, $P = 0.015$; CRP: $\chi^2 = 9.313$, $P = 0.002$). CRP in low-grade synovitis group (KSS 1–4, n = 87) was significantly higher than that in no synovitis group ($\chi^2 = 6.654$, $P = 0.01$). (iii) Spearman's correlation test showed slight but significant correlation between KSS and DAS28-crp ($r = 0.201$, $P = 0.025$) or CRP ($r = 0.225$, $P = 0.005$). However, there was no significant correlation between histological synovitis scores and CDAI, SDAI or PAS. (iv) High disease activity group of RA patients (DAS28-crp > 5.1, n = 55) showed significantly higher stroma activation score and fibrosis subscore (graded from 0 to 3) than in low to moderate disease activity group (DAS28-crp ≥ 2.6 and ≤5.1, n = 97) (stroma activation: $\chi^2 = 5.419$, $P = 0.02$; fibrosis:$\chi^2 = 5.658$, $P = 0.017$). However, histological synovitis scores showed no significant difference among groups of different disease activity according to CDAI, SDAI or PAS.

Conclusion: Our results showed DAS28 was better correlated with grading of histological synovitis (especially stroma activation and fibrosis) than other recommended clinical disease activity measures in RA.

APLAR-0407

Diagnosis of suspected early RA negative for RF by 2010 ACR/EULAR criteria – more close to experts opinion

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Objectives: About 20–30% patients with rheumatoid arthritis (RA) are negative for rheumatoid factor (RF), which is an important element in both the 1987 ACR classification criteria and the 2010 ACR/EULAR criteria. Recognization of patients with RF (−) RA depend mainly on Expert opinion. We want to compare the difference between the both criteria and expert opinion on the diagnosis of suspected early RA negative for RF.

Methods: Patients had arthritis (duration < 6 month, on more than one joint) cannot be explained by other present diseases and negative for RF were studied. Patients also received blood routine test, anti-CCP antibody, ESR, CRP, and X-ray plain film of both hands. Then patients were divided into non-RA group and probable RA group, according to expert opinion, the 1987 ACR criteria, and the 2010 ACR/EULAR criteria.

Results: Eighty-three patients (201 female, 48 male) were studied. 50.6% (126 cases), 32.5% (81 cases), and 61.4% (153 cases) of patients were diagnosed as probable RA according to expert opinion, 1987 ACR, and 2010 ACR/EULAR criteria, respectively. There was moderate level of inter-observer agreement between the two professors ($\kappa = 0.63$, $P < 0.001$). When taking the expert opinion as 'gold standard', the 2010 ACR/EULAR recognized more probable RA patients than 1987 ACR criteria (108 versus 66, $P < 0.05$). There was higher consistency between the 2010 ACR/EULAR criteria and expert opinion than that between the 1987 ACR criteria and expert opinion ($\kappa = 0.69$, 0.43, respectively, $P < 0.05$).

Conclusions: In southern China, the 2010 ACR/EULAR criteria may be superior to the 1987 ACR criteria on recognizing suspected early RA negative for RF, which may need early aggressive treatment.

Clinical Rheumathology: T02 – Rheumatoid arthritis – clinical aspects and co-morbidity

APLAR-0012

Associations between TRAF1-C5 gene polymorphisms and rheumatoid arthritis: a meta-analysis

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Objective: The aim of this study was to determine whether tumor necrosis factor receptor-associated factor 1-complement 5 (TRAF1-C5) polymorphisms confer susceptibility to rheumatoid arthritis (RA) in different populations.

Methods: We conducted a meta-analysis of associations between the TRAF1-C5 rs10818488, rs3761847, rs2900180 and rs10760130 polymorphisms and RA susceptibility, using fixed and random effects models.

Results: A total of 24 comparative studies were included in this meta-analysis, including 22 682 patients with RA and 23 493 controls. The meta-analysis showed an association between the second allele of rs10818488 and RA in all study subjects (OR 1.170, 95% CI 1.082–1.266, $P = 8.2 \times 10^{-6}$). Analysis after stratification by population indicated that the second allele of rs10818488 were associated with RA in Europeans, but not in Asians (OR 1.229, 95% CI 1.094–1.381, $P = 0.001$; OR 1.060, 95% CI 0.930–1.335, $P = 0.092$). The meta-analysis also indicated an association between the second allele of rs3761847 and RA in all study subjects (OR 1.098, 95% CI 1.019–1.184, $P = 0.015$). The second allele of rs3761847 was associated with RA in Europeans, but not in Asians (OR 1.156, 95% CI 1.006–1.327, $P = 0.041$; OR 1.049, 95% CI 0.952–1.156, $P = 0.333$). The meta-analysis revealed an association between the second allele of the rs2900180 polymorphism and the risk of developing RA in all study subjects and Europeans (OR 1.180, 95% CI 1.031–1.350, $P = 0.016$; OR 1.224, 95% CI 1.065–1.405, $P = 0.004$). An association between the second allele of rs10760130 and RA in Europeans (OR 1.072, 95% CI 1.002–1.147, $P = 0.042$) was also noted.

Conclusions: This meta-analysis confirms that the TRAF1-C5 rs10818488, rs3761847, rs2900180 and rs10760130 polymorphisms are associated with RA susceptibility in Europeans. However, the TRAF1-C5 rs10818488 and rs3761847 polymorphisms are not associated with RA in Asians.

APLAR-0034

Treating rheumatoid arthritis to target: a Singapore survey

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Objectives: In recent years, the treatment paradigm for rheumatoid arthritis (RA) has changed significantly. Treat to Target (T2T) is a global initiative that aims to provide guidance to treat RA to specific therapeutic goals. This study aims to assess the agreement and application of the 10 T2T recommendations in Singapore practice.

Methods: An online survey of rheumatologists in Singapore was conducted, asking rheumatologists to score their agreement with each recommendation on a 10-point Likert scale (1 = fully disagree, 10 = fully agree) and to asses the extent of application in their daily practice. Those who were not applying the recommendations were asked if they were willing to change their practice.

Results: Thirty-three out of 41 (80.5%) of rheumatologists responded. Of these, 87.9% were in government hospitals. There was high agreement with the recommendations, with average agreement scores ranging from 8.30 (± 1.61) for recommendation #6 (composite measures of disease activity are necessary) to 9.27 (± 1.40) for recommendation #1 (the target of treatment is remission). A majority of rheumatologists indicated that they apply the T2T recommendations in their practice, but recommendations #5 and #6 (regarding frequency of visits and use of composite measures) had the highest number of responses indicating that they were infrequently applied (24.2% and 33.3%). Lack of time and manpower, inability of the patient to relate to abstract composite scores and the fact that ultrasonography may be more useful than composite scores to assess activity were reasons given for not applying these recommendations, although most were willing to change their practice.

Conclusion: Most rheumatologists in Singapore agreed with and applied the T2T recommendations, although there were specific recommendations that some rheumatologists felt were contentious. A workgroup has been formed to formulate local guidelines for the treatment of RA.

APLAR-0046

Non-steroidal anti-inflammatory drugs have an independent effect on synovial vascularity assessed by musculoskeletal ultrasound in rheumatoid arthritis

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Background: Musculoskeletal ultrasound (MSUS) is useful in monitoring RA and is emphasized its high sensitivity for detecting synovitis. While power Doppler ultrasound (PDUS) is notably accepted for the precise assessment of synovial vascularity, whether the usage of anti-rheumatic drug itself has an effect on PD signal in synovitis has been elusive.

Objectives: To determine whether the usage of anti-rheumatic drugs correlate with the assessment of PDUS of synovitis in RA.

Methods: In this retrospective study, A total of 167 patients with RA were recruited. All the clinical assessment parameters as well as the usage of anti-rheumatic drugs including NSAIDs, prednisolone, methotrexate, and biologic agents were analyzed in this study. MSUS assessment was performed at the bilateral wrists, MCP, and PIP joints. PDUS was graded semi-quantitatively (0–3) in each joint, and the sum of these gradings was estimated as PDUS score. The patient with scoring >1 for PDUS was defined as PDUS positive. The association among PDUS score, the clinical assessment parameters, and the usage of anti-rheumatic drugs was explored by multivariate linear regression analysis. In the group of patients in DAS28 remission, multivariate logistic regression analyses were performed with PDUS positive as dependent variables.

Results: The rate of the patients having DAS28 remission was 23% (39/167) and that of PDUS positive in the group was 48% (19/39). SDAI, mHAQ, and NSAIDs usage were independently associated with increased scoring of PDUS in multivariate linear regression analysis. Within the group of patients with DAS28 remission, only the usage of NSAIDs was independently associated with an increase of PDUS positive patient.

Conclusions: NSAIDs usage may accelerate the PD signal and result in higher scoring despite continuing remission state. Consideration should be given to the NSAIDs effect in assessing disease activity of RA using MSUS, particularly during remission.

APLAR-0052

Determinants of arterial stiffness in Chinese patients with rheumatoid arthritis

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Objective: Rheumatoid arthritis (RA) is associated with increased cardiovascular morbidity and mortality. Arterial stiffness has been shown to be an independent predictor of cardiovascular mortality and become a useful index in the prevention and early detection of cardiovascular disease. Brachial-ankle pulse wave velocity (baPWV), which reflects the stiffness of both central and peripheral muscular arteries, has been frequently used as a simple and noninvasive index for assessing arterial stiffness. Ankle-brachial index (ABI), the ratio of resting ankle to brachial systolic blood pressure, is widely used to screen for peripheral arterial disease. In this study we investigated the relationship between arterial stiffness and its associated risk factors in Chinese patients with RA.

Methods: A total of 137 Chinese RA patients and 100 healthy subjects were included. ABI and baPWV were measured. RA related factors were determined, as well as traditional cardiovascular risk factors.

Results: BaPWV was significant higher in RA group (1695.75 ± 424.91 cm/s) compared to the healthy control group (1478.32 ± 423.05 cm/s; $P = 0.022$). ABI was significant lower in RA group (0.93 ± 0.18) compared to the healthy control group (1.21 ± 0.85; $P < 0.001$).BaPWV of RA group was positively correlated with age, serum cholesterol level, serum low density lipoprotein (LDL) level; and negatively correlated with systolic blood pressure. Meanwhile, ABI of RA group was positively correlated with serum high density lipoprotein (HDL) level, negatively correlated with blood sugar level. Multivariate regression analysis showed that baPWV of RA group was independently associated with age and systolic blood pressure. And ABI of RA group was independently associated with serum high density lipoprotein level and blood sugar level.

Conclusion: The old age and high systolic blood pressure may be the major determinants of arterial stiffness in Chinese RA patients. The low serum HDL level and high blood sugar level may be the major determinants of peripheral arterial disease in Chinese RA patients.

APLAR-0058

Correlation between IL-6 level and DAS28 score in rheumatoid arthritis

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Background and Aim: Rheumatoid arthritis is a chronic inflammation disorder which various cytokines have important roles in inflammatory process and joint destruction. One of these is *interleukin-6* (IL-6), abundantly expressed in the serum and synovial fibroblasts of patients with rheumatoid arthritis and its level correlates with the disease activity and joint destruction. *Disease Activity Score-28* (DAS28) has been the most commonly used to measure the disease activity. This study aimed to determine the correlation between IL-6 level and DAS28 score in rheumatoid arthritis patients.

Method: This was a cross-sectional study. Subjects who fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 criteria for the classification of arthritis rheumatoid were examined routine blood test, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti cyclic citrullinated peptide (anti-CCP) and IL-6. We obtained DAS28 score from the calculation using the number of joints with tenderness or swelling and the ESR.

Result: A total number of 43 subjects were tested using PearsonÕs correlation test, there was no correlation between IL-6 and DAS28 score ($r = 0.234$, $P = 0.131$).

Conclusion: There is no correlation between IL-6 and DAS28 score.

Keywords: rheumatoid arthritis, correlation, IL-6, DAS28.

APLAR-0090

Seasonal changes in fracture incidence among 9987 Japanese patients with rheumatoid arthritis: a prospective observational cohort study

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Background: Although rheumatoid arthritis (RA) is a risk factor for fractures, limited data exist on seasonal changes in fracture incidence. We evaluated seasonal changes in fracture incidence among Japanese RA patients using the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort study.

Methods: The IORRA is a prospective observational cohort study of Japanese RA patients at the Institute of Rheumatology, Tokyo Women's Medical University. A total of 9987 RA patients (82% women; mean age, 56 years) were enrolled in the IORRA cohort study from 2000 to 2010. All participants self-reported occurrence of fracture within the previous 6 months, the site and cause of fracture, and the season in which the fracture occurred (spring/summer, autumn/winter). Statistical analysis was performed using the chi-square test with a 95% confidence interval (CI).

Results: During a mean (SD) duration of 5.2 (3.3) years, 2323 fractures (1098 fractures in spring/summer and 1225 fractures in autumn/winter) were reported in 98 488 self-reports (49 588 self-reports in spring/summer and 48 900 self-reports in autumn/winter). More than 100 clinical fractures were reported in the vertebrae, ribs, shoulder, wrist, hand, hip, ankle, and foot. Overall fracture incidence was significantly higher in autumn/winter than in spring/summer ($P = 0.003$; odds ratio [OR], 1.13; 95% CI, 1.04*1.23); however, only clinical vertebral fracture showed a significant seasonal difference ($P = 0.04$; OR, 1.19; 95% CI, 1.01*1.41). Among clinical vertebral fractures, this seasonal change was only seen in fractures caused by spontaneous events ($P = 0.01$; OR, 1.3; 95% CI, 1.06*1.60) and not in those caused by falls ($P = 0.93$; OR, 1.01; 95% CI, 0.73*1.41).

Conclusions: Overall fracture incidence was significantly higher in autumn/winter. Incidence of clinical vertebral fractures caused by spontaneous events was significantly higher in autumn/winter. Our findings suggest that RA patients should be careful of fractures especially in autumn/winter.

APLAR-0092

Why dont rheumatoid arthritis patients continue to receive regular outpatient treatment?

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Background and Objective: Currently, therapies for rheumatoid arthritis (RA) frequently improve clinical symptom with disease-modifying antirheumatic drugs by induction of OTreat to Target (T2T)O and OTight control (TC)O concept. However some patients do not continue to receive regular outpatient clinic. The aim of the present study was to investigate why they leave clinics.

Method: Ninety RA patients (12 males and 78 females; mean age 55.6 ± 12.7 years, mean disease duration 3.75 ± 1.22 years) were included. They were first seen between 2008 and 2012 at our outpatient clinics. We assessed DAS28 score, HAQDI and satisfaction with current health care, and compared clinical results between attending patients (AP) and non-attending patients (nAP). Moreover we questioned non-attending patients why they leave rheumatoid outpatient clinic.

Result: Nine patients quitted to receive regular outpatient clinic. Among them, four patients (low disease activity (LDA) in two patients, moderate disease activity (MDA) in two patients) hoped to see internal medicine doctor, three patients (all remission) stopped to come outpatient clinic since their rheumatologic symptoms were relieved, and two patients moved (LDA in one patient, remission in one patient). There were no significant changes of background and satisfaction for rheumatoid care between AP and nAP. DAS28 score and HAQDI of nAP were better than AP.

Conclusion: Ninety percent of our patients could continue to receive regular treatment in our rheumatoid clinics. To explain the concepts of OT2TO and OTCO to RA patients helps them understood how important to receive regular outpatient treatment. It still is necessary to explain the importance of maintaining the desired treatment target for RA patients in remission or LDA.

APLAR-0122

Changes in bone mineral density in patients with recent-onset rheumatoid arthritis

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Objectives: Generalized bone loss and an increased risk of fractures are regarded as complications in rheumatoid arthritis (RA). Variable clinical factors, inflammatory activity, and treatment regimens may contribute to the development of bone loss. We evaluated the association between the baseline disease activity and the changes in bone mineral density (BMD) after 1 year of treatment in a cohort of patients with recently diagnosed active RA.

Methods: A total of 106 patients with recent onset RA from ASERA cohort were included in this study. Data on patientÕs demographic factors, disease activity score in 28 joints (DAS28), and anti-rheumatic drugs were obtained. Baseline and 1 year of follow up BMD in proximal femur sites (i.e., the total femur, femur neck, and trochanter) and lumbar spine were measured with dual energy X-ray absorptiometry.

Results: The mean age of women and men was 50 ± 11 years and 59 ± 7 years, respectively and 54 patients in 92 women were postmenopausal status. The mean baseline DAS28 was 5.4 ± 1.2 (range; 2.6–8.6) and 30 (28.3%) patients were diagnosed as osteoporosis at baseline. After 1 year of treatment, the mean annualized rates of bone loss in the total femur, femur neck, trochanter, and L-spine were -1.41%/year, -1.31%/year, -2.07%/year, and -0.78%/year, respectively. Age, smoking, menopause, and high DAS28 were associated with prominent BMD loss in femur neck. Higher cumulative dose of corticosteroids was associated with significant bone loss in the spine and femur. The use of bisphosphonate had no significant protected effect against BMD loss in one year of treatment.

Conclusions: High baseline disease activity and increased dose of steroids are significantly associated with accelerated BMD loss in patients with active RA. Suppression of inflammation at the initial treatment might reduce the bone loss and limited use of steroids can be essential for bone preservation.

APLAR-0125

Incidence of hepatitis B virus reactivation in patients with rheumatoid arthritis during treatment with biologics

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Objective: To examine the incidence of hepatitis B virus (HBV) reactivation in patients with rheumatoid arthritis (RA) with evidence of past HBV infection during treatment with biologics.

Methods: Retrospective observational study. All the patients with RA who were treated with biologics from June 2007 to December 2012 were tested for HBV surface antigen (HBsAg), antibody against HBsAg (anti-HBs) and antibody against HBV core antigen (anti-HBc). In patients with negative for HBsAg and positive for anti-HBs and/or anti-HBc, the results of liver function tests and HBV-DNA level were retrieved from the clinical charts. HBsAg, anti-HBs and anti-HBc were examined using chemiluminescent immunoassay, and the level of HBV-DNA was measured by real-time PCR.

Results: Two hundred and forty-seven patients received biologics, and anti-HBs and/or anti-HBc was positive in 61 patients (24.7%, 10 men and 51 women). Thirty-eight patients were positive for both anti-HBs and anti-HBc. Twelve were anti-HBs negative/anti-HBc positive. Eleven were anti-HBs positive/anti-HBc negative. HBV-DNA was detected positive in only four patients (6.6%): one in etanercept, one in infliximab, and two in tocilizumab, although the levels were below the quantitative detection limit (<2.1 log copies/mL) in all cases. In one patient on tocilizumab, the DNA levels wandered between positive and negative ranges for 4 months. In another case on tocilizumab, the DNA became negative 4 months after the initiation of tocilizumab. Liver function tests were within normal ranges in all examinations, and all the patients continued treatment with biologics. HBV-DNA became negative eventually in all cases without anti-viral treatment.

Conclusions: HBV reactivation was observed in 6.6% of RA patients with past HBV infection during treatment with biologics. However, HBV-DNA levels were too low to be detected quantitatively and liver function tests were normal throughout. Biologics may be used safely in RA patients with the evidence of past HBV infection.

APLAR-0142

Elevated plasma chemerin levels are correlated with disease activity rather than obesity in rheumatoid arthritis

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Objectives: Chemerin is an adipokine that is linked to adipogenesis and chemotaxis of the innate immune system. It has been reported that higher level of chemerin was detected in various chronic inflammatory diseases. Recent studies have showed its expression is increased in the synovium of patients with rheumatoid arthritis (RA), and the chemerin may play an important role in the pathogenesis of RA. However, the association between plasma chemerin level and disease activity in RA patients remains unclear. This study aims to determine whether plasma chemerin level is elevated in patient with RA and its correlation with disease activity and other parameters.

Methods: This study includes 71 RA patients and 42 age- and sex- matched healthy controls. We assessed the clinical characteristics and laboratory parameters including body mass index (BMI), erythrocyte sedimentation rate, C-reactive protein, and disease activity score 28 (DAS28). The plasma levels of chemerin and tumor necrosis factor (TNF)-α were determined using enzyme-linked immunosorbent assay (ELISA).

Results: Plasma chemerin level was significantly elevated in patients with RA than healthy control (9.074 ± 13.513 pg/mL versus 0.370 ± 0.219 pg/mL, $P < 0.001$). In RA patients, the adjusted plasma chemerin level according to BMI was correlated with DAS28($\gamma = 0.340$, $P = 0.004$), but not with plasma TNF-α level. The adjusted plasma chemerin level of active disease group patients (DAS28 ≥ 2.6) was significantly higher than that of remission group patients (DAS28 < 2.6) (0.591 ± 0.879 pg/mL versus 0.220 ± 0.154 pg/mL, $P = 0.015$).

Conclusion: Patients with RA showed higher plasma chemerin levels than those of healthy controls. The adjusted plasma chemerin level according to BMI was well correlated with RA disease activity. These findings suggest that plasma chemerin could play a role in the inflammatory process of RA, and that it may be a useful disease activity marker in RA.

APLAR-0175

The socio-demographic and clinical profile of rheumatoid arthritis patients and its correlation with the disease activity score

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Objective: To determine the socio-demographic and clinical characteristics associated with the disease activity of rheumatoid arthritis (RA) through the disease activity score (DAS-28).

Design: This single-center, cross-sectional analysis examined the characteristics of RA patients.

Setting: The study was conducted at the Makati Medical Center, a tertiary hospital in Metro Manila, Philippines.

Patients: One hundred adult subjects, aged 18–80 years old, through review of clinical charts were selected from the clinics of two Rheumatologists from January 2010 to July 2012.

Results: The mean age of the 100 RA patients was 53.80 years with 7.52 years mean disease duration. Seventy percent of RA patients had low to moderate DAS-28 score (≤3.2 to ≤5.1). Methotrexate and Tocilizumab were the most commonly used modality of treatment in both groups. Overall, no significant correlation was found between the socio-demographic and clinical profile of the selected RA patients with the DAS-28 score. However, in multiple logistic regression analysis adjusted for age, sex and RA disease history, it was found that the RA patients with heart disease (odds ratio (OR) 9.02; 95% confidence interval (CI) 0.41–200.6), hypertension (OR 2.04; 95% CI 0.51–8.11), an abnormal ESR (OR 2.04; 95% CI 0.36–11.66) or an abnormal AST value (OR 4.12; 95% CI 0.18–92.17) had a higher likelihood of obtaining a high DAS-28 score. In contrast to previous literature, no significant association was found between the DAS-28 score and the treatment modality using Chi-square test. Twenty-four percent of RA patients were on biological therapy of whom had a significant difference ($P < 0.002$) between the DAS-28 scores determined at the onset of and during treatment.

Conclusion: The presence of heart disease, hypertension, an abnormal ESR or AST value is a significant predictor in the classification of a high DAS-28 score. A significant difference is seen between the DAS-28 score measured at the onset of and during treatment with biological therapy.

APLAR-0312

Correlation between anti cyclic citrullinated peptides (anti-CCP) with disease activity score-28 (DAS28) in rheumatoid arthritis patients

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Background and Aim: Antibodies to cyclic citrullinated peptides (anti-CCP) have been described in patients with rheumatoid arthritis (RA) and these are the most specific markers of the disease. In this study, we aimed to investigate the relation of the anti-CCP antibodies with disease activity score 28 (DAS28) in a cross sectional study.

Method: A total of 43 RA patients who fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 criteria were included in this study. They were examined routine blood test, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and anti cyclic citrullinated peptide (anti-CCP) and we calculated the DAS28 score using the number of joints with tenderness or swelling and the ESR.

Results: There is a significant correlation between ESR and DAS28 ($P = 0.011$, $r = 0.385$) but no correlation between anti-CCP and DAS28 ($P = 0.965$, $r = -0.007$).

Conclusion: There is no correlation between anti-CCP and DAS28 score.

APLAR-0370

Relationship between change in rheumatoid factor and affected joints in patients with rheumatoid arthritis from the viewpoint of regional assessment

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Background: Rheumatoid factor (RF) is the poor prognosis factor of rheumatoid arthritis (RA). However, the relationship between RF titers and affected joints remains unclear.

Objectives: We examine the relationship between RF change and affected joints from the viewpoint of the joint region.

Methods: Methotrexate-treated patients with RA, excluding who had under the measurable level (<10 IU/mL) of RF, were classified into three groups according to change in RF titers over a period of one to two months: declined (n = 129), no change (n = 18) and elevated (n = 147). Joint indices were calculated as affected joint counts divided by the number of evaluable joints in four joint regions (upper/large, upper/small, lower/large and lower/small) as described[1].

Results: One hundred twenty-two patients with high titer (≥100 IU/mL) of RF had higher DAS28 than 172 patients with low titer (<100 IU/mL) of RF (3.2 ± 1.3 versus 2.5 ± 1.1, $P < 0.001$). Only upper/small region significantly correlated with RF levels (table 1). There was no difference of DAS28 among the three groups classified according to change in RF titers. The declined RF group had higher joint indices in lower/large region (table 2).

Conclusions: Patients with a high titer of RF had high disease activity and joint indices, especially in the upper/small region compared to those with a low titer of RF. We identified a relationship between a decrease in RF and affected joints in the lower/large region.

References: 1. Nishiyama S. et al.: Proposing a method of regional assessment and a novel outcome measure in rheumatoid arthritis. Rheumatol Int 2012:32:2569–71.

Table 1. Correlation between RF levels and joint indices.

	Single regression analysis		Multiple regression analysis		
	r	P	β	95%CI	P
Upper/large	0.08	ns	21.6	−177.7 to 220.9	ns
Upper/small	0.17	<0.0001	314.9	101.5 to 528.3	<0.01
Lower/large	0.06	ns	−41.2	−213.1 to 130.8	ns
Lower/small	0.06	ns	0.8	−119.2 to 120.7	ns

Table 2. Comparison of joint indices between declined RF group and elevated RF group.

	Declined RF group	Elevated RF group	P
Upper/large	0.18 (0.02)	0.15 (0.02)	ns
Upper/small	0.15 (0.02)	0.11 (0.02)	ns
Lower/large	0.25 (0.03)	0.15 (0.02)	<0.01
Lower/small	0.26 (0.04)	0.19 (0.03)	ns

Data was shown as mean (SE).

APLAR-0372

The use of dexilant (dexlansoprazole) in the treatment of hyperacidity associated GI problems in rheumatic conditions

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Purpose: Asians have an increased incidence of Helicobacter Pylorii (Hp) infection compared to Caucasians (up to 50% higher in some series). Hyperacidity problems associated with rheumatic diseases are potentially very troublesome to treat. Many of the medications (NSAIDs, Immune Suppressive Drugs, Corticosteroids, Biologics) used in rheumatology are quite toxic to the GI tract. Dexilant D-R, approved by FDA, for the treatment of Erosive Esophagitis (EE), and symptomatic Non-Erosive Gastro-Esophageal Reflux Disease {N-E GERD}[Reflux Esophagitis (R. E.)], may be useful in treating patients who have significant hyperacidity symptoms while on these medications.

Method and Results: Twenty-five (12M/13F) patients with various rheumatic conditions and hyperacidity problems were recruited into the study. The rheumatic diagnoses included: SLE, RA, Ps. arthropathy, OA, lumbar spondylosis, allergic dermatitis and osteoporosis ± fracture compression and fractures. The hyperacidity problems ranged from: EE, N-E GERD (R.E.), GU, gastritis, DU, duodenitis: Hp +ve infection; gastritis with early metaplastic to dysplastic changes of gastric mucosa on biopsies. Patients were placed on Dexilant DR 60 mg BD/OD or 30 mg BD/OD depending on the onset and severity of their GI symptoms, gastroscopic findings, and ± gastric biopsies.

Discussion and Conclusions: Many of these patients had similar GI conditions treated with other PPIs in the past. This study compared their current treatment response to what occurred in the past. Patients were asked to select which treatment regiment they preferred, if they were given the luxury of choice. Most patients (M: 60% and F: 50%) preferred Dexilant, since it rendered them a quicker pain relief response and continued to maintain them in an extended symptom-free period.

Dexilant has a potential wider clinical use in the treatment of hyperacidity induced problems in rheumatology, and its use should not be just limited to the GI conditions approved by the FDA.

APLAR-0389

Hepcidin is not a reliable parameter reflecting inflammatory anemia in patients with rheumatoid arthritis

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Hepcidin, a key regulator of iron metabolism, has been investigated for its value of indentifying the nature of anemia pattern in patients with rheumatoid arthritis (RA). However, utility of hepcidin to discriminate the cause of anemia in RA patients is till controversial. We sought to address the relationship of hepcidin and inflammatory anemia through longitudinal follow up in RA patients receiving anti-rheumatoid medication. RA patients with anemia of chronic inflammation (ACI) were strictly selected who has normal or increased bone marrow iron store, increased C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Serum hepcidin, TNF-α, IL-6, CRP, ESR and hemoglobin (Hb) were longitudinally assed during the course of rheumatoid disease control. None of the patients received iron supplementation. Serum hepcidin level was higher in RA patients than healthy control. Contrary to other studies assed pro-hepcidin, our study revealed no significant difference of serum hepcidin level between RA with ACI and non-anemic RA patients (56.78 ± 38.26 ng/mL; $P = 0.780$). Serum hepcidin level was positively correlated with CRP ($r = 0.041$; $P = 0.014$) and ESR ($r = 0.436$; $P < 0.005$), but not with the Hb ($r = 0.145$; $P = 0.201$), IL-6 ($r = 0.41$;$P = 0.721$),TNF-α ($r = 0.043$, $P = 0.8$). Hb increment after anti-rheumatoid medication compared to baseline was not correlated with hepcidin alteration ($r = 0.105$, $P = 0.758$). We concluded that serum hepcidin is not a rational parameter to reflect inflammatory anemia in patients with RA.

APLAR-0395

to investigate the significance of serum tartrate resistant acid phosphatase 5b on joint destruction of patients with rheumatoid arthritis

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Objective: Rheumatoid arthritis (RA) is an autoimmune diseases with main clinical manifestations of chronic, symmetry arthritis and extra-articular changes,often occurs in middle-aged women. Serum tartrate resistant acid phosphatase 5b (TRACP-5b) can reflect the activity of osteoclasts and bone resorption as a bone reabsorption marker, which helps to learn the severity of osteoporosis, but the relationship between RA joint damage and serum TRACP-5b is unclear. This study is to investigate this relationship by detecting serum TRACP-5b levels in RA patients.

Methods: Eighty-two cases were enrolled from our department from March 2012 to January 2013, in which 25 male, 57 female. The level of serum TRACP-5b were detected with ELISA, and some patients received bone mineral density detection, we have measured the L1–L4 and upper femur including femoral neck and femoral trochanter. According to the T value the patients were divided into normal group (27) and osteoporosis group (55). DAS28 was calculated at the same time and hands X-ray results were collected as well. On the basis of X-ray RA patients were divided into normal and abnormal groups, while the abnormal group can be further divided into four subgroups–stage ?, ?, ? and ? groups.

Results: The concentration of serum TRACP-5b and DAS28 are positively correlated. In normal group of hands X-ray, the level of TRACP-5b is lower than that of abnormal group, the difference between the two groups is statistically significant ($P < 0.05$), but there were no significant difference among the four abnormal subgroups. The level of TRACP-5b in bone mass normal group is significantly lower than the osteoporosis group, the difference is statistically significant ($P < 0.05$).

Conclusions: There is an obviously positive correlation between the level of serum TRACP-5b and osteoporosis in RA, which may predict joint destruction of RA patients in some extent.

APLAR-0465

correlation of adiponectin serum level with atherosclerosis event in rheumatoid arthritis patients

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Background: Adiponectin are now considered important players in the etiopathogenesis of metabolic and inflammatory disorder including rheumatoid arthritis (RA). Recent data stress the role of adiponectin in inflammation and matrix degradation in RA pathology. Furthermore, it has been reported that adiponectin exerts an anti-atherosclerotic effect in non RA patients. Interestingly, several studies have reported increased level of adiponectin in RA patients, findings which appear paradoxical in light of the higher prevalence of atherosclerosis in RA. Thus, the effect of adiponectin on atherosclerosis has not been clarified sufficiently.

Methods: This was a cross sectional study. Subjects were fifty patients who fulfil Eular Criteria/ACR 2010 for RA from the Rheumatology clinic of Cipto Mangunkusumo Hospital/Faculty of Medicine University of Indonesia Jakarta. Data were collected by taking histories and physical examinations followed by blood test for adiponectin serum level and doppler ultrasonography which was used as atherosclerosis diagnostic tool.

Results: Forty-eight subjects were women and the rest were men. Age mean was 40.26 ± 9.6 years old and the level of adiponectin serum increase in 52% (mean is 9.06 ± 4.88 ng/mL). Atherosclerosis was diagnosed in 26% of this subject. Kolmogorov-Smirnov test showed there was no correlation between adiponectin serum level with atherosclerosis event in RA patients ($P = 0.881$).

Conclusion: From this study, we conclude that adiponectin serum level was increase in rheumatoid arthritis patients, but the increasing of the adiponectin serum level was not correlated with atherosclerosis event.

Clinical Rheumathology: T03 – Rheumatoid arthritis – anti-TNF ALPHA therapy

APLAR-0040

Clinical study on etanercept combined with Tripterygium wilfordii polyglycoside for treatment of eldly rheumatoid arthritis

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Objective: To evaluate the efficacy and safety of etanercept plus Tripterygium wilfordii polyglycoside (TWP) in *elderly* patients with active rheumatoid arthritis (RA).

Methods: Forty-six elderly patients with active RA were randomized to the treatment group (n = 24) and the control group (n = 22).The former was treated with ETN (injected with 50 mg/week subcutaneously, after 3 months, 25 mg/week) along with TWP (10 mg,tid); the latter was treated with ETN and MTX (10 mg/week). The whole course lasted 24 weeks, patients were assessed at weeks 0, 2, 6, 14 and 24.The change from baseline in pain,tender joint count,swollen joint count,health assessment (HAQ), patientOs global assessment,physicianOs global assessment, ESR and CRP were evaluated. The curative effect was statistically evaluated by the United States Institute of Rheumatology ACR 20, ACR50 and ACR70 improvement criteria. Meanwhile adverse events were recorded and evaluated.

Results: At week 2, the ACR20 was achieved in 58% of patients receiving ETN plus TWP,compared with 56% of patients receiving ETN plus MTX ($P > 0.05$).The results for other clinical signs and symptoms and quality of life showed no difference between these two groups ($P > 0.05$).At week 24,the ACR20 improvement was achieved in 80.2% of patients receiving ETN plus TWP,compared with 78% of patients receiving ETN plus MTX ($P > 0.05$).There was no significant difference between the two groups in adverse effects.

Conclusion: These two regimens of ETN plus TWP and ETN plus MTX all can improve the clinical signs and symptoms and quality of life, There was no difference between these two groups in efficacy,and they were well tolerated in the treatment of *elderly* patients with active RA.

APLAR-0102

Postmarketing study to estimate the safety profile of Infliximab in Chinese patients with ankylosing spondylitis or rheumatoid arthritis

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Objectives: A large-scale, single-armed postmarketing study was carried out to determine the safety profile of infliximab in Chinese patients with ankylosing spondylitis (AS) or rheumatoid arthritis (RA).

Methods: This study was conducted in 40 hospitals in China from 2009 to 2011. Infliximab was initiated in patients with confirmed AS or RA. All safety-related events were prospectively monitored during a 2 years study period. All case reports were collected every 4–8 weeks.

Results: A total of 1071 patients (AS: n = 644; RA: n = 427) were enrolled in the study to assess adverse events (AEs), serious adverse events (SAEs), infusion reactions (IRs), and serious infections (e.g. Tuberculosis, TB) during a 2-year study period. The mean ages of AS and RA patients were 28.89 ± 10.97 and 44.47 ± 14.14 years, respectively. Mean durations of AS and RA were 3.01 ± 4.35 and 5.96 ± 7.64 years, respectively. Seventy-six AS patients and 75 RA patients experienced AEs with incidence rates of 11.80% and 17.56%, respectively. Commonly reported AEs included rash, shiver, fever, upper respiratory tract infection, hepatic dysfunction, etc. SAEs were reported in 4 (0.62%) AS patients (two patients with IRs, one with fever and one with lymphatic TB), and in 5 (1.17%) RA patiens (four with IRs and one with pulmonary TB). During the study period, 24 AS patients experienced IRs with an incidence rate of 3.73%. Meanwhile, 27 RA patiens experienced IRs with an incidence rate of 6.33%. Serious IRs were reported in 2 (0.31%) AS patiens and 4 (0.94%) RA patients. Serious infections were noted as 2 cases of TB, in one AS and one RA patients. The incidence rate of TB was 0.18%, lower than those reported in previous studies.

Conclusions: This postmarketing study demonstrated that infliximab was well tolerated in Chinese patients with AS or RA.

APLAR-0217

Association of tuberculosis with anti-tumor necrosis factor therapy in Asia using a number needed to harm approach

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Introduction: Tuberculosis (TB) incidence appears to be lower with etanercept (ETN) than adalimumab (ADA) and infliximab (IFX). (1) Our study estimates TB risk for anti-TNF therapy candidates in Asia where TB is regionally endemic.

Methods: RATIO registry TB incidence ratios (IR) with ADA, ETA, and IFX were used. (1) Worldbank reported TB incidences (15 Asian countries, 2009) provided the absolute risks (AR). (2) Therapy related AR increases were determined: IR x country AR. Assessments included: numbers needed to harm (NNH = 1/AR) and number needed to treat (NNT) to avoid one TB event by ETN use instead of ADA or IFX. An IR sensitivity analysis was performed (95% CI).

Results: The RATIO reported IRs for all therapies was 12.2 (95% CI, 9.7–15.5)1. Individual IR: IFX, 18.6 (95% CI, 13.4–25.8); ADA, 29.3 (95% CI, 20.3–42.4) and ETN, 1.8 (95% CI 0.7–4.3). Results are shown in the Table. Sensitivity analysis indicated consistency.

Country	Population Incidence/ 100 000	Increase AR with anti-TNF use/100 000			NNH			NNT, ETN replacing ADA/IFX
		ADA	ETN	IFX	ADA	ETN	IFX	ADA/IFX
Cambodia	442	12951	796	8221	8	126	12	8/13
Philippines	280	8204	504	5208	12	198	19	13/21
Pakistan	231	6768	416	4297	15	241	23	16/16
Bangladesh	225	6593	405	4185	15	247	24	26/26
Vietnam	200	5860	360	3720	17	278	27	18/19
Indonesia	189	5538	340	3515	18	294	28	30/31
India	168	4922	302	3125	20	331	32	22/27
Thailand	137	4014	247	2548	25	406	39	35/43
China	96	2813	173	1786	36	579	56	38/40
Korea	90	2637	162	1674	38	617	60	62/66
Malaysia	83	2432	149	1544	41	669	65	44/44
Hong Kong	82	2402	148	1525	42	678	66	72/73
Taiwan	62	1817	112	1153	55	896	87	101/59
Singapore	36	1055	65	670	95	1543	149	165/96
Japan	21	615	38	391	163	2646	256	173/283

Conclusions: The risk of harm was higher with ADA and IFX than with ETN. The NNT with ETN instead of ADA/IFX to avoid one TB event was low and may be of clinical relevance given the burden of TB in Asia. Further studies are suggested.

APLAR-0222

Analysis of clinical and functional remissions in switching intensively to Adalimumab after stabilizing disease activity with Infliximab in severe RA

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Objective: Both IFX and ADA are anti-TNF α antibody agents. Bio-switching can be expected to maintain efficacy. Bio-switch to ADA maintenance therapy in RA patients with disease activity adequately reduced by IFX pre-treatment was analyzed.

Methods: Eight RA patients confirmed with decreased disease activity following a mean of five initial treatments with IFX, and switched to ADA were examined. Mean DAS28-ESR at the switch was 2.81. ADA was continued for ≥76 weeks, and the final mean progress observation period was 100 weeks. Statistically significant differences in the primary variables, DAS28-ESR, serum MMP-3 level and HAQ score were examined. Changes in the secondary variables, joint deterioration or bone erosion of several joints in the hands by X-ray, and compliance to steroids, were compared.

Results: Mean DAS28-ESR before the switch, at 12, 24, 52 and 76 weeks after the switch, and at the final progress observation was 5.81, 2.51, 2.25, 2.43, 2.11, 1.89, and 1.63, respectively. Remission was maintained from immediately after switching, and deep remission achieved from 52 weeks onwards. Mean serum MMP-3 level (μg/mL) was 592.9, 43.1, 38.8, 49.4, 44.3, 42.9, and 35.7, respectively. Thus, inhibition of synovial inflammation was maintained. HAQ

score at screening and the final progress observation was 1.89 to 0.16, showing superior improvement by the ADA treatment ($P < 0.01$). X-ray evaluation of several joints in the hands at a mean of 84 weeks revealed restoration of bone erosion and joint destruction in five patients, and inhibition of progression to bone erosion in 2. Mean steroid dose at screening was 3.8 mg/day, however, all patients could be weaned off steroids by the ADA treatment.

Conclusion: Bio-switching to ADA following good control of RA disease activity by IFX produced good results in the clinical, functional and structural evaluations including a high remission rate without recurrence of disease activity.

APLAR-0224

Impact of etanercept-methotrexate therapy on patient-reported outcomes in rheumatoid arthritis patients with up to 12 months of symptoms

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Introduction: Phase 1 of the PRIZE trial (3-phases) included evaluation of PROs in early moderate-severe rheumatoid arthritis (RA).

Methods: Methotrexate- (MTX) and biologic-na•ve patients (RA symptoms ≤12 months; DAS28 > 3.2) received open-label etanercept (ETN) 50 mg/MTX (10–25 mg) QW for 52 weeks. Corticosteroid boosts were administered to patients not achieving low disease activity at weeks 13 and 26. PROs were assessed (Table 1).

Results: Of 306 patients (70% female; mean age 50 years; mean baseline DAS28 6.0 and symptom onset 6.5 months), 222 (73%) completed Phase1. ETN50/MTX therapy resulted in significant, clinically meaningful improvements (CMI) in PROs: HAQ, EQ-5D, SF-36, and FACIT-Fatigue (Table; $P < 0.0001$). Similar improvements were observed in RA-WIS and WPAI:RA.

Conclusion: Combined ETN50/MTX therapy for 52 weeks resulted in significant CMI in physical function, quality of life, fatigue, and work productivity, consistent with findings for patients with more established disease.

Table 1. ETN50/MTX effects on PROs in early RA patients in PRIZE Phase 1 (N = 306).

Parameter (range)	Baseline Mean (SD)	Last observation (LOCF)[§] Mean (SD)	Δ From baseline[§] Mean (SD)
Health Assessment Questionnaire Disability Index (HAQ;0.-3)[¶]	1.3 (0.7)	0.5 (0.6)	−0.8* (0.7)
EuroQol-5 Dimensions (EQ-5D) Utility Score (0–1)/VAS (0–100)**	0.5 (0.3)/50.9 (22.6)	0.8 (0.3)/77.2 (24.1)	0.3* (0.3)/27.4* (28.1)
Short Form Physical/Mental Component (SF-36 PCS/MCS)	33.6 (8.0)/42.9 (10.9)	45.5 (9.7)/50.6 (9.3)	11.9* (9.6)/7.5* (10.6)
Functional Assessment of Chronic Illness Therapy (FACIT-Fatigue, 0–52)[††]	29.1 (12.6)	39.9 (11.4)	10.9* (12.2)
Rheumatoid Arthritis Work Instability Scale (RA-WIS)	13.5 (6.1)	4.8 (6.5)	−8.9* (6.6)
Work Productivity and Activity Impairment (WPAI:RA),% RA activity impairment[‡‡]	57.2 (24.3)	21.5 (25.5)	−36.4* (29.4)
	% Patients (95% CI), LOCF		
Normal HAQ (≤0.5)/CMI (Δ ≥0.22)	66.6[†] (60.9, 71.9)/80.2[‡] (75.2, 84.6)		
RA-WIS Low (0*9)/High (>17)	79.9[†] (74.2, 84.9)/7.7[†] (4.6, 11.9)		

*Paired *t*-test;[†]McNemar's test;[‡]Binomial test, all $P < 0.0001$ versus baseline;[§]observed cases;[¶]lower, less functional disability;**higher, better QoL; Δ ≥0.05, CMI;[††]higher, less fatigue, Δ ≥3.0, CMI;[‡‡]lower%, less impairment.

APLAR-0283

Fatigue and quality of life in the patients with as and RA: is there an effect of anti-tnf therapy

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Objective: Fatigue is a common symptom in many rheumatologic diseases such as ankylosing spondylitis (AS) and rheumatoid arthritis (RA). These diseases can also cause deterioration in the quality of life (QoL). Anti-TNF therapy seems to ameliorate fatigue more than other therapies. In the present study we aimed to determine fatigue and QoL in the patients with AS and RA and also to asssess the effect of anti-TNF therapy on fatigue and QoL.

Methods: Seventy five AS patients (M/F: 56/19, 38.46 ± 10.43 years), and 75 RA patients (M/F: 10/65, 46.54 ± 12.47 years) were enrolled in the study. Fatigue and QoL were evaluated with the Multidimensional Assessment of Fatigue (MAF) and Short Form 36 (SF-36), respectively.

Results: The MAF score was higher in the RA patients than in the AS patients ($P = 0.003$). Scores of physical functioning, physical role and mental health subscales of SF-36 were also significantly better in the patients with AS ($P < 0.05$). When the patients (n = 150) were divided into two groups according to anti-TNF therapy positivity, there was statistically significant difference between the goups regarding MAF score (0.001) and scores of almost all subscales of SF-36 ($P < 0.05$). The patients taking anti-TNF therapy (n = 79) showed better MAF score and SF-36 scores.

Conclusion: In the present study we determined that RA patients had worse fatigue and QoL scores than the AS patients. The patients receiving an anti-TNF therapy displayed decrease fatigue and increased QoL scores.

APLAR-0400

Safety of etanercept therapy in HBsAg carriers with rheumatoid arthritis: a prospective study

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Objectives: To evaluate the influence of etanercept on reactivation of hepatitis B virus (HBV) infection in HBsAg carriers with RA.

Methods: In this 52 weeks observation, HBsAg carriers with active RA (DAS28 > 5.1) despite failed combined treatment with MTX and other non-biological DMARD were enrolled. Patients must have normal liver function prior to study. All patients received therapy with etanercept (50 mg/w) and concomitant MTX (10–12.5 mg/w). Lamivudin were prescribed preventively for patients who had abnormal HBV load (>100 copy/mL) at baseline. Liver enzymes (AST/ALT) and HBV viral load were monitored every 4 weeks. Increased viral load and abnormal liver function were managed according to experts opinion.

Results: Twelve female patients were recruited. At baseline, four patients had abnormal viral load (group 1, with preventive lamivudin), and the other eight patients (group 2) had normal viral load. Two patients from group 2 discontinued etanercept at week 12 due to ineffectiveness. Reactivation of hepatitis B occurred in one patient from group 1, and another from group 2. The patient from group 1 underwent a mild increase of both ALT and AST (63 and 72 IU/L, respectively) at week 32. A elevated viral load (7.9e8 copies/ml, baseline 7.4e6) was also found. After prescription of Entecavir, AST/ALT and viral load decreased to normal range in 12 weeks. The patient from group 2 had mild elevated ALT/AST (66/61 IU/L, respectively) and increased HBV load (5.2e6) at week 20. After prescription of Lamivudin, ALT/AST and viral load decreased to normal range in 8 weeks. For the rest 10 patients, no significant elevated AST/ALT or increased viral load was found.

Conclusions: A aggressive Etanercept + MTX therapy may be a safe option for HBsAg carriers with DMARDs refractory RA. Prophylaxis strategy with more effective anti-viral drugs is recommended to reduce the risk of reactivation of infection.

Clinical Rheumathology: T04 – Rheumatoid arthritis – non-TNF alpha biological therapies

APLAR-0110

DICAM inhibits angiogenesis via suppression of AKT and p38 MAP kinase signaling

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Aims: Dual Ig domain Containing Adhesion Molecule (DICAM), a protein with homology to the junctional adhesion molecule family, has been demonstrated to interact with integrin αVβ3 that plays a critical role in angiogenesis. Here, we determined the role of DICAM during angiogenesis and the molecular mechanisms involved in the inhibition of angiogenesis.

Methods and Results: DICAM was expressed on the endothelial cells of large vessels to small capillaries. In human umbilical vein endothelial cells (HUVECs), DICAM was up-regulated by vascular endothelial growth factor (VEGF) through the MEK/ERK and PI3K/AKT pathways. Furthermore, the exogenous expression of DICAM in HUVECs suppressed angiogenesis *in vitro* Matrigel and *in vivo* plug assays, and conversely, DICAM knockdown enhanced angiogenesis. In addition, DICAM inhibited HUVEC migration and accelerated apoptosis via down-regulation of Bcl-2, but did not affect viability or proliferation of HUVEC. Mechanistically, the exogenous expression of DICAM suppressed VEGF-induced phosphorylarion of AKT and p38 MAP kinase. When integrin signaling was activated by vitronectin, a forced expression of DICAM attenuated integrin β3/FAK signaling and downstream AKT and p38 MAP kinase signaling in HUVECs.

Conclusion: Collectively, DICAM suppressed angiogenesis by attenuating AKT and p38 MAP kinase signaling, which suggests that DICAM may be a novel negative regulator of angiogenesis.

APLAR-0121

Blood B cell counts as predictor of early clinical response after rituximab in patients with rheumatoid arthritis

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Background: B cell depletion with rituximab is effective for reducing the symptoms and inhibiting the progression of joint damage in patients with rheumatoid arthritis (RA).

Objectives: We aimed to investigate the potential value of measurement of peripheral blood B cell counts after rituximab therapy in RA patients refractory to anti-tumor necrosis factor inhibitors.

Methods: A total of 27 active RA patients whom received more than 1 cycle (two 1-gram infusion) of rituximab were included in this study. Absolute B cell counts on day 1 and 15 before each rituximab infusion was measured by conventional flow cytometry. On day 15, peripheral B cell levels below 2.5×10^6 cells/L was defined as B cell depletion and the clinical response was analyzed between the two groups; depletion versus non-depletion. Clinical response at 18 weeks after 1st infusion of rituximab was measured by Disease Activity Score in 28 joints (DAS28) using the erythrocyte sedimentation rate.

Results: The mean age at rituximab treatment was 55 ± 13.8 (25–83) years and the baseline DAS28 was 6.6 ± 0.9 (4.4–8.1). B cells on day 15 was depleted in 17 (56.7%) patients with median value of B cell counts as 1.2×10^6 cells/L [range 0.0–2.5×10^6/L]). Patients in whom B cell depletion was not achieved showed persistently high DAS28 (4.7 ± 0.6 versus 3.3 ± 1.0 [$P = 0.007$]) by 18 weeks and significant short duration of B cell depletion time (4.0 ± 2.3 versus 8.2 ± 4.3, months [$P = 0.008$]) than those in depletions.

Conclusions: Data suggested that measurement of peripheral B cell counts on 15th day might provide clinical information on early response and non-depletion of B cells can be used as a predictive factor of poor response.

APLAR-0237

Abatacept (ABT) equivalent to anti-tumor necrosis factor a (TNFa) in terms of joint destruction inhibition: Multicenter study of 107 patients

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Objective: Evaluation of results of 52-week multicenter clinical study of ABT for RA.

Methods: One hundred and seven RA patients who received ABT at a facility participating in a study conducted by the Academy of Clinical Rheumatoid Arthritis Gunma Institute (ACAGI) for at least 52 weeks were included in the efficacy analysis. Efficacy was assessed based on the SDAI scores stratified by MTX treatment and prior treatment with biologics using the LOCF method. Structural analysis was performed at Week 52 in 49 patients who underwent joint radiography and the annual progression rate was assessed using the modified Total Sharp Score (mTSS).

Results: Mean SDAI scores decreased from 20.18 at Week 0 to 6.12 at Week 52 in biologics-naive patients (n = 37). Fourteen (37.8%) and 15 patients (40.05%) had remission and low disease activity, respectively. The mean SDAI scores decreased from 24.2 at Week 0 to 11.15 at Week 52 in patients who switched treatments (n = 70). Twelve (17.1%) and 30 patients (42.8%) had remission and low disease activity, respectively. The mean SDAI scores decreased from 21.44 at Week 0 to 9.13 at Week 52 in patients who received a combination of ABT and MTX (n = 63). The mean SDAI scores decreased from 24.78 at Week 0 to 9.82 at Week 52 in patients who received ABT only (n = 44). The retention rate at Week 52 was 68.8%. The annual progression rate at Week 52 was 0.1, showing a significant suppression of joint destruction compared to the estimated annual progression rate at baseline of 8.4. Structural remission (mTSS/year ≤0.5) was achieved in 83.7%.

Conclusion: Based on the clinical evaluation and structural analysis at Week 52, more significant effects and better retention can be expected in ABT-treated patients. ABT could be an effective option in RA treatment.

APLAR-0394

Radiographic progression in knee joints with residual local symptoms in rheumatoid arthritis patients receiving tocilizumab

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The effectiveness of tocilizumab in inhibiting the progression of joint damage with rheumatoid arthritis has been evaluated and favorably demonstrated using the total Sharp score. However, the effectiveness of the drug in inhibiting the progression of damage to the symptomatic weight-bearing joint has not been established. In the present study, we investigated the effect of tocilizumab in inhibiting the knee joint damage in patients who had symptoms of swelling or pain.

The subjects consisted of eight patients (14 joints) treated with tocilizumab and who had presented with symptoms in the knee joint. The mean age was 53.9 years, disease duration was 7.9 years, and clinical disease activity index (CDAI) was 26.6. The change in disease activity and X-ray image of the knee joints with time up to 2 years from the start of treatment were evaluated by CDAI and Larsen grade, respectively. The change in presence/absence of tenderness or swelling with time was also examined.

CDAI score improved with time, although progression of damage was observed in two knee joints. In patients who showed improvement in swelling at 3 months from the treatment and whose tenderness disappeared at 6 months from the treatment, inhibition effect of tocilizumab on the progression of damage to the knee joint was observed in all cases.

In our previous study, we reported that the risk factors that limit the effect of TNF-inhibitors on the progression of knee joint damage with symptoms were residual symptoms such as swelling or tenderness. In the present study, a similar tendency has been observed in tocilizumab, IL-6 inhibitor; thus, we consider that the early improvement of the local symptoms as well as the improvement of disease activity is the most important to prevent the progression of knee joint damages.

Clinical Rheumathology: T05 – Rheumatoid arthritis – non biologic treatment

APLAR-0103

the protective role of thalidomide in collagen-induced arthritis

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Objective: To evaluate preventive and therapeutic effects of thalidomide on collagen-induced arthritis (CIA) rats.

Methods: Wistar rats immunized with bovine type II collagen emulsified in adjuvant and treated with thalidomide (50 mg/kg), ibuprofen (27 mg/kg), saline by daily gavages feedings for 48 days. Score of arthritis recorded every day for each paws of animal. Interleukin17, interleukin 6, and interleukin 8 were measured in serums with ELISA. Test the expressions of IL-17 mRNA of CIA rats by using the method of real-time PCR. Have an X-ray to the anklebones of CIA rats in each group and evaluate the injuries of CIA to cartilage and bone.

Result: Treatment with thalidomide resulted in significant delay in time to onset of arthritis as well as significantly ibuprofen incidence, clinical arthritis severity score, histopathological arthritis severity score, X-ray findings were statistical difference compared with CIA group ($P < 0.05$). Administration of thalidomide significantly suppressed the progression of collagen II-induced arthritis and inhibited the production of interleukin17, interleukin 6, and interleukin 8. The expression of IL-17 mRNA in ibuprofen group and thalidomide group were much lower than that in CIA group ($P < 0.05$).

Conclusion: Thalidomide appeared to be a potent immunomodulatory inhibitor of collagen II-induced arthritis in rats. It could delay onset of CIA and reduced cartilage erosion and synovitis inflammation. Therefore, it may be a useful protein in the prevention and treatment of arthritis patient.

APLAR-0157

Tolerability and efficacy of low-dose prednisone chronotherapy for rheumatoid arthritis in Asian patients: a single-centre retrospective study in Singapore

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To evaluate the tolerability and efficacy of modified-release (MR) prednisone chronotherapy, and determine the demographic profile and treatment patterns among rheumatoid arthritis (RA) patients who were prescribed MR prednisone on a named patient basis in a clinic in Singapore.

A retrospective study of patients diagnosed with RA and treated with MR prednisone was conducted in a specialist clinic in Singapore. The relevant data were collected from medical records until the cut-off date of 31 December 2012. Safety assessment was based on abnormalities in laboratory findings. Changes in joint pain or morning stiffness were based on patientsO and investigatorOs assessment.

Of the 38 patients included, the majority were Chinese (57.9%) and over one-third were Indians (34.2%). There was a preponderance of female (92.1%), mean age was 52.8 years, and median disease duration since diagnosis was 1.3 (0.04*8.2) years. Patients received a mean dose of 5.2 mg of MR prednisone per day for a median duration of 15.6 (0.52*52) weeks. Prior to the initiation of treatment with MR prednisone, there was high use of disease-modifying anti-rheumatic drugs (DMARDs) (78.9%), glucocorticoids (78.9%), and non-steroidal anti-inflammatory drugs (NSAIDs) (68.4%). After initiation of treatment with MR prednisone, use of DMARDs (73.7%) and other glucocorticoids (76.3%) remained high while use of NSAIDs decreased substantially (39.5%). The dosage of prescribed concomitant RA medications remained largely the same before and after treatment with MR prednisone except for celecoxib, which was doubled. A small number of patients experienced fasting hyperglycaemia (n = 4), increased triglycerides (n = 2), and increased total cholesterol (n = 2) during treatment with MR prednisone. The majority reported improvement or recovery from morning stiffness (94.7%) or joint pain (70.0*100.0%) after treatment with MR prednisone.

Our clinical experience extends the evidence from clinical trials that MR prednisone chronotherapy is effective and generally well-tolerated in Asian patients with RA.

APLAR-0164

PROFILE study – Leflunomide treatment in Romanian patients with rheumatoid arthritis

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Objectives: Investigate patient characteristics and factors leading to leflunomide therapy initiation in rheumatoid arthritis (RA), routine follow-up measures used in Romania and treatment changes during the first six-months of treatment with leflunomide.

Methods: An open, non-randomized, multicentric, retrospective, non-interventional study was performed. Patients with RA enrolled were initiated and maintained on leflunomide treatment within the last 6 months. Clinical and laboratory parameters were obtained at baseline. Follow-up measures used in current practice in the first six months of leflunomide use were assessed (number of exams performed for: swollen and painful joints, organ involvements, rheumatoid nodes, ESR, CRP, RF, hand and foot Rx, joint ultrasound). Background treatment was registered.

Results: Three thousand, five hundred and forty-seven patients (15.2% male, 84.8% female) with mean age 57.58 years and mean duration of disease 5.9 years were included. At the time of leflunomide initiation mean number of swollen joints was 11.37, mean number of painful joints 14.25; 30.4% patients had rheumatoid nodes, ESR mean value was 48.67 mm/h, RF was positive in 82% patients, CRP was present in 92.5%. ACPA performed in 1367 patients (38.5%) were present in 1222 (89.4%). On Rx erosions were detected in 77.1% and space narrowing in 86.4% patients. Frequent reasons for changing previous background treatment to leflunomide were efficacy (45.3% patients) and tolerability (15.9% patients).

Mean number of clinical/laboratory exams performed during leflunomide treatment has significantly decreased ($P < 0.05$).

No major background treatment changes occurred during the 6 months of leflunomide therapy; mean number of patients requiring anti-inflammatory treatment has significantly decreased ($P < 0.05$): NSAIDs from 56.9% to 51.8% and corticosteroids from 22.1% to 12.8% patients.

Conclusion: Disease activity, extent of articular and extraarticular damage were factors related to physicianOs decision to initiate leflunomide in RA patients in current daily practice. Follow up measures recommended during leflunomide treatment have significantly decreased during 6 months therapy.

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APLAR-0165

Methotrexate-associated non alcoholic fatty liver disease in a Singaporean cohort of rheumatoid arthritis patients

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Background: The second most common adverse event with methotrexate (MTX) therapy is transaminits which may affect up to 20.2% of patients. The aim of this study was to determine the prevalence and risk factors of MTX-associated NAFLD in a Singaporean cohort of rheumatoid arthritis (RA) patients.

Methods: We performed a retrospective review of the computerised medical records of patients on the Tan Tock Seng Hospital (TTSH) RA Registry who had ever received MTX. Patients who developed ultrasound proven NAFLD while on MTX therapy were identified. The demographic and clinical characteristics of the above patients (the cases) were compiled and compared with age and gender-matched controls who were RA patients on long standing MTX therapy without any episode of transaminitis. The ratio of cases to controls was 1: 2. We excluded patients with known alcoholism, chronic hepatitis B, chronic hepatitis C, autoimmune hepatitis and underlying chronic liver disease.

Results: In a total of 978 patients who had received MTX, the prevalence of MTX-associated NAFLD was 4.7% (46 patients). Among the cases, MTX was discontinued in 39.1%. Compared to the controls, the cases had significantly higher mean cumulative dose of MTX (4026.8 ± 2251.8 mg versus 10037.1 ± 9939.1 mg, $P \leq 0.05$), weekly dose of MTX (11.3 ± 4.8 mg versus 13.1 ± 4.4 weekly, $P = 0.033$) and fasting blood glucose ($P = 0.029$). Body mass index, lipid profile, duration of MTX therapy and concomitant use of leflunomide, sulfasalazine and hydroxychloroquine did not differ significantly between both the groups. None of the variables showed significant correlation with the severity of the transaminitis (level of alanine transaminase) on linear regression analysis.

Conclusion: Although the cumulative and weekly doses of MTX were associated with NAFLD, there was no significant correlation between the above variables and the severity of the transaminitis.

APLAR-0218

Clinical, functional and radiographic comparison of tofacitinib monotherapy versus methotrexate in methotrexate-naˇve patients with rheumatoid arthritis

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Background: Tofacitinib is a novel, oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). This Phase 3, double-blind, 24-month study (ORAL Start, NCT01039688) assessed efficacy and safety of tofacitinib monotherapy versus methotrexate in methotrexate-na•ve patients with active RA. We report 12-month interim analyses.

Methods: Patients randomized 2:2:1 to tofacitinib 5 mg twice daily (BID); tofacitinib 10 mg BID; methotrexate (titrated from 10 to 20 mg/week). Co-primary endpoints (Month 6): ACR70 response, mean change from baseline in van der Heijde modified Total Sharp Score (mTSS). Adverse events (AEs) assessed (Months 0–12).

Results: Nine hundred and fifty-two patients were randomized. At Month 6, improvements measured as rates of ACR20/50/70, DAS-defined remission (DAS28-4[ESR]<2.6), mean change from baseline in HAQ-DI, and mean change from baseline in mTSS and rates of no radiographic progression, were significantly superior with tofacitinib versus methotrexate (Table 1).

Table summarizes AEs, serious AEs and discontinuations (0–12 months). Herpes Zoster occurred in 2.2, 2.5 and 1.1% of tofacitinib 5 mg BID, 10 mg BID, and methotrexate patients, respectively. One patient had bone tuberculosis (10 mg BID); one had cytomegalovirus infection (methotrexate); two tofacitinib patients died (occurred after Month 12).

Conclusion: Tofacitinib improved RA signs, symptoms, physical functioning and inhibited progression of structural damage versus methotrexate, with a similar safety profile as reported previously.

	Tofacitinib 5 mg BID (n = 371)	Tofacitinib 10 mg BID (n = 395)	Methotrexate (n = 186)
ACR20/50/70[†] (%)[a,b]	71.0***/46.6***/ 25.5***	75.8***/56.2***/ 37.7***	50.5/27.2/ 12.0
DAS28-4(ESR)<2.6 (%)[a,b]	14.6*	21.6***	7.6
HAQ-DI LS mean change from baseline[b,c]	-0.82***	-0.93***	-0.57
mTSS LS mean change from baseline[†b,d]	0.18*	0.04***	0.84
Patients (%) with no radiographic progression[b,d,e]	83.5*	89.7***	70.5
AEs (%)[f]	70.1	74.4	69.9
Serious AEs (%)[f]	6.5	6.1	7.0
Discontinuations due to AEs (%)[f]	6.5	7.8	9.1

*$P < 0.05$; ***$P < 0.0001$ versus methotrexate; [†]Co-primary endpoint; [a]Non-responder imputation; [b]Month 6; [c]Longitudinal model; [d]Linear extrapolation; [e]mTSS change from baseline ≤0.5; [f]Months 0*12.

APLAR-0265

MRP8 promotes Th17 differentiation via upregulation of IL-6 production by fibroblast-like synoviocytes in rheumatoid arthritis

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Background: Myeloid-related protein (MRP)8/MRP14 is an endogenous Toll-like receptor (TLR)4 ligand and is abundant in synovial fluid (SF) of rheumatoid arthritis (RA) patients. IL-17-producing Th17 cells play a crucial role in RA pathogenesis and IL-6 is the key factor promoting Th17 differentiation. We investigated whether the level of MRP8/MRP14 is positively associated with IL-6 and IL-17 levels in RA SF.

Methods: The expression of MRP8/MRP14, IL-6 and IL-17 in SF and synovial tissue from patients with RA and osteoarthritis (OA) was demonstrated. Human peripheral blood mononuclear cells (PBMC) and $CD4^+$T cells from healthy donor and RA fibroblast-like synoviocytes (FLS) were cultured in presence of MRP8 or MRP14 to investigate the effect on induction of inflammatory cytokines. The differentiation of Th17 cells was determined using the coculture system consisting of $CD4^+$T cells and RA FLS. To explore the downstream signaling pathway associated with MRP8-stimulated increase of IL-6, we used anti-TLR4 antibody and inhibitors of several signaling molecules.

Results: We found that MRP8/MRP14 level had a significant correlation with IL-6 and IL-17 levels in RA SF. We also observed that MRP8 induced IL-17 production by PBMC but MRP14 did not. Upon stimulation with MRP8, IL-6 production was enhanced by RA FLS and was further elevated by coculturing RA FLS with activated $CD4^+$T cells. Moreover, we demonstrated that MRP8-activated IL-6 production by RA FLS promoted differentiation of Th17 cells by the coculture system. Additionally, IL-6 blockade attenuated Th17 polarization of $CD4^+$T cells in the cocultures. Inhibitor studies revealed that MRP8 increased IL-6 production in RA FLS via TLR4/PI3K/NF-κB and MAPK signaling pathways.

Conclusions: Our results show that MRP8 plays a crucial role in stimulating IL-6 expression by RA FLS and subsequently promotes Th17 differentiation in RA, suggesting that neutralizing MRP8 level in RA synovium may be an effective therapeutic strategy in RA treatment.

APLAR-0325

Results of a blinded Phase2b dose-ranging study of baricitinib in combination with traditional disease-modifying antirheumatic drugs in patients with rheumatoid arthritis

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Background: Baricitinib (formerly LY3009104/INCB028050; oral JAK1/JAK2 signaling inhibitor), was evaluated in a 24 week blinded phase 2b study in patients (pts) with moderate to severe RA with inadequate methotrexate (MTX) response. Primary endpoint was assessed after 12 weeks of treatment. Safety and efficacy were also evaluated at 24 weeks and in a 52 week open-label extension.

Methods: Pts (n = 301) with active RA (definition includes ≥8 swollen and eight tender joints based on the 66/68 joint assessment) on stable MTX were randomized to receive 12 weeks of placebo or 1 of 4 once-daily baricitinib doses (1, 2, 4, or 8 mg). Pts assigned to 2, 4, or 8 mg continued same-dose treatment for an additional 12 weeks.

Results: After 12 weeks of baricitinib treatment, significant differences versus placebo ($P < 0.05$) were observed in the proportion of patients achieving ACR20, ACR50 and ACR70, DAS28CRP<2.6, and CDAI≤2.8. Over 12 weeks in the placebo and combined baricitinib groups, there were similar incidence rates of TEAEs (44% versus 41%), infections (12% versus 14%) and SAEs (2% versus 2%), respectively. Over 24 weeks in the combined 2, 4 and 8 mg groups, the rate of TEAEs was 64% (36% mild, 23% moderate, 5% severe), the infection rate was 27% (16% mild, 9% moderate, 1% severe), and the SAE rate was 5%. No opportunistic infections or deaths occurred. Decreased hemoglobin, small increases in serum creatinine, and increased LDL and HDL were observed.

Conclusion: Significant improvements in signs and symptoms of RA with baricitinib treatment versus placebo were observed over 12 weeks. These responses were maintained or improved over an additional 12 weeks of blinded treatment with 2, 4, and 8 mg. In addition, safety signals observed over 12, 24, and 52 weeks were consistent with previously conducted studies of baricitinib.

APLAR-0334

Capsaicine systemic therapy reduces pain and inflammation in adjuvant-induced arthritis in rats

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Freund adjuvant-induced arthritis in rats is an accepted model for understanding the pathogeny of rhematoid arthritis and also for testing new therapy.

Capsaicin (chili pepper extract) is used topical to manage pain in rheumatic disorders.

The present study explored the effects of a chili pepper extract (Capsaicin) on pain and inflammation in a rat model of adjuvant-induced arthritis (AIA).

Arthritis was induced in white Whistar rats by subcutaneous injections with Freund adjuvant in the left hind paw. Four groups were compared-a non-arthritis control group and three AIA groups treated orally with either saline solution, or non-steroidal anti-inflammatory drug (NSAID) Indomethacin 2 mg/kg/day, or with chili pepper extract 2 mg/kg/day.

The change in paw volume (as an indicator of edema) was measured by a plethysmography and nociception was evaluated by applying mechanical pressure on the hind paw in rats with AIA before and after 21 days of therapy with saline solution, or Indomethacin, or chili pepper extract. The data where compared between AIA rats and with the controle group (non-arthritic).

A large increase was observed in the hind paw volume of untreated (saline solution treated) rats compared with non-arthritic rats. Both Indomethacin and Capsaicin treatments significantly decreased the edema and mechanicaly-induced pain in the Freund adjuvant injected paw compared with saline solution treated rats. In our study the efficiency of Capsaicin in reducing both pain and edema was similar to that of Indomethacin.

The study confirms the analgesic and anti-inflammatory effect of Capsaicin in systemic administration. It was also well tolerated.

Capsaicin administered via oral capsules might be an effective therapy for different arthritic conditions.

Further studies are needed on animal models of arthritis and also in humans, but our results on AIA rats sugest that it might be as effective as NSAID but with less toxicity.

This is an important aspect regarding adverse events of NSAID.

APLAR-0387

Evaluating the efficacy of and indications for methotrexate at dosages greater than 10 mg/week in patients with rheumatoid arthritis

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Background: Since February 2011, the maximum approved dosage of methotrexate (MTX) for treatment of rheumatoid arthritis is 16 mg/week in Japan. However, the overall effects of high-dose MTX therapy do not necessarily continue to increase as the dosage is increased.

Object: This study was conducted to investigate the efficacy of and indications for MTX therapy at dosages greater than 10 mg/week in patients with rheumatoid arthritis.

Methods: A total of 30 patients receiving MTX therapy at dosages greater than 10 mg/week for more than 12 weeks were enrolled in the study. We evaluated disease activity scores in 28 joints based on C-reactive protein (DAS28-CRP) values, CRP levels, swollen joint counts (SJC), and tender joint counts (TJC).

Results: The mean CRP levels and DAS28-CRP values at 12 × 20 weeks were significantly lower than initial values when MTX was increased from 8 mg/week. There were no significant differences in the mean values of SJC and TJC. According to clinical responses based on DAS28-CRP values, 17 cases presented no response, and 13 cases presented good or moderate responses. When MTX was increased from 8 mg/week, the mean DAS28-CRP values and CRP levels in the no response group were significantly lower compared with that of the good and/or moderate groups.

Conclusions: This study demonstrated the efficacy of MTX at a dosage >10 mg/week in Japanese patients with rheumatoid arthritis. However, it is possible that improvement of disease activity might not occur in cases with low CRP levels even when treated with MTX at a dosage >10 mg/week.

APLAR-0462

Pain Killers, non-steroidal anti-inflammatory drugs decreases antibody production, acting as an immunomodulators

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Background: Cox-2 selective NSAIDS are commonly prescribed to control inflammation. Little is known whether or not these drugs influence human B lymphocytes and their ability to produce antibodies. Activated B cells have shown high expression of Cox-2 and their inhibitors profoundly inhibit B cells to produce IgG and IgM *in vitro*. This study was conducted to observe the *in vivo* effect of Cox 2 inhibition on immune response.

Material and Methods: Albino Rabbits of either sex were divided into five groups of six animals each were administered Aspirin (100 mg/kg, BD, p.o), Celecoxib (30 mg/kg O.D, p.o), Indomethacin (12.5 mg/kg BD, p.o), Etoricoxib (17 mg/kg O.D, p.o) for seven days starting one day prior to immunization by *S. Typhi* Antigen (0.5 mL in each thighs). The antibody titre were measured weekly for one month using Widal Agglutination test.

Results: The antibody titres in the first week were raised in all the groups but the response was more marked in treated group as compared to Control group. Later on antibody titre fell markedly in the treated groups. Selective Cox 2 inhibitors administration caused higher antibody suppression in comparison to Non-selective Cox inhibitors treatment.

Conclusions: These findings support that NSAIDs and the new Cox-2-selectivedrugs have an unsuspected target, the B cell, and attenuateAb production. Use of NSAIDs may therefore influenceautoantibody production in autoimmune diseases and may dampenhumoral immunity in response to antigenic challenge/vaccination.

Keywords: Nsaids, Autoimmune diseases, Rheumatoid Arthritis.

APLAR-0314

Tuberculosis and tofacitinib therapy in patients with rheumatoid arthritis

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Background: Tofacitinib (CP-690 550) is a novel, oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). More information is needed regarding risk of TB with tofacitinib.

Methods: Phase 2, 3, and long-term extension (LTE) clinical trial data from the tofacitinib RA program were reviewed. Before study entry, potential participants were screened for TB with chest radiography and Quantiferon-TB Gold®, or Mantoux PPD skin test (5 mm cutoff). In Phase 3 trials, patients with latent TB infection (LTBI) were allowed entry after completing 1 of 9 months' isoniazid preventive therapy. Patients with a history of adequately treated active TB were also allowed. Active TB cases, reported by study investigators as of September 29, 2011, were identified and TB incidence rates (IRs; per 100 patient-years [95% CI]) calculated for patients exposed to tofacitinib, by region. Regions were categorized by background TB IR (per 100 person-years): low (≤0.01), medium (>0.01 to ≤0.05), and high (>0.05).[1]

Results: 12/4791 (0.25%) tofacitinib-treated patients developed active TB; median time after drug-start: 43 weeks (range 22–137). Ten cases (83%) occurred in countries with high background TB IR; 11(92%) occurred in patients with negative screening results at study entry, and 4 (33%) were extrapulmonary/disseminated. Nine (75%) occurred in patients receiving 10 mg. TB IR (95% CI) was 0.173 (0.098, 0.305), which varied by regional background TB IR: low, 0.037 (0.005, 0.261); medium, 0.034 (0.005, 0.242); high, 0.781 (0.420, 1.452). In Phase 3 studies, 209 tofacitinib-treated patients received concomitant isoniazid therapy for LTBI, none developed active TB.

Conclusion: Within the RA global tofacitinib developmental program, active TB occurred most frequently in patients receiving 10 mg, and in high TB prevalence regions. Patients with LTBI can be successfully treated with isoniazid prophylaxis while receiving tofacitinib.

Reference: 1. Global tuberculosis control: WHO report 2011; http://whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf

APLAR-0171

1,25-dihydroxyvitamin D3 impacts on the production of osteoclast-activating cytokines in early rheumatoid arthritis

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Objectives: To study effects of 1,25-dihydroxyvitamin D3 ($1,25(OH)_2D_3$) on RANKL signaling pathway and pathway-associated cytokines in patients with rheumatoid arthritis (RA).

Methods: Receptor activator of nuclear factor-kappa B ligand (RANKL), osteoprotegerin (OPG), IFN-γ, IL-6, TNF-α, IL-17 and IL-4 were examined in 54 patients with active RA using a cytometric bead array (CBA) and an enzyme-linked immunosorbent assay (ELISA).

Results: After 72 h of incubation of peripheral blood mononuclear Cell (PBMC) with 1, 25 $(OH)_2D_3$, the levels of RNAKL, TNF-α, IL-17 and IL-6 significantly decreased. 1, $25(OH)_2D_3$ had no significantly impact on the level of OPG, RANKL/OPG and IL-4. The ratios of IL-17/IL-4, TNF-α/IL-4, IFN-γ/IL-4 significantly decreased in 1, $25(OH)_2D_3$ testing groups.

Conclusions: The present study demonstrated that 1, $25(OH)_2D_3$ reduces the production of RANKL and the secretion of TNF-α, IL-17, and IL-6 in PBMC of RA patients, which indicates that 1, $25(OH)_2D_3$ might be able to decrease damage of cartilage and bone in RA patients by regulating the expression of RANKL signaling pathway and pathway-associated cytokines.

Keywords: 1, $25(OH)_2D_3$, RANKL, cytokines.

APLAR-0290

Efficacy of tacrolimus in active rheumatoid arthritis patients shown unsuccessful response against methotrexate: non-comparative, single arm, multi-center, phase 4 study

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Objectives: This phase IV, single arm, non-comparative, multicenter study was conducted to investigate efficacy of Prograf® (Tacrolimus) administration for 4 months in subjects with active rheumatoid arthritis (RA) who showed unsuccessful response against methotrexate (MTX).

Methods: A total of 78 patients were screened and 56 patients were assigned to receive test drug, Tacrolimus 1.5 mg initially and increased to 2.0 mg by investigator's decision after 8 weeks. Subjects orally ingested the assigned agents once a day and visited the clinical center at 2, 4, 8, 12 and 16-week for laboratorial and clinical evaluations. The primary efficacy variable was the change of ACR20 response from baseline after Prograf® (Tacrolimus) administration for 4 months. For the safety assessment, adverse events (AEs) were recorded at each clinical visit.

Results: ACR 20 response rate was 42.9% (24 out of 56 subjects) in ITT population (n = 56) while the ACR 20 response rate was 51.2% (22 out of 43 subjects) in PP population (n = 43). The change from baseline of DAS 28 response rate showed significant difference in visit 4, visit 5 and visit 7 with the mean change of −0.86, −1.04. and −1.42, respectively in ITT population. Similar change was found in PP population where a significant difference in change from baseline were found in visit 4, visit 5 and visit 7 with the mean change of −1.07, −1.23 and −1.69, respectively.

Conclusions: Tacrolimus was effective in subjects with active rheumatoid arthritis who had unsuccessful response to MTX, and might be a useful medication for the treatment of RA as combination with MTX.

APLAR-0301

Resectionarthroplasty with matatarus osteotomy for forefoot deformities in rheumatoid arthritis patients who receiving biologics

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The purpose of this study was to evaluate the efficacy and safety of forefoot surgery in RA patients who receive biologics agents.

Patients and Methods: Forefoot surgery were performed for 26 foots with 18 RA patients who receive biologics agents. The averaged of age was 67 years old. Disease duration was 13 yrs. Swannson Implant for great toe were performed in 23 foots, and at the same time MTP joint resection athropalsty with metatarsus osteotomy were performed in 18 foots. Surgery was evaluated by JJSA (Japanese society for surgery of the foot standard rating system). Wound healing was assessed by the SSI (Surgical site infection). Follow up periods were 1–8 years.

Results: JJSA score was improved from 53 to 64pts after surgery. Especially pain and deformity score was improved comparing to ROM, mobility and ADL score. SSI was not detected in early operative phase but one case suffered deep infection and swannson was removed in delayed phase. Skin wound healing Five patients received bilarthroplasty.

Discussion: These results suggest that the use of biologics does not cause specific AEs. But self foot care is necessary after surgery because foot is easily injured by daily life behavior and easily become infected. The satisfaction of forefoot surgery was very high in biologic patients.

APLAR-0315

Effect of tripterygium glycoside combine with ginsenosides on level of CD4+ CD25+ Foxp3+ Regulatory T cells in rat of collagen-induced arthritis

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Objective: The aim of the study based on rat model of collagen-induced arthritis to investigate the effect of active components of traditional Chinese medicines [Tripterygium glycoside (TG) and Ginsenosides (GS)] and their compatibility on the expression of CD4+ CD25+ Foxp3+ Regulatory T cells (Treg cells), IL-10, TGF-β, IL-17.

Methods: By intragastric administration to CIA rats, they were respectively given TG, TG + GS and MTX for 21 days, and Normal group and Model group were given equivalent volume of saline. On 42nd day after modeling, measuring the paws thickness and weights, rats were drawn blood from orbit, anti-freezing, isolate the peripheral blood mononuclear cells (PBMC), Treg cells were detected by FCM. By enzyme linked immunosorbent assay, the levels of serum transforming growth factor-β1 (TGF-β1), interleukin-10 (IL-10), interleukin-17 (IL-17) were detected, while the expression of TGF-β1, IL-10.

Results: The percentage of CD4+ CD25+ Foxp3+ Regulatory T cells in PBMC of Model group, TG group and MTX group is lower than normal group remarkably ($P < 0.05$). Compared with Model group, there were statistical differences among TG group, TG+GS group, MTX group and it ($P < 0.01$). Comparison of serum TGF-β1 (pg/mL): Compared with Model group, there were statistical differences among TG + GS group, MTX group and it ($P < 0.01$), TG + GS group is higher than MTX group, but there was no statistical differences between them ($P > 0.05$). Comparison of serum IL-10 (pg/mL): Compared with Model group, there were statistical differences among TG + GS group and it ($P < 0.05$). Comparison of serum IL-17 (pg/mL): Compared with Model group, there were statistical differences among TG + GS group, MTX group and it ($P < 0.05$). TG + GS group is lower than MTX group, but there was no statistical differences between them ($P > 0.05$).

Conclusion: By elevating the level of CD4+ CD25+ Foxp3+ Tregs, serum TGF-β1? IL-10, degrading the level of serum IL-17, Tripterygium glycoside combine with Ginsenosides can protect bone tissue in CIA rats. In addition, may also by adjusting the balance between Treg/Th17 to play its immunosuppression function.

Clinical Rheumathology: T06 – Systemic lupus erythematosus, Sjogren's and antiphospholipid syndrome – therapies

APLAR-0248

Clinical outcomes of patients treated with cyclophosphamide for lupus nephritis

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Objective: This study aims to describe the outcomes of patients with lupus nephritis (LN) given intravenous cyclophosphamide (CYC).

Design: We reviewed the medical records of 39 Filipino patients at the Philippine General Hospital, a tertiary care center, from 2007 to 2012 previously treated with intravenous cyclophosphamide for lupus nephritis (LN). Patients were given either the NIH protocol (0.50–0.75 mg/m^2 IV CYC increasing to a maximum of 1.0 g/m^2 for 6 months, then quarterly for two years), a modified NIH protocol (6 doses of 1 g IV CYC monthly, then quarterly for two years) or the Eurolupus protocol (6 fortnightly IV CYC pulses at a fixed dose of 500 mg then daily azathioprine (AZA). Outcomes were assessed within two years of treatment.

Results: Most patients were female (34, 87%) with mean age of 28.2 (16–45) years. Fourteen (36%) had nephritis at the time of diagnosis. Seven of 14 patients with renal biopsy had diffuse proliferative glomerulonephritis. The average baseline creatinine was 1.10 mg/dl (0.32–3.47); 9 (23%) patients were azotemic at baseline. Fourteen (36%) patients had nephrotic range proteinuria. Four patients were given the NIH protocol, 19 the modified NIH protocol, and 16 the Eurolupus protocol. Clinical remission occurred in 21 (53.8%) of the patients, including two who completed the NIH protocol, six who completed the modified NIH protocol, five who completed the induction phases of the same, and 6 of 11 who completed the Eurolupus protocol. Four (10.2%) patients progressed to chronic kidney disease. There were 13 serious and 53 non-serious infections. One patient died from sepsis from urinary tract infection while four were lost to follow-up.

Conclusion: There seems to be higher rates of remission in the patients given the NIH and modified NIH protocols. Further studies are needed to determine the most effective treatment for Filipino patients with lupus nephritis.

APLAR-0273

Hydroxychloroquine inhibits the elevation of IFNa through TLR-9 recognition of nucleotides which is irresponsive to glucocorticoid

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Backgroud: Systemic lupus erythematosus is characterized by constant activation of the innate immune system by endogenous nucleic acids, resulting in the elevation of interferon-α (IFNα). Glucocorticoid have been widely used in autoimmune diseases for their strong anti-inflammatory effects, however, a recent research has found that toll-like receptors (TLRs) recognition of self nucleic acids hampers glucocorticoid' effects in lupus. Though its special mechanisms are still unknown, hydroxychloroquine has been found to block the TLRs.

Objective: To evaluate whether glucocorticoid and/or hydroxychloroquine influence the induction of IFNα through TLR-9 recognizing nucleotides in PBMCs, and whether hydroxychloroquine influences signal proteins in the TLR pathway.

Methods: Freshly isolated PBMCs of healthy donors were stimulated with the TLR-9 agonist, ODN 2216, then treated with hydroxychloroquine and/or different doses of glucocorticoid [hydrocortisone: low dose (10^{-5}M), median dose (10^{-4}M), high dose (10^{-3}M)]. The expression of IFNα, MyD88, AP-1 and IKKα in PBMCs were detected by real time PCR.

Results: (1) Hydroxychloroquine significantly reversed the elevation of IFNα caused by ODN 2216 ($P = 0.033$), and in different doses of glucocorticoid (low dose: $P = 0.028$, median dose: $P = 0.025$, high dose: $P = 0.011$). (2) The glucocorticoid had no effects on the elevation of IFNα by ODN 2216 stimulation ($P = 0.31$). (3) Hydroxychloroquine had no effects on the expression of MyD88, AP-1, IKKα in PBMCs with or without ODN 2216 stimulation in different doses of glucocorticoid [(MyD88: control: $P = 0.054$; low dose: $P = 0.194$; median dose: $P = 0.316$, high dose: $P = 0.378$), (AP1: control: $P = 0.762$; low dose: $P = 0.497$; median dose: $P = 0.052$, high dose: $P = 0.451$), (IKKα: control: $P = 0.324$; low dose: $P = 0.346$; median dose: $P = 0.438$, high dose: $P = 0.485$)].

Conclusions: [1] Hydroxychloroquine hampers the elevation of IFNα, critical in the pathogenesis of lupus and irresponsive to glucocorticoid. [2] Adding hydroxychloroquine can control SLE better. [3] Hydroxychloroquine does not influence MyD88, AP-1, IKKα in TLR pathway.

APLAR-0320

Intensive therapy of SLE at adult patients

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Background: Among the variety of rheumatic diseases occupy a special place SLE, which is a common progressive inflammatory autoimmune disease, mainly affecting the kidneys and lungs.

Objectives: The purpose of the present research: to develop the optimum scheme of intensive therapy for treatment of patients with SLE.

Methods: Fourteen sick patients are included in the research at the age of 15 to 36 years (average age 25.1 ± 5.0 years) with various forms of SLE with high activity of process, resistant to standard steroidal therapies.

Results: At heavy forms of SLE intensive therapy by methylprednisolone (MP) was spent in the form of classical 3 or 5 day time pulse therapy with addition of cyclophosphan for 2-nd day, at the rate of 15–20 mg/kg (1000 mg/1 square m. surfaces). Carrying out of the combined intensive therapy (MP and cyclophosphan) had a positive effect at system necrotizing vasculitises. Most effectively early beginning of treatment because of high risk of development of irreversible necrotizing defeats of the vital part of bodies, first of all kidneys. Further program application of methylprednisolone pulse therapy (MPPT) in a combination with cyclophosphan was conducted with an interval of 1 time within 2 weeks, then 1 time within 4 weeks during 8–12 months.

Conclusions: System purpose of having the MP inside was an obligatory component of treatment of patients with SLE in a doze of 15–20 mg/day. Application of greater dozes is justified at heavy development of diseases at patients with development of multiple organ failure.

APLAR-0362

A multicentre clinical study of umbilical cord mesenchymal stem cells transplantation in active systemic lupus erythematosus

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Aim: To assess the efficacy and safety of allogenic Umbilical cord mesenchymal stem cells (UC MSCs) transplantation in active systemic lupus erythematosus (SLE) patients in China.

Methods: Forty patients with active SLE were enrolled from four clinical centres in China. All patients gave informed consents before transplantation, and allogenic UC MSCs were infused intravenously on days 0 and 7. Adverse event was monitored during and after MSCs transplantation (MSCT). Primary efficacy endpoints were major clinical response (MCR), partial clinical response (PCR) and relapse at 6 and 12 months. Secondary endpoints were improvement in SLEDAI score, British Isles Lupus Assessment Group (BILAG) score, serum levels of creatinine, urea nitrogen, complements and albumin pre- and post-MSCT.

Results: Fourteen and fifteen patients achieved MCR and PCR at 6 months follow-up, respectively. Three and four patients experienced disease relapse at 9 and 12 months follow-up, respectively, after a prior clinical response. SLEDAI score significantly decreased. Total BILAG score markedly decreased 3 months after MSCT, and continued to decrease in the following visit times. BILAG score for renal and hematopoietic system significantly improved. For those with lupus nephritis, 24-h proteinuria declined after transplantation, with statistical differences at 9 and 12 months. Serum creatinine and urea nitrogen decreased to the lowest level at 6 months, while slightly increased at 9 and 12 months. Additionally, Serum levels of albumin, complements 3 and 4 increased after MSCT. Serum ANA and dsDNA antibody decreased after MSCT. Furthermore, hemoglobin and platelet counts increased after MSCT in those with hematopoietic involvement. UC-MSCT was well tolerated and no adverse event was observed.

APLAR-0368

Allogenic mesenchymal stem cell transplantation as a rescue therapy for lupus nephritis patient refractory to conventional induction therapy

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Objective: The aim of this study is to observe the role of allogenic mesenchymal stem cells (MSC) transplantation in renal remission in active and refractory lupus nephritis (LN) patients.

Methods: Eighty-one patients with active and refractory LN were enrolled. Allogenic bone marrow or umbilical cord derived MSC were administered intravenously at the dose of one million cells per kilogram of bodyweight. All the patients were followed up for 12 months to evaluate renal remission as well as possible adverse events. The primary outcomes were renal complete remission (CR) and partial remission (PR) at each visit times, as well as renal flares. The secondary outcomes included renal activity score, total disease activity score, renal function and serologic index.

Results: The overall survival rate during 12 months follow-up was 95% (77/81). The probability of renal remission was 41% (18% CR and 23% PR) at 3 months, 45% (18% CR and 27% PR) at 6 months and 44% (23% CR and 21% PR) at 12 months after allogenic MSCT. Renal remission was not correlated with age, disease duration, MSC source and baseline SLEDAI score, but was significantly correlated with baseline proteinuria ($P = 0.003$, 95%CI 0.336–0.794) and serum creatinine levels ($P = 0.047$, 95%CI 0.224–0.990) by *COX* regression analysis. Eleven in 81 (14%) patients underwent renal flare in 12 months follow up after a prior complete or partial remission. Renal activity evaluated by BILAG score significantly declined after MSCT, in parallel with the obvious amelioration of renal function. Total disease activity evaluation by SLEDAI score also decreased. Additionally, the doses of concomitant prednisone and immunosuppressive drugs were tapered. Four of 81 patients died of uncontrolled LN unrelated to MSCT.

Conclusions: Allogenic MSCT resulted in renal remission within 12 months visit, which could be used early as a potential induction therapy for active and refractory lupus nephritis.

Clinical Rheumathology: T08 – Spondylarthropathies – clinical aspects and co-morbidity

APLAR-0011

Prevalence of cardiovascular risk factors in Filipinos with psoriatic arthritis

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Introduction: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy affecting 1–9% of Asians with psoriasis. Patients have increased mortality mainly due to cardiovascular (CV) disease. Our aim is to determine the prevalence of CV risk factors among Filipinos with PsA.

Methodology: We reviewed charts of patients diagnosed with PsA using the CASPAR criteria from 1999 to 2011 in 2 tertiary clinics. Demographic data, cardiovascular risk factors, and risk factor screening and management were extracted. Descriptive statistics were applied.

Results: Forty-one patients had PsA (73% females). Mean age at diagnosis of psoriasis and PsA were 39 and 43 years, respectively. Mean disease duration was 7.7 years. Majority had RA-like polyarthritis. For traditional CV risk factors: 32% (7/22) were smokers; 32% (7/22) were obese; mean BMI was 23.5 kg/m^2;71% (17/24) had hypertension but only 63% were on antihypertensives; 47% (8/17) and 42% (5/12) had diabetes mellitus and dyslipidemia, respectively, and all were on either hypoglycemics or statins. Only 9 had electrocardiograms (all with normal or with nonspecific changes) and 19% (3/16) had cardiomegaly on radiograph. For disease-related risk factors, 65% still had high disease activity and 88.5% had elevated sedimentation rate (mean 44 mm/h) on latest consult. Sixty-eight percent were on methotrexate and 15% were on biologic agents.

Conclusions: Traditional risk factors such as hypertension, diabetes, dyslipidemia, and obesity were increased in this population. High disease activity and sedimentation rates were predominant disease-related risk factors identified. Approximately half of our patients had documented cardiovascular risk factor screening procedures. Given this data we are thus presented with potential intervention points, including more stringent and routine screening to detect clinical as well as subclinical cardiovascular disease for all patients with psoriatic arthritis, as well as multicenter and prospective studies to expand our cohort of patients and our knowledge about them.

APLAR-0035

Assessment of natural radiographic change in patients with ankylosing spondylitis

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Purpose: The most characteristic bony changes in ankylosing spondylitis (AS) are growth of new bone and formation of syndesmophytes, possibly leading to ankylosis and spinal fusion. The objective of this study was to assess the natural disease progression and to find valuable score sites, by using the modified Stoke ASSpinal Score (mSASSS).

Methods: A total of 207 AS patients who met the modified New York criteria were recruited. Cervical and lumbar spinal radiographs were examined by experienced bone and joint radiologists to validate the results. The inter-observer variability was also assessed. A review of the medical records was conducted to investigate the associations between clinical parameters and the radiographic progression.

Results: Among 207 patients, the mean age was 34.3 ± 9.3, and the mean disease duration was 12.4 ± 7.2 years. 87.2% were men and 176 patients (98%) were HLA-B27 positive. The frequency of juvenile onset AS and peripheral arthritis were 30.4% and 49.8%, respectively. No correlations between clinical parameters and spinal score were found. Over 6 years, radiographic changes were seen in 67% patients (cervical spine 83%, lumbar spine 64%, respectively). Between year 0 and 2, the mean changes in the mSASSS were 2.3 (range 0–5.3), 5.6 (0–12.0) between year 0 and 4, 6.0 (0–16.0) between year 0 and 6 of patients, respectively (paired t testing, $P < 0.01$). The 4th, 5th, 6th cervical, 4th, 5th lumbar, and 1st sacral vertebrae showed most frequently radiological change ($P < 0.01$).

Conclusions: No correlations between clinical parameters and radiographic progression were found. We could find out natural bony changes according to the disease progression over 6 years. The mSASSS is useful for assessing extensive radiographic damage in AS. However, it would be reasonable to examine the vulnerable sites.

APLAR-0085

Analysis for the clinical features and immunological markers of the patients with psoriatic arthritis

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Objective: To investigate the characteristics of clinical features, organ involvement and immunological markers in psoriatic arthritis.

Methods: The clinical and laboratory data are collected from 87 patients with PsA, including features of joint involvement, family history, antibodies, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), immunoglobulins, blood routine, and radiological features.

Results: PsA affects men and women almost equally, the ratio is 40:47. Psoriasis is a prerequisite for the diagnosis of PsA, and 67 of these 87 patients (77%) had psoriasis. Seven of 87 (8%) patients only had spinal involvement manifested as radiographic sacroiliitis. Almost all the patients had peripheral joints involvement, and 55% patients had symmetrical distribution, 31.3% patients had DIP joints involvement. 26.4% patients had nail lesions. 18.3% patients had family history of psoriasis. HLA-B27 was found in 16% (14/87) patients. Anti-CCP antibodies or rheumatoid factor were negative in all patients with PsA. All the patients had elevated ESR, with a average number 45.7 mm/h. In addition, the bone destruction can be seen radiologically.

Conclusion: PsA affects men and women almost equally. Most patients had a skin changes or family history of psoriasis in advance. More than 50% patients had a symmetrical joints involvement. Positive HLA-B27 can be found in patients of PsA, whereas anti-CCP antibodies and rheumatoid factor were negative in patients with PsA.

APLAR-0166

A study of the relationship between serum 25-hydroxyvitamin D level and ankylosing spondylitis

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Objective: Exploring the correlation between serum 25-hydroxyvitamin D level and ankylosing spondylitis (AS). Through testing the level of serum 25-hydroxyvitamin D in AS patients, the deficiency situation of 25-hydroxyvitamin D in AS sufferers was known, then to provide theoretical evidence for the reasonable vitamin D supplement in AS patients.

Methods: Adopting prospective study method, namely, the serum 25-hydroxyvitamin D concentration of 108 AS patients and 66 healthy persons from the Xi'an Institute of Rheumatology during the period from January to November of 2012 was detected and analyzed comparatively.

Results: Theaverage serum25-hydroxyvitamin D concentration of ASpatients and healthy people was (19.98 ± 4.46) ng/mL and (36.86 ± 7.97) ng/mL respectively. Obviously, the average serum 25-hydroxyvitamin D level of AS sufferers was lower than the counterpart of health persons, and the difference was significant ($P < 0.05$). It indicated thatthe serum 25-hydroxyvitamin D were related to ankylosing spondylitis. Conclusion Most AS patients lack of 25-hydroxyvitamin D. Perhaps it is related with the disease itself and lacking of outdoor exercises. In clinical practices, more attention should be paid to the reasonable vitamin D supplement in sufferers during the process of systematic treatment of AS, and the bone density examinationalso should be done according to the specific state of illness. The level of peripheral blood 25-hydroxyvitamin D is closely associated with AS.

Keywords: 25-hydroxyvitamin D Ankylosing spondylitis Correlation.

APLAR-0229

Fatigue in patients with spondyloarthropathies

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Objectives: To establish a correlation among disease activity (objectified by C-reactive protein: CRP), degree of fatigue and quality of life in patients with spondyloarthropaties. Another objective is to assess the way the therapeutic approach influences these parameters.

Methods: During a 3-year period 285 patients from the Western part of Romania were diagnosed with different types of spondyloarthropathies (178 with ankylosing spondylitis (AS),

83 patients with psoriatic arthritis (PsA) and 24 patients with CrohnÕs disease). They were divided into 3 homogenous groups and followed a group differentiated therapy. Group 1 received a symptomatic and DMARD therapy. Group 2 received symptomatic, DMARD and biologic anti-TNF inhibitors. Group 3 followed the same therapy as group 2 and an additional rehabilitation program (30 sessions, twice a year). All patients were evaluated at the beginning of the study, after 3 months, after 6 months and after 1 year. The assessed parameters were CRP, degree of fatigue (Modified Fatigue Impact Scale: IFM-20) and quality of life (Health Assessment Questionnaire Modified for Spondylarthropaties: HAQ-S).

Results: By using correlation and regression tests, a moderate or severe degree of fatigue was recorded in 87% of the patients. The fatigue degree was closely related with CRP levels and HAQ-S scores ($P < 0.001$). After 3 months of therapy, group 2 and 3 patients had an improvement of more than 50% of all parameters ($P < 0.01$ in group 2; $P < 0.001$ in group 3). After 6 months and after 1 year we noticed correlations among CRP, fatigue and quality of life, with no significant differences from the 3-month assessments.

Conclusions: The fatigue degree is closely related with the physical activity and can be a disease activity monitor in patients with spondyloarthropathies. A multiple assessment of these patients is necessary in order to make the right therapeutic choice and to increase their general health status.

APLAR-0286

Factors and outcomes of diagnostic delay in Korean patients with spondyloarthritis

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Objective: To investigate the factors and outcomes of diagnostic delay in Korean patients with spondyloarthritis.

Methods: We performed a cross-sectional, one center study on the patients with spondyloarthritis (SpA) who visited the Rheumatology clinic. The information was obtained by a standardized interview, medical record review, assessment of disease activity and Schober test. Mann-Whitney U-test and partial correlation coefficient adjusted by age and treatment duration were used for statistical analysis.

Results: One hundred and five consecutive patients (81 male and 24 female) were included, 94 (89.5%) axial SpA and 11 (10.5%) peripheral SpA patients. The average age at disease onset was 25.3 ± 10.1 years. The delay from onset of symptoms to diagnosis was 9.3 ± 8.3 years. Diagnostic delay was more remarkable in axial SpA patients than in peripheral SpA patients (10.0 ± 8.5 versus 3.8 ± 3.7 years, $P = 0.011$). Diagnostic delay showed a correlation with BASDAI ($r = 0.230$, $P = 0.019$), BASFI ($r = 0.261$, $P = 0.008$), Schober index ($r = -0.267$, $P = 0.007$), and radiographic damage (mSASSS score; $r = 0.501$, $P = 0.000$). Delayed visit to the hospital and misdiagnosis as having mechanical back pain was associated with diagnostic delay. Presence of peripheral arthritis, enthesitis or dactylitis as initial symptoms helped diagnose SpA earlier (7.2 ± 6.8 versus 11.6 ± 9.2 years, $P = 0.007$). There were no differences in time delay to diagnosis according to the age at onset, sex, HLA-B27, family history or extra-articular involvement.

Conclusions: Time delay to diagnoses SpA was correlated with worse disease activity, function and radiographic damage. Factors of diagnostic delay in Korean SpA patients were time delay to visit the hospital, misdiagnosis as having mechanical back pain, axial SpA, none of peripheral arthritis, enthesitis or dactylitis as initial symptoms.

APLAR-0292

Disease characteristics of Filipino patients with ankylosing spondylitis in rheumatology clinics

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory arthritis affecting the spine, sacroiliac joints, and occasionally the big joints of the lower extremities, with predominance among young males. In a previous descriptive study of fourteen Filipino AS patients seen at a single tertiary centre, the mean age at symptom onset was 21.8 years and the mean age at diagnosis was 29.7 years. This study aimed to further describe the disease characteristics of these patients as seen on a larger scale in several rheumatology clinics.

Method: A Philippine General Hospital database of Filipino patients aged 18 years old and above, diagnosed with AS by the Rome criteria and seen in four rheumatology clinics from January 2000 to May 2012, were included in the study. Demographics, clinical manifestations, radiographic findings, and management were described and tabulated. Descriptive statistics were applied.

Results: Forty seven Filipino AS patients were included in the study. Mean age at diagnosis was 33.2 ± 10.93 years and mean disease duration was 7 years. Male to female ratio was 46:1. Seven patients (14.8%) had a family history of AS and twelve (70.6%) were HLA-B27 positive. Treatment included non-steroidal anti-inflammatory drugs (NSAIDS), methotrexate, sulfasalazine, cyclophosphamide, and biologics. Majority of patients were maintained on NSAIDS combined with exercise. The most common biologic agent used was etanercept followed by infliximab, in less than 15% of cases.

Conclusion: This study showed that Filipino patients with AS are mostly young males presenting with chronic back pain, 70% of which were HLA-B27 positive. Results were consistent with the findings of previous studies done locally and abroad. Furthermore, the data can prove useful in helping local physicians identify AS early in patients presenting with inflammatory back pain.

APLAR-0349

Extra-articular manifestations of ankylosing spondylitis in Chinese Han population

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Objective: To investigate extra-articular manifestations (EAMs) in Chinese Han population with ankylosing spondylitis (AS).

Method: We performed a retrospective analysis of case records of two hundred AS patients hospitalized in our department between January, 2007 and December, 2011 and diagnosed as AS according to modified New York criteria. We compared clinical characteristics between AS patients with and without EAMs.

Results: EAMs were observed in one hundred and ten patients (55%). The most common EAMs was uveitis (thirty-eight, 19%). Kidney damage occurred in twenty-nine patients (14.5%, twenty with proteinuria, four with hematuresis and five with IgA nephropathy). Lung involvement was observed in twenty patients (10%, ten with apical fibrosis and ten with interstitial lung disease). Seventeen patients presented heart involvement (8.5%, seven with valve regurgitation, seven with conduction block and three with aortic insufficiency). There were also neurologic involvement in eight (4%) and vertebral compression fracture in three (1.5%), respectively. Patients with EAMs had significantly longer disease duration (356.38 ± 12.2 months versus 160.42 ± 3.24 months, $P < 0.05$), when compared with patients without EAMs. Patients with EAMs also had higher levels of erythrocyte sedimentation rate, C reactive protein and platelet count ($P < 0.05$).Logistic analysis showed that long disease duration is a risk factor for EAMs [$P = 0.011$,OR = 1.329, 95%(CI)1.230–3.183].

Conclusion: EAMs of AS vary widely in terms of both frequency and severity. Patients with EAMs have longer disease duration and higher level of erythrocyte sedimentation rate, C reactive protein and platelet count. Long disease duration is a risk factor for EAMs.

APLAR-0440

the Correlation between HLA-B27 Polymorphism and Clinical Features of Ankylosing Spondylitis

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Objective: HLA-B27 is closely associated with ankylosing spondylitis (AS), but the exact correlation between HLA-B27 subtypes and AS manifestations is still unknown. The study is to investigate the correlation between HLA-B27 polymorphism and clinical features of AS.

Methods: The study included 846 unrelated AS patients and 959 unrelated healthy controls. Direct HLA-B sequencing procedure was applied to identify the HLA-B27 genotype. Clinical parameters including age, age of onset, family history, low back pain, peripheral arthritis, hip joint involvement, dactylitis, uveitis and sex ratio were compared among patients with different HLA-B27 subtypes.

Results: Six hunderd and fifty-two (87.6%) AS patients and 39 (4.0%) healthy subjects were HLA-B27 positive. HLA-B*2702, B*2704, B*2705, B*2706 and B*2715 were identified in the study. The main subtypes of HLA-B27 were HLA-B*2704 (88%) and HLA-B*2705 (10.1%) in the AS patients. Compared to HLA-B*2704 patients, there was a significant increase of uveitis (16% versus 6.13%, $P = 0.002$) and dactylitis (9.3% versus 3.8%, $P = 0.028$) and older age of onset (23.0 ± 8.0 versus 20.7 ± 6.7, $P = 0.028$) in HLA-B*2705 patients. Binary logistic regression analysis revealed that uveitis was significantly associated with HLA-B*2705 ($P = 0.008$, OR: 2.63; 95% CI; 1.283–5.393). There was no significant difference in family history, low back pain, peripheral arthritis or hip joint involvement among different HLA-B27 subtypes.

Conclusion: Patients with some HLA-B27 subtypes showed a preferential association with some clinical features of AS in the Chinese population. AS patients with HLA-B*2705 had an older age of onset and had higher a risk of uveitis and dactylitis than AS patients with HLA-B*2704.

Clinical Rheumathology: T09 – Spondylarthropathies – biological and non-biological therapies

APLAR-0155

Radiologic findings of variable sacroiliac disorders

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The sacroiliac joint is an underappreciated cause of low back and buttock pain. It is thought to cause at least 15% of low back pain. Sacroiliac joint has two main portions. The inferior two-thirds of the joint is lined by articular cartilage; the upper third is a syndesmosis.

The SI joint can be involved in a wide range of disorders such as infection, inflammation, degeneration and trauma. In this exhibition, variable disease involving sacroiliac joint are shown.

Content organization:

1. Anatomy.
2. Variable disease involving SI joint & radiologic features.
   OA
   RA
   Seronegative spondyloarthropathy
   BehcetOs disease
   Gouty arthritis
   Infection
   Osteitis condensans ilii
   DISH
   Trauma
3. Conclusion
   Purposes (=learning objectives)

1 To know variable disease entities involving sacroiliac joint
2 To understand imaging findings of variable sacroiliac disorders

APLAR-0156

Radiologic manifestations of DISH in spinal and extraspinal structures

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The diffuse idiopathic skeletal hyperostosis (DISH) is a skeletal disorder that produces characteristic alterations by exuberant proliferation of bone at osseous sites of ligamentous and tendinous attachments in spinal and extraspinal structures.

Three strict radiographic features of the spine should serve as a prerequisite for the diagnosis of DISH.

In this presentation, spinal and extraspinal involvements of DISH are demonstrated in plain radiography, computed tomography (CT) and magnetic resonance imaging (MRI), compared with other rheumatic disorders.

Content organization:

1 General concepts
2 Diagnostic criteria
3 Clinical abnormalities
4 Radiolographic abnormalities

- Spinal involvement
- Extraspinal involvement

5 Conclusion

Purposes (=learning objectives):

1 To know imaging features of DISH involving spinal and extraspinal sites
2 To compare imaging findings of DISH with those of other rheumatic disorders in spinal and extraspinal sites

APLAR-0277

Thoughts and perceptions about their medications of patients with ankylosing spondylitis using TNF inhibitors

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Background: Therapies for ankylosing spondylitis (AS) have entered a new era of optimism with the advent of TNF inhibitors (TNFis). However, Oword of mouthÓ uncertainty regarding some of the potential side effects of these agents is a major cause of reluctance among the patients using these agents.

Objectives: To investigate the patients' views about their treatments and the factors that influence patients' treatment decisions in patients with AS who have been using TNFis.

Methods: AS patients from a single rheumatology unit, who had been using TNFis at least 3 months were included to the study. Patients' thoughts and perceptions about their treatment were evaluated with using a standard questionnaire given to the all patients.

Results: A total of 70 patients were recruited. The mean age was 35.9 ± 7.1 (20–50) years, and 94.3% of them were male. Patients described their feelings at the time of prescription as hopefulness (78.6%), anxiety (42/9%), fear (20%), desperate (12.9), and hopeless (10%). The most significant determinant for acceptance of TNFis treatment was stated by patients as hope to heal (81.4%), trust in his/her physician (74.3%), recommendation by other patients (41.4%). After the information regarding TNFis were given through standard forms, patients described their feelings as, increase in anxiety (47.1%), psychologically wearisome (35.7%), and worrying to become worse in the future (28.6%).

Conclusions: This study, to our knowledge, is the first in evaluating the attitudes of patients to TNFis, starting from the stage of informed consent to the stage of post-experience. We found that standard forms of informed consent causes an increase in the level of anxiety among new users of TNFis. In this regard, wording of informed consents can be re-edited in a way to increase the knowledge about these agents without increasing the level of anxiety.

APLAR-0240

Tramadol and acetaminophen in ankylosing spondylitis who had inadequate response to NSAID. a double blind randomize-controlled clinical trial

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Objective: To determine the safety and efficacy of tramadol 37.5 mg/acetaminophen 325 mg combination tablets (Ultracet®) in patients with ankylosing spondylitis (AS).

Methods: This was a 12 weeks' randomized double blind, placebo-controlled study. Sixty patients with active AS according to the Modified New York Criteria were enrolled. Active disease was defined by Bath ankylosing spondylitis disease activity index (BASDAI) for more than 3 cm at randomization. Subjects were randomized equally into two groups: the treatment group received aceclofenac plus Ultracet® 1 tablet twice a day; the control group received aceclofenac plus placebo for 12 weeks. The primary endpoint was difference of ASAS20 response criteria between two groups.

Results: At week 12, ASAS20 was achieved by 53.3% of the aceclofenac plus ultracet group and 31% of the aceclofenac alone group (P = 0.047). For the pain visual analogue scale at week 12, there was a reduction of 45.6% in aceclofenac plus ultracet group and 25.7% in the aceclofenac alone group (P = 0.087). There was no statistically significant difference between two groups in BASDAI, BASFI, BAS-G, physician global assessment, spinal mobility, ESR, hs-CRP and ASQoL. There was no statistically significant difference in adverse events between two groups except for a slight increase in dizziness (7.5 % versus 1.5%), vertigo (4.5% versus 1.5%) and nausea/vomiting (6% versus 0).

Conclusions: The Tramadol 37.5 mg/acetaminophen 325 mg combination tablet was well tolerated and had an adjunctive effect as add-on therapy to non-steroidal anti-inflammatory drugs in the treatment of patients with ankylosing spondylitis.

APLAR-0401

Safety of adalimumab therapy in HBsAg carriers with ankylosing spondylitis: a prospective study

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Objectives: To evaluate the influence of adalimumab on the reactivation of hepatitis B virus (HBV) infection in HBsAg carriers with AS.

Methods: In this 48 weeks observation, HBsAg carriers with active AS (BASDAI $\geq$ 4) despite failed treatment with at least two NSAIDs and sulfasalazine (for patients with persistent peripheral arthritis) were studied. Patients must have normal liver function prior to study. All patients received therapy with adalimumab. Lamivudin were prescribed preventively regardless of individual viral load. Pre-existing NSAIDs and sulfasalazine were allowed. Liver enzymes (AST/ALT) and HBV viral load were monitored every 4 weeks. Increased viral load and abnormal liver function were managed according to experts opinion.

Results: Nineteen patients (18 male, one female) were recruited. At baseline, thirteen patients (group 1, including one female) had normal viral load, other six patients (group 2) had abnormal viral load (>100 copy/mL). Two patients from group 1 and one patient from group 2 discontinued adalimumab at week 12 due to ineffectiveness.

Reactivation of hepatitis B occurred in one patient from group 2. At week 24, the patient underwent a mild increase of both ALT and AST (68 and 57 IU/L, respectively). A elevated viral load (6.9e7 copies/ml, baseline 3.4e4) and a HBV YMDD mutant were also found. The adalimumab treatment continued. After prescription of Adefovir (combined with the pre-existing Lamivudin), both liver enzyme and viral load decreased to normal range in 8 weeks and remained normal. In the rest 18 patients, no significant increase of AST/ALT or viral load was found.

Conclusions: Adalimumab therapy represent a safe and effective option for HBsAg carriers with AS refractory to traditional treatment. Prophylaxis strategy with more effective anti-viral drugs is recommended to reduce the risk of hepatitis B reactivation.

Clinical Rheumathology: T10 – Psoriatic arthritis

APLAR-0043

Treatment of psoriatic arthritis with etanercept, methotrexate, and cyclosporin A

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Background: Psoriatic arthritis (PsA) is seen in approximately 5% to 42% of individuals with psoriasis.

Case Summary: A 37-year-old white male weighing 90 kg presented with erythrodermic psoriasis and PsA. The overall duration of PsA was 3 years. Serum levels of glucose, electrolytes, and tumor markers were normal, as were the results of tests of hepatic and renal function and urinalysis. The findings of posteroanterior radiographic examination of the chest were also normal. However, radiographic examination showed porosis and degeneration in the lumbar vertebrae; narrowing of the L2-L3, L3-L4, and L5-S1 spaces; degenerative changes and narrowing of the proximal interphalangeal and distal interphalangeal (DIP) joints; and osseous ankylosis of the DIP joints of the hands. The cutaneous eruption improved with cyclosporin A (CsA) 3.5 mg/kg p.o., but the severity of PsA did not change. Therefore, parenteral methotrexate (MTX) 15 mg/wk and an indomethacin suppository 100 mg/d were added to the regimen. CsA and MTX were continued for 3 months, during which the patient's PsA symptoms did not abate, based on tender and swollen joint counts, hand-to-floor distance, erythrocyte sedimentation rate, and levels of C-reactive protein (CRP), antistreptolysin O, and rheumatoid factor. Therefore, etanercept 25 mg s.c. twice weekly was added to the regimen. Three weeks after the initiation of this combination, the patient's arthritis had improved. The visual analog scale score decreased from 9 to 4. Tender and swollen joint counts decreased from 28 and 24 to 15 and 10, respectively. The hand-to-floor distance decreased from 20 to 10 cm. The erythrocyte sedimentation rate and levels of CRP, antistreptolysin O, and rheumatoid factor decreased from 72 mm/h, 162 mg/L, 250 IU/mL, and 304 IU/mL at baseline to 23 mm/h, 64 mg/L, 48 IU/mL, and 56.1 IU/mL, respectively. No change was observed in radiographs of the patient's back, hands, and feet. Based on the American College of Rheumatology scoring system, the patient showed 50% improvement in disease severity. Etanercept was discontinued at the end of 4 weeks, and maintenance therapy was continued with MTX alone. No adverse events were reported during or after the completion of etanercept therapy.

Conclusion: In this patient with PsA that was refractory to CsA and MTX, either alone or in combination, the severity of PsA was reduced after 4 weeks of the combined use of etanercept, CsA, and MTX.

Clinical Rheumathology: T13 – Metabolic bone diseases and crystal-induced diseases

APLAR-0041

Urate lowering efficacy of Febuxostat versus allopurinol in patients with hyperuricemia in gout: a meta-analysis

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Background: From the current clinical practice guideline of Philippine Rheumatology Association, Allopurinol should be started at 100 mg/day, with a maximum dose of 300 mg/day to maintain a serum uric acid concentration of <6.0 mg/dl. However, increasing evidence shows that 300 mg dose is ineffective in achieving the target sUA level, limiting allopurinolÕs use on certain subsets of patients who are allopurinol intolerant such as patients with chronic kidney disease, or with multiple comorbidities and in elderly patients.

Objectives: To determine the efficacy and safety of Febuxostat in comparison with Allopurinol in lowering serum uric acid level in patients with hyperuricemia in gout based on the baseline Serum Uric Acid.

Inclusion criteria: Randomized, double blinded, parallel group clinical trial with meta-analysis quality scale of A-B, were included. Intervention included administration of Febuxostat and Allopurinol in determined dosages and duration in each study.

Search Strategy: Electronic searches through COCHRANE, EMBASE, PUBMED, and Manual Search. Free texts used the following: febuxostat, allopurinol, hyperuricemia, gout.

Statistical Analysis: The data were entered in the Cochrane Review Manager Software version 5.0. All outcomes were examined using the random effects model. Dichotomous data were analyzed by calculating the odds ratio, with 95% confidence interval and a significant P value of 0.1 was used.

Results: It showed that there was significant number of lowered serum baseline urate levels in Febuxostat 80 mg than in Allopurinol with OR 3.23 (95% CI, 2.54–4.12, $P = 0.00001$).The risk of having abnormal liver enzymes is higher in the Febuxostat group as compared to the Allopurinol with RRR 1.21 (95% CI, 0.89–1.64, $P = 0.22$).

Conclusions: Febuxostat has significant uric lowering efficacy than Allopurinol, and in patients with renal impairment without requiring dose adjustment, with lower incidence of any adverse events. However, elevated liver enzymes brought about by Febuxostat were noted.

APLAR-0109

A survey of patients and rheumatologists on cognition and the status quo about Gout in China Today

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Objective: To investigate the cognition of Gout patients and the status quo of rheumatologists on the Gout, explore the focus of education on Gout for them in the future.

Methods: In accordance with the concerns of Gout patients and the guidelines for the diagnosis and treatment of Gout, we designed the questionnaires completed by Gout patients and rheumatologists face-to-face. One hundred and twenty-four Gout patients filled in the patient questionnaires and 269 rheumatologists of China filled in the rheumatologist questionnaires.

Results: One hundred and twenty-four patient questionnaires were collected. Eight patients (6.45%) considered that acute Gout flare is caused by bacteria or virus. Seven patients (5.6%) thought that the target value of lowering uric acid is 600 umol/L. Twenty-six patients considered that colchicine, steroids and NSAIDs lower uric acid. One hundred and fifty-six of 269 rheumatologists (61.9%) thought serum uric acid increases during the acute Gout flare. One hundred and thirty-four (51.94%) thought Colchicine is not necessary to prevent Gout flare at the beginning of lowering uric acid therapy. Twenty-five (9.92%) thought that the lowering uric acid drugs can be taken during the acute Gout flare. More than 1/3 of rheumatologists did not understand the guidelines for diagnosis and treatment of Gout including the blood uric acid level during the acute Gout flare, the moment of lowering uric acid, the target value of lowering uric acid and whether to take colchicine or NSAIDs to prevent Gout recurrence at the beginning of the treatment of Gout. The cognition level in Gout of patient was no related with their education degree and Gout duration.

Conclusions: Gout patients will well understand the disease of Gout and cooperate with doctors to be treated systematically through strengthening the Gout knowledge education. The rheumatologist will further strengthen their understanding of Gout and carry on the systematic treatment of Gout through organizing the professional training.

APLAR-0126

Hyperuricemia and bone and joint disease among patients of different age

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Aimof research: To determine uri?acid level in blood serum and incidents of hyperuricemia among patients ofdifferent age and their relation with bone and joint disease.

Object: Women (n = 450) and men (n = 120), age of examined patients was from 20 to 89 years old. Average ageof examined patients was 60.4 ± 0.7 years.

Methods: Uricacid level in blood plasma was determined by uricase-peroxidase method.

Results: Thelevel of uric acid increased with age in women and had a significant differencein women of 80–89 years ($r = 0.18$, $P < 0.05$). Incidence of hyperuricemia among women was 17%, in men * 30%. Significantcorrelation was determined between uric acid and BMD at the trochanter level ($r = 0.31$, $P < 0.05$) among women inpostmenopausal period. Incidence of osteoporosisamong women was 46%, osteopenia * 14%, knee osteoarthritis * 28% and they haveneck pain in 22%, back pain * 35%, lowback pain * 34%; in men: osteoporosis * 11%, osteopenia * 14%, knee osteoarthritis* 11%, gout * 21% and they have neck pain in 18%, backpain * 11%, low back pain * 79%.

Conclusions: It was determined that the level of uric acid wasincreasing with age and a significant correlation was found between uric acidand BMD at the trochanter level among women in postmenopausal period. We found ahigher incidence of bone and joint disease in patients with hyperuricemia.

APLAR-0143

Elevated serum homocysteine levels in gouty patients were related not with serum uric acid levels but with decreased renal function

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Objectives: Both of hyperhomocysteinemia and goutare related with cardiovascular diseases and metabolic syndrome. However, there are few reports about the serum homocysteine levels in gouty patients, and theirresults reveal discrepancy. We investigated whether serum homocysteine levels are elevated in thegouty patients and which factors are associated with thehomocysteine levels.

Methods: This cross-sectional study included 91 male patients with chronic gout and 97 age-matched healthy male controls. The mean ages were 51.19 ± 15.08 and 51.57 ± 17.01 years old, respectively. Serum homocysteine levels were measured by a competitiveimmunoassay using directchemiluminescent. The estimatedglomurular filtration rate (eGFR) was obtained-using modification of diet in renal disease formula, thenthe stages of chronic kidney disease (CKD) were classified according to the KDOQI CKD classification.

Results: The gouty group were not significantly different from the control group in serum uric acid levels (6.15 ± 2.23 mg/dLvs 5.82 ± 1.22 mg/dL, $P = 0.224$), however, had higher serum homocysteine levels than the control group (13.96 ± 4.05 μmol/L vs 12.67 ± 3.52 μmol/L, $P = 0.021$). Serum homocysteine levels showed the positive correlations with serum BUN and Cr levels, and thenegative correlation with eGFR ($r = 0.429$, $P < 0.001$; $r = 0.435$, $P < 0.001$; $r = -0.413$, $P < 0.001$, respectively) in the chronic gouty group. However, serum homocysteine levels are uncorrelated with serum uric acid levels orcholesterolprofiles. The patients at stages1 or 2 of CKD had significantly lower serum homocysteine levels than the patients at stage 3 of CKD ($P < 0.001$). In multiple linear analyses, serum homocysteine level was affected not by the serum uric acid level, but by eGFR ($\beta = -0.385$, $P < 0.001$).

Conclusions: Serum homocysteine levels were higher in the male patients with chronic gout than in the healthy male controls. Hyperhomocysteinemia in gouty patients could be related not with serum uric acid levels, but with decreased renal function.

POSTER SESSION II ABSTRACTS
Clinical Rheumathology: T07 – Systemic lupus erythematosus, Sjogren's and antiphospholipid syndrome – clinical aspects, comorbidities and complications

APLAR-0015

Major infections in a cohort of oriental patients with Systemic Lupus Erythematosus (SLE)

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Background: Patients with SLE have increased risk of infection, which causes morbidity and mortality. We describe the nature and outcome of major infections in a cohort of SLE patients in a single centre in Singapore.

Methods: The cohort consists 1013 patients from 2000 to 2012 who fulfill the American College of Rheumatology 1982 criteria for SLE. We examined data on patients who developed major infections (bacteraemia or infections requiring admission) during follow up.

Results: Eighty patients (7.9%) developed major infections. Fourteen patients had more than one infection. Data was available for 67 patients. Sixty-eight (85.0%) patients were female and 12 (15.0%) male. Mean age of diagnosis of SLE and major infection were 31.1 years (±12.8) and 40.1 years (±14.9) respectively. Mean duration of disease at time of infection was 9.0 years (±8.8). 61.7% of infections were bacterial, 17.3% viral, 1.2% mycobacterial, 19.8% no organism isolated. Gram negative organisms caused 36 (72%) of bacterial infections: Salmonella Group D (n = 13), Salmonella typhi (n = 1), Escherichia coli (n = 5), Klebsiella pneumoniae (n = 2), Pseudomonas aeruginosa (n = 5), Enterococcus spp (n = 5), Acinobacter baumanii (n = 1), Kingella kingae (n = 1), Edwardsiella tarda (n = 1), Citrobacter (n = 1), Morganella morganii (n = 1). Fourteen cases (28.0%) were due to gram positive organisms: Staphylococcus aureus [n = 11(5 MRSA)], Streptococcus pneumoniae (n = 2), and Clostridium difficile (n = 1). Viruses caused 14 incidents: Varicella zoster (10: 8 cutaneous, 2 meningoencephalitis), cytomegalovirus (3) and H1N1 (1). There was 1 case of pulmonary tuberculosis. Main sites of infection were gastrointestinal (n = 16), genitourinary (n = 12), pulmonary (n = 11) and skin (n = 11). The median prednisolone dose at time of infection was 13.75 mg/day (range 0–60).

Most patients recovered without need for intensive care. Of 4 patients who died, 3 had other contributing conditions such as malignancy, intracranial haemorrhage and anoxic encephalopathy.

Conclusions: Gram negative bacteria, especially salmonella, are a major cause of infections among SLE patients.

APLAR-0055

Evaluation of relationship between anti a-actinin antibody and lupus nephritis

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Introduction: Glomerulonephritis is the major complication led to morbidity and mortality in patients with systemic lupus erythematosus (SLE). Deposition of autoantibodies in the glomeruli plays a key role in the development of lupus nephritis (LN). Different studies have investigated the role of α-actinin, as a target for autoantibodies in pathogenesis of LN, however it is still a matter of debate. The aim of this study is to examine the association between serum values of α-actinin antibody (Ab) and LN.

Material and Methods: Eighty lupus patients (Forty patients with and 40 patients without LN) were included in this cross-sectional study. SLE was defined according to American college of rheumatology criteria. Besides, LN was defined as 24/h urine collection proteinurea more than 500 mg. Clinical and laboratory findings of patients were collected. Serum anti-a-actinin-Ab levels were measured by enzyme linked immunosorbent assay (ELISA). Lupus disease activity was calculated in regard with SLEDAI 2k.

Results: The current study demonstrated that the mean anti-a-actinin-Ab serum levels were lower in LN patients compared with patients without LN ($P < 0.001$). There was not any correlation between anti-a-actinin-Ab and proteinurea ($r = -0.163$, $P = 0.406$). Serum values of anti-a-actinin-Ab negatively correlated with SLEDAI ($r = -0.319$, $P = 0.014$).In addition, among different component of SLEDAI only C3 serum values positively correlated with this anti body ($r = 0.249$, $P = 0.032$).

Conclusion: In aggregate, this study could not show any correlation between anti-a-actinin-Ab serum levels and proteinurea. On the other hand, anti-a-actinin-Ab serum levels were significantly higher in patient without LN. Therefore, it seems that this Ab is not a good indicator of lupus nephritis.

Keywords: a-actinin, anti a-actinin antibody, systemic lupus erythematosus, lupus nephritis, proteinurea, SLEDAI.

APLAR-0060

Detection eight cytokines in SLE patients using multiplex immunoassay

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Objective: To measure the serum levels of eight cytokines in SLE patients and healthy controls using multiplex immunoassay and to explore the cytokinesOfunction in SLE and the relationship between cytokines and clinic characteristic of SLE.

Methods: Serum was separated from peripheral blood of 80 SLE patients and 40 healthy individuals. Multiplex immunoassay was performed followed the manual of MILLIPLEX $_{MAP}$ human cytokine detecting kit. Measurements and data analysis of all assays were performed with the Luminex system in combination with the Bio-Plex Manager software. 0.01 pg/mL cytokine level in serum would be detected. The levels of cytokines were expressed as median (25th, 75th). The Mann-Whitney test was used for all 2 sample comparisons (SPSS, version 13.0). $P < 0.05$ was considered significant.

Results: Without any stimulation, IP-10 was expressed the highest in the eight cytokines, the second was IL-8, the third was TNF-α. The level of IL-17 was too low to detected. Only 8 of SLE and 1 of healthy individuals was measured minim level. The level of IP-10, IL-8 and TNF-α were higher in the SLE patients than that in the healthy control individuals ($P < 0.01$; Table 1). The level of IP-10 was positively related with SLEDAI score and the level of TNF-α was negatively related with C3 level.

Conclusions: The serum level of IP-10, IL-8 and TNF-α were higher in the SLE patients than that in the healthy control individuals. The three cytokine may play important roles in the pathogenesis of SLE. Multiplex immunoassay is a reliable, fast, and reproducible technique to measure multiple cytokines with small valumes.

Table. 1 The levels of 7 cytokines in SLE group and control group [Median (25th, 75th), pg/mL].

cytokine	Groups		Z value	P value
	SLE group (80 cases)	Control group(40 cases)		
IP-10	1184.30 (748.73, 1952.32)	541.28 (446.29, 825.53)	−5.283	<0.001
IL-8	370.48 (144.97, 942.00)	149.41 (73.10, 269.96)	−3.719	<0.001
TNF-α	7.81 (1.42, 14.91)	2.21 (0.75, 4.45)	−4.707	<0.001
IFN-γ	1.00 (0.02, 2.13)	0 (0, 0.53)	−4.244	<0.001
IL-10	1.20 (0, 6.31)	0 (0, 0)	−5.646	<0.001
IL-6	0.72 (0,4.18)	0 (0, 0)	−4.684	<0.001
IFN-α2	0 (0, 1.28)	0 (0, 0)	−3.497	<0.001

APLAR-0061

Clinical study of drug allergies in Systemic Lupus Erythematosus

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Objective: To analyze the frequency of drug allergies in patients with systemic lupus erythematosus (SLE), and register the causal drug, the type, and severity of the drug reaction.

Methods: Retrospective investigation and analysis were carried out in 426 patients with SLE and 204 patients with other chronic diseases (including Hypertension, diabetes mellitus, chronic bronchitis, chronic kidney disease,coronary heart disease, and other chronic disease). Demographic data,drug allergies (including the causal drug, the type and severity of the allergic reaction) were registered.

Result: Drug allergies were reported in 121 (28.40%) patients with SLE and 26(12.6%) patients with other chronic diseases ($P > 0.05$). Allergy to penicillin (13.15%) was found more freguently in SLE groups,next were cephalosporin antibiotics (12.69%), Traditional Chinese medicine injection (5.87%), Macrolides (3.76%) and quinolones (3.76%). Most of them presented skin rash as their clinical expression of allergy.Two patients with SLE were allergic to six drugs, three patients were allergic to five drugs and five patients were allergic to four drugs.

Result: Drug allergies are more frequent in SLE than in other chronic diseases. Patients can be allergic to many drugs.Penicillin drugs are still the most frequent cause of drug allergies in SLE Traditional Chinese medicine injection is also prone to allergy in patients with SLE.

APLAR-0065

Malignancy in a cohort of oriental patients with systemic lupus erythematosus (SLE)

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Background: SLE patients have been described to have increased incidence of malignancy. We aim to describe the nature and course of malignancies in SLE patients in a single centre in Singapore.

Methods: The cohort consists of 1013 patients who fulfil the American College of Rheumatology 1982 revised criteria for SLE from 2002 to 2012. We examined data on patients from the cohort who had recorded malignancies.

Results: Twenty-five patients (2.6%) were recorded to have malignancy with a total of 29 incidents. All patients were female. The mean age of diagnosis of SLE and malignancy was 40.5 years (± 12.1) and 51.4 years (± 12.5) respectively. 93.1% of malignancies were diagnosed after diagnosis of SLE.

The majority of malignancies were gynaecological (n = 13, 44.8%) with 7 (24.1%) breast, 3 (10.3%) cervical, 2(6.9%) endometrial and 1 (3.4%) ovarian. Four patients (13.8%) had bladder cancer (out of which one had received cyclophosphamide), 3 (10.3%) lung cancer, 2 (6.9%) thyroid cancer, 2 (6.9%) pancreatic cancer, 2 (6.9%) colorectal cancer, 1 (3.4%) lymphoma, 1 (3.4%) malignant meningioma and 1 (3.4%) metastatic cancer of unknown origin. 44.9% were metastatic. There were 10 (34.5%) deaths due to malignancy.

Conclusion: The majority of malignancies in our cohort of SLE patients were gynaecological, which was unsurprising given the gender predisposition of the disease. Of interest, the percentage of these cancers in our cohort was high, compared to 33% of total cancer incidence in the general population. Bladder cancer was also accounted for a higher percentage than in Singapore females (0.9%). Patients with SLE should be encouraged to receive vaccinations for cervical cancer and undergo routine screening such as PAP smears and mammograms.

APLAR-0067

The study of the predictive factors and the effect of season for flare in systemic lupus erythematosus

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Background: Most of systemic lupus erythematosus (SLE) patients had a relapsing-remitting clinical course.

Objective: To determine the predictive factors and effect of season for SLE flares.

Methods: This study is a prospective inception lupus cohort of newly diagnosed SLE patients seen between May 2007 and June 2012. Only cases that had been observed for a minimum of one year were included.

Results: Ninety-five (88 females) with mean ± SD age and disease duration at the study entry were 33.22 ± 13.24 years and 2.79 ± 3.19 months were enrolled.Their initial modified-systemic lupus erythematosus disease activity index (M-SLEDAI) scrore was 13.33 ± 5.57. Eighty-eight patients (92.63%) reached first remission (M-SLDEAI = 0) during the observing periods of 38.13 ± 16.35 months. Fifty percent of patients reached remission within 7.40 months. The cumulative of disease remission survival at 20 months was 50%. The overall incidence rate of flare was 40.36/100 patient-years. There was no different in rate of flare among winter, summer and rainy seasons (44.33, 41.56 and 37.66/100 patient-years, respectively). From log-rank test, there were different of mean ± SD duration from remission to flare (months) between patients whose age at diagnosis of ≥30 vs. <30 years (18.58 ± 2.70 vs. 38.95 ± 4.64, $P = 0.005$), single vs. married (18.61 ± 2.92 vs. 34.42 ± 4.34, $P = 0.023$), alopecia vs. no alopecia (14.99 ± 2.88 vs. 31.88 ± 3.56, $P = 0.047$), and being treated with vs. without anti-malarial drug (31.76 ± 3.85 vs. 22.21 ± 5.04, $P = 0.030$). However, Cox-regression analysis revealed age at diagnosis of <30 years (Hazard ratio [HR] 2.26, 95%CI1.06, 4.82) and alopecia (HR 2.41, 95%CI1.18, 4.96) were the predictive factors for flares, while used of anti-malarial drug (HR 0.38, 95%CI0.19, 0.73) was the protective factor for flares.

Conclusion: Season has no effect on the flare rate in SLE patients in Thailand. In this study, the predictive factors for SLE flares that need to be taken into account were age at diagnosis of <30 years and alopecia, while use of anti-malarial drug was the protective factor for flare in SLE.

APLAR-0069

sleep disturbances in patients with systemic lupuserythematosus

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Background: Sleep disturbance is a common problem in systemic lupus erythematosus (SLE) patients.

Objectives: To determine the prevalence of sleep disturbance in SLE, the factors that might be associated with sleep disturbance, and the correlation between changes in clinical parameters and sleep quality over time.

Methods: A prospective study conducted at Rheumatology clinic during June 2009 * 2011. The demographic data were recorded at baseline and the clinical data, the Pittsburgh Sleep Quality Index (PSQI) and other standardized assessment tools; disease activity index, damage index, depression, anxiety and fatigue score, were assessed three times: the first visit was at baseline, the second time was one month later, and the third time was three months after the baseline.

Results: Fifty-six female SLE patients from a total of 497 SLE patients (11.3%) agreed to join the study. Thirty-one of these 56 patients (55.36%) were found to have sleep disturbances. All were females with their mean ± SD age of 37.5 ± 12.3 years, and disease duration at study entry of 8.6 ± 7.3 years. There was no association between sleep disturbances and demographic data, disease activity, clinical symptoms, the presence of auto-antibodies and medications. In multiple logistic regression analyses, only moderate to severe depression was the independent determinant of sleep disturbances, $P = 0.036$. During the three monthobservation, with the treatment, the association of changing of total PSQI score and depression score over time showed a moderate correlation ($r = 0.60$, $P < 0.001$).

Conclusion: Sleep disturbances in Thai SLE patients were not uncommon. A depressed mood was strongly associated with sleep disturbances. Awareness of underlying depression as well as sleep disturbances in SLE patients, and treating them properly improve treatment outcomes in SLE.

APLAR-0086

THE clinico-pathologic features and outcomes of lupus nephritis In Filipinos: a 5 year SLMC experience

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Background: Lupus nephritis has variable manifestations and clinical course which is affected by race, ethnicity and geographical region.

Objective: To document various renal manifestation of Lupus, the patient profiles and disease patterns, and outcomes of patients seen at St. LukeOs Medical Center (SLMC) from 2007 to 2012 with the objective of improving the quality of patient care in the local setting.

Results: Renal involvement was seen in 136 of 321 Lupus patients (42.37%). Females outnumber males by 12:1, with males having same incidence of renal disease as do females. Mean age of patients at diagnosis of SLE was 34.96 ± 12.37. Nephrotic syndrome is the predominant glomerular manifestation followed by acute nephritis. Forty of the patients underwent renal biopsy with the main histological types seen as class 3 (17.5%), class 4 (60%). Progression of CKD is significantly affected by age of the patient at diagnosis of disease and ECC at inception, with greater risk of CKD associated with older age and lower ECC. Low ECC at inception is the only significant predictor for renal replacement therapy. The overall mortality rate is relatively low at 5.9%, with sepsis and cardiovascular complications as the usual causes of death. The presence of anti-dsDNA antibodies and hypertension were seen as strong predictors of death. Response of 61 Filipino LN patients to Euro Lupus and NIH protocol was investigated and there is no statistically significant difference in terms of risk for relapse, infection for between the low dose Cyclophosphamide and high dose Cyclophosphamide. Filipino LN patients post transplant generally has good outcome.

Conclusion: Presentation ofLupus nephritis in Filipinos is comparable to LN from other countries. In patients with LN, Hypertension and presence of anti-dsDNA antibodies are independent risk factors for death while old age and low ECC at diagnosis are predictors of progression of CKD.

APLAR-0088

A study of systemic lupus erythematosus in the medical intensive care unit, southern Thailand: epidemiology and predictors of survival

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Sixty-one patients with Systemic Lupus Erythematosus (SLE) who admitted to the medical intensive care unit (ICU) over a 6-year period (from July 2004 to August 2010) were reviewed, based on the setting of tertiary referral university hospital in Songkhla, Thailand. We examined the demography, reasons for admission, APACHE II- severity scores, outcome, and causes of death as well as prognostic factors. The main reasons for ICU admission were acute respiratory failure (69%) and/or shock (62%). The overall mortality rate during ICU stay was 57%, mainly caused by the infections, especially in the lower respiratory tract. Most patients had high severity scores, with a mean (SD) APACHE II score of 24.8 (10.8). The SLE patients who had APACHE II score 20 or more comprising up to 65 percent, and had significantly lower probability to survival from Kaplan-Meier method ($P = 0.004$). The need of vasopressor was significantly correlated to non-survivor (OR 6.98, 95% CI 1.91–25.49) and the occurrence of ventilator associated pneumonia tended to bad outcome (OR 4.17, 95%CI 0.91–19.03). On the contrary, the use of azathioprine as steroid sparing agent for SLE was negatively associated with mortality (OR 0.08, 95%CI 0.01–0.58), that had never been previously reported. Our findings emphasized the important of the early aggressive interventions in the SLE patients with a critical illness to improve better outcome.

APLAR-0098

Ocular manifestations in SLE patients in Saudi Arabia

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Objectives: To study the ophthalmic manifestations in systemic lupus erythematosus patients in a tertiary hospital in Saudi Arabia.

Methods: SLE patients (fulfilling ACR criteria) attending KKUH clinics, Riyadh were studied.

Results: A total of 624 patients, 566 (90.7%) females, were diagnosed to have SLE with a mean age of 34.3 ± 11.9 (range 8–71) years, and mean duration of SLE of 9.3 ± 5.3 (range 0.3–30) years. Various ocular manifestations were found in our patients and are shown in Table 1. A total of 105 (16.8%) ocular manifestations were noted, 87 (13.9%) patients manifested with one or more ocular symptoms;. Blurred vision was reported by 25(4.0%) patients followed by dry eyes (sicca) in 16 (2.6%). Cataract was seen in 11(1.8%) patients, conjunctivitis in 11(1.8%),SLE retinopathy in 2(0.3%),optic atrophy in 2(0.3%), papilloedema in 1 (0.2%),maculopathy in8(1.3%) and chloroquine keratopathy in3(0.5%) patients.

Conclusions: Ocular manifestations occured with a frequency of 16.8% in this group of SLE patients. Blurred vision dry eyes and cataract occurred with high frequency. Chloroquine toxicity was negligible in our patients. As ocular morbidity and vision loss may occur in SLE patients, close monitoring by referral to opthalmologists and appropriate local and systemic treatments are necessary.

Table 1. Ocular manifestations among 624 SLE patients.

Manifestation	No. (%)
Conjunctivitis	11 (1.8)
SLE retinopathy	2 (0.3)
Cataract	11 (1.8)
Sicca (Dry eyes)	16 (2.6)
Angioedema of eyelids	2 (0.3)
Blurred vision	25 (4.0)
Optic atrophy (devics disease)	2 (0.3)
Steroid related – inactive trachoma	2 (0.3)
Chloroquine keratopathy	3 (0.5)
Papilloedema	4 (0.6)
Recurrent loss of vision	1 (0.2)
Bilateral keratoconus	3 (0.5)
Uveitis	1 (0.2)
Maculopathy	8 (1.3)
Cotton wool spots	3 (0.5)
Bilateral retinal vein thrombosis	1 (0.2)
Blepharitis	5 (0.8)
Xanthelasma eye	1 (0.2)
Bilateral corneal verticillata 2° to chloroquine	1 (0.2)
Perforated corneal ulcer, corneal transplant	1 (0.2)

APLAR-0100

Pulmonary hypertension in systemic lupus erythematosus

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Background: Pulmonary arterial hypertension (PAH) is an increasingly recognized complication of Systemic Lupus Erythematosus (SLE). The reported prevalence of PAH in SLE ranged from 0.5% to 14% in previous review. The prognosis of patients with PAH has been reported to be very poor and the mean survival from the onset of PAH was 2 years. There was still limited data about this complication especially in our country.

Aim: To know the incidence of PAH in SLE patient.

Methods: This cross sectional study was done in Siloam General Hospital, Karawaci, Tangerang, Banten, Indonesia in 2012. The SLE patients with symptoms of heart failure were done the trans-thoracic echocardiography (TTE) to find signs of PAH. Diagnosis PAH was made when the resting pulmonary arterial systolic pressure (PASP) was >30 mmHg at rest by TTE. Excluded were other forms of PAH due to left heart disease, chronic lung disease, and or hypoxemia, chronic thromboembolism.

Results: A sum of 43 patients as comprise of 40 females and the others were male. The mean of age was 24 years old (ranged 13–51 years). Cardiac abnormalities were found in 78% as comprise of five systolic dysfunction patients, 12 diastolic dysfunction patients, 13 patients with pericardial effusion, 28 patients with valve abnormalities, and one patient with thrombus in left atrial. There were 8 patients identified having PAH.

Conclusion: The incidence of PAH in our study was 18.6%. The others abnormalities were systolic and diastolic dysfunctions, pericardial effusion, valve abnormalities, and one patient with thrombus in left atrial.

Key words: Pulmonary arterial hypertension, Systemic lupus erythematosus.

APLAR-0144

Risk factors for avascular necrosis in patients with systemic lupus erythematosus

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Objective: To identify associated factors for the development of avascular necrosis (AVN) in patients with systemic lupus erythematosus (SLE).

Methods: We conducted a retrospective case-control study from SLE patients who attended the Affiliated Provincial Hospital of Anhui Medical University from 1992 to 2011. Who had clinically apparent AVN (confirmed by plain radiographs, computer tomography or magnetic resonance imaging). For each case, two controls were selected and matched to the case by gender, age and time of onset. The clinical and laboratory variables thought to be risk factors of AVN variables were compared between patients who did and did not develop AVN.

Results: Of 219 SLE patients, we identified 73 patients who developed AVN during the course of follow-up. Fifty-three patients were available for data analysis. From the univariate analysis, incidence of renal involvement, oral ulcer, raynaud phenomenon, CNS disease, triglycerides, cholesterol, the use of cyclophosphamide and the maximum dose of steroids were significantly higher in the ON group than in controls. The use of antimalarials was significantly lower in patients with AVN than in controls. No difference in disease activity, or anticar-diolipin antibody was found between groups. In the logistic regression, the presence of CNS involvement as a positive associated factor for AVN (OR = 2.759, CI = 1.138*6.691, $P = 0.025$) and the use of antimalarial drugs was a negative associated factor for ON (OR = 0.532, CI = 0.345*0.820, $P = 0.004$).

Conclusion: The AVN relatively high risk of CNS lesions in patients with SLE. The hydroxychloroquine can avoid the occurrence of AVN. We found that in most SLE with AVN lesions elevated renal involvement, oral ulcers, Raynaud's phenomenon, elevated triglycerides and cholesterol, and most had used larger steroid.

APLAR-0162

Concomitant cryptococcal and tuberculous meningitis in a patient with systemic lupus erythematosus

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Introduction: Infection is a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Cryptococcal and tuberculous meningitis are opportunistic infections that can be fatal, especially among immunocompromised patients. Concomitant central nervous system infection with cryptococcosis and tuberculosis (TB) has been reported in immunodeficiency states such as infection with human immunodeficiency virus. However, there has been no report of such co-infection in a patient with SLE.

Objective: To describe a unique case of concomitant cryptococcal and tuberculous meningitis in a patient with SLE.

Case: A 23 year old female with a two-year history of SLE, maintained on low dose prednisone and hydroxychloroquine, presented with one week history of intermittent dizziness, nape pain, headache, vomiting and fever. On admission, she was alert and oriented. She was normotensive, tachycardic, afebrile, with alopecia, malar rash, tenderness on the acromioclavicular-sternoclavicular joint and otherwise unremarkable systemic findings. She had supple neck, grade two and three papilledema on the right and left respectively and horizontal nystagmus. There was no cranial nerve, motor and sensory deficits, no cerebellar, Babinski sign or clonus elicited.

Pertinent work-up include anemia and a communicating hydrocephalus with cortical calcifications on cranial computed tomography. Gram stain and cultures of lumbar cerebrospinal fluid were negative for bacteria but cryptococcal india ink test and TB polymerase chain reaction were positive.

She was treated with quadruple anti-KochÕs with vitamin B, intravenous amphotericin B which was later shifted to oral fluconazole, mannitol and corticosteroids with resolution of presenting symptoms. She was discharged after a month with successful recovery on follow-up visits.

Conclusion: We presented a case of concomitant cryptococcal and TB meningitis in a patient with SLE. This case highlights the need to be vigilant in detecting serious infections in our patients with SLE, which would lead to timely and life-saving treatment.

APLAR-0167

The clinical significance of anti-CENP-B antibody in rheumatic diseases

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Abstract Objective: Investigating clinical value of anti-centromere protein B (anti-CENP-B) in rheumatic diseases.

Method: Data of 2592 patients with positive anti-nuclear antibodies in Xi'an City Fifth Hospital during the period from October 2009 to October 2012 was analyzed retrospectively, including 186 cases with positive anti-CENP-B antibody (7.2%), and the anti-nuclear antibody test results and disease types of the 186 cases was analysis statistically.

Results: One Hundred and Fifty cases had autoimmune diseases (81%) in the 186 patients, including 48 cases with Localized Systemic Sclerosis (32%), 27 cases with Systemic Lupus Erythematosus (18%), 27 cases with Raynaud's disease (18%), 18 cases with Rheumatoid Arthritis (12%), 13 cases with Sjogren syndrome (8.7%), 10 cases with Connective Tissue Diseases (6.7%), 7 cases with other diseases such as Polymyositis/Dermatomyositis, Mixed Connective Tissue Disease, Osteoarthritis, Overlap Syndrome, Autoimmune Hepatitis and Ankylosing Spondylitis (4.6%). And 36 cases with non-autoimmune diseases (19%), mainly had lung and liver diseases, which were 20 cases and 8 cases, respectively, the remaining 8 cases suffered other diseases. In the 186 patients, 177 cases had positive anti-nuclear antibodies (95.2%), and the other 9 cases were negative anti-nuclear antibodies (4.8%). As for the fluorescence karyotype, the centromere type, the dot type, the homogeneous type had and other types were 117 cases, 54 cases, 36 cases and 12 cases, respectively.

Conclusion: The anti-CENP-B antibody is mainly associated with autoimmune diseases, especially Localized Systemic Sclerosis, SLE, Raynaud's disease and RA. In the patients with autoimmune diseases, anti-CENP-B antibody is mainly related with the lung and liver diseases. When the anti-CENP-B antibody is positive, the fluorescence karyotype is mainly the centromere type, but other karyotypes may also occur, and many karyotypes often appear in one specimen synchronously, the combined detection of anti-nuclear antibodies and the anti-nuclear antibodies spectrum help to improve the detection rate of autoimmune diseases.

APLAR-0176

A clinical analysis of adult patients with autoimmune- and infection-associated hemophagocytic lymphohistiocytosis

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare but potentially life-threatening disease. Secondary HLH is associated with various clinical conditions, including infections, malignancies, and autoimmune diseases. Although many previous studies reviewed the autoimmune- or infection-associated HLH, respectively, only a few studies have evaluated the differences between autoimmune- and infection-associated HLH to these factors.

Objective: To identify and compare the clinical features, treatments, and outcomes in patients with secondary HLH caused by diseases other than malignancy.

Methods: We retrospectively collected medical data on 33 adult patients who were diagnosed with autoimmune- or infection-associated HLH from 1997 to 2011 at a single tertiary hospital.

Results: Twelve patients were diagnosed as having autoimmune-associated HLH, including nine with systemic lupus erythematosus and three with adult-onset stillÕs disease. Steroid therapy was commenced for all patients and 11 of the patients recovered (91.7%). Twenty-one of our patients were diagnosed with infection-associated HLH, most commonly EBV (n = 19) followed by hepatitis A (n = 1) and parvovirus B19 (n = 1). Thirteen patients were treated according to a HLH protocol and only four patients survived (19.0%). With respect to clinical characteristics, splenomegaly was more common in patients with infection-associated HLH ($P = 0.010$). With respect to laboratory characteristics, the platelet count and the level of ESR were lower in the infection-associated HLH group ($P = 0.009$ and $P = 0.020$, respectively). Hyperbilirubinemia was more prominent in the infection-associated HLH group ($P = 0.015$). Concerning treatment, patients with infection-associated HLH were more commonly administered cyclosporine A and etoposide therapy.

Conclusions: Secondary HLH is a syndrome-based diagnosis as it encompasses various heterogeneous conditions. In the present study, autoimmune-associated HLH has mild disease activity and is considered a mild disease entity. In secondary HLH, an exhaustive search for an underlying cause, such as infection or autoimmune disease, is warranted because the results of such research may guide treatment regimens and help predict outcomes.

APLAR-0185

Comparison of anti-CRP antibodies in incomplete lupus and systemic lupus erythematosus

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Introduction: Anti-C-reactive protein (CRP) antibodies have been described in patients with systemic lupus erythematosus (SLE). We investigated the anti-CRP antibody as a disease activity marker in Korean patients with SLE and as a predictor of progression to SLE in patients with incomplete lupus.

Methods: IgG anti-CRP antibodies were measured with an enzyme-linked immunosorbent assay (ELISA).

Results: The anti-CRP antibody levels in the SLE (35.6 ± 35.1 AU) were higher than those in the incomplete lupus (23.1 ± 25.8 AU, $P = 0.016$) and NC (21.0 ± 14.3 AU, $P < 0.001$). However, only 18 patients with SLE (19%) revealed positive anti-CRP antibodies. Anti-CRP antibody levels were significantly higher in SLE patients with arthritis than those without arthritis and in patients who had antichromatin antibody those who did not. Also, a marginally significant correlation was found between the level of anti-CRP antibodies and leukocytes, platelets, C-reactive protein, complement 3, complement 4, anti-dsDNA antibody, antichromatin antibody, and Systemic Lupus Erythematosus Disease Activity Index. No significance difference in anti-CRP levels was observed in patients with incomplete lupus whether they progressed to SLE or not.

Conclusion: These data suggest that anti-CRP antibodies appear not to be a useful biomarker to aid in the assessment of SLE, nor can they predict which patients with incomplete lupus will progress to SLE.

APLAR-0186

The effects of psychological stress in disease activity in SLE

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Stress has been known as a triggering factor in systemic lupus erythematosus (SLE). Saliva has several advantages as a source of biological fluid to assess stress because it is less intrusive and easier to collect than blood. We investigated stress hormones and disease biomarkers in saliva, and collected the questionnaire representing psychological distress in patients with SLE and normal controls saliva were acquired from patients with SLE (n = 110) and age, sex-matched healthy control (n = 59). Salivary cortisol, α-amylase, and IL-1β were measured with ELISA. All participants filled out perceived stress scale (PSS) and Beck depression index (BDI) to quantify their stress and depression. The mean level of salivary α-amylase was higher in SLE than that in NC (128.09 ± 60.61 vs 101.56 ± 54.30, $P = 0.004$), however levels of cortisol and IL-1β were not different between SLE and NC ($P = 0.79$ and $P = 0.162$, respectively). Salivary α-amylase was correlated with ESR and IL-1β. Salivary IL-1β was correlated with BDI, α-amylase, disease duration, and ESR in patients with SLE. The BDI was more increased in SLE than NC (10.86 ± 9.25 vs 5.37 ± 4.82, $P < 0.001$). Though PSS had no difference between SLE and NC, the change of it was significantly correlated with that of SLEDAI for 3 months ($r^2 = 0.262$, $P = 0.006$) in SLE salivary α-amylase was elevated in patients with SLE, though it wasnÕt related with disease activity. The patients with SLE were suggested be more depressed than normal healthy control. There was no difference in recognizing stress, however, the activity of SLE became worse with increasing stress levels.

APLAR-0198

Serum cystatin C levels may be a useful marker for disease activity of systemic lupus erythematosus

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Background: Cystatin C (CysC) has been postulated to be a useful marker of glomerular filtration rate (GFR). A pilot study we performed earlier, however, serum CysC levels may relate with disease activity of systemic lupus erythematosus (SLE).

Objective: We examined the relationship between serum CysC levels and SLE disease activity with or without nephropathy.

Patients: We enrolled 48 female patients with SLE who visited our hospital from July 2012 to February 2013. Twenty-three patients who met one of the following abnormalities were classified into nephropathy group: persistent proteinuria, previous history of nephrosis, glomerulonephritis confirmed by renal biopsy, or estimated GFR≤60 mL/min. Mean age ±SD of nephropathy and non-nephropathy groups were 51 ± 12 and 45 ± 13 years, respectively.

Results: In nephropathy group, serum CysC levels significantly correlated with SLEDAI ($r = 0.43$), serum creatinine ($r = 0.60$), and inversely correlated with estimated GFR ($r = -0.56$), although they did not correlate with anti-DNA antibody titers, and serum C3 and C4 levels. On the other hand, whereas CysC did not correlate with serum creatinine, estimated GFR, SLEDAI, and anti-DNA antibody titers, there was significant inverse correlation between serum CysC levels and each of serum levels of C3 ($r = -0.41$) and C4 ($r = -0.47$) in non-nephropathy group.

Discussion: Because low C3 and C4 levels are thought to be a predictive marker of lupus nephritis, increase in serum CysC may predict the development of lupus nephritis before renal impairment appears clinically.

Conclusions: Serum CysC level was a useful marker for disease activity in patients with SLE and may be a predictive marker for development of lupus nephritis.

APLAR-0231

Pulmonary hypertension in systemic lupus erythematosus (SLE) is associated with severe outcome

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Pulmonary hypertension (PH) is rare complication of SLE and it is associated with bad prognosis.

We evaluated retrospectively the medical records of SLE patients which were followed in our rheumatology outpatient clinic between 2001 and 2012. The pulmonary artery systolic

pressure was more then 30 mmHg at rest on echocardiogram were enrolled into the PH group.

Of the 72 patients under follow-up, results of echocardiografic evaluation were available in 70; among these, 5 had PH (7%). Four patients with PH (mean age 44.0 + 16.1) and 55 patients without PH (mean age 40.1 + 11.9) were female. In patients with and without PH, the age at onset were similar (33.0 ± 12.6 and 36.4 ± 18.4 years). The duration of follow up was also similar (25.8 ± 23.2 vs 24.1 ± 19.4 months). In patients with PH the time interval between disease onset and diagnosis was longer (42.0 ± 83.9 months vs. 20.6 ± 30.8 months; $P = 0.001$). None of the patients in the PH group had antiphospholipd syndrome and antiphospholipid antibodies. In 18 patients without PH, at least one antibody was positive and 6 (9.2%) had the antiphspholipid syndrome. Twenty percent of the patients with PH had the Raynaud's phenomenone and 6.2% had livedo reticularis. None of the patients without PH had Raynaud's phenomenone or livedo.The frequency of oral ulcer (80%, 30.8%; $P = 0.04$), pleuritis (40%, 18.5%; $P = 0.026$), renal (60%, 40%; $P < 0.05$), neurological (20%, 9.2%; $P < 0.05$) and haematological (80%, 61.5%; $P < 0.05$) involvement and anti-dsDNA positivity (80%, 60.3%; $P \leq 0.05$) was significantly higher in the PH group. Vasculitic lesions (40% and 3.1%, $P = 0.02$) and venous thrombosis (20% and 6.2%; $P < 0.05$) were more frequent in the PH group. Mean damage index was 3.0 ± 2.9 in the PH group and 0.9 ± 1.3 in without PH ($P = 0.001$).

The time interval between disease onset and diagnosis was longer in the PH group. In patients with PH, organ involvement was more frequent and damage index was higher.

APLAR-0262

Increased expression of interleukin 33 in sera and salivary gland from patients with Sjogren syndrome

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Background: Interleukin 33 (IL-33), a member of IL-1 superfamily, exerts pro-inflammatory effect by binding with ST2 expressed on many cell types. Recently, the association of IL-33 with autoimmune disease has been increasingly reported.

Objective: The aim of this study is to identify the expression of IL-33 and ST2 in sera and salivary gland tissues from patients with Sjogren syndrome (SS).

Methods: Serum IL-33 and was measured in patients with and without SS. Expression of IL-33 and ST2 in salivary gland tissue from patients with and without SS was assessed by immunohistochemistry. The source of IL-33 in salivary gland of patients with SS was investigated using confocal microscopy system after staining with cytokeratin antibody, CD31 antibody and IL-33 antibody. Additionally, we examined the expression of IL-33 mRNA and ST2 mRNA. The level of IL-33 mRNA in salivary gland cell line (human head and neck squamous cell carcinoma A253 cell) was determined after stimulation with inflammatory cytokines. Also, we measured the level of ST2 mRNA from peripheral blood mononuclear cell (PBMC) isolated from blood of patients with and without SS.

Results: Serum IL-33 level was significantly higher in SS group than that of control group ($P = 0.004$). Immunohistochemistry of salivary gland revealed increased expression of IL-33 and ST2 in SS group. We demonstrated the expression of IL-33 in epithelial and endothelial cells from salivary gland of patients with SS. The expression of IL-33 mRNA in A253 cell was considerably increased after stimulation with interferon gamma. The level of ST2 mRNA in PBMC was higher in SS group than control group, although statistically not significant ($P = 0.093$).

Conclusions: Our result shows that IL-33 is involved in the pathogenesis of SS. Further research would suggest a new therapeutic approach associated with IL-33/ST2 pathway in SS.

APLAR-0274

Association of anti-C1q antibodies with clinical manifestation, disease activity, and some activity markers in SLE

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Objective: Serum antibodies to C1q has been reported to be elevated in many patients with systemic lupus erythematosus (SLE). Some studies also showed association of anti-C1q with nephritis, leucopenia, hypocomplementemia, and anti ds-DNA. The association of high titer anti-C1q with different clinical manifestations and disease activity in SLE, however, are not definitely understood.

Methods: All new SLE patients were included from February * July 2012, every clinical presentation was recorded. We measured the levels of IgG type anti-C1q using an ELISA method. Disease activity was measured using SLAM (Systemic Lupus Activity Measure). Complete blood count, anti ds-DNA, C3, and C4 were also performed.

Results: There were 40 new SLE patients (39 females, 1 male). The mean anti-C1q level was 42.18 ± 52.16 U/mL, 31 subjects (77.5%) had highanti-C1q titer. There were 17 subjects (42.5%) with kidney manifestation, 12 (30%) had serositis, 6 (15%) with neuropsychiatric lupus, 32 (80%) with arthritis, and 9 (22.5%) had leucopenia. The mean C3 level was 68.70 ± 37.08 mg/dL. Twenty-six (65%) had low C3 level. The mean C4 level was 18.75 ± 10.69 mg/dL,13 (32.5%) had low C4 level. The mean anti ds-DNA titer was 224.96 ± 298.62, 23 (57.5%) had negative titer.

There was a significant correlation between anti-C1q and disease activity ($P = 0.011$ and $r = 0.399$). There was also a negative correlation between anti-C1q and complement C3 and C4 ($P = 0.004$ and $r = -0.443$ for C3 and $P = 0.006$ and $r = -0.429$ for C4), There was a significant correlation between anti-C1q and anti ds-DNA ($P = 0.009$ and $r = 0.410$). There was no significant correlation between anti-C1q and leucocyte level. There was no association of anti-C1q level with specific clinical manifestations.

Conclusion: High titer anti-C1q are associated with disease activity, level of C3,C4, and anti ds-DNA, but had no association with specific clinical manifestations of SLE.

Keywords: Anti-C1q, SLE, disease activity.

APLAR-0288

The coagulation function of 77 biopsy-proven lupus nephritis patients in Southern China

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Objective: To evaluate the coagulation function of 77 biopsy-proven lupus nephritis patients in Southern China, and analyze their relationship with other clinical features.

Methods: Seventy-seven biopsy-proven LN patients from Southern China were recruited, including 12 type I, 12 type II, 4 type III, 38 type IV, 11 type V patients. There were 66 females and 11 males, averagely 29.3 ± 10.9 years old. The coagulation functional biomarkers, such as PT, PTA, Fib, APTT, TT, the SLEDAI, laboratory tests such as ALB, C3 et al., were analyzed.

Results: (1) The Fib ascended in 25 (35.2%) LN patients, including 2 LN I, 2 LN II, 2 LN III, 14 LN IV, 5 LN V patients. (2) The PTA elevated in 28 (26%) LN patients, including 0 LN I, 3 LN II, 2 LN III, 18 LN IV, 5 LN V patients ($P = 0.037$). (3) The ALB ($P < 0.001$) and C3 ($P = 0.001$) differed in LN patients, the ALB highest in LN I (40.98 ± 1.092), lowest in LN IV (30.3 ± 1.065, $P < 0.001$) patients, while the C3 highest in LN I (0.95 ± 0.062), lowest in LN IV (0.51 ± 0.051, $P < 0.001$) patients. (4) SLEDAI differed in LN patients ($P = 0.004$). The highest were found in type IV LN (17.21 ± 1.029), while LN I (8.50 ± 1.848) was lower than other types ($P < 0.05$). (5) No significant correlations were found between the coagulation function and clinical features.

Conclusions: (1) The coagulation function (Fib, PTA) seems more frequently elevated in LN III, IV, V than LN I and II patients. (2) LN IV patients frequently have elevated Fib and PTA levels, the highest SLEDAI, the lowest levels of ALB and C3, while the LN I patients have the normal coagulation function, the lowest SLEDAI, the highest levels of ALB and C3. We should pay more attention to the type IV LN patients, especially in the coagulation function.

APLAR-0317

Correlation TNF a serum levels with SLE disease activity

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Objective: SLE is a chronic systemic autoimmune disease with vary widely clinical manifestations. Controversial on the role of TNFα in the pathogenesis of SLE probably reflects the spectrum in different tissues. Increased levels of TNF α have been observed in the serum of SLE patients, but correlation with disease activity has varied among studies. Several studies linking elevated levels serum TNFα and SLEDAI.

Methods: A cross sectional study with 40 samples fulfilled ACR 1997 criteria. The level of TNFα serum were measured with ELISA Kit. Disease activity were measured by SLAM (Systemic Lupus Activity Measurement). Collected data was analyzed using Spearman 's correlation test.

Results: Of the patients studied SLE mean aged was 31 ± 7.89 years old. Most patients were female (97.2%). The mean level of TNFα was 3.905 ± 1.1554. The mean score SLAM in SLE patients was 21.06 ± 6.26. There is a significant correlation between the level of TNFα serum with SLAM score ($P = 0.0001$, $r = 0.971$).

Conclusion: This study showed that TNFα levels significantly correlated with SLE disease activity as measured by SLAM.

Keywords: TNFα, disease activity, SLAM.
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APLAR-0356

The role of Axl receptor tyrosine kinase in systemic lupus erythematous

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Background: Axl is receptor tyrosine kinase important in regulation of innate immunity and phagocytosis of apoptotic cells and may involved in the pathogenesis of systemic lupus erythematous (SLE).

Objective: To investigate the clinical relevance of Axl in SLE, we evaluate the membrane expression of Axl (mAxl) on the surface of CD 14$^+$monocytes/macrophages and measure the plasma levels of soluble Axl (sAxl).

Methods: One hundred and five SLE patients and 40 normal controls were recruited. mAxl on the surface of CD 14+ monocytes/macrophages in peripheral blood mononuclear cell

(PBMC) was evaluated by Flow cytometry (FCM). The plasma sAxl levels were measured by ELISAs.

Results: Overall, the concentrations of sAxl was significantly higher ($P < 0.01$) in the serum of the patients with SLE (45025 ± 1827 pg/mL) than that in normal controls (31640 ± 1290 pg/mL), but the MFI of mAxl expression on $CD14^+$ monocytes/macrophages was significantly lower (8.09 ± 1.37 vs. 14.66 ± 2.16, $P = 0.01$). In patients with SLE, the MFI of mAxl expression on CD14+ monocytes/macrophages was significantly correlated to the serum concentration of component 3 (C3) ($r = 0.504$, $P = 0.009$). The sAxl levels were positively correlated to SLEDAI ($r = 0.245$, $P = 0.007$).It was also found that sAxl levels were correlated to decreased haemoglobin ($r = -0.263$, $P = 0.007$), thrombopenia ($r = -0.225$, $P = 0.021$), decreased C3 ($r = -0.364$, $P = 0.00021$) and C4 ($r = -0.301$, $P = 0.003$) and increased levels of anti-dsDNA antibody ($r = 0.28$, $P = 0.007$) and anticardiolipin antibody ($r = 0.282$, $P = 0.011$). Meanwhile, the sAxl level was positively correlated to sedimentation rate ($r = 0.205$, $P = 0.046$). The SLE patients with AnuA showed higher concentrations of sAxl than those without AnuA (52138 ± 4653.95 pg/mL vs. 39449 ± 1709.14 pg/mL, $P = 0.021$).

Conclusions: The expression of mAxl on the surface of $CD14^+$ monocyte/macrophage was significantly decreased while circulating sAxl concentrations were significantly elevated in SLE patients, especially in those with severe disease activity. Our study indicated that Axl tyrosine kinase receptor might have important role in the pathogenesis of systemic lupus erythematous.

APLAR-0364

Increased mTOR activity in CD4+ T cells from SLE patients causes their resistance to activation-induced death

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Background: As we know, over-activated CD4+ T cells play an important role in the pathology of SLE. They can secret many pro-inflammatory factors without normal regulation. Previous studies have found that mTOR activity was up-regulated in T cells from SLE patients and mTOR inhibitors such as rapamycin could improve their disease activity. However, itOs unclear whether defective activation-induced cell death (AICD) of CD4+ T cells from SLE patients was attributed to increased mTOR activity.

Objectives: To investigate whether resistance to AICD of CD4+ T cells from SLE patients was due to their increased mTOR activity.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood of SLE patients and healthy donors. mTOR level and frequency of CD4+ T cells were measured by flow cytometric analysis.

Results: Baseline mTOR activity was significantly higher in both CD4+ and CD4- T cells from SLE patients compared with that from healthy controls. And CD4+ T cells have a higher mTOR level than CD4-T cells in SLE patients. After cultured *in vitro* with anti-CD3/CD28 antibodies for 3 days, we found that mTOR activity of both CD4+ and CD4-T cells from SLE patients decreased to normal level, even lower than that from healthy controls, though without significant difference. However, CD4+ T cells still had a higher mTOR activity than CD4- T cells in SLE patients. Meanwhile, the frequency of CD8+ T cells rather than CD4+ T cells was robustly reduced, in a degree much higher than controls, which was negatively correlated with their mTOR activity.

Conclusion: Increased mTOR activity in CD4+ T lymphocytes causes their resistance to activation-induced cell death.

APLAR-0365

SLE Serum induced senescence of mesenchymal stem cells via activation of NF-kB signaling pathway

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Background and Objective: We have demonstrated that bone marrow-derived mesenchymal stem cells (BM-MSC) from systemic lupus erythematosus (SLE) patients showed abnormal morphology and dysfunction, including cytoskeleton changes, enhanced apoptosis and senescence, decreased migration. It has been reported that transplantation of BM-MSC from young NZB/NZWF1 mice (clinically unaffected) into lupus mice could be as effective as that from C57BL/6 mice, much better than that from old mice (clinically affected). The objective of this study is to explore whether microenvironment of SLE patients (such as SLE serum) affected MSC senescence.

Methods: Serum were isolated from SLE patients and healthy controls, and BM-MSCs were cultured in these serum. MSC proliferation were examined by CCK8, and apoptosis detected by flow cytometry, and senescence of MSCs was evaluated by SA-b-gal staining, expression of p53 and p21 (tested by western blot and real time PCR), DNA damage response 53BP1 (detected by immunofluorescence). In addition, NF-kB p65 was tested by western blot analysis and real time PCR.

Results: MSCs cultured in SLE serum showed significantly increased apoptosis (39.18 ± 3.36%), compared with those in normal serum (9.48 ± 2.67%). Proliferation capacity of MSCs in SLE serum was notably impaired. SLE serum treatment could induce higher number of SA-b-gal positive cells, higher expression of p53 and p21 of MSCs. The expression of 53BP1 was markedly enhanced in SLE serum. In addition, NF-kB p65 expression was increased significantly after MSCs were treated with SLE serum.

Conclusion: SLE serum could induce MSC senescence, which may be mediated by activation of NF-kB signaling pathway.

APLAR-0367

Treg/Th17 imbalance mediated by miR-663 through down-regulating TGF-O1 secretion of bone marrow-derived mesenchymal stem cells inSLE

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Background: Our previous study demonstrated that bone marrow derived mesenchymal stem cells (BMSCs) from systemic lupus erythematosus (SLE) patients are defective in immune modulation, which might be involved in its Treg/Th17 imbalance, but the mechanisms are not clear yet. As computer predicted target of miR-663, Transforming growth factor-beta1 (TGF-β1) is an important immune regulatory factor secreted by BMSCs which could modulate SLE Treg/Th17 imbalance.

Objectives: To investigate whether miR-663 could contribute to SLE Treg/Th17 imbalance though down-regulating TGF-β1 of SLE BMSCs.

Methods: BMSCs were expanded from bone marrow of four healthy donors and four SLE patients. Real-time PCR was used to determine miR-663 and TGF-β1 expression. As a computer predicted target, TGF-β1 was directly determined using the luciferase reporter assay system. MSCs were transfected with pre-miR-663a, miRNA control, and anti-miR-663a and co-cultured with PBMCs from SLE patients, flow cytometry was used to detect their effect on ratio of Treg/Th17.

Results: The expression of miR-663 was markedly up-regulated in SLE MSCs compared to normal controls, while TGF-β1 mRNA was significantly lower in SLE MSCs. Transfection of SLE MSCs with pre-miR-663a caused markedly upregulation of miR-663a and lower synthesis of TGF-β1, while anti-miR-663a led to an opposite effect. Compared to SLE MSCs, MSCs from normal controls exhibited a better immune suppression effect through up-regulating SLE Treg/Th17, and transfection of normal MSCs with pre-miR-663a caused significant downregulation of Treg/Th17, while anti-miR-663a led to an opposite effect.

Conclusions: Treg/Th17 imbalance in SLE patients might be associated with down-regulated TGF-β1 secretion of SLE MSCs mediated by miR-663.

APLAR-0369

Eveluated level of Serum antibodies against human lipocalin 2 in systemic lupus erythematosus

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Background: Human lipocalin 2 was involved in the pathogenesis of systemic lupus erythematosus (SLE). There was increased urine lipocalin in SLE patients, leading to self lipocalin loss. Nevertheless, the serum lipocalin antibody level remains controversial. The aim of this study was to evaluate the value of serum IgG antibody against lipocalin in diagnosis of SLE.

Methods: The level of serum anti-lipocalin IgG antibodies was detected by ELISA in 103 SLE patients, 93 rheumatoid arthritis (RA) patients, 30 primary Sjogren's syndrome (pSS) patients, 13 systemic sclerosis (SSc) patients, and 91 healthy controls. The antibody titer was expressed as AU values. Diagnostic properties of anti-lipocalin IgG were determined by receiver-operating characteristic curve analysis.

Results: The serum anti-lipocalin IgG antibody level in patients with SLE was significantly higher than that in patients with RA, pSS, SSc, and in healthy controls ($P < 0.05$), with more sensitivity and specificity (49.5% and 90.7%, repectively). Anti-lipocalin antibodies are present in 48.1% of anti-Sm negative SLE patients, and anti-lipocalin antibodies may also exist in SLE lacking of anti-dsDNA (52%) and anti-nucleosome antibodies (46.3%), respectively. Moreover, anti-lipocalin IgG positive SLE patients revealed higher CRP and IgG levels than anti-lipocalin IgG negative patients ($P < 0.05$). Anti-lipocalin IgG antibody level was positively correlated with the levels of CRP and IgA.

Conclusions: Higher levels of anti-lipocalin IgG antibody were demonstrated in the sera of SLE patients. This antibody might be served as a novel diagnostic marker for SLE.

Table 1. The sensitivity and specificity of IgG anti-lipocalin antibodies in SLE and other rheumatic diseases.

	N	Sensitivity (%)	Specificity (%)
SLE	103	49.5	90.7
RA	93	9.6	73.3
pSS	29	27.5	78.6
SSc	13	15.3	77.8
HC	91	2.1	NN

Table 2. The frequency of anti-lipocalin in SLE lacking of anti-dsDNA, Sm and nucleosome antibodies

Antibodies	n	Anti-lipocalin positive	
		n	%
Anti-nucleosome (-)	41	19	46.3
Anti-Sm (-)	81	39	48.1
Anti-dsDNA (-)	50	26	52

Table 3. Comparison of clinical and laboratory features between patients with anti-lipocalin and those without anti-lipocalin

	Anti-lipocalin (+) (n = 51)	Anti-lipocalin (−) (n = 52)	*P*
dsDNA, n (%)	28 (54.90)	23 (44.23)	0.278
Sm (+), n (%)	8 (15.68)	11 (21.15)	0.474
SLEDAI	13.62 ± 9.67	13.84 ± 7.63	0.899
RF, median U/mL	20 (0.1Ñ868)	20.7 (20Ñ2510)	0.768
ESR, median, mm/h	45 (9Ñ156)	26 (3Ñ166)	0.037
CRP level, median mg/L	5.22 (1Ñ155)	2.04 (0Ñ203)	0.002
IgA, mean ± SD, g/L	3.04 ± 1.37	2.21 ± 1.32	0.004
IgG, median g/L	17.45 (1Ñ62)	14.3 (0Ñ26.5)	0.095
IgM, median g/L	0.86 (0Ñ4.74)	0.99 (0Ñ4.06)	0.766

APLAR-0375

Pulmonary manifestations in systemic lupus erythematosus

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Introduction: Systemic lupus erythematosus (SLE) is a complex systemic autoimmune disease, with numerous immunologic and clinical manifestations. More than half of all patients with SLE will experience involvement of the lung parenchyma, pulmonary vasculature, pleura, or chest wall, which are collectively considered pulmonary manifestations of lupus.

Objectives: Purpose of our study was the identification of pulmonary manifestations in patients with systemic lupus erythematosus, their assessment in relation to immunological alterations and their relation to gender.

Patients and Methods: This is a cohort prospective study that analyzed 60 patients with systemic lupus erythematosus. History of disease taking. Patients were examined by immunological tests such as: anti-nuclear antibody test, anti double stranded DNA antibody and anticardiolipin antibodies. Chest x-ray, pulmonary high-resolution computed tomography, computerized tomographic pulmonary angiography, pulmonary function tests and echocardiography doppler were performed for the patients.

Results: Pleural effusion are 17(28%) patients. Interstitial lung disease is found in 7 (12%) patients, acute lupus pneumonitis 2 (3%) patients, pulmonary tromboemboli 7 (12%) patients and pulmonary arterial hypertension were 3 (5%) patients. Restrictive ventilator insufficiency are 19 (32%) patients.

Conclusions: Pulmonary manifestations are common in SLE and have a wide spectrum. These injuries are anatomical and functional. Immunological alterations are important factor in pulmonary injuries. Gender is a factor that influences the pulmonary injuries.

Keywords: lupus, pulmonary, pleural effusion.

APLAR-0379

Relationship between systemic lupus activity measurement (SLAM) score and mortality on systemic lupus erithematosus inpatients in Sardjito Hospital Yogyakarta

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Background: SLE is a chronic autoimmune disorder that can be severe and life threatening. Death in SLE may be due to lupus activity or long-term sequelae. SLAM score is one tool that can count lupus activity in our patients.

Objective: To analyze relationship between SLAM score and mortality in lupus inpatients.

Method: Retrolective cohort study was used for reaching objective of the study. Lupus inpatients was used as research population. Medical record was used as study data collection over period of 2004 until 2011. Independent variable was SLAM score. The cut of point of SLAM score was made based on the mean of SLAM score (16.7 point score). Dependent variable was mortality.

Result: We got 106 medical records of lupus inpatients. Fifty five (51.4%) of samples had SLAM score more than mean value (16.7 point score). Twenty three (22%) of samples were passed away while discharge. There was a difference of median survival between less and more than 16.7 point score, 346.73 and 316. 03 respectively (p 0.37). There was a relationship between SLAM score (more than 16.7 point score) and mortality HR 2.76 (95%CI 1.01–7.53).

Conclusion: There was a relationship between SLAM score and mortality in lupus inpatients.

APLAR-0390

Kikuchis disease related to systemic lupus erythematosus

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Objectives: The aim of this study is to expand the number and the understanding of the cases of Kikuchi's disease in SLE.

Results: We found eight cases of Kikuchi's disease occurring in SLE patients and analyzed the clinicopathological features of our collected cases. Table showed the characteristics of Kikuchi's disease in SLE. Kikuchi's disease in SLE is predominant in young female. The sequence of occurrence of both diseases is not consistent. When the Kikuchi's disease and the lupus evolve simultaneously, the clinical manifestations were varying from lymphadenopathy alone to lupus flare up. Mostly, systemic manifestation is related to lupus rather than Kikuchi's disease.

No	Age	Sex	Skin lesion	ANA	Other Ab	Diagnosis SLE	Treament	Other findings
1	26	F	face, trunk	640, sp	Sm	concomitant	Pr	vasculitis on Brain MRI
2	23	M	malar	160,sp	Ro, La	concomitant	MP (IV)	nephritis, serositis
3	30	F	malar	1280, sp	Ro	Before	antibiotics	recurrence
4	20	F	malar	640, sp	ds DNA,Sm, Ro, U1 RNP,	Before	MP (IV)	recurrence
5	29	F	-	1280,sp	negative	concomitant	Pr	myositis, serosittis
6	24	F	malar	1280, sp+homo	ds DNA,	concomitant	Pr	nephritis
7	36	F	malar	320,sp	ds DNA,	concomitant	Pr	serositis
8	27	F	face, neck	320, nucleolar	UI RNP, Ro	Before	Pr	

Methods: We retrospectively reviewed the medical record of patient who had Kikuchi's disease and SLE from 2000 to 2009. The patients were from four tertiary medical centers. Kikuchi's disease was proven by pathologically. The diagnosis of SLE was based on the 1982 Revised ACR Criteria.

Conclusion: First, flare up of lupus was more common in both disease simultaneously onset than in Kikuchi's disease following the onset of lupus. Second, lymphadenopathy in Kikuchi's disease with lupus can be recurrent. Third, skin lesion is commonly found in Kikcuhi's disease in SLE.

APLAR-0409

End-organ damage in a cohort of Filipino patients with systemic lupus erythematosus at two tertiary hospitals

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Objective: This retrospective study describes the prevalence and characteristics of end-organ damage among Filipino systemic lupus erythematosus (SLE) patients.

Design: We reviewed the medical records ofadult (≥18 years old) patients seen at the lupus clinics of two tertiary hospitals (University of Santo Tomas, St. LukeOs Medical Center) from January 2012 to January 2013. Patients with incomplete charts and who were lost to follow-up for at least 6 months were excluded from the study. Patients were assessed for the presence of end-organ damage using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/SDI). Other characteristics of SLE patients with end-organ damage, such as presenting manifestations at diagnosis, average steroid dose per day and cyclophosphamide use were also analyzed.

Results: Two hundred and twenty-one patients (210, 95% females), with mean age at diagnosis at 28 ± 10.52 years and mean disease duration of 10 ± 6.56 years were included in the study. One hundred and thirty-six (61.5%) had at least 1 end-organ damage. The most commonly damaged organ systems were the renal (59, 43%), ocular (38, 28%), neuropsychiatric (30, 22%), and musculoskeletal (29, 21%). Damage occurred at an average of 6 years after diagnosis. Development of a subsequent damage occurred at an average of 2 years after the first damage. Among those with end-organ damage, mucocutaneous, hematologic, and musculoskeletal were common presenting manifestations. Average prednisone dose was >10 mg/day, and 59 (43%) of these patients had received cyclophosphamide.

Conclusion: In this cohort of SLE patients, majority were found to have end-organ damage. The renal, ocular, neuropsychiatric, and musculoskeletal were the most damaged organ systems. Mucocutaneous, hematologic, and musculoskeletal were most common presenting manifestations. Average prednisone dose was >10 mg/day among patients with end-organ damage, reiterating the contributory role of therapy to damage in SLE.

Funding: Lupus Inspired Advocacy (LUISA) of Rheumatology Educational Trust Foundation, Inc.

APLAR-0413

Reasons for admission in hospital and the outcome of systemic lupus erythematosus patients

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with variable manifestation, high morbidity as well as mortality. During the course of disease, SLE patients have risk to develop severe condition which required admission in hospital. The bimodal pattern of mortality is infection and flare in the early of disease course, and cardiovascular event in the long term period which should be anticipated during manage of this disease. The objective of this study to determine the cause of admission of SLE patients in our hospital and their outcomes during 2012.

Method: This is a retrospective study by reviewing the medical record of SLE patients who had been admitted in Hasan Sadikin Hospital in Bandung, Indonesia, from January to December 2012. Data of sex, age, duration of disease, reasons for admission, lupus involved during admission, length of stay in hospital and the outcomes were recorded.

Result: There were total 60 SLE patients had been admitted in our hospital with total of 70 admissions (6 patients had readmission) during 2012. Fifty five (91.67%) were female, with the mean of age 29.55 ± 9.53 years and duration of disease of 26.04 ± 35.76 months. The reasons for admission were: cardiovascular event (2 cases, 2.9%), disease flare (41 cases, 58.6%) with most of neuropsychiatry and nephritis, and infection (27 cases, 38.6%), most of respiratory tract infection. The length of stays was 10.93 ± 8.37 days. The outcomes of these patients were: 50 (83.3%) improved, however 10 (16.7%) died, most of them due to severe infection.

Conclusion: Infection was one of the major reasons SLE patients admitted in hospital, beside activity of disease itself. The outcome of SLE patients who were admitted was poor.

Keyword: hospital admission, systemic lupus erythematosus, infection.

APLAR-0435

The application of systemic lupus erythematosus-specific quality of life questionnaire in systemic lupus erythematosus

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Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease associated with high mortality rate. We investigated the application of a new Chinese used disease-specific health related quality of life (HRQOL) instrument for adults with SLE, Specific Quality of Life questionnaire in Systemic Lupus Erythematosus (SLEQOL), so as to improve the quality of life of SLE patients.

Methods: A total of 157 Chinese SLE patients were included in this investigation. We measured the quality of life with SLEQOL and the Short Form-36 (SF-36) questionnaire. Disease activity was measured using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). The information of patients, gender, disease duration, age, education was also recorded.

Results: The scores of patients with severe disease activity are significantly increased in the physical functioning of SLEQOL than patients who do not have activity, as well as who with mild and moderate activity ($P < 0.05$). For health transition the SF-36 scores of patients with moderate and severe disease activity are higher than those who have no disease activity ($P < 0.05$). For role emotional the SF-36 scores of patients with mild or severe disease activity are higher than those who have no disease activity. Lupus disease activity was positive correlation with the physical functioning of SLEQOL and negative correlation with the health transitioning of SF-36 (the correlation coefficients was 0.36 and -0.24 respectively, $P < 0.05$). On multivariate regression models both disease duration and education were predictive factors of the SLEQOL.

Conclusions: SLEQOL was a valid and reliable instrument in assessing HRQOL in Chinese SLE patients. Quality of life of SLE patients is related to the disease activity and impacted by disease duration and education.

APLAR-0447

Effects of vitamin D supplementation on disease activity and fatigue conditions of systemic lupus erythematosus patients with hypovitamin D

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Background: Vitamin D have received particular attention in recent years as immunomodulator. On previous studies, low level of vitamin D linked with autoimmune disease, such as systemic lupus erythematosus (SLE). There was an inverse relationship between levels of vitamin D and fatigue degree, and so was autoantibody production.The purpose of this study was to determine the association between vitamin D level with disease activity and fatigue in systemic lupus erythematosus with hypovitamin D.

Methods: This study was conducted in twenty active disease SLE patients (SLEDAI score>5) with clinical trial double blind by supplementation each patient for 3 months. The level of vitamin D [25(OH)D3] was assayed by ELISA. The patient which was hypovitamin D would include as sample, then disease activity would measured with SLEDAI and fatigue would measure with Fatigue Severity Scale (FSS). After supplementation with vitamin D 1200 IU/day and placebo (as control), level of vitamin D,SLEDAI, FSS would evaluated again. Difference level of vitamin D, SLEDAI, and FSS pre-post trial were analized with Chi square test. Correlation of vitamin D level, SLEDAI, and FSS pre-post trial were analized by Spearman test. P value <0.05 was considered significant.

Results: This study still on going. From February – March 2013, we had 10 patients to be studied. All patient were female, age 16–39 years old (mean = 30.8 years). Onset of SLE disease were 0.5–12 months (mean = 2.68 month). All patients had hypovitamin D, the lowest 14 ng/mL and the highest 29.8 ng/mL (mean = 23.04 ng/mL). SLEDAI score the lowest were 7 and the highest were 26 (mean = 12.18). FSS score, the lowest were 5.1 and the highest were 6.8(mean = 6.09). Within one month follow up 6 (60%) patient showed FSS score improvement and 7 (70%) patient also showed MEXSLEDAI improvement (we have to wait 3 months to recheck SLEDAI).

Key words: SLE, vitamin D, FSS, SLEDAI.

APLAR-0448

The association between vitamin D and bone mineral density in systemic lupus erithematosus patients

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Background: Evidence showed high prevalence of vitamin D deficiency and low BMD in SLE patients.

Aim: To evaluate the association between vitamin D and BMD in women with systemic lupus erythematosus (SLE).

Method: A cross-sectional observational study was conducted among 28 consecutive SLE women based on ACR 1997 criteria and 20 healthy women. Serum $25(OH)D_3$ measured by ELISA method, bone mineral density (BMD) measured by dual X-ray absorptiometry (DXA). Comparison between vitamin D level in SLE patients and healthy control analyzed using independent *t*-test. The association vitamin D and BMD analyzed using Pearson's correlation. Variables influence the BMD analyzed using multiple linier regression.

Result: Mean of vitamin D level was 19.5 ± 9.02 ng/mL. 57.1% patients had vitamin D deficiency, and 32.1% patients had vitamin D insufficiency. 60.7% patients had low BMD, 10.7% patients had low BMD at lumbar spine, 21.4% patients at hip, and 28.6% patients had low BMD at lumbar and hip. There was significant difference vitamin D level in SLE patients and healthy control. There was significant association between vitamin D level with BMD ($r = 0.390$ $P = 0.040$) and ESR with BMD ($r = -0.423$ $P = 0.03$).

Key Words: Systemic lupus erithematosus, vitamin D, bone mineral density.

APLAR-0450

The association between molecular heterogeneity of prolactin and autoantibodies and complement levels in patients with systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease commonly found among reproductive women, suggesting that prolactin (PRL) hormone may play role. There are three PRL isoforms: small, medium, and large. Small PRL has been reported to play role in activation of immune system. This study was aimed to investigate the relationship between molecular heterogeneity of PRL and anti-dsDNA, anti-C1q, and Complement C3 levels in patients with SLE.

Subjects and Methods: This study included 30 premenopausal women diagnosed with SLE at Rheumatology Clinic of Doctor Saiful Anwar Malang Public Hospital and 30 healthy women as control group. PRL heterogeneity (small and large) was examined using ultra filtration method and ECLIA. Total PRL, anti-dsDNA, anti-C1q and C3 levels were measured by ELISA.

Results: There were significant differences in mean total PRL (13.83 ± 8.78 vs 9.14 ± 3.85 ng/mL; $P = 0.01$), small PRL (4.45 ± 1.88 vs 2.49 ± 0.29 ng/mL; $P = 0.00$), anti-dsDNA (153.62 ± 99.1 vs 19.20 ± 3.21 U/mL; $P = 0.00$) and C3 (9.50 ± 1.40 vs 75.6 ± 7.46 mg/dL; $P = 0.00$) levels between SLE patients and healthy control group. Significant correlations were found between small PRL and anti-dsDNA ($r = 0.978$; $P = 0.00$) and C3 ($r = -0.970$; $P = 0.00$) levels. Small PRL was not associated with anti-C1q level.

Conclusions: Small PRL is associated with anti-dsDNAantibody and C3 levels in term of the higher small PRL level, the higher antibody anti-dsDNAthe lower C3 levels.

Key words: PRL, anti-dsDNA, anti-C1q, C3, SLE.

APLAR-0455

Serum levels of IL-18 as an indicator of disease activity in Iranian females with systemic lupus erythematosus

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IL-18 is a member of the IL-1 family of cytokines but due to its unique inflammatory and immunoregulatory properties it is suggested that it plays important roles in autoimmune and inflammatory diseases like as systemic lupus erythematosus (SLE). The current study was sought to evaluate serum levels of IL-18 as prognostic factor of disease activity and organ involvment in Iranian females with SLE. Serum samples of 25 patients with low disease activity, SLE-DAI score <7, 25 with high disease activity, SLE-DAI score ≥7 and 25 normal subjects were assessed for IL-18, anti-ds-DNA, C3, C4 and other lab findings using appropriate methods. Level IL-18 in patients with SLE-DAI score ≥7 was significantly higher than patients with low disease activity and controls ($P = 0.026$ and $P = 0.005$, respectively). In patients with high disease activity, a positive correlation was found between serum levels of IL-18 with DsDNA antibody, protein levels in 24 h collected urine, platelet counts and it correlates negatively with serum C-3 levels.The findings point to important role of IL-18 in SLE patients with disease activity higher than SLE-DAI score 7.

APLAR-0460

Correlation between inflammation, disease activity, corticosteroid therapy with atherosclerosis in systemic lupus erythematosus patients

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Background: Systemic Lupus Erythematosus is a chronic autoimmune inflammation disease, with a high prevalence in young female. Coronary artery disease is major caused mortality and morbidity in late case of SLE patients. Female with SLE at 35–44 years old have fifty times greater to had myocardial infarction than control. Premature atherosclerosis cannot be explained by traditional risk factors alone, it has been attributed to complex interaction between traditional risk factors and factors associated with the disease itself or its treatment.

Objective: To assess the premature atherosclerosis in SLE patient, measured by the intima media thickness of carotid artery by using B mode USG.

Methods: This observational analytic is a cross sectional study, carried out from June 2007 to February 2008. Forty Indonesian female SLE patients were recruited that fulfils criteria of ACR 1997.

Results: From 40 patients, we found 10 patients with premature atherosclerosis (25%). Patients presented with fever 7.5%, rash 60%, arthritis 53%, edeme 45%.With baseline characteristic: female 17–57 years old. The mean age 31.22 ± 8.5228, mean age SLE patients without atherosclerosis Vs premature atherosclerosis (29.70 ± 7.35 Vs 34.90 ± 11.87; $P = 0.108$). The mean BMI 21.51 ± 4.27 mean BMI SLE patient without atherosclerosis Vs with premature atherosclerosis (20.87 ± 3.59 Vs 23.43 ± 5.68 $P = 0.207$). Mean duration of SLE (in month) 31.85 ± 33.19, mean duration of SLE without atherosclerosis Vs with premature atherosclerosis (24.8 ± 29.8 Vs 52.9 ± 35.44 $P = 0.041$). Mean of CRP0.73 ± 0.89 mean CRP SLE patient without atherosclerosis Vs with atherosclerosis (0.53 ± 0.22 Vs 1.33 ± 0.71 $P = 0.046$). Mean duration of corticosteroid therapy (in month) 20.97 ± 22.67 mean duration of corticosteroid therapy SLE patient without atherosclerosis Vs with atherosclerosis (15 ± 9.70 Vs 38 ± 10.36 $P = 0.003$).

Conclusion: LDL level, Sugar Level, and Blood pressure, as traditional risk factors in SLE patients are not significantly different in both premature atherosclerosis and non atherosclerosis patients. Age, BMI and other specific risk factors in SLE; duration of SLE, CRP levels and duration of corticosteroid therapy was significantly different in patients with atherosclerosis than in patients without atherosclerosis.

Keyword: Premature atherosclerosis, disease severity, corticosteroid therapy, SLE.

APLAR-0461

High level of interleukin-12 serum increase activity index and renal flares in lupus nephritis

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Background: Level of Interleukin-12 serum was increased in lupus nephrits, particulary those in the active disease such as renal flares and activity index represent a significant problem because of the potential for cumulative damage that may lead to deterioration of renal function.

Aim: To determine whether high level of interleukin-12 will increase activity index and renal flares, and relation of activity index and renal flares in lupus nephritis.

Methods: Twenty-seven consecutive patiens with systemic lupus erythemotosus having active renal disease were recruited. They were required to undergo renal biopsy for lupus nephritis classification and activity index score. Renal biopsy was evaluated according to the world Health Organization (WHO) classification of lupus nephritis. Interleukin-12 serum was examined with ELISA. Renal flares was determined by active sediment urine, proteinuria, increased creatinin serum, low level of C3, and high level of dsDNA.

Results: There were 13 patients class III nephritis, 10 patients with class IV and V nephritis, 3 patients with class IV nephritis, and 1 patient with class III and V. The median value interleukin-12 was 30 pg/mL (range 0.26–1415 pg/mL), activity index 3 (range 1–7), and renal flare 2 (range 0–4). There was a significant correlation between activity index and renal flares (Correlation Coefficient/$r = 0.414$; $P = 0.32$) but there were not correlation between interleukin-12 with activity index and renal flare in lupus nephritis.

Conclusions: High level of interleukin-12 can not describe the severity of activity index and renal flares in lupus nephritis. However high score of activity index can describe the severity of renal flare in lupus nephritis.

Key word: lupus nephritis, interleukin-12, activity index, renal flare.

APLAR-0469

Organ involvement and treatment effect of tuberculosis on steroid requirement among Filipino patients with systemic lupus erythematosus

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Objectives: This study describes the organ involvement, extent and outcomes of TB infection among Filipino SLE patients seen in a single institution. We further analyzed the effect of adequate TB treatment on corticosteroid requirement in this cohort of Filipino patients.

Methods: This is a retrospective review of medical records of Filipino SLE patients seen at the Rheumatology Clinics of the University of Santo Tomas Hospital who had completed a minimum 6-month therapy for TB. The involvement, extent (pulmonary, extra-pulmonary site, miliary-pattern, disseminated) and outcomes of TB infection were described. The average

prednisone or prednisone-equivalent in mg/daywas recorded before, during, and upon completion of anti-TB therapy.

Results: A total of 153 episodes of TB infection in 122 SLE patients (112 females, 92%) were included in the analyses. The average age was 29.30 ± 12.97 (range 7–67) at SLE diagnosis, with SLE disease duration of 88.5 months ± 64.2 (range 1–276) to TB diagnosis. Pulmonary TB (PTB) involvement was seen in 76 patients (62.29%). Fifty-three (43.44%) had extra-pulmonary TB (EPTB), with 11.76% having solely EPTB involvement while 13.73% presented with both PTB and EPTB involvement. EPTB involvement included meningitis (26%), soft tissue (22%), arthritis (20.75%), genitourinary (17%), gastrointestinal (5.66%), spine (3.77%), and pericarditis (3.77%). Average daily prednisone dose (mg/day) decreased from 16.56 ± 12.59 SD before therapy to 10.85 ± 7.9 SD during, and 7.13 ± 5.36 SD after TB therapy.

Conclusion: The relatively high occurrence of extrapulmonary involvement in this cohort of SLE patients, without pulmonary involvement in approximately 12% poses a special diagnostic challenge. The potential contributory and confounding role of TB infection to SLE disease activity is suggested by our findings of decreasing steroid requirement during the course of TB treatment.

Funding: Lupus-Inspired Advocacy (LUISA) Project of Rheumatology Educational Trust Fund Inc. (RETFI).

APLAR-0471

Validation of the Filipino version of LupusPro® questionnaire among Filipino patients with systemic lupus erythematosus

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Objective: The English version of LupusPRO®, a disease-targeted patient reported outcome questionnaire has previously been validated among Filipino patients with systemic lupus erythematosus (SLE). This study reports the translation and validation of the LupusPRO into the Filipino language.

Methods: The LupusPRO® questionnaire was translated by an independent translator into the Filipino language. The instrument underwent intensive focused group discussion among 10 adult SLE patients from which a revised consensus version was produced. Back translation of this version was then performed by an independent translator; there were no significant discrepancies from the original English version. After obtaining informed consent, this revised Filipino version was administered to 78 SLE patients with minimum high school level educational attainment who were consecutively seen at the Rheumatology Clinics of University of Santo Tomas Hospital.

Results: A total of 78 Filipino SLE patients (96% females, mean age 30.2 ± 10 years) participated in the study. SLE disease duration was 68.2 ± 51.6 months. Baseline demographic data, Mexican SLE Disease Activity Index (MEX-SLEDAI), Physicians Global Assessment (PGA) and SLE Damage Index (SDI) were recorded. The final version of the Filipino LupusPRO® questionnaire was administered along with Short Form-36 (SF-36). There was good internal consistency reliability (CronbachÕs alpha >0.8) and test-retest reliability. Convergent validity with corresponding Short Form-36 (SF-36) domains, as well as criterion validity with disease activity and damage index were seen.

Conclusion: This study showed that the Filipino version of the LupusPRO® questionnaire has good structural characteristic and is a valid instrument that can be used for Filipino patients with SLE.

Funding: Lupus-Inspired Advocacy (LUISA) Project of Rheumatology Educational Trust Fund Inc. (RETFI).

APLAR-0472

Physical, social, psycho-emotional and spiritual impact of systemic lupus erythematosus and rheumatoid arthritis in Filipino patients

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Objectives: To describe SLE and RA patientsÕ responses to structured questions along four aspects affected by a chronic illness: physical, social, psycho-emotional and spiritual.

Study Design and setting: Descriptive study on the responses from a self-reported, facilitator-assisted survey of SLE and RA patients derived from structured ÒLiving wellÓ workshops conducted.

Methods: Seven workshop sessions for SLE and RA patients were conducted in Metro Manila, Quezon City, Iloilo, Davao, Bacolod, facilitated by rheumatologists and selected patient-volunteers adept in the module contents and conduct of ÒLiving wellÓ program and had undergone training in workshop dynamics. The survey instrument consisted of open-ended questions to elicit individual concerns on four aspects of a patientÕs life. Responses in English and Filipino were analyzed using the constant comparison method.

Results: Two hundred and seventy patients consisting of 163 SLE (158 females) and 107 RA (102 females) participated in the workshop. Most common physical concerns were: [self] difficulty taking care of self (33%,SLE) and limited mobility (41%,RA); [homes] inability to perform household chores (57%,SLE) (56%,RA); [work/school] inability to perform assigned tasks (21%,SLE; 33%,RA); [community] restricted outdoor activities (35%,SLE), limited mobility (30%,RA). In the social aspect, qualities of people around them which the patients considered essential included patience (22%,SLE), and being caring (11%, RA). Concerns and coping strategies were common in psycho-emotional aspects where majority (77.73%) spontaneously cited keeping a positive outlook despite the illness. RA and SLE patients centered their spiritual aspect on prayer or religion (41.90%), family members (22.63%), friends (12.04%) and doctors (15.03%).

Conclusions: This patient-reported survey on the physical, psycho-emotional, social and spiritual aspects reflects a range of individual and common concerns, insights and coping strategies in a group of Filipino patients with SLE and RA. Data derived from these structured workshops can enhance self-help programs and develop a holistic management approach to these patients.

Funding: Rheumatology Educational Trust Foundation.

APLAR-0473

Profile of Filipino SLE patients with end stage renal disease at the University of Santo Tomas Hospital

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Background and Objectives: Renal involvement is a potentially serious complication of SLE with 10–30% of patients progressing to end-stage renal disease (ESRD) requiring hemodialysis and/or transplantation. This paper describes the clinical profile of a cohort of Filipino lupus patients with ESRD seen at a single tertiary care hospital.

Methods: We reviewed the medical records of patients diagnosed with ESRD included in the Lupus Database of the Section of Rheumatology at University of Santo Tomas (UST) Hospital in Manila, Philippines from 2001 to 2011. Demographic, clinical, serologic and histopathologic profiles, therapeutic modalities and outcomes were described.

Result: Included were 47 SLE patients with ESRD (42, 89% females), mean age at SLE diagnosis 25 ± 11.2 (range 7–57) years, mean age at ESRD diagnosis 31 ± 11.5 (range 14–64) years, with average disease duration of 73 ± 482 (range 0–204) months from SLE diagnosis to development of ESRD. The common presenting manifestations were malar rash 33(70%), arthritis 30(64%), hematologic 25(53%) and immunologic 34(72%), 19(49%) with positive anti-dsDNA; 25(53%) with hypocomplementemia. On SLE diagnosis, 12(25%) had active lupus nephritis, 11(23%) with elevated baseline creatinine and 14(31%) had hypertension. Renal biopsy in 21(44%) patients were interpreted as: Class IV in 17, Class II in 3, class III in 1 patient. Lupus nephritis therapeutic regimens included: methylprednisolone pulse therapy 17(36%), cyclophosphamide pulse therapy 40(85%) (24 completed 1 minimum 1 year therapy) and mycophenolate mofetil 11(23%). Forty-six (97%) had renal replacement therapy, 7 (15%) had kidney transplant (KT). At this report, 18(38%) had died, 2 of whom had received KT.

Conclusion: This report substantiates the high morbidity associated with lupus nephritis among Filipinos, with occurrence of ESRD even among patients who apparently received adequate therapy.

Funding: Lupus Inspired Advocacy (LUISA) Project of Rheumatology Educational Trust Foundation, Inc.

APLAR-0478

Renal outcomes comparing low-dose versus high-dose cyclophosphamide induction regimen for lupus nephritis

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Objective: To describe the renal outcomes of patients who completed the induction phase of intravenous cyclophosphamide pulse therapy (CyPT) using low-dose Euro-Lupus Nephritis Trial (ELNT) vs high-dose National Institutes of Health (NIH) regimens in the treatment of lupus nephritis (LN).

Design: Descriptive retrospective study.

Results: Of 177 patients who were started on CyPT for LN, 81 (71;87.65% females) completed the induction phase and comprised the cohort for this analysis. Mean age at SLE diagnosis was 28 ± 8.5 years (range15–57), mean age at initiation of CyPT 31.8 ± 8.52 years (range 18–57), and mean disease duration of 51.9 ± 51.7 months (range 0–221) from SLE diagnosis to CyPT. Thirty (37%) were on ELNT and 51 (63%) on NIH regimen. Immediately after completion of induction therapy, complete response was seen in 11 (36.7%) with ELNT vs 29 (56.9%) with NIH; partial response in 9 (30%) and 10 (19.6%) with ELNT vs NIH, non- response in 7 (23.3%) and 7 (13.7%) with ELNT vs NIH and deterioration in 3 (10%) and 5 (9.8%) with ELNT vs NIH, respectively; P = NS. At 6 months following completion of induction, complete response was seen in 4 (3.3%) with ELNT vs 27 (52.9%) with NIH, partial response in 5 (16.7%) with ELNT vs 11 (21.6%) with NIH; $P < 0.001$; non-response in 15 (50%) and 7 (13.7%) with ELNT vs NIH and deterioration in 6 (20%) and 6 (11.8%) with ELNT vs NIH, respectively; P = NS. Infections were reported in 62.8% on NIH vs. 37.2% on ELNT. Infections included respiratory tract infection, oral candidiasis, non-healing wound, abscess, onychomycosis and herpes zoster.

Conclusion: This study among Filipino patients showed that the high-dose CyPT was better than low- dose ELNT regimen in achieving complete and partial response in terms of renal outcomes in LN patients observed at 6 months post-induction therapy, regardless of maintenance therapy in the 6 months following induction. On the other hand, the high-dose regimen was associated with more adverse events compared to the low-dose regimen.

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APLAR-0481

Analysis of uNGAL and uIL-17 as biomarkers for lupus nephritis

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Background: Lupus nephritis (LN) is the most common and serious complication of SLE, occured in 30–50% in first presentation of patients. Renal biopsy is the gold standard for LN diagnosis which is an invasive procedure and less convenient for the patient. Recently, urine biomarker has been studied for early detection of kidney injury on NL patient, such as urine Neutrophil Gelatinase-Associated Lipocalin (uNGAL) and urine Interleukine-17 (uIL-17) with various results. The purpose of this study is to determine the diagnostic value of urinary biomarker NGAL and IL-17 urine for the diagnosis of NL.

Research Methods: his study was carried out in dr. Saiful Anwar General Hospital Malang February 2011-April 2013. The study included 50 SLE female patients, 38 patients are LN patients (Biopsy class III, IV), 12 patients are non-LN (Biopsy class I,II,normal) according to American Rheumatology Association (ARA) 1997 and 21 female for healthy control with matched for age. Urine NGAL and IL-17 levels are measured with ELISA.

Result: Significant difference of uNGAL concentration found between non-LN SLE patients and healthy control ($P = 0.013$) with LN and healthy controls ($P = 0.000$), and also between concentration of uIL-17 in LN with healthy controls ($P = 0.029$) and LN and non-LN ($P = 0.005$). uNGAL with AUC 75.7% and cut-off value of 593.0 pg/mL had sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 69.70%, 68.42%, 65.71%, and 72.22%, respectively. uIL-17 with AUC 69.5% and cut-off value of 44.3 pg/mL had sensitivity, specificity, PPV, and NPV of 60.61%, 60.53%, 57.14%, and 63.89%, respectively. Combined diagnostic value for uNGAL and uIL-17 are AUC 74.2% and cut-off value 0.426 pg/mL with sensitivity 66.67%, specificity 65.79%, PPV 62.86% and NPV 69.44%.

Conclusion: According to above results, uNGAL and uIL-17 have a low diagnostic value for LN.

Key words: SLE, Lupus Nephritis, uNGAL, uIL-17.

APLAR-0482

Analysis uMCP-1 and uTGF-Ô1 as biomarkers for lupus nephritis

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Background: Lupus nephritis (LN) is a serious manifestation of systemic lupus erythematosus (SLE). Renal biopsy is the gold standard for LN diagnosis, but since it is an invasive procedure, a variety of biomarkers has been investigated, such as urine transforming growth factor beta 1 (uTGF-β1) and urine monocyte chemoattractant protein 1 (uMCP-1), with varying results. This studyÕs aim is to determine whether uTGF-β1 and uMCP-1 can be used for LN diagnosis.

Research Methods: This study was conducted at Dr. Saiful Anwar Hospital Malang, from February 2011 till April 2013. SLE was diagnosed by 1997 ARA criteria. The samples were divided into 3 groups: LN patients (renal biopsy showed class III/IV/V, n = 38), SLE controls (renal biopsy showed class I/II/normal, n = 12), and healthy controls with comparable age and sex (n = 20). uTGF-β1 and uMCP-1 levels were determined by ELISA, using spot urine.

Result: Significant difference of uTGF-β1 value was found between LN patients and healthy controls ($P = 0.014$). For uMCP-1, it was observed between LN patients and healthy controls as well as SLE controls and healthy controls ($P = 0.000$, $P = 0.000$). Positive correlation between uTGF-β1 and uMCP-1 was weak ($P = 0.002$; $r = 0.387$). uTGF-β1 AUC was 63.60%, with cut off 35.38 pg/ml showed sensitivity, specificity, PPV, NPV 62.00%, 64.00%, 61.76%, 63.89% respectively. uMCP-1 AUC was 67.80% with cut off 7.19 pg/mL showed sensitivity, specificity, PPV, NPV 59.00%, 58.00%, 100.00%, 100.00% respectively. Sensitivity, specificity, PPV, NPV for the combined biomarkers were 78.95%, 37.84%, 56.60%, 63.64% respectively.

Conclusion: uTGF-β1 and uMCP-1 have weak diagnostic value for LN diagnosis.

Key words: LN, SLE, uTGF-β1, uMCP-1.

APLAR-0483

Effect of vitamin D [1,25(OH)2D3] on dendritic cells differentiation and production of IL-12, in SLE patients with hipovitamin D

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Objective: To determine the effect of vitamin D [1,25$(OH)_2D_3$] on dendritic cell differentiation (expression of CD40, CD86, and HLA-DR), and the amount of IL-12p70 levels, in SLE patients with hipovitamin D.

Research Methods: PBMCs from blood samples of 5 SLE patients with hipovitamin D were cultured using RPMI medium containing L-Glutamine to, continue with culture media using GM-CSF and IL-4. After TNF-α stimulation, and treated with various doses of 1,25$(OH)_2D_3$ (P0: 0 M, P1:10^{-9}M, P2: $10^{*\ 8}$ M, P3: 10^{-7} M), we analyzed the surface activation markers expression: CD40, CD86, and HLA-DR by flowcytometri and IL-12p70 levels using ELISA method.

Result: Compared with P0 (42.43 ± 6.32%), the mean expression of CD40 in P1 (36.87 ± 5.60%; $P = 0.006$) and P2 (31.66 ± 6.43%; $P = 0.009$) were significantly lower. The mean expression of CD86 in P2 was significantly lower compared with P0 (29.93 ± 7.28% vs 53.53 ± 13:40%; $P = 0.011$). Compared with P0 (39.53 ± 17.74%), the mean expression of HLA-DR in P2 (27.69 ± 14.77%; $P = 0.018$) and P3 (31.98 ± 6.17%; $P = 0.038$) were significantly lower. Further, the mean levels of IL-12p70 in P2 was significantly lower compared with P0 (28.9 ± 6.8 pg/mL vs 57.1 ± 16.9 pg/mL; $P = 0.018$).

Conclusion: Administration of 1,25$(OH)_2D_3$at various doses are significantly inhibit dendritic cell differentiation and IL-12 production, in SLE patients with hipovitamin D.

Key words: vitamin D, SLE, dendritic cells, IL-12.

APLAR-0485

Effect of vitamin D [1,25 (OH) 2D3] on percentage of T reg (CD4+ CD25+ Foxp3+) cells

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Objective: To determine the effect of vitamin D [1,25 (OH) $_2D_3$] on percentage of T Reg (CD4+ CD25+ Foxp3+) cells and TGF-β expression in SLE patients with hipovitamin D.

Research Methods: CD4 + T lymphocytes from PBMCs of 5 SLE patients with hipovitamin D were cultured using RPMI 1640, PMA, ionomycin, Golgiplug, 10% heat-inactivated FCS, penicillin (100 IU/mL), and streptomycin (100 IU/mL). After stimulation with 10 ng/mL IL-6, 5 ng/mL TGF-β1, 10 μg/mL anti-IFN-γ, and 10 μg/mL anti-IL-4, and treated with various doses of 1,25 (OH) $_2D_3$(P0:0M, P1:10^{-9}M, P2:$10^{*\ 8}$M, P3:10^{-7} M), we analysed the the number (percentage) of CD4+ CD25 + FoxP3 + (Treg) cells with flowcytometri. The levels of TGF-β were measured using ELISA method.

Result: There was no significant difference in the mean percentage of Treg cells between P0 (13.76 ± 8.52%), and P1 (14.74 ± 9.20%; $P = 0.886$), P2 (8:32 ± 4.13%; $P = 0.280$), and P3 (16.82 ± 7:33%; $P = 0.536$). As for the levels of TGF-β indicates a significant difference between P0 and P2 (6571 ± 3359.21 pg/mL vs 4192.6 ± 544.40 pg/mL; $P = 0.043$).

Conclusion: Administration of vitamin D [1,25 (OH) $_2D_3$] did not reduce the number (percentage) of Treg (CD4 + CD25 + Foxp3 +) cells, but reduce their TGF-β expression in CD4 + Tcells culture of SLE patients with hipovitamin D.

Key words: vitamin D, SLE, Treg, TGF-β.

APLAR-0486

Effect of vitamin D [1,25 (OH) 2D3] on the Nb and function of thelper 17 cells in SLE patients with hipovitamin D

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Objective: To determine the effect of vitamin D [1,25 (OH) $_2D_3$] in the number and function of Th17 cells (CD4 + IL-17A+) in SLE patients with hipovitamin D.

Research Methods: CD4 + T lymphocytes from PBMCs of 5 SLE patients with hipovitamin D were cultured using RPMI 1640, PMA, ionomycin, Golgiplug, 10% heat-inactivated FCS, penicillin (100 IU/mL), and streptomycin (100 IU/mL). After stimulation with 10 ng/mL IL-6, 5 ng/mL TGF-β1, 10 μg/mL anti-IFN-γ, and 10 μg/mL anti-IL-4, and treated with various doses of 1,25 (OH) $_2D_3$(P0:0M, P1:10^{-9}M, P2:10^{*8}M, P3:107 M), we analyzed the number and function of Th17 cells. The number (percentage) of Th17 cells was measured by flowcytometry, while Th17 cell function is measured by the levels of IL-17A expression using ELISA method.

Result: Compared with P0 (17:07 ± 2.99%), the mean percentage of Th17 cells in P1 (8:39 ± 3:29%; $P = 0.043$) and P2 (7:17 ± 3.81%; $P = 0.038$) were significantly lower. Similarly, the levels of IL-17A, in P1 (25.90 ± 11.90 pg/mL; $P = 0.024$) and P2 (15.75 ± 1.22 pg/mL; $P = 0.047$) were significantly lower than P0 (59.18 ± 26.95 pg/mL).

Conclusion: Administration of vitamin D [1,25 (OH) $_2D_3$] can reduce the number (percentage) of Th17 cells and IL-17A levels in CD4 + Tcells culture of SLE patients with hipovitamin D.

Key words: vitamin D, SLE, Th17, IL-17A.

APLAR-0409

End-organ damage in a cohort of Filipino patients with systemic lupus erythematosus at two tertiary hospitals

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Objective: This retrospective study describes the prevalence and characteristics of end-organ damage among Filipino systemic lupus erythematosus (SLE) patients.

Design: We reviewed the medical records of adult (>18 years old) patients seen at the lupus clinics of two tertiary hospitals (University of Santo Tomas, St. Luke's Medical Center) from January 2012 to January 2013. Patients with incomplete charts and who were lost to follow-up for at least 6 months were excluded from the study. Patients were assessed for the presence of end-organ damage using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/SDI). Other characteristics of SLE patients with end-organ damage, such as presenting manifestations at diagnosis, average steroid dose per day and cyclophosphamide use were also analyzed.

Results: Two hundred and twenty-one patients (210, 95% females), with mean age at diagnosis at 28 + 10.52 years and mean disease duration of 10 + 6.56 years were included in the study. One hundred and thirty-six (61.5%) had at least 1 end-organ damage. The most commonly damaged organ systems were the renal (59, 43%), ocular (38, 28%), neuropsychiatric (30, 22%), and musculoskeletal (29, 21%). Damage occurred at an average of 6 years after diagnosis. Development of a subsequent damage occurred at an average of 2 years after the first damage. Among those with end-organ damage, mucocutaneous, hematologic, and musculoskeletal were common presenting manifestations. Average prednisone dose was >10 mg/day, and 59 (43%) of these patients had received cyclophosphamide.

Conclusion: In this cohort of SLE patients, majority were found to have end-organ damage. The renal, ocular, neuropsychiatric, and musculoskeletal were the most damaged organ systems. Mucocutaneous, hematologic, and musculoskeletal were most common presenting manifestations. Average prednisone dose was >10 mg/day among patients with end-organ damage, reiterating the contributory role of therapy to damage in SLE.

Funding: Lupus Inspired Advocacy (LUISA) of Rheumatology Educational Trust Foundation, Inc.

APLAR-0278

Urinary sCD25 as a potential biomarker for lupus nephritis

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Background: Lupus nephritis (LN) is a common manifestation of SLE that has impact on mortality. Traditionally proteinuria has been used as the major biomarker for lupus nephritis, however it can also occur because of damage. Thus other urinary biomarkers that reflect immune events are being explored.

Methods: Patients who fulfilled ACR criteria for diagnosis of SLE and had either active or inactive nephritis were enrolled. They were divided into two groups, active LN and inactive LN. Urinary sCD25 was measured by ELISA and normalized to urinary creatinine excretion. Patients with active LN were treated with Eurolupus nephritis protocol and followed up 3 monthly. At 6 months clinical response as well as biomarker was assessed. Data were analyzed using non-parametric tests.

Results: There were 72 patients (70 females, median age 27 years). Forty-two patients with active LN (SLEDAI 18, rSLEDAI 8) of these 26 had 6 months of follow up (23 responders) and 30 patients had inactive LN (SLEDAI 2, rSLEDAI 0).

The median levels of sCD25 (49.92 pg/mL, 31.69 pg/mL: $P < 0.006$) were higher in the active LN as compared to inactive LN. Levels of sCD25 correlated with SLEDAI ($P < 0.05$) and as well as with rSLEDAI ($P < 0.05$).

In longitudinal analysis, among 26 patients with active LN, sCD25 levels reduced (49.92 pg/mL, 33.12 pg/mL: $P < 0.05$) after 6 months of treatment.

Conclusion: Urinary sCD25 is a good biomarker for LN.

APLAR-0020

Clinical analysis of systemic lupus erythematosus patients with peripheral neuropathy in China

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Introduction: The nervous system in systemic lupus erythematosus (SLE) is frequently involved, but peripheral nervous system involvement has been less investigation. Pain, numb and weak in limbs and trunk caused by periphery neuropathy (PN) seriously reduced the quality of life. Our aim is to investigate the clinical characteristics of SLE patients with PN in China.

Methods: The data of 67 consecutive SLE-PN (PN related with SLE) patients admitted in Peking Union Medical College Hospital from January 1995 to August 2011 were prospectively analyzed. All patients fulfilled American College of Rheumatology (ACR) classification criteria in 1982 for SLE and case definitions for seven PN of 19 Neuropsychiatric SLE (NPSLE) in 1999. At the same time, a total of 201 cases were randomly selected as control from 4447 SLE patients without SLE-PN in PUMCH during the same period.

Results: (i) The prevalence of SLE-PN in patients was 1.5%(67/4514). Seventy-two cases of PN were happened in 67 patients. Polyneuropathy was the most frequent and diagnosed in 62.5%, monoeuropathy in 12.5%, myasthenia gravis in 11.1%, cranial neuropathy in 9.7%, autonomic disorder in 2.8% and acute inflammatory demyelinating polyradiculoneuropathy in 1.4%. No plexopathy was diagnosed. (ii) No symptoms were observed in 6.9% PN. There were significant differences between SLE patients with and without SLE-PN in age (36.6 ± 13.9 versus 31.9 ± 13.7 years), fever (65.7% versus 47.8%), myositis (17.9% versus 5.0%), involvement of skin and mucous (80.6% versus 59.7%), central nerve system involvement (38.8% versus 19.9%), gastrointestinal involvement (6.0% versus 18.4%) and SLEDAI score (13.2 ± 8.5 versus 10.2 ± 6.3; $P < 0.05$). (iii) There were more rates of anti-Sm antibody positivity, anti-RNP antibody positivity and more elevation of IgG in patients with SLE-PN ($P < 0.05$).

Conclusions: SLE-PN is not rare in patients with SLE. It is easier to ignore the PN. The patients with SLE-PN were always active in SLE. Cooperation with neurologist and physiotherapist are necessary for rheumatologist to improve quality of life.

APLAR-0309

Serum IL-6 and IGF-1 levels correlate with the development of pulmonary arterial hypertension in patients with systemic lupus erythematosus

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Background: Studies of connective tissue disease associated PAH have been mainly focused on scleroderma patients. A reliable and sensitive screening method for identifying risk factors or early diagnosis of PAH in SLE (SLE-PAH) has been lacking.

Objective: To survey the profile of a broad range of circulating molecules as early predictive tools and biomarkers for SLE-PAH.

Materials and Methods: Serum markers, including angiotensin converting enzyme and endothelin-1 (ET-1) for *endothelial dysfunction*; tumor necrosis factor-α, interleukin-2 (IL-2), IL-4, IL-6, IL-17, monocyte chemotactic protein-1 (MCP-1), and macrophage inflammatory protein-1α (MIP-1α) for *inflammation*; vascular endothelial growth factor, placental growth factor-1 (PlGF-1), stem cell factor (SCF), nerve growth factor (NGF), fibroblast growth factor-β, leptin, and endoglin for *angiogenesis*; and platelet-derived growth factor (PDGF), transforming growth factor-b (TGF-β), epidermal growth factor, insulin-like growth factor-1 (IGF-1), and angiopoietin-1 for *remodeling*; were serially detected in the year 2010–2012 by enzyme immunoassay in patients with SLE-PAH (n = 11), and 56 SLE patients with normal pulmonary arterial systolic pressure (PASP) including 6 patients with anti-phospholipid antibody syndrome, 25 high-risk patients with moderate to severe RaynaudOs phenomenon, and 25 low-risk patients without RaynaudOs phenomenon.

Results: ET-1, IL-6, IL-17, MIP-1α, MCP-1, PlGF-1, SCF, NGF, PDGF, TGF-β and IGF-1 were significantly elevated in SLE-PAH at screening. In the serial measurements of these candidate markers for five newly-diagnosed and four early-treated SLE-PAH patients during follow-up, compared with patients who remained normal PASP, we found that only IL-6 and IGF-1 elevated along with the development of PAH and declined with sildenafil treatment. There were significant differences between baseline and peak levels during evolution of PAH ($P = 0.009$ for IL-6, and 0.025 for IGF-1). The fluctuations were not associated with lupus clinical or serological activity.

Conclusion: IL-6 and IGF-1 could be biomarkers of predicting SLE-PAH.

APLAR-0406

Diagnosis of anti-SSA/SSB negative Sjögrens syndrome by 2012 ACR classification criteria – more close to expert opinion

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Objectives: About 20–35% patients with Sjögren's syndrome (SS) are negative for anti-SSA/SSB antibody, which is an important element in both 2002 AECG criteria and 2012 ACR classification criteria for SS. Recognization of these patients depend mainly on Expert opinion. We aimed to compare the difference between the both criteria and expert opinion on the diagnosis of suspected SS negative for anti-SSA/SSB.

Methods: Patients had both dry eyes and dry mouth cannot be explained by other present diseases or any underlying causes, and negative for anti-SSA/SSB in twice time, were studied. According to demand of both 2002 and 2012 criteria, patients received routine assessment of SS (including symptom, sign, RF, ANA, salivary gland scintigraphy and labial salivary gland biopsies). After 3 months follow-up (which allow a further clinical assessment), patients were divided into non-SS group and SS group, according to experts opinion, the 2002 criteria, and the 2012 criteria. When judged by expert opinion, SS was diagnosed if both two experienced professors make a diagnosis of SS without consulting each other.

Results: Twenty-one patients (17 female, four male) were studied. 71.4% (15 cases), 52.3% (11 cases), and 81.0% (17 cases) of patients were diagnosed as SS according to expert opinion, 2002, and 2012 criteria, respectively. There was moderate level of inter-observer agreement between two professors ($\kappa = 0.64$, $P < 0.001$). When taking the expert opinion as 'goldstandard', 2012 ACR criteria recognized more SS patients than 2002 criteria (14 versus 9, $P < 0.05$). There was higher consistency between 2012 ACR criteria and expert opinion than that between 2002 criteria and expert opinion ($\kappa = 0.72$, 0.48, respectively, $P < 0.05$).

Conclusions: The 2012 ACR classification criteria may be superior to the 2002 criteria on recognizing suspected anti-SSA/SSB negative SS patients in southern China.

APLAR-0415

Association of anti-nucleosome, anti-dsDNA and anti-dsDNA-NcX with systemic lupus erythematosus

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Objective: To test the levels of anti*double-stranded DNA (anti-dsDNA) antibody,Anti-nucleosome (AnuA) and Anti-dsDNA-NcX in serum of patients with systemic lupus erythematosus (SLE), analyze the sensitivity and specificity of anti-dsDNA, AnuA and Anti-dsDNA-NcX and the correlation between others laboratryindexs in SLE, to supply the evidence of diagnostics and treatment for SLE, for clinical practic of association detecting to make initial investigate.

Methods: ELISA were used to detect serum Anti-dsDNA, Anti-nucleosome and Anti-dsDNA-NcX in 91 patients with SLE, as well as 45 disaese controls and 46 heathy controls. We analysed sensitivity and specificity of three antibodies, evaluated the correlation between others laboratory index.

Results: The positive rate of Anti-dsDNA, Anti-nucleosome and Anti-dsDNA-NcX was 56%, 49.5% and 61.5% respectively, Specificity was 94.5%, 94.5% and 100% respectively? Anti-nucleosome, Anti-dsDNA and Anti-dsDNA-NcX were positively associated with SLEDAI (Spearman correlation coefficient r = 0.496, P = 0.000 r = 0.486, P = 0.000 r = 0.42, P = 0.000)? The titers of ANA was positively correlated with AnuA and Anti-dsDNA-NcX concentration (Spearman correlation coefficient r = 0.303, P = 0.004 r = 0.499, P = 0.000), ANA titres was not correlation with Anti-dsDNA (Spearman correlation coefficient r = 0.188, P = 0.076)? There was no statistics difference of ESR among negative and positive groups of Anti-dsDNA and Anti-dsDNA-NcX ($\chi^2 = 0.758$, P = 0.384; $\chi^2 = 0.134$, P = 0.175), there was statistics difference between the negative with positive grops of AnuA ($\chi^2 = 20.313$, P = 0.000)? The difference of CRP and UPRO were not statistic significant in the three antibodies? Complement 3? Complement 4 was statistic significant in the negative with positive grops of AnuA? Anti-dsDNA and Anti-dsDNA-NcX ($\chi^2 = 9.84$, P = 0.002)? ($\chi^2 = 16.533$, P = 0.000) ($\chi^2 = 10.33$, P = 0.001) and ($\chi^2 = 11.611$, P = 0.001)? ($\chi^2 = 12.688$, P = 0.000) ($\chi^2 = 8.766$, P = 0.003), respectively? There was no statistics difference of CysC among negative and positive grops of Anti-dsDNA and AnuA ($\chi^2 = 0.758$, P = 0.384) ($\chi^2 = 0.134$, P = 0.175), there was statistics difference between the negative with positive grops of Anti-dsDNA-NcX ($\chi^2 = 4.038$ P = 0.044)?

Conclusion: Anti-dsDNA-NcX regarded as an important serologic marker in the diagnosis and determination of disease activity, and the sensitivity and specificity were higher than AnuA and Anti-dsDNA. Three antibodies were associated with disease activity with SLE. It could help to evaluate the disease condition.

APLAR-0328

Correlation of interleukin -6 serum with systemic lupus erythematosus disease activity

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Background: To determine disease activity in SLE patients is very complex because great variety manifestations, broad spectrum organs involvement, and non spesific symptoms that could leads to delayed treatment by clinicians, high morbidity and mortality. So it is important to find a specific biomarker for disease activity. Interleukin-6 plays important role in lupus pathogenesis and several studies show raised levels in SLE flare.

Methods: A cross sectional study with 36 samples fulfilled ACR 1997 criteria. The level of IL-6 serum were measured by ELISA kit. Disease activity were measured by SLAM (*Systemic Lupus Activity Measurement*). Levels of IL-6 were correlated with disease activity measured by SLAM.

Result: SLAM scores obtained with mean 20.17 (range 7–35) and IL-6 serum with mean 23.93 pg/mL (range 3.15–83.35 pg/mL). There is significant correlation between the level of IL-6 serum with SLAM score ($P \leq 0.005$, $r = 0.640$).

Conclusion: This study result is Interleukin-6 correlates with SLE disease activity measured by SLAM.

Keywords: SLE, IL-6, SLAM, biomarker, disease activity.

APLAR-0467

Correlation between lymphopenia and disease activity in Indonesian SLE patients

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Background: Lymphopenia is one of SLE clinical manifestation, occurs in 75% patients with active SLE, and 18% during their period of life. Lymphopenia is one of ACR criteria to establish diagnosis of SLE. In some studies there was also association between lymphopenia and disease activity in SLE. The aim of this study was to know the correlation between lymphopenia and disease activity in Indonesian new patients of SLE.

Methods: A cross-sectional study was done in 40 new SLE patients (using ACR criteria 1997). Patients were from in-patient and outpatient rheumatology clinic. They all had never got any therapy for SLE. Disease activity was measured using SLAM, and value less than 20 was considered low activity, and equal or more than 20 was considered severe SLE. Level of lymphopenia was measured using flowcytometry (mm^3).

Result: There were 40 newly SLE patient, 39 women (97.5%) and one man (2.5%). Average of age was 30.43 ± 8.102 years old. Average of lymphocyte count was 1048.15 ± 706.380/mm^3. Severity of lymphopenia was divided into four groups. There were 5 pts (12.5%) with lymphocyte count 1500–4000/mm^3, 10 pts (25%) 1000*1499/mm^3, 19 pts 500*999/mm^3, 6 pts (15%) <500/mm^3. Average of SLAM score was 20.98 ± 6.678 (range 7–35). There were 18 pts (45%) with SLAM <20 and 22 pts (55%) with SLAM ≥ 20. There was signicant negative correlation between lymphopenia and SLAM score ($r = 0.494$, $P > 0.01$)

Conclusion: There was a significant negative correlation between severity of lymphophenia and disease activity of SLE with $r = 0.494$, $P > 0.01$.

Keywords: SLE, SLAM, lymphopenia.

APLAR-0468

A systemic lupus erythematosus patient with manifestation of lupus nephritis and lupus cerebral: A case report

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Introduction: SLE is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding autoantibodies and immune complexes. Prevalence is between 30 and 50 in 100 000 people with ratio between female and male is 10–12 to 1. Approximately 50% of patients with SLE will develop lupus nephritis, which increases the risks for renal failure, cardiovascular disease and death. Most (50*60%) neuropsychiatric lupus events occur at disease onset or within the first year after SLE onset. It is a major cause of morbidity and mortality.

Case: A 41-year-old female had complaint of arthralgia, photosensitive, and history of lupus nephritis. During the admission, she got general seizure. From physical diagnosis we found thin hair, falling hair, anemic conjunctiva, oral ulcer, and hepatomegaly. From laboratorium findings, there were anemia, lymphopenia, increase serum creatinin, hypoalbuminemia, dyslipidemia, hyperuricemia, proteinuria, erythrocyturia, bacteriuria, strong positive ANA test, and positive anti dsDNA. X-ray showed lung inflammation and bilateralostheoarthritis of genu, USG showed hepatosplenomegaly, minimal pericardial effusion on echocardiography, and abnormal EEG. She was diagnosed of lupus nephritis, suspect UTI, pneumonia, and lupus cerebral. She had been given high calories with 0.8–1 mg/kg/day protein and low salt diet, *pulse dose* methyl prednisolon, cyclophosphamid, valsartan, metamizole, omeprazole, simvastatin, allopurinol, calsium and vitamin D3. This patient has a bad prognosis.

Keywords: SLE, lupus nephritis, lupus cerebral.

APLAR-0470

Causes of mortality among Filipino patients with SLE at a single tertiary care center

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Objective: This describes the causes of mortality in a group of Filipino patients with systemic lupus erythematosus (SLE) seen at a single tertiary care center.

Methods: Retrospective study to describe the causes of mortality in a cohort of Filipino lupus patients seen at the Rheumatology Clinics of the University of Santo Tomas (UST) Hospital who were recorded to have died within the 5-year period from January 2008 to December 2012. The primary and secondary causes of death were obtained from clinic and hospital records, death certificates, and first-hand information from bereaved family members. Excluded were patients whose cause of death were unknown.

Results: A total of 117 SLE patients (105, 89.7% females) were included in this analysis. The average age at SLE diagnosis was 26.6 ± 11.4 (range 15.2–38.0) years. Mean age at death was 34 ± 13 (range 21–47) years, with mean disease duration of 90 ± 84 (range 6–174) months. Primary cause of death was active SLE with concomitant infection in 60 patients (51.3%), active SLE alone in 50 (42.7%), non-SLE related in seven patients (three acute coronary syndrome, two malignancies, one each stroke and status asthmaticus). Organ involvement among those with active SLE included renal (61, 55.4%), hematologic (29, 6.4%) and pulmonary (24, 21.8%). The most common infection recorded among SLE-related deaths was sepsis (40%). Within the first 5 years of illness, the most common cause of death was SLE flare with concomitant infection, reported in 61% of patients.

Conclusion: Active SLE with concomitant infection was the most common cause of death in this cohort, usually within the first 5 years of illness. This underscores the need for aggressive control of disease activity and vigilance in the prevention and control of infections.

Funding: Lupus Inspired Advocacy (LUISA) Project of Rheumatology Educational Trust Foundation, Inc.

Clinical Rheumathology: T11 – Osteoarthritis

APLAR-0064

Increased risk of severe acute inflammatory reactions to chemically cross-linked hyaluronic acid among Japanese patients with osteoarthritis of the knee

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Increased risk of severe acute inflammatory reactions to chemically cross-linked hyaluronic acid among Japanese patients with osteoarthritis of the knee.

APLAR-0136

Increased expression of acid sensing ion channel and transient receptor potential vanilloid in mouse anti-type II collagen antibody-induced arthritis

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Background/Purpose: Different acid-sensing ion channel (ASIC) isoforms and Transient receptor potential vanilloid (TRPV) have been identified and critical for development of secondary hyperalgesia in peripheral sensory neurons innervating skin and muscle. This study was aimed to investigate the ASIC and TRPV expression in mouse anti-type II collagen antibody-induced arthritis (CIA).

Method: Mice were divided into 2 groups; control, CIA. The expression of ASIC, TRPV, type II collagen specific antibodies, IL-17, and IL-16 were determined from the synovial membrane of control and CIA by performing immunohistochemistry. The expression of ASIC and TRPV were measured by real time reverse transcriptase polymerase chain reaction (RT-PCR). The expression of type II collagen specific antibodies, IL-17 and IL-16 were measured by enzyme linked immunosorbent assay (ELISA) analysis.

Result: Histological and X-ray assessment revealed increased infiltration of inflammatory cells, synovial hyperplasia, and the destruction of the articular cartilage and bone in CIA group. ASIC1, ASIC2, ASIC3, TRPV1 and TRPV4 were markedly increased compared with those in control. The concentrations of anti-type II collagen antibody in CIA were significantly higher than those in control. Serum concentration of IL-6 in CIA group were also increased.

Conclusion: Taken together, these results implicate that increased ASICs and TRPV involved in the joint pain in mice anti-type II collagen antibody-induced arthritis.

APLAR-0255

Coenzyme Q10 ameliorates pain and cartilage degradation in a rat model of osteoarthritis by regulating nitric oxide and inflammatory cytokines

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Objective: To investigate the effect of CoenzymeQ10 (CoQ10) on pain severity and cartilage degeneration in an experimental model of rat osteoarthritis (OA)

Materials and methods: OA was induced in rats by intra-articular injection of monosodium iodoacetate (MIA) to the knee. Oral administration of CoQ10 was initiated on the day 4 of MIA injection. Pain severity was assessed by measuring secondary tactile allodynia using von Frey assessment test. The degree of cartilage degradation was determined by cartilage thickness and the amount of proteoglycan. Mankin scoring system was also used. The expressions of matrix metalloproteinase-13 (MMP-13), interleukin-1β (IL-1β), IL-6, IL-15, inducible nitric oxide synthase (iNOS), nitrotyrosine and receptor for advanced glycation end products (RAGE) were analyzed by immunohistochemistry.

Results: Treatment with CoQ10 demonstrated an antinociceptive effect in OA animal model. Secondary tactile allodynia was significantly reduced represented by increased pain withdrawal latency and pain withdrawal threshold. CoQ10 also attenuated cartilage degeneration in OA joints. The expressions of MMP-13, IL-1β, IL-6, IL-15, iNOS, nitrotyrosine and RAGE were upregulated in OA joints and significantly reduced with CoQ10 treatment.

Conclusion: CoQ10 exert a therapeutic effect on OA by suppressing pain and cartilage degeneration through inhibition of inflammatory mediators which have emerged as central players in OA pathogenesis.

APLAR-0259

Fibronectin fragment-induced expression of matrix metalloproteinases is mediated by MyD88-dependent TLR-2 signaling pathway in human articular chondrocytes

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Background/Purpose: Fibronectin fragments (FN-fs) are increased in the synovial fluid of osteoarthritis patients and have a potent chondrolytic effect. However, little is known about the cellular receptors and signaling mechanisms that are mediated by FN-fs. Here we investigated whether the 29-kDa amino-terminal fibronectin fragment (29-kDa FN-f) regulate cartilage metabolism through Toll-like receptor-2 (TLR-2) signaling pathway in human articular chondrocytes.

Method: In order to investigate whether 29-kDa FN-finduce MMPs production through TLR-2, human chondrocytes were transfected with TLR-2 expression plasmid or small interfering RNAs (siRNAs) targeting TLR-2 and Myeloid differentiation factor 88 (MyD88). In 29-kDa FN-f-stimulated chondrocytes, the relative levels of mRNA for MMP-1, MMP-3, and MMP-13 were analyzed by real-time quantitative reverse transcription-polymerase chain reaction. Protein expression levels of MMP-1 and MMP-3 and the regulatory effect of TLR-2 on 29-kDa FN-f-mediated signaling pathways were assessed by immunoblotting. MMP-13 production was measured by ELISA assay.

Result: When human chondrocytes were stimulated with various fibronectin fragments, TLR-2 expression was highly increased by 29-kDa FN-f stimulation. Knockdown of TLR-2 expression using siTLR-2 significantly suppressed 29-kDa FN-f-induced MMPs production in human normal and OA chondrocytes. Conversely, overexpression of TLR-2 enhanced 29-kDa FN-f-stimulated MMPs production. Moreover, we found that knockdown of MyD88, a downstream adaptor in TLR-2 signaling pathways, led to marked reduction of MMPs production induced by 29-kDa FN-f. In addition, 29-kDa FN-f-mediated phosphorylation of IkBa and p38 was apparently inhibited by transfection of siTLR-2. However siTLR-2 treatment did not affect 29-kDa FN-f-induced activation of JNK and ERK. Notably, fluorescence microscopic analysis showed direct interaction between TLR-2 and 29-kDa FN-f in human chondrocytes.

Conclusion: MyD88-dependent TLR-2 signaling pathway plays an important role in 29-kDa FN-f-stimulated procatabolic responses of human chondrocytes. Modulation of TLR-2-mediated signaling may be as a potential therapeutic strategy for the prevention of cartilage degradation in OA.

APLAR-0263

Synovial fulid vascular endothelial growth factor(VEGF) as a biomaker for predicting severity of osteoarthritis according to radiological and ultrasonographic findings

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Objective: To examine serum and synovial fluid biomarkers related to osteoarthritis(OA) progression, we measured biomarkers and examined the correlation with radiologic and ultrasonographic findings of knee joints.

Method: The study was conducted with 34 consecutive patients with clinical and radiographic evidence of knee OA with joint effusion detected clinically. The questionnaire included the duration of knee pain, 100 mm visual analog scale (VAS), and Western Ontario McMaster Universities (WOMAC) Osteoarthritis Index. All patients were examined by x-ray on the same day as ultrasonography. Knee X-rays were analyzed by Kellgren-Lawrence (KL) grading system. Plasma and synovial fluid (SF) VEGF and MMP 13 levels were determined by ELISA.

Results: Thirty four patients with knee OA included two men and 26 women, with a mean age of 65.5 ± 7.9 years and mean disease duration of 38.2 ± 48.9 months. Mean pain VAS was 56.8 ± 23.9 mm and total WOMAC score was 89.9 ± 42.9. Fourteen patients were categorized as grade 2 (KL 2), 16 as grade 3 (KL 3), and 4 as grade 4 (KL 4). The median value of SF VEGF were higher in KL grade 4 than those of KL grade 2 (845.0 ± 82.3 pg/mL vs 624.6 ± 37 pg/mL, $P = 0.025$). SF VEGF levels positively correlated with KL scores ($r = 0.444$, $P = 0.009$). No significant difference in SF and plasma levels of MMP-13 as well as plasma levels of VEGF were found according to KL grade. The SF VEGF correlated positively with the length of the medial osteophytes ($r = 0.502$, $P = 0.012$), lateral osteopytes ($r = 0.528$, $P = 0.008$) and joint capsule distension ($r = 0.423$, $P = 0.048$). The SF MMP-13 did not show any correlation with ultrasonographic finding.

Conclusion: SF VEGF levels increased in advanced OA according to KL scores and correlated well with ultrasonographic finding such as length of medial and lateral osteophytes and joint capsule distension.

APLAR-0268

The association between levels of TNF-α, IL-10 and ratio TNF-α /IL-10 joint fluid with the degree of osteoarthritis

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Aim: To determine the association between levels of TNF-α, IL-10 and ratio TNF-α/IL-10 joint fluid with the degree of osteoarthritis (OA) according to Kellgren-Lawrance (KL) classification.

Methods: This study is a descriptive analytic method using a cross sectional observational study among 41 knee osteoarthritis subjects aged 45–72 years old (13 male and 28 female). The levels of TNF-α and IL-10 joint fluid (pg/mL) was measured by using the method of quantitative sandwich immunoassay. Radiographic examination to classified the degree of OA by using the Kellgren-Lawrence (KL) grading (1–4).

Result: The results of study showed that the levels of TNF-α ranged from 0.39 to 1062.33 with a mean of 94.35 pg/mL, levels of IL-10 ranged from 0.77 to 66.83 with a mean of 8.35 pg/mL and the ratio TNF-α and IL-10 ranged from 0.46 to 192.56 with a mean of 16.34. Levels of TNF-α, IL-10 and TNF-α/IL-10 ratio were significantly associated with the degree of OA by Spearman's correlation coefficient respectively 0.819; 0.355, and 0.620.

Levels of TNF-α on the degree of OA (1–4), respectively are 5.76 ± 3.81 pg/mL; 18.83 ± 3.33 pg/mL; 153.42 ± 150.36 pg/mL; and 733 286 61 pg/mL. Levels of IL-10 on the degree of OA (1–4), respectively are 2.91 ± 3.66 pg/mL; 5.86 ± 8.62 pg/mL; 13.25 ± 22.24 pg/mL; and 28.70 ± 16.41 pg/mL. TNF-α/IL-10 ratio on the degree of OA (1–4), respectively are 2.92 ± 2.66; 8.86 ± 8.89; 46.83 ± 63.10, and 27.65 ± 6.47.

Conclusion: The level of TNF-α, IL-10 and ratio TNF-α/IL-10 have significantly association with degree of OA according to Kellgren-Lawrance classification.

APLAR-0285

Examination of Sauve-Kapandji method (S-K method) as reconstruction surgery of the wrist for RA patients using the biologics

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Purpose: It was inspected whether Sauve-Kapandji method (S-K method) was effective as reconstruction surgery of the wrist for RA patients who have been treated using the biologics.

Patients and methods: 26 RA patients (27 joints) during treatment with biologics were performed S-K method. Distal tenodesis with half-slip of ECU of the proximal end of ulna was performed. All cases were female, age at surgery was 57.4 years on average. On X-ray findings, Larsen grade of the radiocarpal joint was grade III or IV. As X-ray parameter, carpal height ratio (CHR), ulnar carpal distance ratio (UCDR), radial rotation angle (RRA), palmar carpal subluxation ratio (PCSR) were evaluated over time. In addition, in X-ray finding, a change of the articular surface of radiocarpal joint was considered. The RA disease activity was evaluated in DAS28-ESR.

Result: At the time of surgery, all cases were low disease activity in DAS28-ESR.

By the X-rays evaluation, CHR decreased in predominance. UCDR and the RRA showed a tendency to decrease just after surgery. In addition, PCSR did not have a change just after surgery at an investigation. In few cases, intercarpal joint became ankylosis.

ROM: Rotation angle and joint pain were improved in all cases, but extension-flexion range was not improved. In many cases, remodeling of the radiocarpal joint surface was observed.

Conclusions: In RA case with good response for treatment with biologics, SK method is an effective method, even though radiocarpal joint was severe destructed.

APLAR-0293

No association of Abdominal Adiposity quantified by CT and Hand Osteoarthritis in Korean Elderly Population

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Objectives: Obesity has been reported to be associated with hand osteoarthritis (OA) and visceral fat is a key player in the development of obesity-related health problems. The aim of this study was to evaluate the association between hand OA and visceral fat area quantified by CT.

Methods: Two hundred and seventy subjects (142 males and 128 females) were enrolled from a population-based KLoSHA cohort consisting of Korean elders over 65 years. Clinical and laboratory findings including body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and lipid profiles were collected. Their hand radiographs were evaluated to determine the presence of OA using Kellgren-Lawrence (KL) grading system. Visceral adiposity areas were calculated at the umbilicus level by a single scout CT scan. Body fat proportion was measured by tetrapolar bioelectrical impedance analysis

Results: Hand OA was present in 84 (59.2%) of men and 83 (61.9%) of women. In total subjects, visceral fat area was positively correlated with BMI, WC, serum fasting glucose level, triglyceride level, and HbA1C level. However, we did not observe any significant difference in visceral fat areas between hand OA and non-hand OA groups. Additionally, there was no association between hand OA and different measures of body mass or body fat proportion.

Conclusion: Visceral fat area was not significantly associated with hand OA in this cross-sectional study. A further larger study is warranted to establish a pathogenetic association between visceral fat and OA in the non-weight bearing joints.

APLAR-0311

The Prevalence of hand Osteoarthritis in dentists in Tehran, Iran

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Background: Pattern of the joint involvement in osteoarthritis (OA) can be affected by the individualOs life style and occupation. In the present study, we detected the prevalence of hand osteoarthritis (HOA) in Iranian dentists who worked in Tehran. In addition, characteristics of the OA were determined.

Materials and Methods: The study population consisted of the Iranian dentists who had attended in The Annual Scientific Dental Congress in Tehran. Four hundred participants of Tehran were questioned by a self answering questionnaire. After filling the questionnaire, the dentists were examined by a rheumatologist. Then in the (HOA) cases, X-ray of hands was done.

Results: The response rate was 90% in this study. The mean age of respondent was 43.5 + 8.8 and the mean Body Mass Index was 25.5 + 3.4. Among respondent 27 cases suffered from OA (6.8% CI: 4.5–9.7). The prevalence of hand OA was 18 from 291 among men, and 9 from 109 among women, 6.2% and 8.3 respectively. The most involved joints were the first Carpometacarpal (CMC I), Distal Interphalangeal (DIP) and Proximal Interphalangeal (PIP) joints. The only significant risk factor for HOA was family history, OR: 2.8 CI: 1.23 * 6.37.

Conclusion: The prevalence of HOA was higher in dentists in comparison to Iranian normal population (2.9% HOA in normal population according to the COPCORD study, 2008). The prevalence of the disease was higher in Iranian dentists in comparison to some other countries. In this study the differences were due to the family history and the long working hours of Iranian dentists.

Keywords: Hand Osteoarthritis, Occupation, Iranian Dentists.

APLAR-0313

Effectiveness and safety of hydrogel patch containing loxoprofen sodium in patients with knee osteoarthritis

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Objective: To investigate the effectiveness and safety of hydrogel patch containing loxoprofen sodium (LX-P) in patients with knee osteoarthritis.*Methods:* 169 patients from 11 rheumatology referral centers in China were enrolled in this randomized, controlled, double-blind, double-parallel, multicenter, phase ? trial. Patients were randomly assigned in a 1:1 ratio to either LX-P group (n = 84, LX-P 100 mg per day plus oral placebo t.i.d) or loxoprofen sodium tablet (LX-T) group (n = 85, LX-T 60 mg t.i.d plus patch placebo per day) for 4 weeks.

Results: The full analysis set population included 164 patients. There were more patients with an overall improvement rate of ≥50% in the LX-P group compared to those in LX-T group, although there was no statistically significant difference (72.8% *vs* 60.2%, respectively, P = 0.088). The treatment difference between two groups was 12.6% [95% confidence interval (CI): −1.7–26.9], and the lower margin of the 95% CI was above the predetermined noninferiority margin. No significant differences were found in tenderness, pain on motion, swelling, effusion, burning, or disability in daily activities, such as squat, standing and moving up/downstairs, at week 2, 4 or at the discontinuation point, but not in rest pain at the discontinuation point (86.3% *vs* 69.8%, P = 0.043), in both groups. There was a lower incidence of adverse events in the LX-P group than in the LX-T group, but there was no statistically significant difference (16.9% *vs* 28.2%, P = 0.078). No serious adverse events were reported in the LX-P group, whereas 1 case was reported in the LX-T group. *Conclusions:* LX-P has equivalent efficacy and safety as LX*T for the management of knee osteoarthritis. Therefore, it is assumed

that LX-P will be a highly useful therapeutic option with advantages such as easier administration and lower systemic exposure, compared with LX-T.

APLAR-0408

The new frontier: early diagnosis of osteoarthritis of the knee

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Background: The marked improvement in disability and survival in diseases such as RA and SLE has rested on early diagnosis and early intervention. Yet, knee osteoarthritis (OA) alone affects 6% >30 years, disables the majority and is diagnosed years after onset.

Hypothesis: That early diagnosis and a cost-effective intervention in early disease are possible.

Methods: A population based cohort of individuals with knee pain aged 40–79 years was assembled from greater Vancouver, British Columbia, Canada and assessed by standardized clinical examination, knee x-rays and magnetic resonance imaging (MRI) (J Cibere, PI, funding Canadian Institutes of Health Research). Subsequently, a cluster randomized clinical trial using the resultant diagnostic algorithm was conducted to assess the impact of pharmacist diagnosis and collaboration with physiotherapist and primary care physician in knee OA treatment (C Marra, PI, funding Michael Smith Foundation for Health Research). Cost-effectiveness analyses used standard approaches from perspective of both the Ministry of Health and society.

Results: 255 persons formed the knee pain cohort. 89% had OA on MRI and 49% had pre-radiographic OA (normal x-rays) (Cibere J, Arthritis Rheum 2010;62:1691–8). A clinical diagnostic algorithm was developed that allowed simple early identification of pre-radiographic knee OA in the majority. Following a pilot study demonstrating that early diagnosis of person with knee pain and previously undiagnosed knee OA was readily possible (Marra C, Arthritis Rheum 2007;57:1238–44), the trial enrolled 139 participants at 32 pharmacies, randomized to usual care, or to pharmacist medication review and physiotherapy intervention. In addition to significant improvement in pain and disability, the intervention was cost-saving (i.e, it dominated the usual care arm).

Conclusion: Early diagnosis of the knee OA allows intervention that is not only effective but cost-saving. This opens the door to the improvement in outcome for knee OA that is currently expected for inflammatory arthritis.

APLAR-0289

Efficacy of PG201 and celecoxib in symptomatic knee OA; a double blinded, randomized, multi-center, active drug comparative, parallel-group non-inferiority, phase 3 study

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Objectives: To define the non-inferiority of PG201 600 mg in comparison to celecoxib 200 mg in the treatment of symptomatic knee osteoarthritis (OA).

Methods: A total of 309 patients were randomly assigned to receive either the test drug, PG201 600 mg (n = 154) or the comparative drug, celecoxib 200 mg (n = 155). Subjects orally ingested the assigned agents twice a day and visited the clinical center at 4 and 8-week for laboratorial and clinical evaluations. The primary efficacy variable was the improvement in mean 100 mm pain VAS score from the baseline to the final visit (weeks 8), and it was compared between the two treatment groups. For the safety assessment, adverse events (AEs) were recorded at each clinical visit.

Results: At week 8, 100 mm pain VAS score significantly decreased by PG201 600 mg ($P < 0.0001$) and celecoxib 200 mg ($P < 0.0001$) from baseline scores. There were no statistically significant differences between groups ($P = 0.312$). These results met prespecified criteria for non-inferiority for both the Intent-to-Treat (ITT) and Per-Protocol (PP) populations. PG201 600 mg and celecoxib 200 mg were well-tolerated, with no statistically significant differences in tolerability profile between two groups.

Conclusions: PG201 600 mg was at least as effective and safe as celecoxib 200 mg in the treatment of symptomatic knee OA, and might be a useful medication for the treatment of knee OA.

APLAR-0223

Assessing the risk factors for osteoporosis in women aged from 50 years and above in the northern part of Vietnam

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Osteoporosis is a disease of bones with complication of bone fractures that lead to consequences in economy, decreasing quality of life and increasing mortality rate. Identification of risk factors for osteoporosis helps to give interventions to minimise bone fracture rate.

Objective: (i) To describe feature of risk factors for osteoporosis in women aged from 50 and higher in northern part of Vietnam, (ii) Determine risk factors for osteoporosis by analysis using multiple regression techniques.

Methods: Women from 50 years of age who visited outpatient clinics, Bach Mai hospital for general health-check and were not previously treated for osteoporosis. One hundred and eighty-three patients with T-score ≤ -2.5 were selected and age-matched with 183 women without osteoporosis (T-score > -2.5). All subjects (366) were determined bone mineral density (BMD) at lumbar spine and hip using DEXA scan (Hologic).

Results: Risk factors for osteoporosis included height below 145 cm (OR = 3.79), weight under 42 kg (OR = 6.16), BMI < 18.5 (OR = 4.37), having more than two children (OR = 1.71), first period after age of 15 (OR = 1.65), early menopausal before 45 years of age (OR = 3.38), post menopausal > 5 years (OR = 1.73), rheumatoid arthritis (OR = 1.82), long use of medications (glucocorticoids, thyrozol) (OR = 1.97), and elderly people. Among these factors, weight < 45 kg and early menopausal significantly had impact on osteoporosis according to multiple regression technique analysis. Conclusions

In northern part of Vietnam, women with weight less than 45 kg and early menopausal before 45 years of age are 2 factors significantly associated with osteoporosis ($r = 0.52$, $P < 0.001$)

Keywords: osteoporosis, risk factors, menopausal, women in northern part of Vietnam.

Clinical Rheumathology: T12 – Osteoporosis

APLAR-0054

Costunolide inhibits rankl-induced osteoclast differentiation by suppressing rankl-mediated c-fos transcriptional activity

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Background: Costunolide, a sesquiterpene lactone, exhibits anti-inflammatory and anti-oxidant propertiesand mediates apoptosis. However, its effects and mechanism of action in osteoclasts remains unknown.

Objectives: We investigated the role of Constunolide in RANKL-induced osteoclast differentiation.

Methods: Osteoclast formation was evaluated in bone marrow cells (BMC) in the presence or absence of Constunolide. The expression of c-fos and NFATc1 mRNA in osteoclast precursor were assessed by RT-PCR. The levels of c-fos and NFATc1 protein were assessed by western blot. Also the MAPKs and NF-κB pathways were measured using Western blot analysis.

Results: We found that costunolide significantly inhibited RANKL-induced BMM differentiation into osteoclasts in a dose-dependent manner without affeting cytotoxicity. Costunolide did not regulate the early signaling pathways of RANKL, including the mitogen activated protein kinase (MAPK) and NF-κB pathways. However, costunolide suppressed nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) expression via inhibition of *c-Fos* transcriptional activity without affecting RANKL-induced *c-Fos* expression. The inhibitory effects of costunolide were rescued by overexpression of constitutively active (CA)-NFATc1.

Conclusions: Taken together, our results suggest that costunolide inhibited RANKL-induced osteoclast differentiation by suppressing RANKL-mediated *c-Fos* transcriptional activity.

APLAR-0059

AG490 inhibits NFATc1 expression and STAT3 activation during RANKL induced osteoclastogenesis

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Objective: The role which JAK2/STAT3 signaling has on receptor activator of nuclear factor-κB ligand (RANKL)-induced osteoclastogenesis is still elusive. Therefore, this study was undertaken to investigate how specific inhibition of JAK2 with AG490 affects RANKL-mediated osteoclast differentiation in vitro.

Methods: RAW264.7 cells were cultured in the presence of RANKL and specific JAK2 inhibitor AG490. After 2 days culture, morphologic changes were observed under a light microscope. Osteoclasts were determined to be tartrate-resistant acid phosphatase (TRAP) positive staining multinuclear cells and counted under light microscopy. The expression of specific osteoclast markers (TRAP and RANK), two macrophage makers (CD11b and Emr1) in mRNA level and two transcription factors (NFATc1 and c-Fos) was analyzed by using real time polymerase chain reaction. The influence of AG490 on cell proliferation was assessed by using the Cell Counting Kit (CCK-8). The cell cycle distribution following AG490 treatment was determined through Flow cytometry. The activation of Akt, ERK1/2 and STAT3 signaling was detected by Western blotting.

Results: AG490 significantly inhibited osteoclastogenesis in murine osteoclast precursor cell line RAW264.7 stimulated by RANKL. AG490 suppressed cell proliferation and delayed the G1 to S cell cycle transition. Furthermore, AG490 repressed the expression of NFATc1 but not c-Fos in RAW264.7. Subsequently, we investigated various intracellular signaling proteins associated with osteoclastogenesis. AG490 has no effects on RANKL-induced activation of Akt, ERK1/2 and Tyr705-STAT3 pathways. Interestingly, AG490 suppressed RANKL-induced phosphorylation of Ser727 in STAT3.

Conclusion: We demonstrated that AG490 inhibited RANKL-induced osteoclastogenesis by suppressing NFATc1 production and cell proliferation via the STAT3 pathway. These results suggest that AG490 has potential application for treating inflammatory and metabolic bone-resorptive disease, such as rheumatoid arthritis and osteoporosis.

APLAR-0104

Study of bone density in type 2 diabetic patients and non-diabetics in Milad hospital, tehran, in 2011, comparisons and insights

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Aim: Osteoporosis is the most common reported bone metabolic disease, on the other hand Outbreak of diabetes type 1 and 2 are increasing in the world nowadays. Currently, the accepted opinion among experts is that type 1diabetes mellitus increases the risk and intensity of osteoporosis and the common question among the medical community is to understand the relation between diabetes type 2 (DM2) and Osteoporosis. DM 2 is the most common type of diabetes as it includes higher percentage of diabetic patients in the world. We design this study to review bone densitometry differences between our DM2 patients and other non diabetics.

Method: This study is based on a case-control method in which case group includes patients suffering from diabetes type 2 and control group consists of non-diabetics referred to bone densitometry. We selected 148 postmenopausal women have referred to densitometry center of Milad hospital. These cases include 69 patient with DM2 and 79 people without diabetes. We tried to select these two group equal in different parameters. We excluded many interventional factors in two groups. Information regarding variables of interest was collected through questionnaire and bone density was measured by Norland bone densitometry machine.

Results: This study analyzes 148 cases, including 69 diabetic (59 ± 8 years old) and 79 non-diabetic (58.1 ± 7.9 years old) patients, categorized in case and control groups, respectively. Based on statistical results, in terms of background and confounding variables, the two groups were statistically identical ($P > 0.05$). Bone mineral density (BMD) of lumbar spine in DM2 group was 0.93 ± 0.17and in control group was 0.94 ± 0.13, shows that there isn't a significant difference between two groups in the variable of bone density in the lumbar spine area ($P > 0.05$). The average bone density in femoral area for diabetic patients (0.79 ± 0.13) was significantly higher than that of nondiabetic (0.74 ± 0.10) group ($P < 0.05$).

Conclusion: No significant difference in bone density of lumbar spine and increase of mean densitometry of femoral neck area in cases of DM2 of this study is supportable by some of the current theories. Maybe we can expect DM2 doesnÖt not only lead to osteoporosis but also seems to have protective effects on bones. The caveat here is that this study did not take into account the impact of anti-diabetic drugs (medicines), which can have impact on the relationship between DM2 and Osteoporosis. Further studies, focusing on controlling the effects of anti-diabetic drugs in this relationship, can lead to more robust insights.

Key words: Type 2 diabetes, Osteoporosis, bone densitometry

APLAR-0132

Effects of an adapted physical activity program in osteoporotic women with rheumatoid arthritis

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Object of the study: To assess the effects on bone mineral density and muscular strength of a long-term adapted physical activity program in osteoporotic postmenopausal women suffering of rheumatoid arthritis.

Methods: Eighty-five osteoporotic postmenopausal women diagnosed with rheumatoid arthritis were divided into two groups (exercise group and control group). All patients underwent two assessments: before and after the training period. The bone quality was assessed by bone mineral density (quantified by T score measured through dual-energy x-ray absorptiometry). The maximal strength of lower limbs extensors was also evaluated. The exercise group participated in a specific adapted physical activity program performed during a 12-month period, twice a week. The program included aerobic, balance and strengthening exercises adapted according to the disease activity.

Results: After the training period, we noticed statistically significant increase of bone mineral density in exercise group (initial Tscore = −3.21 ± 1.23, final T score = −1.96 ± 0.45; $P < 0.001$). Instead, no significant changes were recorded in the exercise group (initial T score = −3.16 ± 0.92, final T score = −2.77 ± 1.17; $P > 0.05$). The women in the exercise group had also large gains in lower limb maximal strength.

Conclusions: An active exercise adapted to disease activity and disability should be included in the management of all patients suffering from rheumatoid arthritis. The current study proved that a long-term training protocol, lasting 12 months, can improve lower limbs strength and bone quality. These are two of the most important determinants of fall and fracture risk, improving thus patientsÖ general health status especially in elderly women diagnosed with both autoimmune inflammatory rheumatic disease and osteoporosis.

APLAR-0133

Correlation of parathyroid hormone level in elderly patients with or without fracture

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Aims: The purpose of this study was to compare parathyroid hormone levels in elderly patients with or without fractures and to evaluate a corelation between, age, BMI (Body Mass Index), CCT(Clearence Creatinin Test) and fractured in elderly.

Methods: Between Maret 2012 * Desember 2012we review 18 elderly patients with fracture (fracture group) and also reviewed 20 elderly patients without fracture(control group).In all subjects (38 patients), the correlation between parathyroid hormone level and sex, BMI, CCT was evaluated.

Result: Of the 38 elderly patients who were selected in this study, 18 with fractures (seven men, 11 women) and 20 non fractures (11 men nine women), mean age in fractured subjects 75 ± 9 years and non fractures 72 ± 5 years ($P > 0.05$). In this study there were significant differences of the serum parathyroid hormone level between the two groups patients, median PTH are 126.41 pg/dL (62.39–292.40) in fractured subjects and 32.28 pg/dL (22.55 * 58.55) in non fractures ($P = 0.0001$) and parathyroid hormone level were significant different in each group according to sex, in male fractured subjects : PTH mean 99.63 ± 33.28 pg/dL; and PTH mean 32.40 ± 8.96 in male without fracture ($P = 0.0001$). In female fractured subjects PTH mean 169.41 ± 74.62 pg/dL, and: PTH 32.13 ± 11.43, in female without fracture ($P = 0.0001$). But BMI and CCT were not significantly different in each group ($P > 0.05$) and ($P > 0.05$).

Conclusion: Parathyroid hormone level was increase in elderly patients and patients with fracture were found to have significantly higher parathyroid hormone levels than patients without fracture.

APLAR-0140

Effects of exercise on low density lipoprotein receptor related protein 5 gene expression in patients with postmeopausal osteoporosis

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Introduction: Osteoporosis (OP) is a common metabolic bone disease which is characterized by a low bone mass and deterioration in the micro-architecture of the bone tissue In this study, we investigated the effects of aerobic exercise on Low Density Lipoprotein Receptor Related Protein 5 (LRP5) gene mRNA expression

Methods: Seven patients with postmenopausal OP (median age 60 ± 5.3) were included in the study. An exercise protocol consisting of treadmill exercising for 30 min, 3 days a week for six weeks was performed at a moderate intensity. LRP5 gene expression levels were evaluate before the onset of exercise program, then 4 hours after the end of the 1st, 12th (4th week) 18th (6th week) sessions of exercise.

Results: Our results demonstrated variable changes in the LRP5 gene expression after the aerobic exercise sessions. Excluding one patient, the LRP5 gene expression levels showed a slight tendency to increase. In spite of this tendency, gene expression differences during the exercise sessions were not significant.

Conclusion: These results suggest that interindividual variations of LRP5 gene expression exists after moderate intensity aerobic exercises in patients with postmenopausal OP. Despite of this variability, LRP5 gene expression levels showed a slight increase except for one patient in peripheral blood.

APLAR-0212

The mechanism of the Chinese medicine in the treatment of postmenopausal osteoporosis

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Objective: To analysis the mechanism of the Chinese medicine in the treatment of postmenopausal osteoporosis.

Methods: A total of 134 cases of PMOP patients completed the study. Patients were randomly divided into active vitamin D + calcium group (control group) and the Chinese medicine of tonifying the kidney + Ca + active vitamin D group (Chinese medicine group), all treated for 1 year . At 0 month, 3 months, 6 months all patients were tested urinary calcium / creatinine (Ca / Cr), urinary type I collagen cross-linked C telopeptide / creatinine (CTX-I/Cr).And at 0 month, 12 months they were examined the bone mineral density(BMD).

Results: All patients of urinary Ca /Cr were not significantly different in three time points. But the Chinese medicine group's urinary CTX-I/Cr decreased ($P < 0.01$) at 3 months, and femoral neck BMD increased significantly ($P < 0.05$). Urinary CTX-I/Cr changes was positively correlated with the changes of femoral neck BMD ($P < 0.05$). Urinary CTX-I/Cr, femoral neck /lumbar spine BMD of the control group were not change after one year treatment.

Conclusion: The Chinese medicine of tonifying the kidney may decrease bone resorption, and at the same time enhance bone formation, increase bone mineral density. The mechanism may be related to inhibition the resorption of osteoclast and promottion apoptosis of osteoclast, and promoting the differentiation and proliferation of osteoblast.

APLAR-0300

Prevalence and Risk factors of Low Bone Mineral Density in young Indian Information Technology (IT) Professionals

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Introduction: Osteoporosis, defined as a Òprogressive systemic skeletal disease characterised by low bone mass and micro architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractureÓ (WHO), is recognised as a major concern globally especially in older age. However, the prevalence of osteopenia (low bone density) or osteoporosis (significantly low bone density) in young populations is not known.

Objective: The Objective of this study was to identify the prevalence and risk factors of osteoporosis and osteopenia among young Indian adult IT professionals.

Methods: The study involved identification of self reported risk factors of osteoporosis and measurement of bone mineral density (BMD) among 426 subjects aged between 20 years and 40 years at on-site occupational health clinics, using an ultrasound BMD analyser at the heel.

Result: The mean (±SD) age (years), height (cm) and weight (kg) of the subjects were 29.41 (±7.41), 168.43 (±8.47) and 67.4 (±11.0). 70% of the subjects were male. The results indicated that 10.7% subjects were exposed to the risk factors of osteoporosis. The study results also revealed that prevalence rate of osteopenia was 33.5% and osteoporosis was 11.6% among the affected population as compared with the reference value. The commonest self reported risk factors were lack of exercise (52%), lack of exposure to sunlight (47%), consumption of caffeine/alcohol (47%) and associated joint pain (37%).

Conclusion: Larger studies using BMD measurement by Dual Energy X-Ray Absorptiometry and Vitamin D levels in young IT professionals are recommended. We also recommend that occupational health physicians consider the possibility of osteopenia and osteoporosis in young IT professionals, including males, and incorporate on-site education and screening programmes for these conditions.

Key words: Osteoporosis, Osteopenia, Bone Mineral Density

APLAR-0359

Dietary calcium intake – a pathogenetic link between hypertension and osteoporosis

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A low dietary calcium intake is a well recognised risk factor for osteoporosis and recent studies suggest an influence of low dairy intake on high blood pressure.

Dysregulation of calcium homeostasis appears to be a fundamental factor linking these conditions (3). Dietary calcium is an important modulator of blood pressure in humans (1).

Serum ionized calcium levels are lower among hypertensive subjects with inappropiately low levels of the renal pressor hormone, renin, than among normotensive individuals. Low renin hypertensive subjects exhibited higher parathyroid hormone (PTH). Lower average serum ionized calcium levels observed in these pacients suggests a calcium deficit in the low renin hypertensive state (2). Thus, available evidence indicates that increasing dietary calcium intake may result in reduction in blood pressure (3).

Objectives: Aim of this study was to investigate if a low dietary calcium intake could play a role as a pathogenic link between hypertension and osteoporosis. We examined the effect of calcium plus vitamin D supplementation on blood pressure and the incidence of hypertension in osteoporotic postmenopausal women.

Methods: We examined 55 postmenopausal womenn with osteoporosis (defined as T Score BMD ≥−2.5) and high blood pressure (between 140 mmHg/90 mmHg and 160 mmHg/ 105 mmHg). All pacients were on antihypertensive treatment. All pacients had normal calcium serum and urinary level and declared a hypocacemic diet. 50% pacients received calcium supplements 1500 mg/day and vitamin D 800 UI/day for 8 weeks and 50% did not received calcium supplements.

Outcome measurements: Blood pressure measurements were taken at baseline and during follow-up examinations (4 weeks and 8 weeks).

Results: Univariate analysis showed that subjects with hypertension had a significant lower calcium intake and a higher prevalence of osteoporosis (31.3% vs.23.1%; $P < 0.001$). Multiple logistic regression analyses demonstrated that a low calcium intake was associated with an increased risk of hypertension (OR 1.39;92%CI:1.23–1.87) and osteoporosis (OR 1.44; 92%

CI:1.18–1.86). Calcium supplements lowered the top number of the blood pressure reading (the systolic pressure) by about 1.5 points on average and the bottom number (dyastolic pressure) by about 0.9 points on calcium supplemented pacients.

Conclusion: A low calcium intake from dairy sources can be responsible for a higher prevalence of osteoporosis in subjects with high blood pressure values and can be considered as a possible pathogenic factor linking hypertension and osteoporosis.

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APLAR-0373

The Use of Prolia (denosumab) in Hard-to-treat Cases of Osteoporosis

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Purpose: In rheumatology, patients who are symptomatic and severely incapacitated by severe osteoporosis are quite common. The usual treatment with NSAIDs, analgesics, calcium + vitamin D supplements, calcitonin (miacalcic) injections, strontium ranelate (Protos), oral bisphosphonates, or a combination of these; may not be effective; since treatment depends on patientsO compliance. Prolia 60 mg injected s.c., q 6 months, may be an effective and simpler therapy for some of these patients.

Methods and Results: Nine post-menopausal, female patients, with mean average age 69.2 years, with proven severe osteoporosis: T-score <−2.5 on DEXA Scan, with background diagnoses of: RA (6); Psoriatic Arthropathy (1); AddisonOs Disease (1); Hypothyroidism (5); On long-term LOW dose corticosteroid [< Prednisolone 5 mg/day] (4); Proven fractures (5); Diabetes Mellitus (2) or a combination of one or more of these diagnoses were injected with Prolia (With Ca + Vitamin D) according to protocol. Improvements were monitored by the clinician and patients, q8 weeks, and followed for 14 months. Patients were maintained on their previous medications for their pre-existing diagnoses.

Discussion and Conclusions: All patients were satisfied with the treatment and subjective improvements (less pain, less symptoms with weather changes, improvements in ADL and exercises) were noticed within 8 weeks of Prolia injection. The symptomatic improvements were consistent and continued over the treatment period. Some patients (4/9) [44.4%], noticed further improvements in symptoms after the second injection and (6/9) [66.7%] noticed great improvements in symptoms by 9–10 months.

No patients experienced any of the major complications: hypocalcemia, infections, rashes, osteonecrosis of the jaw (ONJ), pancreatitis, new malignancies while on treatment. Except for the cost, all patients preferred the current therapy for their osteoporosis: they find the therapy to be simple and effective. Barring cost considerations, Prolia injections should be considered in patients with long-duration, severe and symptomatic osteoporosis.

APLAR-0396

Osteoporosis-related life habits and knowledge about osteoporosis among adults in Beijing: A cross-sectional study

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Objective: The aim of this study was to determine the osteoporosis knowledge, the influence of osteoporosis-risk factors on osteoporosis, the diagnosis and treatment data of osteoporosis of adults in Beijing China.

Mathods: In this cross-sectional study, an osteoporosis knowledge assessment questionnaire was used to collect data and it was delivered through a face-to-face interview. Survey data included sociodemographics, osteoporosis risk factors, prior fractures and osteoporosis testing, health beliefs about osteoporosis, prior diagnosis and medications of osteoporosis. All residents underwent dual-energy-x ray absorptiometry (DXA) bone mineral density assessment during interview.

Results: Study indicated that women are more likely to respond the survey and had more knowledge about osteoporosis than men. The sample comprised of 2482 women and 553 men. 19.7% had fracture history. Only 7.9% had BMD test before. 6.3% had a pre-existing treatment of osteoporosis. Osteoporosis rate is 15.4% with only 2.5% in the younger group (<50 years). Osteoporosis treatment was not significantly associated with age, gender and history of fracture. Calcium and Vit D intake were only in most cases of those who had fracture history or osteoporosis. Smoking and alcohol intake are not correlate to osteoporosis. With all female residents received survey, no one received HRT. There is no relationship between fracture history and prior BMD test. Women are more likely to have fracture than men ($P < 0.01$).

Conclusions: osteoporosis related data in Beijing are different from other parts of the world. BMD test rate is very low; calcium and Vit D intake are not sufficient. It is important to make the long-term effects of programs on improving awareness, diagnosis and treatment of osteoporosis.

APLAR-0397

Expression of circulating advanced glycation end-products in menopausal women with osteoporosis

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Objective: Advanced glycation end-products (AGEs) can accumulate in organs and tissues during ageing and diabetes. Increased levels of AGEs are found in the bone tissue of patients with osteoporosis. The purpose of this study was to evaluate circulating AGEs in patients with osteoporosis.

Methods: We evaluated plasma AGEs, osteoporosis-related biomarkers, and bone mass in 82 menopausal women with osteoporosis or osteopenia, 16 young women with osteopenia, and 43 healthy women without osteoporosis or osteopenia.

Results: Higher levels of serum AGEs were found in the osteoporosis or osteopenia group compared to healthy women ($P = 0.004$). A negative correlation was observed between serum AGEs and lumbar spine bone density (BMD of lumbar spine, $r = -0.249$, $P = 0.028$; T-score of lumbar spine, $r = -0.261$, $P = 0.021$). Women with a high level of serum AGEs (>16.22 U/mL) had a 9.41-fold risk of osteopenia regarding lumbar spine T-score and a 2.81-fold risk of osteopenia regarding the hip T-score. No significant correlation was found between AGEs and age ($P = 0.087$) or serum estrogen ($P = 0.823$).

Conclusion: Serum AGEs could be used to monitor the severity and progression of osteoporosis. An increased serum level of AGEs was associated with impaired bone formation and was a risk factor for the development of osteoporosis. Targeting AGEs may represent a novel therapeutic approach for primary or secondary osteoporosis.

APLAR-0414

The effect of soft tissue on BMD in premenopausal women

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Aims: Fat mass and muscle mass (lean mass) of the two the main variables that make up our body weight and Have different effects on bone density. In this study, we examined the relationship between lean mass and fat mass to bone mineral density (BMD) in different parts of the body in pre-menopausal women were studied volunteer military.

Methods: Fat mass, lean mass and BMD of 42 women military personnel, with an age range of 35–45 years who were pre-menopausal, were measured by DEXA. Relationship between Fat mass and lean mass with BMD in different parts and whole body of the subjects were measured.

Results: The mean and standard deviations of whole body bone density in women was: 1/09 ± 0/15 g/cm^2, total body fat mass: 24901/55 ± 6021/90 g, percent body fat: 37/02% ± 3/86 of the total lean mass: 39657/2 ± 6369 /24 g. The amount of total BMD with fat mass and between left and BMD of right lower limb with fat mass, there is a negative correlation. Between BMD in upper and lower limbs with same of lean mass, there is a significant positive relationship.

Conclusion: The results of this study concluded that fat mass had a negative effect on bone density. Lean mass as a strong predictor of BMD in premenopausal women is the upper and lower limbs. Also, a positive relationship between lean mass with whole body and lumbar bone mass density observed.

Keywords: Body composition, BMD, Lean mass, Fat mass, Perimenopause.

APLAR-0443

Modifiable risk factors of osteoporosis on background of rituximab therapy with rheumatoid arthritis patients

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Purpose: To assess the influence of rituximab therapy on modifiable risk factors (RF) of osteoporosis with rheumatoid arthritis (RA) patients.

Materials and methods: We observed 56 patients with a documented diagnosis of RA. All the patients were divided into two groups according to the level of bone mineral density (BMD): Group 1 – patients with osteopenia (n = 20) and group 2 – patients with osteoporosis (n = 36). To assess the risk factors the thematic map of RA patients was used developed by Rheumatology Research Institute of Russian Academy of Medical Sciences by the program "Osteoporosis in rheumatoid arthritis: diagnosis, risk factors, fractures, treatment." BMD was

measured by dual-energy x-ray absorptiometry. Osteoporosis risk factors and BMD were assessed in the dynamics of the therapy with rituximab.

Results: The treatment with rituximab positive trend was observed in both groups of patients in two risk factors. Thus, 6 patients with osteoporosis had a statistically significant increase in BMD and T-criterion (BMD 0.813 ± 0.10 g/cm^2, T-criterion −2.61 ± 0.09 g/cm^2, $P < 0.05$ and $P < 0.05$) and levels of physical activity was increased with seven patients (19.4%). In the patientsÕ group with osteopenia the number of patients with low body weight – One person (4.2%) and low levels of physical activity – two patients (8.3%) decreased .Osteoporotic fractures occurring with minimal trauma, reported with 3 osteoporosis patients (8.3%).

Conclusions. Rituximab therapy is associated with increased levels of physical activity with all RA patients, regardless of the degree of bone density reduction, and with the positive dynamics of BMD with RA and osteoporosis patients.

APLAR-0445

Disease activity in Rheumatoid Arthritis patients affected Bone Mass Density

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Background: Osteoporosis frequency in rheumatoid arthritis ranged 4–24% and osteopenia ranged 28–61.9%, while fracture prevalence ranged 0–25%. Bone destruction related to inflammation in RA manifest as bone erosion and osteoporosis. Quantitative bone mass examination with highest sensitivity is needed, to detect earlier disease.

Aim: To determine correlation between bone mass density with inflammation severity and disease activity in rheumatoid arthritis patients.

Method: Cross-sectional study, with consecutive sampling in 31 premenopause females with rheumatoid arthritis, using steroid prednison ≤10 mg/day. Bone mass density was measured by dual x-ray absorptiometry, while ESR was assessed using westergreen method, CRP using ELISA method, and disease activity was measured by DAS(28(4))-CRP. The data obtained will be processed using SPSS and performed correlation analysis with Pearson / Spearman. From the overall data and analysis carried out, a link between BMD with disease activity of RA will be obtained.

Results: Thirty one patients with RA were studied in this study. One patient (3.22%) suffered from femoral osteoporosis, three patients (9.67%) Ò*ward triangle*Ó osteoporosis. No fracture history in all subjects. Twenty one patients (67.74%) with positive rheumatoid factor. Lumbar 2 and total hip had positive correlation with body mass index; total hip with disease activity; Ò*ward triangle*Ó, great trochanter, and total hip correlated with ESR; total hip with CRP; Lumbar 2, and total lumbar with disease duration. BMD of great trochanter, total hip and disease activity were correlated with rheumatoid factor positivity. BMD lumbal 2 and total femoral had positive correlation with VAS. There was negative correlation between bone mass density with inflammation severity and disease activity in RA patients.

Key word: bone mass density, disease activity, rheumatoid arthritis

APLAR-0456

The relationship of BMI and chronic systemic inflammation with bone mineral density in elderly Indonesian men with COPD

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A decrease in bone mineral density is a frequent complication in elderly patients with Chronic Obstructive Pulmonary Disease (COPD) but still lacking of studies this topic. Understanding the role of other risk factors that also affect the severity of COPD and decrease bone density, such as body mass index (BMI) that associated with muscle mass, serum 25-OH Vitamin D, calcium, IL-6 and TNF-α serum are crucial for early detection of osteopenia or osteoporosis in COPD. The purpose of this study was to determine the relationship of BMI and chronic systemic inflammation with bone mineral density in COPD.

The study was a descriptive analytic cross-sectional design of the elderly male outpatients with COPD that went to Geriatric and pulmonology clinics at Dr.Hasan Sadikin General Teaching Hospital Bandung, Indonesia. Patients are screened through history taking and physical examinations as according to the inclusion and exclusion criteria. The research variables were BMI, levels of total calcium, 25-OH D Vitamin, Interleukin-6, TNF-α, and osteoprotegerin (OPG) serum and bone mass density (BMD) based on Dual Energy X-Ray absorbtiometri (DEXA). Relationships between variables were analyzed by Pearson correlation test.

A total of 76 male subjects age 50 (65.8%) without osteoporosis and 26 (34.2%) with osteoporosis. Pearson correlation test results showed a weak positive correlation between BMI and T-Score ($P = 0.007$, $r = 0.282$), and a weak positive correlation between the levels of 25-OH Vitamin D with a T-score ($P = 0.018$, $r = 0.242$). BMI and the level serum 25-OH vitamin D were lower in osteoporotic COPD group compared with COPD without osteoporosis, and levels of osteoprotegerin, IL-6, TNF-α was higher in osteoporotic COPD group compared with COPD without osteoporosis. Based on these results it can be concluded that the lower IMT and the levels of 25-OH Vitamin D, the lower of the value of T-Score.

Clinical Rheumathology: T15 – Scleroderma, myositis and related syndromes

APLAR-0017

The incidence of pulmonary hypertension in asymptomatic systemic sclerosis: Is annually echocardiography screening necessary?

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Background: AnnuallyECHO screening is recommended for early detection of pulmonary hypertension (PH) in patients with systemic sclerosis (SSc), however, beneficial effect of this high cost procedure in asymptomatic cases is not well established.

Objectives: To determine the incidence and clinical predictors of ECHO diagnosed PH in asymptomatic Thai SSc patients.

Methods: Historical cohort study of adult SSc patients at Srinagarind Hospital, KhonKaen University, Thailand, between January 1, 2005 and December 31, 2011 was performed. All included study patients had annually ECHO screening for PH at least 2 times. PH is defined by estimate right ventricular systolic pressure (RVSP) over 40 mmHg.

Results: A total of 143 medical records of SSc patients were reviewed. The female to male ratio was 1.7:1. Majority was diffuse cutaneous SSc (94 cases; 69.6%). Of the total 779.5 person-years under observation, 14 events of ECHO diagnosed PH were detected. The incidence rate of PH was 1.7 per 100 person-years (95%CI 0.9–3.0). Diagnosis of PH was confirmed by right heart catheterization (RHC) in nine of them (64.3%). Seventy five patients (52.4%) were asymptomatic throughout the follow up period, among these only one had PAH diagnosed by RHC. The incidence of PH in asymptomatic SSc was 0.2 per 100 person-years (95%CI 0.006–0.01). Overall, the median disease duration at the time of PH detection by ECHO was 5.2 years (IQR 1.7–13.6), and 5.1 years in asymptomatic patient. Functional class (FC) II and III were associated with PH by ECHO screening with the incidence rate ratio 2.45 (95%CI 1.10–5.74) and 3.98 (95%CI 1.19–10.64), respectively. Meanwhile sex, age, skin tightness, SSc subset, anti-Scl70 antibody, and internal organ involvement were not increased rate of PH detection.

Conclusion: The incidence of ECHO diagnosed PH in asymptomatic Thai SSc patients was low. PH was found 4–5 years after disease onset and associated with declining functional class in most cases. Annually ECHO has less beneficial effect in asymptomatic SSc patients; rather repeated ECHO should be performed in one who has declining FC during follow up.

APLAR-0026

Rehabilitation effect on hand range of motions in patients with systemic sclerosis

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To evaluate the efficacy of a 3-week inpatiens couse on Systemic Sclerosis Questionnaire, SySQ (Rouf et al.,Viitanen JV) and wrist and four fingers' range of motions (ROMs), measured in degrees (¡) or millimeters (mm), and fingers' mean extension deficit (MED) as distance (mm/¡) from the level of a table(?, and hand grip force as kPa (Jamar grip-2). Together 23 patiens with mild or moderate scleroderma, who did not suffer from axial restrictions or cardiovascular symptoms, were included.

Assessments in 4 cathegorical scales, comprising 12 subgroups out of 32 questions in SySQ, evinced small improvements in General Symtoms (0.18), but not at all in other three scales (between −0.03 and 0.05) – scoring 0–3 (the most sever symptoms). Any marked functional improvements were not to be observed. SySQ did'nt correlate with fitness test (N 12) results. The ROMs results correlated, however, markedly with assessments of 12 subgroups in SySQ, rho 0.42–0.74 ($P < 0.05$), except for PIP-joint MED. At entry to the course the mean finger and wrist ROMs were slightly restricted, and the squeeze force markedly deteriorated. Hand ROMS improved markedly by intensive rehabilitation means after a 3-week course.

Table 1. Results of grip stregh and right hand ROMs added in six subgroups. N = 23 At entry After 3-week course.

	Mean (SD)	Changes (SD)	95 % C.I.
Grip force, kPa	20.0 (10.5)	3.45 (3.3)***	5.0–1.9
Fingers II-IV[33]			
Extension deficit ? (¡)	3.7 (8.5)	−1.5 (2.3)*	−0.2−−2.1
Extension deficit? (¡)	4.6 (9.0)	−1.6 (2.7)*	−0.4−−2.8
Thumb			
MCP+IP flexion (¡)	101.3 (29.0)	3.7 (7.12)*	6.8–0.6
MCP flexion (¡)	73.1 (13.0)	6.0 (5.2)***	8.2–3.8
Wrist			
Flexion-extension (¡)	111.2 (20.6)	10.8 (15.3)**	17.4–4.1
Supination-pronation (¡)	103.2 (21.7)	6.3 (9.1)*	10.3–2.4

***$P < 0.001$, **$P < 0.01$, *$P < 0.05$; [33]) Little finger excluded.

APLAR-0030

New centromere autoantigens identified in Systemic Sclerosis using centromere protein microarray

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Background: Anti-centromere antibodies (ACA) were useful biomarkers in the diagnosis of systemic sclerosis (SSc). To date, several centromere proteins(CENPs) have been identified as ACA autoantigens. However, whether other CENPs have autoimmune activity has not been comprehensively surveyed.

Objective: To identify novel CENP targets of ACA and investigate their association with clinical manifestations.

Methods: A CENP-focused protein microarray was fabricated by spotting 14 purified CENPs (A, B, C, H, I, J, K, L, M, N, O, P, Q, T). These microarrays were incubated with 35 ACA-positive SSc sera and 20 ACA-negative healthy controls. Newly identified CENP autoantigens with high sensitivities were validated and characterized by ELISA and Western blotting and analyzed their association with clinical manifestation.

Results: Eleven CENPs are target antigens of ACA in SSc. Five of them (CENP-P, CENP-Q, CENP-M, CENP-J, and CENP-T) are novel, in which CENP-P and CENP-Q showed high sensitivities in ACA-positive SSc sera of 34.3% and 28.6%, respectively. 186 SSc sera (35 ACA-positives and 151 negatives) were assayed for the presence of anti-CENP-P and -Q autoantibodies by ELISA followed by western blotting analysis. Anti-CENP-P was also found in 9 of the 151 ACA-negative sera. Analyses of the correlation with clinical information showed anti-CENP-P positive patients had higher levels of IgG, IgA and ESR among the ACA-positive cohort and were more vulnerably to renal disease in the ACA-negative SSc patients. Regardless of ACA status, anti-CENP-P or -Q negative patients seem to be predominantly affected by interstitial lung disease.

Conclusion: Five CENPs were identified as novel ACA targets in SSc by using a CENP-focused protein microarray. Of them, CENP-P and -Q showed high sensitivities in ACA-positive sera followed by validation of ELISA and western blotting. Both of them have prognostic utility for interstitial lung diseases. In addition, CENP-P is associated with renal disease in ACA-negative cohort.

APLAR-0068

Predictors of complete remission at 1-year-follow up in patients with inflammatory myositis

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Objectives: To determine the clinical and muscle pathology findings as predictors of complete remission(CR) at 1-year-follow up in inflammatory myositis(IM) patients

Methods: 40 IM patients who were attended at the Rheumatology clinic, Chiang Mai University Hospital from January 2003 to December 2010 with available data at baseline visit when muscle biopsy performed and having data at 1-year-follow up were retrospectively identified. Their fresh frozen sample muscle biopsies were evaluation by one muscle pathologist. Four domains of the muscle pathological findings consisted of inflammation(IF), vasculitis(V), muscle(M), and endomysial fibrosis(E) were scored.The demographic data, medications, combined muscle strength (CMS) [0–40] and creatine kinase(CK) were recorded. Logistic regression analysis was performed to determine the predictor of complete remission(CR) at 1 year. CR was defined as having normal values both muscle strength and enzyme.

Results: Mean (SD) age was 46.7(13.4) years. 31(77.5%) were female. There were four subgroups of IM patients including 45% IM associated with connective tissue disease, 32.5% idiopathic polymyositis, 15.0% idiopathic dermatomyositis, and 7.5% IM associated with malignancy. 21(52.5%) and 17(42.5%) patients were treated with methotrexate and azathioprine, respectively. Mean(SD) values at baseline were: CMS 32.1(4.08), CK 5124.3(5165.8); IF 1.5(1.7); V 0.2(0.7); M: atrophy 1.7(0.7), degeneration 0.8(0.9), internal nuclei 0.4(0.5), invasion of non-necrotic fiber 0.2(0.6), E: 0.8(0.8); combined scores 5.7(3.8). Mean(SD) values at 1-year were CMS 37.9(2.6) and CK 345.3(489.9). 15(37.5%) patients were classified as CR.

In univariate analysis, myositis subgroup ($P = 0.029$), CMS at baseline ($P = 0.008$), CK ($P = 0.025$), and E score(0.046) were associated with CR. In multiple logistic regression analysis, combined muscle strength was the independent determination of CR at 1-year follow-up (B [S.E.] = 0.32[0.15], $P = 0.03$, OR 1.37, 95% CI: 1.027–1.841, R^2 0.349).

Conclusions: We found that demographic data, medication, muscle pathology scores and CK could not independently determine CR in our study population. However, only the better muscle strength at baseline predict good outcome.

APLAR-0072

Left ventricular diastolic dysfunction is early cardiac impairment in patients with polymyositis/dermatomyositis: A Tissue Doppler Imaging Study

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Objective: To investigate early cardiac involvement in patients with polymyositis/dermatomyositis(PM/DM), and to evaluate the risk factors for early cardiac involvement.

Methods: The study population included 46 PM/DM patients without overt cardiovascular manifestations and 21 age and gender matched healthy controls. Traditional echocardiography and Tissue Doppler Imaging(TDI) were used to evaluate the cardiac function in both groups. PatientsÓ clinical characteristics were recorded. Multivariate logistics regression analysis was applied to investigate the risk factors for early cardiac impairment in patients with PM/DM.

Results: No significant difference was found by traditional echocardiography between patients and healthy controls. However, compared to healthy controls, PM/DM patients had a significantly lower ratio of early diastolic mitral annulus velocity to late diastolic mitral annulus velocity (Em/Am) [(1.23 ± 0.52)?(1.79 ± 0.37), t = −4.485, P < 0.001] and a higher ratio of E/Em [(8.26 ± 2.57)?(6.76 ± 1.17), t = 3.287, P < 0.05] as found by using TDI measurement. There was no significant difference in TDI parameters between PM and DM patients as well as between untreated cases and treated cases in the past. The multivariate regression analysis showed that female gender (OR 11.044, 95%CI 1.066~114.357, P = 0.044), late onset (OR = 1.157, 95%CI 1.047~1.278, P = 0.004) and duration of disease (OR = 1.060, 95%CI 1.008~1.115, P = 0.023) were risk factors for abnormal left ventricular filling pressures.

Conclusion: TDI is a useful tool to detect early cardiac impairment in PM/DM patients. Left ventricular diastolic dysfunction is an early feature of cardiac involvement. Female gender, late onset and long course of disease are three independent risk factors for predicting the left ventricular diastolic dysfunction in patients with PM/DM.

APLAR-0118

Palosuran treatment, effective as bosentan in the treatment of pulmonary arterial hypertension (PAH) model

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Objective: Due to its high morbidity and mortality rates, pulmonary arterial hypertension is a life threatening and a progressive disease. Endothelin-1 (ET1) is a vasoactive peptide that plays important role in the pathogenesis of PAH, and ET1 inhibitors have been widely used in the treatment. ET1 and Urotension-II (UII) have similar effect profiles and features. In our previous studies, UII acts similarly as ET1 and increased in patients with SSc, especially with vascular pathologies. Also we have demonstrated the positive effect of UII inhibitor Palosuran in an animal model on pulmonary arterial pressure (PAP), ET1, UII, Cardiac Muscle Mass and pathology. In this study we aimed to compare the ET1 inhibitor bosentan which is regarded as standard therapy with different dose regimens of palosuran.

Material and Methods: Seventy male mice were randomly divided into seven groups, with each group comprising 10 rats. The first level of the study has been terminated at twenty-first day, after determining the optimum dose regimens and drug combinations the study was prolonged to investigate the efficiency of palosuran and bosentan combinations and monotherapy. The extended study group was also sacrificed at the twenty-first day of the experiment. Single dose moncrataline (MCT) were injected subcutaneously to create the PAH model. Palosuran and bosentan were given twice a day by gavages. Group 1 (control group) received the serum physiologic (SP); Group 2 (untreated MCT control group) received subcutaneous MCT and SP; Group 3 (Palosuran 30 mg therapy group) received subcutaneous MCT and 30 mg/kg/day palosuran; Group 4 (Palosuran 100 mg therapy group) received subcutaneous MCT and 100 mg/kg/day palosuran; Group 5 (Bosentan 30 mg therapy group) received subcutaneous MCT and 30 mg/kg/day bosentan; Group 6 (Bosentan 100 mg therapy group) received subcutaneous MCT and 100 mg/kg/day bosentan; Group 7 (Combination therapy group) received subcutaneous MCT and 300 mg/kg/day bosentan and palosuran. ET1 and UII levels, PAP and all cardiac indexes of all groups have been measured and recorded. Among the cardiac indexes, right ventricular hypertrophy (RVH) (right and left ventricule + septum) and right ventricular mass indexes (right ventricule and total body weight) have been used.

Results: ET1, UII and PAP findings of all groups have been presented in Table-1. The ET1 and UII levels of untreated rats (group 2) were significantly higher than the other groups (P < 0.05). Moreover, PAP levels of group 2 were significantly higher than the other groups (P = 0.001).

Conclusion: When we have compared the different dose regimens of palosuran with bosentan, UII inhibitor is at least as effective as standard therapy bosentan. Findings of this study consolidates that palosuruan could be a new future promising therapeutic option in PAH. Further human studies may require the findings of our study.

Table 1. ET1, UII and PAP Measurements of all groups.

	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7
ET1 (pg/mL)	0.753 ± 0.08	0.865 ± 0.11	0.574 ± 0.13	0.658 ± 0.18	0.618 ± 0.17	0.719 ± 0.15	0.653 ± 0.05
UII (ng/mL)	1.02 ± 0.17	1.11 ± 0.08	0.55 ± 0.17	0.58 ± 0.16	0.55 ± 0.17	0.88 ± 0.31	0.93 ± 0.17
PAB (mmHg)	12.9 ± 3.1	22.5 ± 6.4	11.8 ± 1.9	13.2 ± 2.9	11.7 ± 1.4	10.6 ± 0.8	11.2 ± 2.1

APLAR-0152

Vascular endothelial growth factor (VEGF), sVEGFR-1 and sVEGFR-2 in the sera of patients with systemic sclerosis

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Introduction: Systemic sclerosis(SSc) is a connective tissue disorder affects skin and internal organs(1). The significant loss of small vessels in SSc patients lead to disturbance in the angiogenesis process(2). Hypoxia and tissue ischemia lead to the expression of angiogenic growth factors, e.g. vascular endothelial growth factor (VEGF)(2,3,4).Soluble fms-like tyrosine kinase (FLt)1 is an endogenous anti-VEGF and causes microangiopathy(5). Also soluble form of VEGFR-2, termed sVEGFR-2 has been showed potent antiangiogenic effects(6).

In this study we determined the serum levels of VEGF as an angiogenic factor, the sVEGF-R1 (sFLt-1) and R2 (as anti-angiogenic factors), the VEGF/sVEGFR1 and VEGF/sVEGFR2 ratios in SSc patients and their correlation to main clinical manifestations of scleroderma patients like pulmonary fibrosis, digital ulcer and skin score.

Method & Materials: In this case control study we selected 44 patients with systemic sclerosis referring to clinic of scleroderma of Hafez Hospital of Shiraz University of Medical Sciences, from April 2011 to April 2012. The study sample was based on the LeRoy Criteria. The demographic data and clinical manifestations have been recorded. Serum levels of VEGF, sFlt1 and sVEGFR-2 were measured in all samples using ELISA kits.

Results: In 44 cases and 44 age and sex matched controls there was no statistically significant difference in VEGF-R1 serum level (P = 0.9) but higher level of VEGF (P = 0.018) and lower level of VEGF-R2 (P = 0.034) in scleroderma group comparing to control group.

Comparing the patients with diffuse(26.59%) and limited sclerosis(16.40%) serum level of VEGF, VEGF-R1, VEGF-R2 were higher in patients with diffuse SSc comparing to limited subtype, although it was not statistically significant. Also VEGF serum level in patients with digital tip ulceration was higher than patients without this presentation (P = 0.34). But VEGF-R1 (P = 0.54) and VEGF-R2 (P = 0.80) level were more in patients without digital tip ulceration.

Conclusion: This paper indicates that VEGF is significantly higher in patients with scleroderma comparing to control population. Also lower sVEGF-R2 in our patients can suggest its antiangiogenic effect in scleroderma patients. There was suggestion of pathogenic role of VEGF and protective role of sVEGF-R1 and sVEGF-R2 in vasculopathy and digital ulcer of scleroderma patients.

APLAR-0226

Prevalence and clinical significance of arthritis in systemic sclerosis: a report from the database of Chinese population

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Objective: To explore the prevalence of and independent factors associated with arthritis in Chinese patients with systemic sclerosis(SSc).

Methods: This study was a prospective cross-sectional study based on data collected from 248 SSc patients of Peking Union Medical College Hospital(PUMCH), Beijing, China. Arthritis was clinically diagnosed as one or more joint disorder with tender and swollen for more than two weeks. Demographic, clinical and laboratory data were analyzed in groups with and without arthritis. Systematic examinations of modified Rodnan skin score(mRSS), six-minute walk test, and pulmonary function test were also performed.

Results: Of 248 Chinese SSc patients whose mean age was 45 ± 9 years old and disease duration was 7 ± 5 years, 144 had a limited cutaneous subset. Overall prevalence of arthritis was 41.13%(102/248). The presence of Raynaud phenomenon (94.11% vs. 90.41%), muscle weakness(38.23% vs. 24.66%), gastrointestinal symptoms(67.65% vs. 53.42%), intestinal lung disease(ILD) (64.7% vs. 49.31%), and all joint manifestations occurred significantly more frequent in patients with arthritis than those without arthritis. The elevation of erythrocyte sedimentation rate(ESR), IgG, anti-Sm and anti-CCP were more frequent in arthritis group than in non-arthritis group(50.00% vs. 40.46%, 41.30% vs. 31.78%, 8.82% vs. 2.05% and 8.82% vs. 1.37%, respectively). There were no obvious differences in the mRSS score, digital ulcers, pulmonary arterial hypertension (PAH), and six-minute walk test between two groups.

Conclusion: Our results underline the significant prevalence of arthritis in a large cohort of SSc patients in China. Compared to non-arthritis patients, the SSc patients with arthritis have a more severe inflammation response and a more frequency of intestinal lung disease.

APLAR-0227

Comparing the four diagnostic criteria for idiopathic inflammatory myopathy

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Objective: To analyze and compare the specificity and sensitivity of four common diagnostic criteria of idiopathic inflammatory myopathy(IIM).

Methods: The sensitivity and specificity of these four sets of diagnostic criteria in 1975, 1995, 1997 and 2004 were determined by retrospective analyzing of our hospital diagnosed idiopathic inflammatory myopathy patients and non idiopathic inflammatory myopathy patients.

Results: Ninety-four cases of idiopathic inflammatory myopathy patients and 98 cases of non idiopathic inflammatory myopathy patients were analyzed by four sets of diagnostic criteria. The sensitivity of the diagnostic criteria in 1975, 1995, 1997 and 2004 are 56.4%, 87.2%, 61.7 % and 52.1% respectively,the specificity are 78.6%, 20.4%, 78.6% and 90.8% respectively, the Youden index are 35%, 7.6%, 40.3% and 42.9% respectively,the odd product are 4.74, 1.75, 5.91 and 10.77 respectively,kappa test values were 0.351 ($P < 0.05$), 0.075 ($P > 0.05$), 0.404 ($P < 0.05$) and 0.433 ($P < 0.05$) respectively.

Conclusion: Thesensitivity of diagnostic criteria in 1995 is high,but the specificity is too low, the misdiagnosis rate is high, it is the worst in four sets of diagnostic criteria in clinical application value. The sensitivity of diagnostic criteria in 2004 is slightly lower, but the specificity is high.The Youden index, the odd product and the kappa test results showed that the value of clinical application of the diagnostic criteria in 2004 is better than the other three criteria.

APLAR-0258

Echocardiography Evaluation In Scleroderma Patients

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Background: Transthoracic Echocardiography (TTE) has emerged as important noninvasive method of studying cardiac abnormality. The study was carried out to detect the cardiac abnormalities in patient with scleroderma.

Aim: To know an incidence cardiac abnormality in scleroderma patients.

Methods: This a descriptive study, we took data retrospectively from medical record,we studied a resting TTE findings in 19 patients with scleroderma and were evaluated for incidence of cardiac abnormality.

Results: Following results of TTE in 19 scleroderma patients, 17 (89.5%) patients most were females. Mean age of the patients was 37.3 $\pm$ 12.9 years old. TTE revealed abnormality in 14 patients (73.68%). Of these findings, two patients (10.52%) had pericardial effusion. Eight patients (42.10%) had some valvular involvement and there were two patient (10.52%) had low left ventricular ejection fraction. Four of the 19 patients (21.05%) were diagnosed having pulmonary hypertension. Some degree diastolic dysfunction was found eight patient (42.10%). We did not find any thrombus from TTE in our patient.

Conclusion: The incidence of cardiac abnormality in our study was 73.68%. Cardiac involvement is common in patients with scleroderma with other abnormalities findings.TTE can be helpful as a non-invasive, easily available detection of cardiac abnormalities in scleroderma.

Key words: Echocardiography, Cardiac abnormalities, Scleroderma.

APLAR-0291

Anti-NXP-2 antibodies in Chinese patients with idiopathic inflammatory myopathies

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Objectives: To investigate the prevalence and clinical associations of anti-NXP2 antibody in the serum of Chinese patients with IIM.

Methods: Serum levels of anti-NXP2 antibodies were detected by ELISA in 198 patients with IIM, 70 patients with systemic lupus erythematosis(SLE), 60 patients with rheumatic arthritis (RA), 25 patients with systemic sclerosis(SSc), 46 patients with sjogren syndrome(SS) and 40 healthy controls. The associations between anti-NXP2 antibody and clinical characteristics of patients with IIM were analyzed.

Results: The cutoff value was set at 0.137, based on four SDs above the mean value obtained from 40 healthy control serums. Serums of 10 patients with IIM were positive for anti-NXP2 antibodies. None of the patients with other CTDs and healthy controls had these autoantibodies. 2/12(16.7%) JDM cases were positive in comparison with 5/135(3.7%) adults with DM and 3/51(5.9%) adults with PM. There were no significant differences in anti-NXP2 -positive rate among patients with JDM, adult DM and PM. Compared with anti-NXP2 antibodies and clinical features of IIM patients, age at onset was younger in anti-NXP2 (+) ($P = 0.038$). Between anti-NXP2*positive and anti-NXP2*negative IIM patients, there was no significant difference in the female-to-male ratio, arthritis, dysphagia, GottronOs lesions, mechanic's hand, Raynaud's syndrome or rashes. Among 10 anti-NXP2*positive patients, 9 adult patients showed myalgia and myasthenia, seven patients showed rashes. In the two JDM patients with anti-NXP2-antibodies, one patient who died later had severe calcinosis, myasthenia and rapid progress. None of them had malignancy.

Conclusions: This is the first report of anti-NXP2 antibodies from a Chinese single center cohort. The positive rate of anti-NXP2 antibodies in Chinese IIM was 5%. The patients with anti-NXP2 presented with younger ages. Positive antibodies in JDM suggest calcinosis and severe condition.

APLAR-0388

Pulmonary involvement in scleroderma

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Introduction: Systemic sclerosis is a chronic systemic disease characterised by autoimmunity, vascular lesions and progressive fibrosis, with heterogeneous clinical presentation. This disease affects various organs as lung, heart, kidneys and gastro intestinal tract

Objectives: Purpose of this study is the identification lung injuries in patients with scleroderma, the impact of anti-nuclear antibody, anti-topoisomerase and anti-centromere antibody and the sensitivity of the examinations that are used to detect lung injuries.

Methods: This is a prospective study that analyzed 58 patients with scleroderma. Patients were examined by immunological tests such as anti-nuclear antibody (ANA), anti-topoisomerase (anti-Scl 70) and anti-centromere (ACA) antibody. Chest x-ray (CXR), pulmonary high-resolution computed tomography (HRCT), pulmonary function tests (PFTs) and echocardiography doppler were performed for the patients.

Results: Patients with positive ANA are 46 (79%), anti-Scl 70 positive are 23 (40%) patients and ACA positive are 16 (28%) patients. CXR changes are seen in 10 (17%) patients, pulmonary injuries in HRCT are found in 42 (72%) patients, pulmonary arterial hypertension were 6 (10%) patients with echocardiography doppler and PFTs abnormalities are 32 (55%) patients.Interstitial lung disease is found in 42 (72%) and restrictive ventilator insufficiency are 32 (55%) patients. Pulmonary injuries in the group of patients with abnormal immunological laboratory tests are found in 85% of patients, while in the other group of patients who do not have positive ANA, anti-Scl 70 and ACA antibody, pulmonary injuries are found in 25% of patients

Conclusions: Lung injury in scleroderma occur frequently and includes parenchymal and vascular disease. Immunological alterations are important factor in pulmonary injuries. High-resolution computed tomography is the most sensitive examination for the detection of pulmonary injuries in scleroderma.

Key words: scleroderma, pulmonary, interstitial lung disease

APLAR-0457

Clinical characteristics and pathogen analysis of idiopathic inflammatory myopathies with pneumonias

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Objectives: To analysis risk factors, clinical characteristics, constituent ratio of pathogens and tolerance of antibiotics of idiopathic inflammatory myopathies with pneumonias.

Method: Retrospective analysis of 93 cases of idiopathic inflammatory myopathies with pneumonias from 2009 to 2011.

Results: The risk factors of IIM with pneumonias were age of onset and interstitial lung disease. The most common pathogen was gram negative bacteria. *Klebsiella pneumoniae* was the most common bacteria and *Candida albicans* was the most common fungus. The third-genera-

tion and forth generation of cephalosporin, fluoroquinolones and aminoglycoside had relatively higher sensitivities.

Conclusion: Older patients with interstitial lung disease were prone to have pneumonia, especially gram negative bacterial pneumonia, as well as other atypical pathogens. Timely and reasonable anti-infection treatment was essential.

APLAR-0305

Expression of TRAIL in T cells of PM/DM patients

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Objective: To detect the expression of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) and its death receptor DR4, DR5 in T cells of polymyositis (PM)/dermatomyositis (DM) patients.

Methods: The peripheral blood of 20 PM/DM patients and 10 healthy volunteers were collected to test the expression of TRAIL, DR4, DR5 by flow cytometry (FCM).

Results: The PM/DM patients had significantly lower expression (%) of TRAIL 19.87 $\pm$ 8.40 ($P = 0.01$), DR4 19.72 $\pm$ 8.59 ($P = 0.02$) and DR5 19.22 $\pm$ 9.2 ($P = 0.01$) than healthy volunteers, which was 28.39 $\pm$ 9.16, 27.09 $\pm$ 10.34, 29.06 $\pm$ 9.54, respectively.

Conclusion: The apoptosis of T cells in TRAIL signal pathway may be down-regulated in PM/DM, which may play an important role in the pathogenesis.

POSTER SESSION III ABSTRACTS
Clinical Rheumathology: T14 – Systemic vasculitis

APLAR-0108

Cardiac features of Churg Strauss syndrome among an Indonesian population: a case series of three patients

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Background: Churg Strauss Syndrome (CSS) is a rare systemic vasculitis occuring in patients with a history of asthma or allergy and eosinophilia. Although lungs, skin, and peripheral nervous system are the most common sites of involvement, many other organ especially cardiac can be affected. Many autoimmune diseases differ in individual of different cases, but there were very scarce information on cardiac features of CSS among Asian patients, especially in Indonesia.

Aim: To know the cardiac features of Indonesian CSS patients.

Methods: The medical records and Trans-Thoracic Echocardiography (TTE) of CSS patients hospitalized in Siloam General hospital in 2012 were carefully reviewed.

Results: There were three patients fullfilled the latest American College of Rheumatology criteria and the TTE results were reviewed for cardiac abnormalitites. The ages were 10, 13, and 29 years old. Two patients were males. The median of body mass index was 24.9 kg/m^2. One patient has got normal cardiac feature. The others have got diastolic dysfunction, consentric enlargement of left ventricle, one patient with the sign of coronary artery disease, two patient with mild valve abnormalities mitral regurgitation and tricuspid regurgitation. All patients have got normal systolic function. There were no sign of pulmonary hypertension found.

Conclusion: The cardiac abnormalities of Indonesian CSS patients were diastolic dysfuction, sign of coronary artery disease, concentric enlargement of left ventricle, and mild valve abnormalities.

Key words: Churg strauss syndrome, cardiac abnormalities.

APLAR-0172

Gastrointestinal bleeding in adult patients with henoch-schönlein purpura

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Objectives: Adult Henoch-Sch*nlein purpura (HSP) has a significantly higher frequency of gastrointestinal (GI) bleeding, compared with pediatric HSP. However, the clinical characteristics of adult HSP with GI bleeding are still largely unknown. We investigated the clinical features including endoscopic findings in adult HSP patients with GI bleeding.

Methods: Twenty-four adult HSP patients, who had evidence of GI bleeding and underwent both upper GI endoscopy and colonoscopy, were included for this study. The controls were 27 adult HSP patients without GI bleeding.

Results: Patients with GI bleeding showed a significantly higher frequency of palpable purpura on the upper extremities ($P < 0.001$) and trunk ($P = 0.006$), and elevated serum CRP ($P < 0.001$), compared with controls. Multivariate analysis showed that palpable purpura on the upper extremities and elevated serum CRP were independent risk factors for GI bleeding (purpura, OR 79.4, 95% CI 4.2–1486.3, $P = 0.003$; CRP, OR 32.3, 95% CI 1.4–742.2, $P = 0.030$). Mucosal lesions were found in all patients on the upper GI endoscopy and in 22 patients (91.7%) on the colonoscopy. The second portion of duodenum (70.8%) and terminal ileum (75.0%) were the most frequently and severely involved regions in upper and lower GI tract, respectively. In the subgroup analysis with small bowel involvement in 16 patients who underwent both abdominal CT and endoscopy, jejunum involvement was observed in 31.3%. Pathologically, leukocytoclastic vasculitis was detected in severe lesions and significantly correlated with ischemic changes (upper GI tract, $P = 0.041$; lower GI tract, $P < 0.001$). Most mucosal lesions were dramatically improved after one week of glucocorticoid treatment. Two patients with severe multiple ulcers were dead even with treatment of immunosuppressants as well as glucocorticoid.

Conclusions: This study suggested that both upper and lower GI examinations were necessary for proper evaluation of HSP patients with GI bleeding and provided a good evidence of therapeutic importance for severe mucosal lesions.

APLAR-0358

Clinical Characteristics of Patients with Takayasus Arteritis in Different Age and Gender

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Objective: Takayasu's arteritis (TA) is a heterogeneous disease. We aimed to explore the clinical features in distinct ages and/or gender populations, to improve diagnosis of TA.

Methods: Weretrospectively analyzed manifestations and helpful tests in 53 TA patients.

Results: (1) Ratio of onset age in male and female was 1:4; Age of male was (35 ± 11) years and female was (28 ± 11) years. Onset age in 17% patients was aged over 40. Onset symptom of TA was chest pain or tightness in male and high blood pressure or dizziness in female ($P < 0.05$). (2) Fever and pulselessness were found in first-visit patients aged over 40 ($P < 0.05$, $P < 0.05$). Chest pain, tightness and fever appeared also more in the patients aged over 40, especially young men. (3) Laboratory tests were no differences between male and female groups, but lower glumerular filtration rate was found in more male patients. (4)In imaging investigations, more male patients, mainly young male, had multiple vascular involvement, ($P < 0.05$); patients aged over 40 had less renal artery, abdominal aortic and multiple vascular involvement ($P < 0.05$, $P < 0.05$, $P < 0.01$).. More male patients had renal dysfunction than female patients ($P < 0.05$); (5) Thoracic aorta involvement was independent risk factor of elevated blood pressure ($P < 0.05$); ascending aorta involvement was independent risk factor of aortic regurgitation ($P < 0.01$) and combined aneurysm formation ($P < 0.05$). There were no independent risk factors of renal dysfunction. Conclusion

Onset age of TA was older in male than in female patients, obvious clinical symptoms, severe complications, and diffuse vascular involvements were more likely found in male especially young male than that in female patients. Range of lesions of arteries was relatively localized in patients aged over 40. We should pay more attention to early diagnosis and treatment to young male patients.

APLAR-0324

Treatment and clinical outcomes in vasculitis with renal involvement. Single center experience. Bogotá – Colombia

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Renal involvement associated systemic vasculitides. We described the experience of 5 years of follow up in Bogota, Colombia. Observational descriptive study, between August 2007 and December 2012 were included.

25 patients where included (8 pANCAS, 11 cANCAS and 6 negative ANCAS), with mean age of 58 years, 52% males. 16 patients had microscopic polyangiitis, nine had granulomatosis with polyangiitis. We divided the population in two groups according to the systemic involvement (Group A: 15 patients with renal involvement and Group B: 10 with systemic compromise). In the first group mean serum creatinine before treatment was 2.9 mg/dL, mean GFR by MDRD4 was 50 mL/min, three patients required dialysis and mean hemoglobin was 10.7 mg/dL. All patients had proteinuria, hematuria, normal values of serum complement. FFS scale was 1 in 8 patients, more than 2 in 5 patients and there was no information in rest. 14 (93%) patients received metilprednisolone, 12 (80%) cyclofosfamide, 1 metrotexate and 1 plasmapheresis. No patients required chronic renal replacement therapy. Three patients died due to severe sepsis after a mean of 79 days after received treatment. In the group B, whit systemic compromise for pulmonary, renal and neurologic involvement. Mean serum creatinine before treatment was 7.9 mg/dL, mean GFR by MDRD4 was 17.8 mL/min, eight patients required dialysis (four continue on dialysis after hospital discharge) and mean hemoglobin was 9.8 mg/dL, 5 had positive ANAS and all had negative antiDNA. FFS scale was 1 in 8 patients, more than 2 in 5 patients and there was no information in rest, all patients (100%) received metilprednisolone, cyclofosfamide, and plasmapheresis. Two patients died due to severe sepsis after a mean of 52 days after received treatment. The level of systemic and renal involvement at presentation in our population is highly predictive of survival and required chronic renal replacement.

APLAR-0466

A Pregnant Woman with Takayasus Arteritis and Intracerebral Haemorrhage

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TakayasuÕs arteritis is a chronic inflammatory disease that affects aorta and its major branches. Fibrosis and thickening of the arterial wall often occur in later stages, resulting in a cerebrovascular accident. It is reported a 22 year-old woman at 22 weeks of gestation with TakayasuOs arteritis and intracerebral hemorrhage. She got a sudden headache and left hemiparesis. She had history of hypertension since she was 10, sometimes the blood pressure was more than 200/110 mmHg.

The patient looked pale with weak radial pulse, carotid bruit, and asymmetrical blood pressure (180/80 mmHg right, 140/60 mmHg left). Left extremities muscle strength was 0 with positive pathological reflexes. ESR was elevated. Haemoglobin level was 8.1 g/dL (hypochromic microcytic anemia), albumine was 3.1 mg/dL. ANA test and anti-cardiolipin antibodies were negative. Head CT scan showed right temporoparietal hemorrhage (±42.5 cc). Occlusions in other arteries were diagnosed by magnetic resonance angiography (MRA) and Doppler USG. Echocardiography was normal.

The most common central neurological manifestation of Takayasu arteritis is brain ischemia due to artery occlusion, but in this patient we found intracerebral hemorrhage which might be caused by chronic hypertension. Hypertension is probably the most serious major complication that can develop, possibly leading to intrauterine growth retardation, maternal heart failure, and fetal haemorrhage. The baby was delivered using caesarian section at 33 weeks of gestation (2000 g/41 cm), Apgar score 7–9. The patient got methylprednisolone during pregnancy and then methotrexate after delivery. Anti hypertensions given were methyldopa 250 mg tid. and bisoprolol 1.25 mg daily.

Keywords: Takayasu arteritis, pregnancy, intracerebral hemorrhage

APLAR-0021

Clinical analysis of polyarteritisnodosa with cardiovascular manifestations

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Objective: To investigate the prevalence and clinical characteristics of polyarteritisnodosa (PAN) with cardiovascular manifestations.

Method: A total of 64 consecutive PAN patients admitted into Peking Union Medical College Hospital from January 2002 to August 2012 were enrolled in this study. 41 had the cardiovascular involvements. All patients fulfilled 1990 American College of Rheumatology and CHCC criteria. The vascular involvements were defined as arterial lesions that could be found in radiographic inspection.

Results: (i) The prevalence of cardiovascular involvements was 64%. Onset age was 35.1 ± 13.6 years. Sex ratio (Female/Male) was 14/27. (ii) The prevalence of heart involvement was 17.2% (11/64). Five patients suffered from symptoms of cardiac ischemia such as chest pain and short of breath, and the other patients had no corresponding symptoms. In addition, seven patients with coronary artery involvement, two patient with pericardial effusion. (iii) Mean arterial involvement was 5 ± 3 arteries per patient. Most of patients had no corresponding ischemia symptoms. Involvements of arteries in viscera (25 cases) and low limbs (19 cases) were most frequent. On the other hand, renal arteries and branches (19 cases), anterior (15 cases) and posterior tibial arteries (12 cases) were most frequent. Asymmetric artery involvement (55%) was common. (vi) Forty patients were treated with steroid and immunosuppressant, and 5 patients (12.2%) died or suffered from irreversible organ injury after a median follow-up of 6.5 months. (v) There were significant differences between patients with and without vascular involvements in skin rash (46.3% versus 91.3%), higher diastolic pressure (68.3% versus 34.8%) and microscopic hematuria (4.9% versus 26.1%) and glucocorticoid treatment (methylprednisolone bolus/>30 mg/day_prednisone/≤30 mg/day_prednisone) (13/25/3 vs. 2/19/2).

Conclusions: Cardiovascular involvement were common in patients with PAN, and correlated to irreversible organ injury. Most of patients lacked corresponding symptoms, thus we should pay attention to patients with risk factors such as higher diastolic pressure. Early diagnosis and therapy will improve prognosis.

Clinical Rheumathology: T16 – Infection-related rheumatic diseases

APLAR-0083

Tuberculosis infection in Primary Sjögrens Syndrome: A Nationwide Population-based Study in Taiwan

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Background: This nationwide population-based study aimed to explore the incidence, hazard and risk factors of Mycobacterium tuberculosis (TB) infection in patients with primary Sj*gren's syndrome (pSS).

Methods: We identified 4822 patients with pSS from the Taiwan National Health Insurance database between 2000 and 2006, and compared the incidence rates of TB with 48 220 randomly selected age-, sex- and comorbidity-matched subjects without pSS. The Kaplan*Meier method was employed for comparison of cumulative TB incidence between pSS and control cohorts. Cox proportional hazard model was used to identify risk factors for TB in patients with pSS.

Results: During the study period, the risk of TB was higher in the pSS cohort with an incidence rate ratio (IRR) of 1.58 (95% CI 1.13*2.18; P = 0.006) than in the control cohort, mainly contributed by an excess risk of pulmonary TB (IRR 1.58, 95% CI 1.08*2.25; P = 0.015). The risk factors for TB in the pSS cohort were age ≥60 years (HR 3.22, 95% CI 1.78*5.84; P < 0.001) and corticosteroids using with a dose-dependent effect compared to non-users (daily prednisolone dose or equivalent less than 5 mg/day: HR 2.34, 95% CI 1.14–4.78; P = 0.020; 5 mg/day to less than 10 mg/day: HR 4.79, 95% CI 2.15–10.68; P < 0.001; 10 mg/day or more: HR 12.19, 95% CI 4.42–33.63, P < 0.001).

Conclusions: Patients with pSS had higher pulmonary TB risk in Taiwan, which was related to age and corticosteroid using.

APLAR-0160

The diagnostic utility of serum procalcitonin in acute bacterial septic arthritis

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Introduction: Septic arthritis is a common and serious problem. Early detection and prompt treatment can improve outcomes.

Objective: To evaluate serum procalcitonin to distinguish between acute bacterial septic arthritis and acute inflammatory non-septic arthritis and to compare itOs diagnostic utility with other tools such as erythrocyte sedimentation rate (ESR) and high sensitivity C reactive protein (hs-CRP).

Method: A prospective cross-sectional study was performed in 78 Thai patients with acute arthritis. Patients with concomitant infections were excluded. Acute bacterial septic arthritis was diagnosed by the New Man criteria. Twenty eight patients were diagnosed acute bacterial septic arthritis, 50 patients were diagnosed with acute inflammatory non-septic arthritis. Blood samples were collected for complete blood count, ESR, hs-CRP, procalcitonin, and hemoculture. Synovial fluids were sent for cell count, Gram stain, crystals, and culture. Baseline characteristics and other relevant variables were recorded. The diagnostic accuracy by area under ROC curve was calculated.

Result: Patients with acute bacterial septic arthritis had higher procalcitonin levels than in acute inflammatory non-septic arthritis (median 0.78 versus 0.11 ng/mL, P = 0.032). The best cut-off level of procalcitonin was 0.66 ng/mL which sensitivity, specificity and accuracy for diagnosis of bacterial septic arthritis are 59.3%, 86% and 76.6%, respectively. Patients with acute bacterial septic arthritis also had higher hs-CRP levels than in acute inflammatory non-septic arthritis but not the ESR. The ROC curve analysis showed that procalcitonin had the higher diagnostic accuracy (area under the curve = 0.80, 95% CI 0.69–0.89; P < 0.01) than hs-CRP (0.67, 95% CI 0.55–0.79, P = 0.01). Combination of procalcitonin with other markers did not provide better sensitivity or specificity than procalcitonin alone.

Conclusion: Procalcitonin may have a potential role in differentiate acute bacterial septic arthritis from other acute inflammatory non-septic arthritis and has higher diagnostic accuracy for diagnosis of acute bacterial septic arthritis than hs-CRP.

APLAR-0168

Does use of biologic agent increase the incidence of postoperative infection?

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Objective: The use of biologic agent has improved rheumatoid arthritis (RA), but orthopedic procedures are still required. There is no consistent evidence for an effect of biologic agents on surgical site infection and late infection. We investigated whether use of biologic agent increased the rate of postoperative infection in patients with RA.

[Methods] The subjects were 356 RA joints treated with biologics in our department (bio group) and 331 RA joints that were not treated with biologics (control group). The biologic used were etanercept (ETN) in 285 joints, infliximab (INF) in 18 joints, tocilizumab (TCZ) in 31 joints, adalimumab (ADA) in 20 joints, and abatacept (ABT) in 2 joints.

Results: In the bio group, surperficial infection in one joint, deep infection in three joints and late infection in three joints were found. In the control group, surperficial infection was found in two joints and no deep or late infection was detected. Prosthesis removal was performed in patients with deep or late infection. Pathogenic bacteria were commonly MSSA and P. aeruginosa. Infection subsided in all patients and biologics were re-administered with no relapse of infection.

Conclusion: Biologics did not increase the incidence of postoperative infection. However, careful intra- and postoperative observation is required due to the increased number of cases treated with surgery and biologics.

APLAR-0287

A Three-Month Follow-up of Arthritis in Chikungunya Fever

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Background: Chikungunya virus (CHIKV) is a mosquito-borne alphavirus of the family Togaviridae transmitted to humans by the Aedes spp. mosquitoes, causing Chikungunya Fever (CHIKF).

Objectives: This study aims to describe the course and outcome of arthritis in patients with CHIKF seen over a 3-month period.

Methods: This is a prospective descriptive study. Fifty-one patients with fever, rash, and arthritis seen at the Philippine General Hospital and private arthritis clinics were collected from August – December 2012. Demographics and course of arthritis were described.

Results: Fifty-one patients, 38 females, 13 male, with a mean age of 38.76 (range 8–61) were diagnosed with CHIKF. All cases were from the Metropolitan Manila area. Of these, 13 had 3–4 family members affected. The most common presenting symptoms were fever (94.1%), arthritis (88.2%), and rash (88.2%). The most common joint areas involved were the ankles (68.9%), the wrists (42.2%) and the small

joints of the hand (53.3%), the knees (28.9%), the tarsals (15.6%) and the 1st MTP (11.1%). At week 6, 28 of 35 patients seen (80%) had persistent arthritis. Eleven (31.4%) patients had arthritis lasting at least eight weeks. At 12 weeks, three patients continued to have arthritis. At least half of the cases had to stop work due to arthritis.

Twenty-one patients had (+) CHIKV IgM by ELISA, and 1 had (+) CHIKV PCR. Sixteen of these had chronic arthritis of 6 weeks or longer (range, 6–16). Treatment consisted of continuous NSAIDs for at least 2 weeks and some received steroids.

Conclusions: This is a report of a recent outbreak of CHIKF, manifesting as a triad of fever, rash, and arthritis, severe enough to cause work stoppage. More females were affected. At least a third had chronic form of rheumatoid arthritis-like polyarthritis.

Clinical Rheumathology: T17 – Fibromyalgia

APLAR-0071

Altered intrinsic brain connectivity in the salience network of fibromyalgia patients at rest

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Objective: To investigate the possible alteration in the salience processing of pain in patients with FM.

Methods: Twenty female FM patients and 24 healthy controls underwent resting-state fMRI. Independent component analysis was used for evaluation of resting-state salience network (SN) connectivity.

Results: Significant increase in functional connectivity of anterior insula within the SN was found in patients with FM. The increase in functional connectivity within the SN was not associated with symptoms of depression and anxiety.

Conclusion: Increased functional connectivity suggests spontaneous altered activity in the salience of pain in patients with FM implicating enhanced spontaneous salience to pain.

APLAR-0130

Assessment of enthesopathy in patients with fibromyalgia by using new sonographic enthesitis index

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Purpose: The aim of the present study is to determine the frequency of enthesopathy in fibromyalgia (FM) via by using a newly developed ultrasonography (US) method, the Madrid Sonography Enthesitis Index (MASEI).

Methods and Materials: The study was conducted on 38 consecutive patients with FM and 48 healthy sex- and age-matched controls. Six entheseal sites (olecranon tuberosity, superior and inferior poles of patella, tibial tuberosity, superior and inferior poles of calcaneus) on both lower limbs were evaluated. All US findings were identified according to MASEI. Scores of patients and controls were compared by Student's t-test, Mann-Whitney U-test. Validity was analysed by receiver operating characteristic curve. Values of $P < 0.05$ were considered significant.

Resullts: Total enthesitis score was 7.39 ± 4.99 (mean±SD) among FM patients and 3.7 ± 3.22 among healthy controls ($P < 0.001$). Receiver operating characteristic curve established an ultrasound score of >3.5 in FM group, as the best cut-off point for differentiation between cases and controls. No statistically significant correlation was found between MASEI score and FM disease duration, the localization of tender points.

Conclusion: Misdiagnoses of FM are damaging for patients and the community, and the increased presence of enthesopathy among FM patients with MASEI may helpful tool in order to discriminate FM patients presenting with ill-defined symptoms and signs in order to prevent mistreatment.

APLAR-0146

Prevalence of Fibromyalgia in Rheumatoid Arthritis patients referred to Tohid Hospital in Sanandaj and association with patients activity

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Background and Objectives: This study evaluates the prevalence of Fibromyaliagia in patients with Rheumatoid arthritis referred to Tohid hospital in Sanandaj and its relationship with measures of disease activity based on DAS28 and demographic characteristics.

Methods: Two-hundred patients have been to referred to the clinic and Rheumatology ward at Tohid hospital and according to criteria ACR Rheumatoid arthritis was diagnosed, randomly selected by Rheumatologist. Then all of those patients by The same Rheumatologist have been examined and the results have been recorded in this examination for patients who have the diagnosis according to criteria ACR was considered Fibromyaliagia. In this study patients were divided into two groups the one with Rheumatoid arthritis and the one with Rheumatoid arthritis and Fibromyaliagia.

Results: NO important and significant difference between the two groups of age, sex, occupation, education level, location, situation, marital status, drugs including Corticosteroid and DMARDs(HCQ and MTX,É) were observed ($PV > 0.005$), between the two groups were not also observed.Positivity of RF and Anti Ccp Ab significant differences($PV = 0.003$), anxiety disorder($Pv = 0.99$)and depression ($Pv = 0.25$) no statistically significant differences were seen between the two groups.Sleep disorder significant differences were seen between the two groups($Pv = 0.001$).

Disease activity based on DAS28 no statistically significant differences ($Pv = 0.59$) were seen between the two groups,although the average of DAS28 were different ($Pv = 0.001$)

Conclusion: The results of our expriment againest others expriments do not confirms that the addition of Fibromyalgia to Rheumatoid arthritis Fibromyalgia causes the actual number is estimated to be too high. although the average of DAS28 were different.

It is recommanded that any patient with rheumatoid arthritis with general musculoskeletal pain more than three months, especially in the shoulder belt and hip should be reviewed of having Fibromyalgia with tenderness in 18-fold spots.

Key word: Fibromyalgia, Rheumatoid Arthritis, DAS28

APLAR-0150

The effectiveness of aerobic exercise and education in fibromyalgia syndrome

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Background: Fibromyalgia is a common syndrome found predominantly in women. It is characterized by chronic, diffuse, musculosceletal pain and a sleep disorder, without evidence of arthritis or myositis.

Objectives: The purpose of this study was to compare the effectiveness of aerobic exercise and education with the control group in fibromyalgia syndrome and to evaluate the patients treated with this method after the treatment program

Methods: Sixty women, aged 18–55 years, diagnosed as fibromyalgia according to 1990 ACR criteria were randomly divided into two groups. Group I was given aerobic exercise and stretching exercise for 8 weeks following an education program. Group II was the control group. Both groups took sertralin 50 mg/day. The patients were evaluated before and after the treatment. We used VAS, number of tender points, total myalgic score for pain, Beck depression inventory (BDI) for depression, Patient and doctor global assessment scale, Fibromyalgia attitudes index (FAI) for global assessment, Fibromyalgia impact questionnaire (FIQ), Health assessment questionnaire (HAQ) for functional evaluation, Astrand test for aerobic capacity.

Results: The results of VAS, number of tender points, total myalgic score, BDI, FAI, FIQ, HAQ and patient and doctor global assessment scale showed significant improvement in both groups ($P < 0.001$, $P < 0.01$). In the first group, the results of VO2max showed significant improvement ($P < 0.001$).The results of some groups of FIQ, SELF function subscale, FAI and BDI were not statistically different among the two groups ($P > 0.05$). We found significant improvement in other parameters in exercise group than the control group.

Conclusion: Fibromyalgia is a multifactorial syndrome, and the best treatment will encompass multiple strategies, that include education, stress management treatment and aerobic exercise.

APLAR-0228

The Impact of Associated Fibromyalgia on Inflammatory Rheumatic Diseases

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Introduction: The patients with inflammatory rheumatic diseases develop often fibromyalgia.

Objectives: We assessed, in the patients with inflammatory rheumatic diseases and associated fibromyalgia, the pain and the number of days every month in which patient used symptomatic medication (anti-inflammatory, analgesic and muscle relaxant).

Material and Method: 208 patients with inflammatory rheumatic diseases (127 with rheumatic arthritis and 81 with ankylosing spondylitis) were assessed over a period of 1 year. All patients underwent complex symptomatic treatment (anti-inflammatory, analgesic and muscle relaxant medication), DMARDS with or without biologic therapy and also medical rehabilitation treatment. We carried out the assessment of mean VAS score, number of days every month in which the patients used symptomatic medication and also the number of medical rehabilitation sessions.

Results and Discussion: The results are presented in the table below:

	Rheumatoid arthritis		Ankylosing spondylitis	
	With fibromyalgia	Without fibromyalgia	With fibromyalgia	Without fibromyalgia
Patients number	23	104	14	67
Mean VAS score	3.15	2.67	3.08	2.51
Average number of days / month with symptomatic medication	12.87	9.72	13.09	10.14
Average number of medical rehabilitation sessions	27.93	21.19	29.72	23.42

Conclusions: Owing to pain, fibromyalgia associated with inflammatory rheumatic diseases leads to a negative impact on the patient quality of life. The increase of days every month, in which patients used symptomatic medication, results in an increase of the adverse reaction risks. The number of medical rehabilitation sessions is also higher in the patients with associated fibromyalgia.

APLAR-0339

Personal experience in the Fibromyalgia management – a local cohort study

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Fibromyalgia is characterized by chronic widespread pain and allodynia. Its exact cause is unknown but is believed to involve psychological, genetics and neurobiological factors. The sympoms are not restricted to pain. Other symptoms include fatigue, sleep disturbance and joint stifness. Fibromyalgia is frequently comorbid with psychiatric conditions such a depression and anxiety. Not all fibromyalgia patients experience all assocoated symptoms. Fybromyalgia is estimated to affect 2–4% of the population.

APLAR-0398

The impact of thyroid autoimmunity on arterial stiffness in postmenopausal female patients with fibromyalgia

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Objective: The exact mechanism of the arterial stiffness in fibromyalgia (FM) remains unclear. The present study aimed to evaluate the association between thyroid function and markers of arterial function in postmenopausal female FM patients.

Methods: This study included 163 postmenopausal female FM patients without any known cardiovascular diseases and within a normal reference range of thyroid-stimulating hormone (TSH) level. Clinical parameters including the Fibromyalgia Impact Questionnaire (FIQ), the pain visual analogical scale (VAS) and tender point counts were measured. Vascular function was assessed by brachial-ankle pulse wave velocity (baPWV) and flow-mediated dilation (FMD). We evaluated the associations between arterial markers and serum TSH, free thyroxin, as well as serum thyroidperoxidase autoantibody (TPO Ab).

Results: Patients with a high baPWV (≥1.490 cm/s) showed more positive TPO Ab (65% vs. 10%, $P = 0.006$) than those with a normal baPWV. Additionally, the baPWV values of patients with positive TPO Ab were significantly different from those with negative TPO Ab. Age, FIQ and TPO Ab were significantly correlated with baPWV and FMD (all $P < 0.05$). Multiple linear regression analysis revealed that the only significant predictors of baPWV were age, FIQ, and the presence of TPO Ab after adjustment for traditional risk factors. A significant association was also found between FMD and positive TPO Ab.

Conclusion: Age, functional status, and presence of TPO Ab were significantly associated with increased arterial stiffness in postmenopausal female FM patients. Given the combined thyroid autoimmunity in FM patients, a re-evaluation of the effects on the vasculature may be necessary.

APLAR-0306

Outcome analysis in fibromyalgia following a multidisciplinary rehabilitation protocol- a follow up

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Aim: To evaluate various outcomes among the patients with fibromyalgia after 1 year, following a multidisciplinary rehabilitation in a tertiary level rehabilitation centre in India.

Materials and Methods: It is a retrospective experimental follow up in which 30 subjects diagnosed to have Fibromyalgia participated in the study. All the subjects were evaluated and diagnosed by a physician which is followed by drug prescription and treatment using a novel multidisciplinary rehabilitation protocol which included medication, patient education, CBT, nutritional intervention, myotherapy, aerobic conditioning etc. Various outcome measured before the treatment were reassessed during the follow-up and are analysed statistically. Outcomes measured were Visual Analog Scale (VAS) for pain, fatigue using Borg C 10 scale, sleep using VAS, depression with help of BECK Depression Inventory, Fibromyalgia Impact Questionnaire (FIQ) and SF-36.

Results: Out of the samples 18 were males and 12 females. Four were between the age group of 20 and 25 years, 11 between 25 and 30 years and 15 above 30 years of age. 26 were IT professionals, three house wife and one was a teacher among the subjects. Results suggested a significant reduction in pain ($P < 0.01$), fatigue level ($P < 0.01$), Depression ($P < 0.01$) and sleep disturbance ($P < 0.01$) after 1 year follow-up. There was a significant functional improvement following a sequenced protocol based treatment which was noted by analysis the FIQ and SF-36.

Conclusion: A Multidisciplinary team Approach is needed for treatment of Fibromyalgia and Rehabilitation with a Multidisciplinary approach shows a significant improvement in pain reduction, sleep, decrease fatigue, decrease depression and general quality of life

Key words: Fibromyalgia, SHARAN'S Protocol.

Clinical Rheumathology: T18 – Soft tissue rheumatism

APLAR-0005

Upper limb musculoskeletal abnormalities and relation with metabolic control in type 2 diabetes

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Introduction: An increased prevalence of musculoskeletal disease is recognised in diabetes and is a common source of disability. It is known to predominantly affect the upper limbs especially the hand and shoulder. The relationship with other complications of diabetes and glycaemic control is uncertain. We designed this study to clarify these relationships.

Methods: We identified a group of 188 people with established type 2 diabetes attending the diabetes clinic in Firouzgar hospital .After an interview a complete rheumatologic examination was done for all patients for the presence of musculoskeletal disease focusing on the upper limbs. We recorded the mean HbA1c and the presence of diabetic neuropathy and retinopathy. We explored correlations between musculoskeletal disease and these variables using logistic regression.

Results: Upper limb musculoskeletal disease was present in 48.4% of diabetics. This prevalence was significantly higher in females than males (OR = 2/27, 95% CI: 1.22–4.22). and Dupuytrens contracture (20.2%),trigger finger(18%), limited joint mobility(LJM) (18.6%) carpal tunnel syndrome (10%),, rotator cuff tendinitis (8%), Shoulder capsulitis (6%) were the most frequent findings and were much commoner in longstanding diseases. we couldnOt find any relation between mean HBA1c of one year and frequency of rheumatologic complications.LJM usually coexisted with nephropathy (OR = 3.44, 95% CI: 1.60–7.36). And best predicted the presence of nephropathy.Patients were unaware of their rheumatologic problem in more than 70% of cases. And only 6% was aware about musculoskeletal complication of DM generally.

Conclusion: Thorough rheumatologic examination should be included as an integral part of care in Type 2DM patients. Diabetic patients and physicians need more education and attention respectively to this disabling complication of DM.

APLAR-0304

Co morbidities of Neck Pain among Computer users in India

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Aim: The Aim of the study is to identify the co morbidity of musculoskeletal discomfort with neck pain among IT professional in India.

Methods: The data was collected from 5357 IT professionals from various IT companies who visited the on-site clinics situated at their office campus of three cities in India. Demographic data were collected from the participants including age, gender, computer usage per day, and the type of use (Laptop/Desktop). Data regarding type and intensity of the musculoskeletal problems were collected from a Rehabilitation Physician and a Physical Therapist. EmployeeOs feedbacks were also used for evaluating the status of musculoskeletal health of the IT professional. PhysicianÕs diagnosis revealed type and severity of the clinical features. Data were analyzed statistically for significance

Results: The study participants were predominantly males (71%). The mean age of the male and female subjects were 31.10 ± 5.99 years and 29.68 ± 5.59 years respectively. 41% of the population used laptops, 35% desktops and 24% both. Neck pain is the commonest followed by low back, shoulder and arm pain respectively. Statistical analysis also revealed that neck pain was significantly associated with low back pain ($P < 0.001$), shoulder pain ($P < 0.001$), arm pain ($P < 0.001$) and wrist pain ($P < 0.001$). Thoracic Outlet Syndrome was found to be co morbid with neck pain in both male (40.10%) and female (45.23%). On the other hand co morbidity of Fibromyalgia Syndrome was found to be 16.61% for male and 22.80% for female respectively. Further analysis revealed that there was a significant association between presence of neck pain and Thoracic Outlet Syndrome ($P < 0.001$) and Fibromyalgia Syndrome ($P < 0.001$).

APLAR-0377

Influence of cyclosporine therapy on the severity of psoriasis

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Psoriasis is a chronic skin disease with recurrences . Psoriasis affects quality of life to a great extent. Although, the efficacy of cyclosporine A on psoriasis is well known, a few reports have been found that investigates the effects of cyclosporine therapy on quality of life. In this study, we aimed to examine the effect of psoriasis on quality of life and the effect of cyclosporine-A therapy on both psoriasis area severity index (PASI) and quality of life.

Materials and methods: One hundrand and forty patients diagnosed with psoriasis from five different centers were taken into our study. The cases with psoriasis that were recalcitrant to the other therapies were enrolled prospectively in the study. Dermatologic examinations of the patients were made before the treatment.. PASI was measured and the dermatology life quality index (DLQI) was answered by all patients before the treatment. Cyclosporine-A was started at a dose of 3.5 mg/kg/day and patients were followed up with intervals of 15 days. The comparison of PASI and DLQI between the15 th day, first, second and third months of the treatment was evaluated statistically.

Results: The mean of PASI score was 13.73 ± 7.87 before the treatment. PASI was measured as 5.04 ± 4.89 on the first month, 2.76 ± 4.11 on the second month and 2.33 ± 4.26 on the third month respectively. The mean of DLQI was 12.1 ± 7.67 before the treatment. DLQI was3.44 ± 4.98 on the first month, 2.39 ± 4.1 ve on the second month and on 1.71 ± 3.43 the third month respectively. Significant difference was detected in the PASI and DLQI between the comparison of first, second and third months ($P < 0.05$). No significant side effect was observed.

Conclusion: Cyclosporine therapy in psoriasis have an important and rapid influence on severity of psoriasis and quality of life of the patients.

APLAR-0432

Starting dose of prednisolone and clinical course of patients with polymyalgia rheumatica in a general hospital in Japan

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Objectives: We explored to establish the optimum initial doses of prednisolone (PSL) for the Japanese patients with Polymyalgia rheumatica (PMR).

Patients and Methods: Fourteen patients were given a diagnosis of PMR according to modified BirdÕs criteria (CRP positive instead of ESR>40). They presented to our hospital from April 2011 to March 2014 and were followed more than one month.

Results: Of the 14 patients, four were men and 10 women. The median age at the diagnosis was 74.5 (IQR 70.5–81). The median follow-up was 11 months (range 1–18 months). The standard treatment for PMR in our clinic was initiated with 15 mg/day of PSL, which was proposed by Hernandez-Rodriguez J et al. (Arch Intern Med 2009; 169:1839). We modified the dose of PSL by the patientOs age and/or body weight, because Japanese elderly women patients are often smaller and lower-weighted than western country patients. As a result, five patients were treated with 10 mg/day PSL and one with 5 mg/day. There were no significant differences between the patients treated with 15 mg and patients treated with 5 or 10 mg in our study.

Conclusion: PSL dosage based on BW (mg/Kg) might be more effective for especially elderly low-body weight women in Japan than uniformly fixed dose.

	patients with 5 or 10 mg PSL n = 6	Patients with 15 mg PSL n = 6	
PSL dose per BW (mg/kg/day)	0.21 ± 0.04	0.34 ± 0.04	<0.01*
Sex; women %	67%	83%	0.03*
Age at diagnosis	78.5 ± 4.64	73.0 ± 6.13	0.09
Body weight at diagnosis	44.8 ± 6.21	44.3 ± 6.65	0.94
Follow-up months	11.5 ± 5.47	10.5 ± 6.00	0.87
Serum CRP(mg/dL)	8.0 ± 5.68	6.5 ± 3.96	0.42
Days until the beginning of PSL tapering	46.4 ± 13.69	40.3 ± 22.17	0.94
Days until PSL 7–8 mg/day	47.5 ± 15.55	79.2 ± 40.23	0.049*
Relapse	2 (33%)	1 (17%)	
PSL off	1 (17%)	2 (33%)	

Clinical Rheumathology: T19 – Pediatric rheumatology

APLAR-0437

Clinical features & complications of henoch-schoenlein purpura in Bandung Indonesia

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Background: Henoch*Sch*nlein purpura (HSP) is a systemic vasculitis syndrome. This disorder involves non-thrombocytopenic purpura, arthritis/arthralgia, abdominal pain, and glomerulonephritis. Clinical manifestations is caused by inflammation of polymorphonuclear cells occuring in the walls of small vessels. HSP generally resolves completely in most children. However, serious complication in HSP patients such as severe gastrointestinal and renal manifestations can happen. These patients should be carefully treated and adequately monitored.

Aim: The objective of this study was to identify clinical symptoms and complications of HSP patients.

Method: We performed a retrospective study of children with the HSP diagnosis who came to Allergy & Immunology Clinic, Department of Child Health Hasan Sadikin Hospital, Bandung, Indonesia during 2006–2012. We identified the clinical symptoms and complications of the HSP patients. Diagnostic criteria was ACR 1990 and EULAR/PRINTO 2008 revised criteria. The standard therapeutic protocol given was corticosteroid.

Results: We enrolled 146 patients consisting of 93 (63.7%) boys and 53 (36.3%) girls. The mean age of HSP onset was 8.05 ± 2.9 years, ranging from 6 month to 15 years. In 93 cases (63.7%), HSP occured before the age of 10-years-old. Most of the patients (102 patients; 69.9%) had purpura as their initial symptom. All of the patients had purpura during HSP episode. About 59 patients (40.4%) had arthritis or arthralgia and 97 patients (66.4%) had abdominal pain as their clinical symptoms at the time of diagnosis. The complications of HSP were nephritis in 41 patients (28.1%), acute abdomen in six patients (4.1%).

Conclusions: Most of the patients 69.9) had purpura as their initial symptom of HSP. Furthermore, purpura was seen in all of the patients (100% cases) as their clinical symptom at the of diagnosis. The most frequent complications occured was nephritis, which was seen in 28.1% of HSP patients.

Keyword: children, clinical features, complication, Henoch-Sch*nlein Purpura

APLAR-0439

Dental infection as the trigger factors of henoch-schönlein Purpura in children in Bandung, Indonesia

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Background: Henoch-Schonlein Purpura (HSP) is the most common vasculitis in children which manifests as purpura, abdominal pain and nephritic that brings poor prognostic, commonly occur in children between 2–10 year-old. HSP commonly triggered by infections such as rhinopharyngitis, tuberculosis and most common by dental infection. There were no data about risk factors and possible triggering factors especially dental infection of children with HSP in Indonesia.

Methods: We performed a retrospective study of children with the HSP diagnosis who came to Allergy & Immunology Clinic, Department of Child Health Hasan Sadikin Hospital, Bandung, Indonesia during 2006–2012. Diagnostic criteria was ACR 1990 and EULAR/PRINTO 2008 revised criteria. Data was characteristics, clinical profiles, and infections, dental and other than dental as possible triggering factors for HSP.

Results: Totally 146 children with HSP. Male to female ratio is 1.75:1, age range was 6 month to 15 year old, with mean of 8.05 ± 2.9 year old. In 19.2% there were possible triggering factors with upper respiratory airway infection, in 13.7% dental infection, diarrhea, pyoderma, and tuberculosis in 2.1%, 1.4%, dan 0.7%. All patient complaint of palpable purpura, along with abdominal pain (66.4%), arthritis (40.4%), and nephritis (28.1%).

Conclusions: After upper respiratory airway infection, dental infection plays important role as trigger factors of HSP, it needs concerning the hygiene of dental and mouth among patients that diagnosed as HSP.

Key words: children, dental infection, Henoch-Schonlein Purpura

Clinical Rheumathology: T20 – Behcet's disease and miscellaneous rheumatic conditions

APLAR-0047

Immune Complexome Analysis of Serum and Its Application in Screening for Immune Complex Antigens in Behcet Disease and Further Analysis

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Objects: The aim of this study is to promote seeking of candidate autoAgs in CIC in BD patients, and detect antibody levels to candidate autoantigen through ELISA in different kinds autoimmune diseases.

Methods: We developed a novel proteomic strategy (immune complexome analysis) in which circulating immune complexes (CICs) are separated from serum, digested directly with trypsin, and then subjected to LTQ-orbitrap mass spectrometry for identifying and profiling antigens in CICs.10 Behcet Disease pooling Serum sample and 10 healthy control pooling serum samples were detected. Enzyme-linked immunosorbent assay (ELISA) were performed using sera from 45 BD patients, 51 SLE patients, 51 SSc patients, 40 RA patients, 51 SS patients, 22 OA patients, 22 RAU patients and 59 healthy volunteers against human α-tubulin.

Results: CICs containing protein of ECT2, TAOK3, BAG3 and a-tubulin et al were found in the serum of BD patients, while not in healthy coontrols. The autoAbs to a-tubulin was investigated byELISA using a recombinant protein . The autoAbs to a-tubulin were detected in 26 (57.8%) of the 45 patients with BD, 12 (23.5%) of the 51patients with SLE, 12 (23.5%) of the 51patients with SSc, 4 (10%) of the 40 patients with RA and 5 (9.2%) of the 51 patients with SS. Further analysis demonstrated that anti-a-tubulin was correlated with deep venous thrombosis and erythema nodosum of BD ($P < 0.05$), levels of anti-a-tubulin were correlated with levels of ESR and IgG ($P < 0.05$).Our data indicate that the generation of autoAbs to a-tubulin may reflect vasculitis of BD and other autoimmune diseases. And would help understanding of the deep venous thrombosis and erythema nodosum of BD. In addition, the CIC containing autoantigen sepration and proteomic approach would be useful way to investigate autoAgs in autoimmune diseases.

Key words: Behcet Disease

APLAR-0084

A survey of hospitalisation in behçets syndrome

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Background: We are unaware of previous studies on hospitalisation in Beh*etÕs syndrome (BS). We surveyed the causes and outcome of hospitalisations among BS patients in a dedicated center.

Methods: We surveyed the records of all hospitalisations in our clinic between 2002 and 2011 to identify patients with a diagnosis of BS. We reviewed both the inpatient and outpatient charts of all BS patients who were hospitalised to identify the demographic and clinical features, causes of hospitalisation and outcome. We tried to contact the patients to determine their current condition.

Results: 178 BS patients (74% men, mean age 42.9 ± 11.3) had been hospitalized for a total of 211 times during the last ten years. We were able to contact 104(58%) of them. The reasons for hospitalisation were directly related to BS organ involvement in 118(56%) and to complications in 93(44%). The most common BS related reasons were vascular involvement in 74/118(63%) (including 21 patients with pulmonary artery aneurysms, 10 with peripheral artery aneurysms and 11 with serious venous thrombosis such as vena cava superior and Budd-Chiari syndrome), neurologic involvement in 14/118(12%), gastrointestinal involvement in 6/118(5%) and eye involvement in 6/118(5%). Hospitalisations caused by complications of BS were infections in 39/93(42%), and other drug related adverse events in 15/93(16%). Neoplasias were diagnosed in five patients. Among the 178 patients, 16(9%) had died. Most common causes of death were vascular involvement (n = 5), infections (n = 4) and malignancies (n = 4).

Discussion: Vascular involvement is the leading cause of hospitalisation among BS patients, followed by infections related to therapy. Adverse events related to immunosuppressives are problematic. The predominance of men among hospitalized patients underlines the more severe course of BS in this sex. The relatively low frequency of gastrointestinal involvement among hospitalisations is in line with our previous observation that this type of involvement is rare in our BS patients.

APLAR-0123

The ESSPRI as an independent determinant of health-related quality of life in Sjögrens syndrome patients

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Objectives: To investigate the significant determinants of health-related quality of life (HRQOL) and the association of the EULAR Sj*gren's Syndrome Patient Reported Index (ESSPRI) with clinical parameters including HRQOL in Korean patients with primary Sj*grenÕs syndrome (pSS) compared to non-SS sicca patients.

Methods: We prospectively analysed 104 pSS (according to the American-European Consensus Group criteria) and 42 non-SS sicca patients. Clinical data including scores of SF-36 scales, self-assessments for symptoms, patient global assessment, and ESSPRI, were collected in a cross-sectional manner.

Results: Even though most self-assessments and HRQOL status were comparable, different association patterns between HRQOL and symptoms were observed in pSS and non-SS sicca patients. pSS patients with low HRQOL had significantly higher ESSPRI scores and ESSPRI scores showed a significant association with all SF-36 scales in pSS patients. However, in non-SS sicca patients, xerostomia inventory (XI) scores were higher in the low HRQOL subgroup and this correlated with five scales of SF-36. Moreover, in multivariate analyses, depression and ESSPRI significantly correlated with the mental component summary (MCS) and the physical component summary (PCS), respectively. On the other hand, in non-SS sicca group, anxiety and XI scores were the main determinants of the MCS and the PCS, respectively.

Conclusion: HRQOL levels were differentially associated with clinical facets in pSS and non-SS sicca patients, despite of the fact that the groups had similar clinical symptoms and HRQOL reduction. Because depression and ESSPRI are major determinants of HRQOL in Korean pSS patients, ESSPRI is suggested to be a disease-specific for pSS.

APLAR-0135

Clinical features of the patients who have relapsing febrile inflammatory diseases without infectious or autoimmune evidence

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Background: Autoinflammatory disease (AID) is a newly proposed category of disorders that encompasses a wide clinical spectrum of abnormally increased inflammation mediated by innate immune system. However, clinical phenotypes of non-hereditary AID have been poorly described due to considerable heterogeneity of the disease. We aimed to characterize the clinical features of a particular subset of patients who suffered relapsing fever and inflammation without infectious or autoimmune evidence.

Methods: Medical records of 1775 patients who visited our Rheumatology Clinic between March 2009 and December 2010 were reviewed to identify diagnostically challenging patients with recurrent fever and/or non-infectious inflammation and in lack of serum autoantibodies.

Results: We identified 20 patients (1.1%) who had recurrent febrile episodes and inflammation in two or more organ systems, were in lack of anti-nuclear antibody, rheumatoid factor, anti-CCP antibody, and anti-neutrophil cytoplasmic antibody, and failed to satisfy any specific classification criteria. Because the clinical features of these 20 patients consisted of those commonly seen in autoimmune diseases, other well-known AIDs, or viral infections (table 1), these patients underwent extensive work-up for infection and autoimmune causes, but remained un-classified.

Conclusion: A small number of patients were identified to show relapsing fever and inflammation without any infectious or autoimmune evidence. Although they did not belong to any particular disease classification, the clinical features of these patients were not unique compared with autoimmune diseases or other AIDs.

Table 1. Clinical features of 20 patients who had recurrent fever and inflammation without infectious or autoimmune evidence.

Clinical features	n (%)
Peripheral arthritis/arthralgia	8 (40)
Oral ulcer	8 (40)
Headache	7 (35)
Macular rash	7 (35)
Lymphadenopathy	6 (30)
Sore throat	6 (30)
Genital ulcer	5 (25)
Myalgia	5 (25)
Buttock pain	3 (15)
Erythema nodosum	3 (15)
Serositis	2 (10)
Abdominal pain and diarrhea	2 (10)
Meningoencephalitis	1 (5)
Hepatitis	1 (5)
HLA-B27 or HLA-B51	0 (0)

APLAR-0138

The association between Behcets disease and single nucleotide polymorphisms in IL-10 mediated signaling pathways in a Korean population

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Objective: Our recent GWAS did not replicate the association between *IL-10* and BD in a Korean population [1]. To fully examine the relationship between IL-10 and BD, the associations between BD and single nucleotide polymorphisms (SNPs) in IL-10 mediated signaling pathways were examined in Korean BD patients.

Methods: DNA samples were obtained from 181 BD patients and 181 age- and sex-matched healthy controls. Eighteen tag SNPs in *JAK1* (rs17127024, rs310245, rs2991269, rs2230587, rs2780898, rs2274948, rs310222, rs2256298, rs3818753, rs2780831, rs10889502, rs12563017, rs11208537, rs11208538, rs1353595, rs17127171, rs7553101, and rs4244165), five in *TYK2* (rs34536443, rs12720356, rs2304256, rs280523, and rs12720217), and five in *STAT3* (rs3744483, rs2293152, rs6503695, rs744166, and rs12948909) selected using the Japanese panel of international HapMap data with a minor allele frequency of >5% and with $r^2 > 0.8$ were genotyped. Genetic loci with a deviation from Hardy-Weinberg equilibrium in controls (rs11208538 in *JAK1*), or without any polymorphism in study subjects (rs34536443 and rs12720356 in *TYK2*) were not included in the analysis.

Results: The frequency of C allele at rs12948909 in *STAT3* was higher in BD patients than controls (OR[95%CI] = 1.54[1.00–2.38], P = 0.047), which, however, lost statistical significance after permutation-based correction for multiple testing. No significant associations were found between alleles of the rest 24 SNPs and BD. In addition, there was no genotype found to have a significant association with BD. In linkage disequilibrium (LD) analysis, eight haplotypes from two LD blocks in *JAK1* and three haplotype from one LD block in *STAT3* were identified but showed no association with BD.

Conclusion: The result of this study suggests that genetic dysregulation of IL-10 mediated intracellular signaling is not a predominant pathogenic mechanism for BD in Koreans.

[1]. Lee YJ et al. Genome-wide association study identifies GIMAP as a novel susceptibility locus for Behcet's disease. Ann Rheum Dis. 2013 Feb 25.

APLAR-0266

Macrophage activation syndrome an under recognized hematological manifestation: Experience from a tertiary Rheumatology referral institute from south India

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Introduction: Anemia of chronic disease, iron deficiency anemia, Evan's syndrome are the common hematological problems in rheumatology.The macrophage activation syndrome is the other condition often under recognized by rheumatologist.Macrophage activation syndrome (MAS) is characterized by excessive activation of well differentiated macrophages and T cells which clinically presents as fever, cytopenias, lymphadenopathy, hepatosplenomegaly, coagulopathy and in severe cases multiorgan failure mimicking sepsis and high mortality rate, posing a big clinical challenge to the physician in the diagnosis and treatment.It's reported incidence is 7–13% in systemic onset JIA and 0.9–4.6% in SLE.

Aim: To analyze clinical, laboratory parameters and outcome of rheumatology patients with suspected macrophage activation syndrome.

Patients and Methods: Patients satisfying criteria for hemophagocytic lymphohistiocytosis (HLH-2009) were identified from inpatient case sheets and discharge summaries from department database from 2008 to 2012, collected: age, sex, clinical features, complete blood counts, ESR, bone marrow examination, renal and liver function tests, serum ferritin, LDH, Fasting triglyceride levels, underlying rheumatic disease and short term outcomes and analyzed.

Results: Eighteen patients (12 females)(twelve were SLE,2 were JIA,one each of Adult onset Still's,dermatomyositis,RA,primary HLH)were identified, Median duration of the underlying disease was 6 (range:3–60)months,Mean duration from first symptom to diagnosis is 19.1 ± 11.5 days; Mean Hospital stay 15.5 ± 11.5 days,Pancytopenia was observed in 16, and bicytopenia in two patients.Bone marrow examination done in 16,marrow hemophagocytosis is seen in three patients .Multiorgan failure occurred in 6(33.33%) of which 3(3/18 = 16.66%) died.Infection in 10(55.55%) and cyclophosphamide in one was the triggering cause of MAS.**Conclusions:** (i) Fever and sepsis like syndrome,elevated serum ferritin, altered liver enzymes, pancytopenia are the most common findings in Macrophage activation syndrome (MAS). (ii) Infections are common triggers. (iii) Mortality is high (50%) in patients with multi organ failure. (iv) Absence of Marrow hemophagocytosis does not negate the diagnosis. (v) High index of clinical suspicion and early treatment may improve the outcome.

Clinical Rheumathology: T21 – Imaging techniques and diagnosis

APLAR-0045

Assessment of the link between inflammation and fat metaplasia in patients with spondyloarthritis on non-biological therapy

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Background: There is growing awareness of the importance of fat metaplasia in the pathogenesis of spondyloarthritis (SpA). In particular, recent data has demonstrated fat metaplasia at vertebral corners after resolution of inflammation in patients receiving anti-TNF therapies.There is no data that assesses this link in patients receiving non-biological therapies. We aimed to compare these findings in patients with SpA according to treatment.

Objectives: To prospectively assess and compare the link between inflammation and fat metaplasia in patients with SpA receiving anti-TNF therapy and/or non-steroidal anti-inflammatory agents (NSAIDs).

Methods: Two readers blinded to treatment STIR and T1W MRI scans from 103 patients with SpA in a prospective cohort. MRI was conducted at intervals up to 4 years, 56 patients received anti-TNF while 47 received non-Biologic therapies. Fat metaplasia was scored on T1W scans using a the CanDen FAt SpA Spine Score (FASSS) method, which scores 6 different types of fat lesions defined according to anatomical location. Fat lesions are recorded at each vertebral endplate from C2 lower to S1 upper. Inflammation was scored on STIR scans using the SPARCC MRI Spine 23DVUI method with lesions being scored at each DVU. We calculated change scores, responsiveness by standardized response mean, and associations by Pearson c2 and multivariate regression adjusting for age, sex, disease duration, BASDAI, CRP.

Results: Change (a decrease) in SPARCC 23-DVU score from baseline was significant in anti-TNF treated patients but not non-BIOLOGIC treated patients. A significant increase in FASSS was evident in both anti-TNFand non-BIOLOGIC treated patients.

Conclusions: Long-term follow up reveals a strong link between resolution of inflammation and development of fat metaplasia in patients on anti-TNF therapy. There is a disconnect between change in inflammation and development of fat metaplasia in patients receiving non-Biologic therapies. This may have implications for pathways leading to new bone formation.

CIC, Mass spectrum, anti-a-tubulin antibody

APLAR-0124

Sarcopenia in Ukrainian women of different age

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The aim of this study: The aim of this study is evaluating of bodycomposition and frequency of sarcopenia in women depending on age.

Materials and methods: WeÕve examined 8637 women aged 20–89 years (mean age * 56.7 ± 0.14 years; mean height * 162.5 ± 0.07 cm; mean weight * 73.5 ± 0.16 kg). The patients were divided intotwo groups depending on age: 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89 years. Lean and fat masses and total body, lumbar spine, femoral neck bone,forearm bone mineral density (BMD) were measured by DXA using a densitometerProdigy, GE.

Results: We have found thesignificantly differences of fat andlean masses in women with age:

-fatmass: 20–24 years * 18630.12 g; 25–29 years * 18630.12 g; 30–34 years * 19201.00 g;35–39 years * 21528.15?.; 40–44 years * 24611.77 g, 45–49 years* 2750.54 g; 50–54 years * 27501.54 g; 55–59 years * 29909.92 g; 60–64 years * 31600.27 g; 65–69 years * 33508.25 g; 70–74 years * 33155.54 g; 75–79 years * 32284.86 g,80–84 years * 30595.53 g; 85–89 years * 30303.68 g; F = 83.19; P < 0.0000001;
-leanmass: 20–24 years * 37271.57 g; 25–29 years * 37954.09 g; 30–34 years – 39019.72 g; 35–39 years * 39928.62 g; 40–44 years * 40929.67 g, 45–49 years * 41407.19 g; 50–54 years * 41936.27 g; 55–59 years * 42564.79 g; 60–64 years * 42519.73 g; 65–69 years * 41758.95 g; 70–74 years * 41233.77 g; 75–79 years * 41105.52 g, 80–84 years * 40308.00 g; 85–89 years * 38454.61 g; F = 29.15; P < 0.0000001.

Frequency of sarcopenia in women aged 65 years and older was 7 % (women aged 65–69 years (n = 943) * 7.6% (n = 72), 70–74 years (n = 877) * 6.1% (n = 54), 75–79 years (n = 384) * 6.3% (n = 24), 80–84 years (n = 204) * 6.9% (n = 14), 85–59 years (n = 48) * 10.4% (n = 5).

Conclusion: Fat and lean masses weresignificantly decreased with age. The maximal accumulation of fat and lean masseswas in women aged 50–59 years. Frequency of sarcopenia in women aged 65 years andolder was 7 %.

APLAR-0243

Correlation of median nerve cross sectional area (CSA), tunnel diameter and CSA-tunnel diameter ratio with disease severity in carpal tunnel syndrome

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Introduction: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy resulting from the compression of the median nerve at the wrist. It is confirmed by nerve conduction velocity studies and electromyography (EMG-NCV) and can be classified as mild, moderate or severe. Musculoskeletal ultrasound (MSUS) of the wrist has been advocated as an alternative in the diagnosis of CTS because of its non-invasiveness and real-time assessment. However, no ultrasound criteria have been defined yet for the diagnosis of CTS and the classification of its disease severity.

Objective: To determine the correlation of the median nerve CSA, tunnel diameter and the CSA -carpal tunnel diameter ratio measured by MSUS with disease severity as determined by EMG-NCV.

Methodology: A cross-sectional study involving seventeen patients (29 hands) with a mean age of 50.6 years with CTS from the out-patient clinic of the Department of Rehabilitation Medicine at the Philippine General Hospital were recruited to undergo both EMG-NCV and MSUS of the wrist. Carpal tunnel syndrome severity was classified using the American Association of Electrodiagnostic Medicine (AANEM) criteria for mild, moderate and severe CTS. Median nerve CSA using direct and indirect methods and the tunnel diameter were measured using MSUS.

Results: SpearmanÕs rank correlation showed significant direct positive correlation between the median nerve CSA (by direct method) and disease severity of CTS at the proximal carpal tunnel (P = 0.0221). There was also significant positive correlation between the tunnel diameter and disease severity both at the proximal and distal tunnel (P = 0.0095 and P = 0.0470, respectively). Indirect median nerve CSA and CSA-tunnel diameter ratios were not significant

Conclusion: MSUS is a possible alternative in diagnosing CTS and determining its severity using the direct median nerve CSA.

APLAR-0267

Protracted febrile myalgia of familial Mediterranean fever can be reliably detected by magnetic resonance imaging: a comprehensive analysis of 20 cases

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Background: Protracted febrile myalgia (PFM) is a rare and least well recognized manifestation of familial Mediterranen fever (FMF), characterized by prolonged excruciating muscle pain, tenderness, fever. While the diagnosis of PFM in the setting of previously diagnosed FMF is mostly clinical, diagnosis of PFM when it is the sole manifestation of FMF might be challenging.

Aim: To analyse clinical, laboratory, and magnetic resonance imaging (MRI) findings in a series of patients who presented to our department with myalgia and diagnosed as having PFM secondary to FMF.

Methods: We describe a retrospective cohort PFM patients seen at our department between 2009 and 2012.

Results: Study group consisted of 20 patients. Four (20%) of the patients had a previous diagnosis of FMF, while PFM occurred as the presenting symptom of FMF in 40%. M694V allelic involvement was noted in 80% of the patients. Muscle enzymes were in normal range in all patients, and EMGs were normal in all studied patients (n = 13), but one. None of the patients in whom muscle biopsy was available (n = 8) showed features compatible with myositis. All of the patients underwent MRI of the symptomatic extremity and showed different degrees of involvement on the MR images of the affected extremities. On MR images, the muscle involvement was either patchy or diffuse, displayed with the high signal intensity on fluid sensitive and gadolinium-enhanced fat saturated T1-weighted images. Extension of the inflammation around individual muscles and muscle groups (myofascial distribution) was observed, as well as subcutaneous tissue edema.

Discussion: This series of patients with PFM, to our knowledge, is the largest one reported in the literature. With the appropriate clinical history, detection of MRI findings compatible with myositis in the absence of other features suggestive of myositis (muscle enzymes, EMG, etc.) can help make or confirm the diagnosis of PFM.

APLAR-0296

Usefulness of musculoskeletal ultrasonography of haemophilic arthropathy

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Objectives: Recurrent haemarthrosis in haemophilia results in synovitis and joint arthropathy, therefore sensitive tool for detecting haemarthrosis and synovitis are required. Recently, musculoskeletal ultrasonography (MSUS), especially power-Doppler ultrasonography (PDUS) has became a standard tool for assessment of synovitis. Using this technique, we discriminated haemarthrosis and synovitis in haemophilic arthropathy.

Patients and Methods: We obtained MSUS (especially PDUS) of 21 joints in 16 haemophilia patients from December 2010 to November 2012. All of these patients was haemophilia A (n = 14) or haemophilia B (n = 2), and aged 5–58 (mean 20.5 years). 8 patients had a high titer inhibitor. To quantify synovial vascularity, we adopted a semi-quantitative scoring system (grade 0–3) which is used for rheumatoid arthritis. We performed arthroscopic synovectomy seven patients 10 joints and assessed macroscopic and pathohistological analysis of synovium.

Results: PD grade 2 or more with haemarthrosis were 10, PD grade 1 or less with haemarthrosis were 3, PD grade 2 or more without haemarthrosis were 7. In all cases of PD grade 2 or more, the results of pathohistological examination showed vascularization and the synovium demonstrated hypertrophic appearance in arthroscopy.

Conclusion: MSUS (especially PDUS) for haemophilic arthropathy were useful and specific in evaluation of chronic synovitis, and it could be promising tools.

APLAR-0444

Infrared thermography of big toe for diagnosis of Raynauds phenomenon

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Background: The thermography measures blood flow indirectly by measuring skin surface temperature [1]. The characteristic of Raynaud phenomenon is cold-induced vasoconstriction in distal extremities which in turn, lowers skin temperature.

Objectives: The aim of this study was to determine whether the infrared thermography on hands and feet is useful for diagnosis of RaynaudÕs phenomenon (RP).

Methods: Fifty-seven patients with RP (primary RP, n = 33; secondary RP, n = 24) and 120 healthy volunteers were recruited. After acclimation to room temperature for 30 min, patients were evaluated by thermal imaging of the palmar aspects of hands and dorsal aspects of feet. Temperature drop from palm (center) to each finger and from foot dorsum (center) to each toe were compared between RP patients and controls.

Results: Temperature drop from palm to fingers and from foot dorsum to toes differed significantly between RP patients and controls. Area under the curve analysis showed that the temperature difference drop in 1st (big) toe (cutoff value: 3.11?) best differentiated RP patients from controls (sensitivity: 72–74%, specificity : 65–67%).

Conclusions: Thermographic assessment of the skin temperature drop from the foot dorsum to 1st toe is useful for diagnosing RP. It was previously reported that about 90% of patients presented with features of RP of the feet [2]. Thus it clearly indicates that infrared thermography of the feet as the initial workup of Raynaud phenomenon could provide reliable data for diagnosis. In particular, the 1st toe provided the best thermographic parameter for diagnosis of RP among toes. The 1st toe is larger in size and has more obvious boundaries in imaging, which allows confident location for regions of interest to be drawn.

Clinical Rheumathology: T22 – Epidemiology, health care system and pharmacoeconomics

APLAR-0016

Confidence Levels of Medical Students in Rheumatological Skills and Diagnosis: Assessment of Attitudes and Intervention

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Introduction: Studies have shown that doctors are poorly equipped to handle rheumatological complaints, possibly due to poor exposure at the undergraduate level. This study aims to describe the attitudes and confidence of final year medical students towards rheumatology and assess if attending a rheumatology workshop improves this.

Methodology: An interactive workshop focusing on arthritis and joint examination was organised for final year students in the Yong Loo Lin School of Medicine. Participants were invited to complete pre and post workshop surveys looking at their attitudes and self-rating of confidence in rheumatology and joint examination on a five point Likert scale, as well as factors that might affect it.

Results: 80.9% and 91% participants answered the pre and post surveys respectively. Exposure to rheumatology was low and 83.6% had been taught the GALS screen. Prior to the workshop, the mean confidence ratings for rheumatology were significantly lower than those for cardiology, pulmonology and gastroenterology. Figure 1 shows rheumatology rated as the most difficult subject at 3.93 + /- 0.76 ($P < 0.05$). After the workshop, confidence in rheumatology increased significantly ($P < 0.05$).

Conclusion: Confidence in rheumatology is poor and students feel ill-prepared to face these cases. More emphasis needs to be placed on rheumatology and musculoskeletal medicine at the undergraduate level.

APLAR-0230

Epidemiology of chronic backache in NZ

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The lifetime prevalence of spinal pain has been reported to be 54% to 80%. The costs of chronic disability to the injured worker, his or her family, employers, and society are enormous. Although there have been many epidemiological studies of risk factors for lower back pain, there are few risk factors established in prospective studies.

We are reporting the epidemiological findings for over 500 cases of Grade II to IV lower back pain assessed by a single orthopaedic surgeon over the period of last 4 years [2008–2012] for Accident Compensation Corporation, New Zealand.

Various demographic factors and risk factors including psychological factors and their significances are being reviewed. Factors such as work environment, cigarette smoking, prior episodes of backache, psychosocial factors consistently predict chronic disability.

The purpose of this study is to develop a statistical model that accurately predicts chronic work disability. Accurate early identification of risk factors for chronic disability could enable these individuals to be targeted for early intervention and promote their return to work.

APLAR-0245

Development of the United Arab Emirates Rheumatological Disease Registry

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Background: A recent study[1] suggested that patients with rheumatoid arthritis living in the United Arab Emirates (UAE) have a delayed diagnosis, high active disease and low biologic and disease modifying antirheumatic drugs (DMARDs) utilisation. However, there remains a scarcity of longitudinal clinical data from the region.

Aims: Mafraq Hospital, a third-level, public hospital in Abu Dhabi, is creating the UAE Rheumatological Disease Registry (URDR), consisting of longitudinal clinical data with the ultimate aim of improving outcomes for patients. We will determine the long-term effectiveness and safety of drug therapies for rheumatoid arthritis, ankylosing spondylitis, juvenile arthritis and other inflammatory arthritides.

The specific objectives of the URDR are to:

1. Describe the population and disease characteristics of inflammatory arthritis patients in the UAE;
2. Determine the short- and long-term effectiveness and safety of biologic and DMARD therapies, as measured by mortality/survival, function and disability, quality of life, incidence of adverse events, treatment side effects, and reasons for withdrawing or switching therapy;
3. Determine the relative contributions of disease factors and other treatments in any risks or benefits observed;
4. Determine the economic impact of pharmaceutical therapy and other resource utilisation, using government-linked data;
5. Establish an on-going data resource which will answer important questions that may arise in the future.

Methodology: The URDR will be undertaken in collaboration with the Ontario Biologics Research Institute from Canada, a long standing successful rheumatological registry. Tools utilised will include the Health Assessment Questionnaire Disability Index, Rheumatoid Arthritis Disease Activity Index, Ankylosing Spondylitis Disease Activity Index, Patient Global Assessment, Work Productivity Questionnaire, European Quality of Life Questionnaire, specific and non-specific biological parameters.

Conclusions: The URDR will become a valuable source of epidemiological data essential for clinicians, consumers, policymakers, drug development tract companies, approval agencies and others.

Refs: [1]Badsha H, et al (2007) Ann Rheum Dis

APLAR-0269

The frequency of occult hepatitis B infection in rheumatic diseases and the role of Anti-HBc test in routine practice

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Background: Most of the drugs used in rheumatic diseases suppress the immune system, especially corticosteroids and anti-TNF agents, therefore may cause reactivation in patients with hepatitis B virus (HBV). Studies have shown that HBV reactivation due to immunosuppression is not a case only in patients with chronic HBV infection, but also in patients with occult diseases. Evidence is accumulating that HBV is present in patients who are HBsAg negative, but have antibody to hepatitis B core antigen (anti-HBc).

Objective: To determine the prevalence of occult HBV infection in patients receiving immunosuppressive agents and examine the role of anti-HBc as a screening test for occult infection in Turkish patients with rheumatic diseases.

Methods: Consecutive patients using immunosuppressive agents for rheumatic diseases seen in rheumatology outpatient clinic and who are negative for HBsAg were included. HBsAg, Anti-HBs and anti-HBc IgG tests were studied in all participants along with the quantification of HBV-DNA by real-time PCR.

Results: Total 116 patients included to the study (59 spondylarthritis, 39 romatoid arthritis, and 18 others). Patients were given corticosteroids (36%), methotrexate (27%), anti-TNF agents (35%). In this HBsAg negative group, 27 patients (23%) were found to be positive for anti-HBc IgG. In this subgroup, 19 patients were anti-HBs Ab positive while isolated anti-HBc IgG positivity were detected in other eight patients. None of the patients was found as HBV-DNA positive.

Conclusion: Since none of our patients with isolated anti-HBc positivity had detectable levels of HBV-DNA in their serum, using anti-HBc test for screening seems not to be justified. While our results suggest that prevalence of occult HBV infection is ignorable among patients with rheumatic diseases in Turkey, considering the preliminary feature of our results (target study population is 300) full results should be waited to reach such a definite conclusion.

APLAR-0391

COPCORD 30 years progress

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COPCORD

The community oriented program for the control of rheumatic disease
30 years progress
Richard Wigley and Arvind Chopra

Cross sectional studies of the prevalence of rheumatic disease, in developing countries, have now been completed in 23 countries with multiple studies in China, India, Iran and Mexico. More than 100 publications are listed on the COPCORD website.

The prevalence of rheumatic diseases is as great as in lethal diseases such as cancer though the effect is on disability rather than on mortality. Ie, in Iran 25.5% had pain and 13% of

these had some physical disability. In Pune, India, RD is more prevalent than the mortal diseases of the west such as hypertension, heart disease diabetes, obesity and cancer.

In Han Chinese a gradient in latitude in back and knee pain suggests an effect of climate. There is a high prevalence of rheumatic pain In Mexico City (43.7) at high altitude than in Sinaloa province (7.1%) at a lower level. Rheumatoid arthritis is common in the Yucatan (2.8%). Fibromyalgia is less prevalent than in the west, where it averages 4–5%. It only affects 0.7% Iran and 0.6% in Mexico. The exception is Bangladesh at 4.4%

In Bhigwan village near Pune in India regular intervention has been continued over 15 years by Dr Chopra. Comparison is now to be made with the initial and current COPCORD data and with similar village population where there has been no intervention. The endpoints will be 1. Health 2. Educational level 3. Economic status.

Future COPCORD studies will include the effects of occupation on RD and of RD on employment, The causation of knee osteoarthritis in Iran is currently being assessed. A COPCORD study in Subsaharan Africa, probably in Kenya.

APLAR-0154

Work disability in patients with rheumatoid arthritis: a cross-sectional study in China

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Objective: To evaluate the impact of rheumatoid arthritis (RA) on work ability and identify predictive factors of work disability in patients with RA.

Methods: A cross-sectional multicentre study was performed in 21 tertiary care hospitals across China. A consecutive sample of 846 patients with RA was recruited. Of which, 589 patients in working age at disease onset constituted the study population. Socio-demographic, clinical, working and financial conditions of the patients were collected. Logistic regression analyses were used to identify predictors of work disability.

Results: The rate of work disability was 48.0% in RA patients with a mean disease duration of 60 months (IQR 14–134 months), including 11.7% retired early from work, 33.6% reduced work hours and 2.7% changed jobs. In 135 patients with disease duration less than 12 months, the rate of work disability was also high (45.2%, 61/135). There was a significant positive correlation of lower education ($P = 0.001$), current smoking ($P = 0.01$), lower monthly income ($P < 0.001$), having no medical insurance ($P = 0.004$), manual labor ($P < 0.001$), worse patient pain assessment ($P < 0.001$), worse patient global assessment ($P < 0.001$), worse physician global assessment ($P < 0.001$) and higher HAQ score ($P = 0.031$) with work disability of RA patients. Furthermore, the multivariate logistic regression analysis confirmed that current smoking (OR 2.516, 95% CI 1.165–5.436), manual labor (OR 2.010, 95% CI 1.273–3.173), lower monthly income (OR 1.633, 95% CI 1.007–2.649) and higher HAQ score (OR 1.534, 95% CI 1.198–1.964) were independent risk factors for work disability of Chinese RA patients.

Conclusion: There is a substantial impact of RA on work ability of RA patients in China, and it is associated with current smoking, manual labor, lower income and higher HAQ score.

Clinical Rheumathology: T24 – Advances in pain management

APLAR-0134

Effectiveness and safety of hydrogel patches containing loxoprofen sodium in patients with myalgia: a randomized, controlled, double-blind, double-parallel, multicenter Phase 3 trial

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Objective: To evaluate the effectiveness and safety of hydrogel patches containing loxoprofen sodium in patients with myalgia.

Methods: From November 2010 to August 2011, 182 patients from 9 rheumatology referral centers in China were enrolled in this randomized, controlled, double-blind, double-parallel, multicenter phase III trial. Patients were randomly assigned to either the LX patch (LX-P) group (n = 91, 100 mg of LX patch per day plus oral placebo t.i.d.) or a loxoprofen sodium tablet (LX-T) group (n = 91, LX-T 60 mg t.i.d. plus patch placebo) for 2 weeks. The primary efficacy endpoint was the proportion of patients with an overall improvement rate of ≥50%.

Results: The study was completed by 175 patients. There were more patients with an overall improvement rate of ≥50% in the LX-P group compared to those taking LX-T, although there was no statistically significant difference (81.3% *vs* 72.2%, respectively, P = 0.147). The treatment difference between the two groups was 9.1% [95% confidence interval (CI): −3.1%, 21.3%], and the lower margin of the 95% CI was above the predetermined non-inferiority margin (−10%). No significant differences were found in rest pain, tenderness, pain on motion, or in disability in daily activities at week 1 and at the discontinuation point in both groups. There was a lower incidence of adverse events in the LX-P group than in the LX-T group, but there was no statistically significant difference (14.3% *vs* 22.0%, P = 0.178). No serious adverse events were reported in either group.

Conclusions: LX-P has non-inferiority in efficacy and safety to LX*T for the management of myalgia, and demonstrates a superior trend compared to that of LX*T. Therefore, it is assumed that LX-P, with advantages such as better compliance and lower systemic exposure, will be more appropriate than LX-T for the treatment of myalgia.

APLAR-0153

Double-blind, multicenter trial to evaluate safety and efficacy of hydrogel patch containing loxoprofen-sodium in treating swelling and pain caused by Trauma

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Objective: To evaluate the safety and efficacy of hydrogel patches containing loxoprofen sodium in treating the swelling and pain caused by trauma.

Methods: From December 2010 to August 2011 162 patients from 7 hospitals in China were enrolled in this randomized, controlled, double-blind, double-parallel, multicenter clinical trial. Patients were randomly assigned to either the LX patch (LX-P) group (n = 80, LX patch 100 mg per day plus oral placebo 60 mg t.i.d.) or the loxoprofen sodium tablet (LX-T) group (n = 82, LX-T 60 mg t.i.d. plus patch placebo 100 mg). The treatment course was 7 days. The symptomatic efficiency rate, the overall efficiency rate, the overall safety, and the treatment compliance were evaluated.

Results: All of the 162 patients completed the study as the trial was designed. The overall efficiency rate at the last visit for the patients in LX-P group was 91.3%, slightly higher than that of the patients from the LX-T group (89.0%), although there was no statistically significant difference between the two groups (P = 0.635). However, the difference between the groups and the 95% confidence interval (CI) were 2.2% (−6.9–11.4%), and the lower margin of the 95% CI was above the predetermined non-inferiority margin (−10%). The symptomatic efficiency rates, including pain (rest pain, tenderness, kinesalgia), inflammatory symptoms (swelling, local burning sensation), and limited movement, were found no statistically significant differences between two groups, although the efficiency rate of the LX-T group was superior to that of the LX-P group by 5% in relieving rest pain and swelling. There was a lower incidence of adverse events (AE) in the LX-P group than in the LX-T group, but there was no statistically significant difference (8.8% vs 12.2%, P = 0.474). No Serious AE or deaths were reported during the trial. All of the patients in the two groups showed a similar excellent treatment compliance. The total drug exposure for each patient in the LX-P group was lower than that in the LX-T group, while the number of drug exposure days was the same.

Conclusions: LX-P demonstrated non-inferiority to LX-T in treating the swelling and pain caused by trauma. However, because of its lower drug exposure, the incidence of AEs in LX-P was lower than that seen with LX-T. Therefore, LX in a patch formulation may be more suitable than the oral form for treating the swelling and pain caused by trauma.

APLAR-0307

Low back pain of myofascial origin among it professionals and treatment using a sequenced protocol

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Aim: To estimate the prevalence and to describe the clinical features and outcome of treatment of MPS of the lower back among cases of Work Related Musculoskeletal Disorders (WRMSD).

Materials and Methods: This retrospective study covered 7385 clients diagnosed with WRMSD, with a mean age 30 ± 5.92 years. The relevant clinical data were extracted from the treatment chart of WRMSD patients who received treatment at a Rehabilitation Centre. A single Orthopaedic Surgeon performed the clinical assessment and made the diagnosis of MPS using the modified Simons Criteria. All the clients received a sequenced, multidisciplinary treatment protocol incorporating manual therapy techniques.

Results: Low Back pain is the second commonest with 46% of the total population. Among the subjects with low back pain 61% were diagnosed to have MPS of the lower back. Among the cases of MPS, 75% were male and 25% were female. 41% of the participants were working for 8–12 hours. The commonest job categories of the participants were Managerial (28%), Software engineers (27%) and Application Engineers (22%). Prolonged sitting with static loading of the lower back was found to be the risk factor. Commonest co morbidities were neck pain, upper back pain, leg and foot pain. Significant reduction in pain or discomfort ($P \leq 0.05$) is noted among the subjects following a sequenced rehabilitation protocol.

Conclusion: In view of the high prevalence of MPS, clinical practitioners dealing with pain management need to be familiar with the current approaches to diagnose Low Back pain. Skilled hands on manual techniques along with mind body approaches, exercise and ergonomics found to be an effective method of treatment of MPS.

Key words: MPS of the lower back, SHARAN'S Protocol, Prevalence.

Allied Health Research Topics: T25 – Nursing

APLAR-0111

Professional support to ad hoc needs in rheumatology care – A review of Telephone Advice Line (TAL) service

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Introduction: Despite advance in the management of rheumatic diseases, patients encountering problems from their disease or treatment before their scheduled visits often have limited access to professional assistance. The Rheumatology nurse-led TAL service has been developed since July 2011 to provide professional advice on disease and drug management, and to enhance patient self-efficacy and reduce stress.

Objectives: (1) To review patientsÕ needs and satisfaction level using TAL; and (2) to estimate the effectiveness of TAL in reducing utilization of Accident and Emergency Department (AED) service.

Methodology: A review of TAL record was performed to analyze the reasons for calls. A questionnaire was designed to measure patientsÕ satisfaction level towards the service and to evaluate their potential alternatives if the TAL service was not available.

Results: From September 2011 to December 2012, there were 677 calls from rheumatology patients or their carers. Majority (404 cases) was related to physical discomfort and drug problems. Among these cases, 80 questionnaires were administered by convenience sampling in Jan 2013 with 76 (95%) responses.

Most patients (61.8%) reported that they would attend AED if TAL service was not available. 22.4% would seek assistance from the public out-patient or private clinics. 13.2% would call Specialist Out-patient Department for advice, only 6.6% would try to seek help from related wards. Regarding satisfaction level, 88.2% expressed that their problems were solved by the TAL service; 89.5% were satisfied with the service; and nearly all cases (96.1%) agreed or strongly agreed that continual provision of TAL service is essential.

Conclusion: Disease or treatment related problems are commonly encountered by patients in between their scheduled visits. With TAL, patients can receive professional advice and support by rheumatology nurse to address these problems. It also effectively alleviates patientsÕ demand on AED service.

APLAR-0128

Nurse-led biologic infusion – a safe service that saves

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Introduction: In the conventional practice of biologic infusion, patients have to be seen by rheumatologist for every visit to get the prescription followed by drug purchase and administration. To streamline the workflow and to reduce doctorÕs workload on routine visits, a pilot project of nurse-led biologic infusion (NLBI) clinic has been launched.

Objectives: (1) To evaluate the effectiveness and safety of the NLBI service; (2) to assess the reduction in patient waiting time from admission to discharge in day ward and (3) to quantify the reduction in workload of rheumatologists.

Methodology: Patients receiving biologic therapy for more than one year with stable conditions were recruited to the NLBI clinic by rheumatologists. Alternating follow-up sessions by NLBI clinic and rheumatologist was arranged. Rheumatologists would assess the patient and prescribe the appropriate drug regime for the next NLBI clinic. During NLBI clinic visit, patientÕs clinical conditions, including their disease activity, laboratory results and vital signs were assessed according to standardized protocol to ensure treatment safety. After the infusion therapy, rheumatology nurse will make proper discharge record to ensure continuity of care. For patients with unstable conditions or infusion reactions, rheumatologists are readily available for timely management.

Results: 11 patients were recruited with a total of 20 attendances from April to December of 2012. All cases were given biologic infusion safely and successfully without any adverse effects. Patients saved 45 min in each visit since there is no need to wait for drug prescription and collection. The alternating follow-up arrangement also reduced doctorÕs workload by 50%.

Conclusion: Nurse-led biologic infusion is smooth and safe. It saves patientÕs time in terms of the total duration of the treatment session. Furthermore, it spares the time of rheumatologists spent on routine visits and enables them to concentrate on the management of more complex cases.

Allied Health Research Topics: T26 – Physiotherapy

APLAR-0295

Assessment of spinal mobility in juvenile healthy volunteers using supine and standing posture

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Introduction: Spinal mobility is commonly assessed during the evaluation of functional status and therapeutic outcomes of ankylosing spondylitis, however, performance of some measures is time-consuming and may not be feasible in clinical practice. This study were designed (1) to explore the influence factors of spinal mobility, and (2) to compare the results of spinal mobility were measured by sitting and supine posture respectively.

Materials and Methods: Initial recruitment identified 223 healthy participants (188 males, 35 females) aged 18–23 years from community residents of north and south city in China.

Results: Statistical difference was found with tragus to wall distance, cervical rotation (sitting position), intermalleolar distance (standing position), modified SchoberÕs test, fingertip-to-floor distance and chest expansion between males and females ($P < 0.05$). Northerners had significantly higher levels of tragus to wall distance, intermalleolar distance and chest expansion than southerners ($P < 0.05$). Weekly exercise volumewere positively correlated with cervical rotation (supine position), intermalleolar distance (standing and supine position) and chest expansion ($P < 0.05$). Height was positively correlated with intermalleolar distance ($P < 0.01$) after controlling for body weight and exercise. Body weight was positively correlated with tragus to wall distance and modified SchoberÕs test ($P < 0.05$). There were statistical difference between standing and supine position intermalleolar distance ($P < 0.05$), and between sitting and supine position cervical rotation in females ($P = 0.025$).

Conclusions: Spinal mobility was affected by gender, height, weight, exercise and geographical factors. The affecting factors should be considered when the standard of spinal mobility was formulated. The intermalleolar distance can not reflect very well activity of hip joint for the height because of differences of height. The measurement of cervical rotation by supine position could reduce the influence of shoulder rotation than sitting position, this way may be more scientific.

APLAR-0354

High-fluence low-level laser irradiation treatment reduces TNF-alpha and MMP3 expressions in early stage of rat rheumatoid synovium

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Rheumatoid arthritis (RA) is a chronic, inflammatory and systemic autoimmune disease that leads to progressive synovitis. Treatment of RA is very complex, severalstudies have investigated the use of low-level laser therapy (LLLT) in pain symptoms of RA. However, it remains unknown if LLLT can modulate early stage of RA on synovitis in a dose-dependent fashion. With this perspective in mind, we evaluated the anti-inflammatory effects of LLLT at low and high fluences in early RA progression stage. Monoarthritis was induced in adult male Sprague-Dawley rats (250–300 g) via intraarticular injection of complete Freund's adjuvant (CFA, 50 μL) into the tibiotarsal joint. All CFA-induced arthritic (CIA) animals were randomly divided into four groups: (1) animals with CIA and treated with 660-nm GaAlAs laser at high fluence (72 J/cm^2); (2) animals with CIA and treated with sham-high-fluence laser irradiation (0 J/cm^2); (3) animals with CIA and treated with laser at low fluence (4.5 J/cm^2); and (4) animals with sham-low-fluence laser irradiation (0 J/cm^2). LLLT treatments were performed 3 days after CIA for 10 consecutive days. All animals were sacrificed at the 14th day from RA induction and articular tissue was collected in order to assess inflammation in synovium by immunofluorescent studies with 5B5, ED1, TNF-α and MMP3. We observed that LLLT at a fluence of 72 J/cm^2 significantly reduced the expressions of 5B5-, ED1- TNF-α- and MMP3-like immunoreactivities when compared to the other groups at early stage of RA ($P < 0.05$). We suggest that high-fluence LLLT is able to modulate inflammatory responses in early progression stages of RA.

APLAR-0355

Comparative effects of low- and high-intensity laser combined with intraarticular hyaluronan injection in an animal model for rheumatoid arthritis

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Purpose: Many studies demonstrated that supplement of hyaluronan (HA) could decrease hyperanalgesic, inflammation and lubricates joint. Recently, intraarticular injection of HA (IAHA) for treating rheumatoid arthritis (RA) is more common, but the efficacy was limited due to its side effects of pain at the injection site and inflammatory pain. Low-level laser therapy is the proven and recommended intervention for managing pain, but the dosage of laser therapy is still controversy on RA-related pain. The purpose of this study was to investigate the effects of combined use of low- or high-intensity laser therapy (LILT or HILT) combined with IAHA on pain and inflammation in rats with complete Freund's adjuvant-induced arthritis (CIA).

Materials and Methods: Monoarthritis was induced in adult male Sprague-Dawley (250–300 g) via intraarticular injection of complete Freund's adjuvant into the tibiotarsal joint. The CIA animals were divided into four groups: control (no treatments), IAHA, LILT (4.5 J/cm^2)+IAHA, and HILT (72 J/cm^2)+IAHA groups. Seven days after CIA, combined use of laser therapy and IAHA were administered for 8 consecutive days and once every other day respectively. Functional evaluations of pain behavior, histology, and pro-inflammatory cytokines were performed. Results: The mechanical withdrawal pain threshold were significantly improved in HILT+IAHA group when compared with those in the IAHA, LILT+IAHA and control groups. Both HILT and LILT combined with IAHA can reduce inflammation by suppressing TNF-α, iNOS and ED1 accumulation at synovium.Conclusions: Our findings suggest that HILT combined with IAHA can decrease hyperanalgesia by increasing mechanical pain threshold. IAHA combined with LLLT at either high- or low-intensity can modulate inflammatory mediators. Therefore, LLLT has a synergistic effect in providing greater improvement combined with IAHA on RA treatment.

Allied Health Research Topics: T29 – Alternative medicine (eg. acupuncture)

APLAR-0025

Effect of cadmium on experimental arthritis

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Exposure of humans and animals to toxic metals is widespread. Cadmium is one of the most prevalent nephrotoxic heavy metal but it may cause other systemic toxicity as well. Cadmium may cause adverse health effects by impairment of immune system, disrupting endocrine system and induction of reactive oxygen species. The present study has been designed to find out the effect of cadmium exposure on pathogenesis of rheumatoid arthritis (RA) in the animal model (CIA) of the disease. Arthritis was induced in male Wistar rats by intradermal injection of emulsion containing bovine type II collagen in Complete Freundós adjuvant. Rats were treated with cadmium chloride dissolved in drinking water at concentration of 5µg/ml and 50µg/ml for 21 days after immunization. The effects of treatment were analysed by studies on morphogical changes, biochemical parameters and histological evaluation of the joints. Exposure to animals at the two dose levels of cadmium elicited remarkably contrasting response. While exposure at 5µg/ml tended to attenuate inflammation as compared to collagen type ?? treated rats whereas a dose of 50µg/ml accelerated the response profoundly. The results suggest that elicited mechanism of immune and inflammatory response to cadmium exposure in RA follow different pathways depending on the exposure level.

APLAR-0053

A study of additional combination therapy with bucillamine in patients with escape response to methotrexate

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Purpose: We examined the usefulness of additional therapy with bucillamine (BC) in patients with rheumatoid arthritis (RA) showing inadequate response or escape response to methotrexate(MTX).

Methods: Additional combination therapy with BC was performed in 32 patients with RA (five males and 27 females; mean age, 60.7 years) showing inadequate response or escape response to MTX, in order to examine the usefulness of the treatment. Time to escape response to MTX was 13–27 months with a mean period of 21 months.

Results and Discussion: Clinical response evaluation in the 32 patients included in the present study was performed with Disease Activity Score 28 (DAS 28). Because 10 out of 28 patients responding to the treatment later needed an increase in MTX dose, the dose was not changed. The additional combination therapy with BC had an efficacy rate of 56.3%. The duration of response to the additional combination therapy was 18–36 months with a mean period of 24 months. BC also has a 50-mg formulation, and is a disease-modifying antirheumatic drug (DMARD) less likely to cause serious side effects at low doses and easy to use. Therefore, when MTX teratment is not as effective as expected, the additional combination therapy with BC is considered to be useful.

APLAR-0080

Standardization of design and reporting of yoga interventions for musculoskeletal conditions: A Delphi survey approach

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Objective: Evidence suggests yoga may result in clinically relevant improvements in pain and functional outcomes across a range of musculoskeletal conditions including rheumatoid arthritis, osteoarthritis, and fibromyalgia. The aim of the current study was to develop a set of standardized core components for yoga therapy in clinical intervention trials for patients with musculoskeletal conditions.

Methods: Forty one panelists from six countries were recruited. The 3-round Delphi was conducted via electronic surveys. Round 1 consisted of an open-ended question to generate items for consideration as core yoga intervention components. These items were rated for importance for inclusion in the Delphi list in Round 2. Any items not reaching consensus were forwarded to Round 3 for re-rating.

Results: Thirty six participants (88%) completed the survey. Round 1 generated 348 comments, which were analyzed using thematic analysis and grouped into 49 items for rating in Round 2. Thirty one items not reaching consensus were subsequently re-rated in Round 3. Final consensus was reached on 33 items, grouped under 5 themes: 1) defining the yoga intervention: intervention parameters, minimum parameter values, appropriateness of the intervention; 2) types of yoga practices; 3) delivery of the yoga protocol: instructors, best practice, resources; 4) outcome domains; and 5) reporting of the intervention. Comments regarding items not reaching consensus highlighted areas of divergence among researchers regarding some parameter values and reporting of the interventions.

Conclusions: The 33-item Delphi list provides a reference tool for standardization of best practice in the design and reporting of future clinical yoga trials for musculoskeletal conditions. The use of this list will address the challenge of balancing a need for standardization with the ability to adapt interventions to the specific clinical population and outcome measures being studied, and the style of yoga being taught.

Case Report: T30 – Case report

APLAR-0010

Multiple infections in a Filipino with polyangiitis overlap syndrome

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Background: Polyangiitis overlap syndorme (POS) refers to primary vasculitis not classifiable into a well-defined syndrome. Infections may play etiologic roles not just in secondary but also *primary* vasculitis.

Objective: Our objective is to present POS with features of 2 ANCA-associated vasculitides (AAVs) – granulomatosis with polyangiitis (GPA) and Churg-Strauss syndrome (CSS) – and infections.

Case: A 25-year-old Filipina had 6 years of recurrent purpura and debilitating arthralgia, hemoptysis, epistaxis, eye redness, dyspnea. She had cachexia, oral ulcers, rhinorrhea, crackles, and polyarthritis. She had anemia, elevated ESR and CRP, c-ANCA and anti-proteinase 3, chronic sinusitis on rhinoscopy and lung vasculitis on chest CT. Skin biopsy showed leukocytoclastic vasculitis. There was eosinophilia without parasitism, but negative p-ANCA and anti-myeloperoxidase, also ANA and anti-dsDNA. She had high ASO titers, chronic hepatitis B, bronchial pseudomonas aeruginosa and sinus methicilin-resistant staphylococcus aureus infections. HIV infection was ruled out.

There were incomplete features of limited GPA and CSS with multiple infections. She was given naproxen and culture-guided antibiotics with partial resolution of symptoms. Prednisone was started 2 weeks after hepatitis B reactivation prophylaxis. Complete resolution of skin lesions, joint pains, and airway symptoms, and improvement of inflammatory markers were seen after twelve weeks. She is maintained on prednisone 10 mg OD.

Discussion and Conclusion: There have been no more than 30 reported POS cases worldwide, and none in Southeast Asia. Our patientOs case is unique * POS as a combination of 2 AAVs, further compounded by multiple pathogens, either current infections or colonizers, that may have triggered or perpetuated vasculitis, necessitating use of both antimicrobial and anti-inflammatory drugs to achieve remission. Knowledge of existence and early recognition of POS are essential to avoid treatment delay and prevention of irreversible organ damage.

APLAR-0019

Cutaneous necrosis of lower extremity as the first manifestation of catastrophic antiphospholipid syndrome

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This is a report of a young woman with extensive skin necrosis in her right flank, right thigh and left leg, which was misdiagnosed as warfarin induced skin necrosis. Further investigations revealed that she is suffering from catastrophic antiphospholipid syndrome. She recovered from this life-threatening variant of antiphospholipid syndrome.

APLAR-0028

A case of primary Sjögrens syndrome admitted with autoimmune hepatitis

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Introduction: Primary Sj*gren's syndrome is a chronic autoimmune disease characterized by dry mouth and dry eye and is capable of involving locomotor system and systemic organs. Besides its classical setting, it may be presented with different findings.

Case Report: 42-year-old female patient was admitted to hospital with complaints of pain in wrist, MCP, PIF joints, morning stiffness lasting more than an hour, dyspnea on effort and dryness of the mouth and eyes. Her medical history is composed of the onset of fatigue, jaundice, abdominal pain and arthralgia about 8 months ago and she was hospitalized to Hepatology clinic. She was diagnosed as autoimmune hepatitis and primary biliary cirrhosis after liver biopsy, and therapy with corticosteroid 1 mg/kg/day, azathioprine 100 mg/day and ursodeoksikolik acid 500 mg/day was started. Since locomotor system complaints continue to increase, the patient was directed to our out-patients clinic. Her physical examination revealed tenderness and limitation of motion in both wrist, MCP and PIF joints. Laboratory tests were as follows; RF: positive, ESR: 59 mm/h and CRP: 1.74 mg/dL. Protein electrophoresis revealed polyclonal gammopathy. Serology tests were as follows; ANA: 1/320 granular, anti-Ro: positive, BUT: positive, anti-dsDNA: negative, anti-CCP: negative, C3 and C4 were normal. Ophtalmology consultation reported Shirmer: 3/4 mm and BUT: 4/4sn. Lip biopsy was reported as Chisholm grade 3. The patient was diagnosed as primary Sj*gren's syndrome according to the clinical, laboratory and pathological data and was evaluated with the American-European classification criteria. In addition to the immunosuppressive treatment she has been taking, hydroxychloroquine 400 mg/day was started.

Conclusion: Autoimmune hepatitis may be associated with different rheumatic diseases and/or may be a part of these systemic diseases. In order to rule out an underlying systemic rheumatic disease in a patient with autoimmune hepatitis, performing good systemic questioning is required and full laboratory and serological tests should be done.

APLAR-0029

A case of leukocytoclastic vasculitis applied with ischemic Jejunitis

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Introduction: Leukocytoclastic vasculitis is defined as vascular inflammation resulting from hypersensitivity and referred to as hypersensitive or allergic vasculitis. It is noticed as palpable purpurea and maculopapillary skin rashes.

Case Report: 30-year-old male patient applied to the family physician with the onset of purpuric skin lesions on the pretibial area of lower extremity, pain and limitation of motion in both wrists in April 2012. As the patient started complaining of stomach pain, he was directed to our Rheumatology out-patients clinic. Physical examination on admission revealed sensitivity in epigastrium, increase in bowel sounds and diffuse purpuric lesions were detected in the skin. Laboratory tests were as follows; WBC: 19000/Ul, ESR: 49 mm/h, CRP: 2.07 mg/dL; RF was negative. Routine urine analysis was normal, occult blood in the stool was positive. Serological tests for ANA, ANCA, C3, C4 and anti-CCP were normal. Abdominal angiographic CT reported marked diffuse thickening of intestinal wall startin from the second segment of duodenum and involving the proximal jejunum and submucosal edema; these findings were in favor of the vasculitic process in the ischemic bowel disease. Skin biopsy of purpuric skin lesions in the lower extremity interpreted the skin lesions as leukocytoclastic vasculitis. The case was considered as leukocytoclastic vasculitis with GI involvement according to the clinical, laboratory, radiologic and pathologic evaluation. Therapy was started with 3 days pulse corticosteroid (1 g/gÝn) treatment followed by 1 mg/kg daily dose, and subcutaneous methotrexate 15 mg/week. Abdominal angiographic CT was taken on the third month of the treatment, all of the previous findings disappeared when compared to the first CT findings.

Conclusion: As in our case, in patients presenting with acute abdominal pain and locomotor system complaints, investigations should be performed to exclude a vasculitic process. If it is accompanied by the involvement of internal organs, early diagnosis and treatment will be life saving.

APLAR-0042

Case report on ANA negative systemic lupus erythematosus with co-existing thrombotic thrombocytopenic purpura presented as pancytopenia

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Introduction: ANA negative Systemic Lupus Erythematosus is rare case with only 1–5% of SLE population. Diagnosis of ANA negative SLE is made when the patient was able to meet the 4 out of 11 of diagnosis of SLE by ACR. Thrombotic thrombocytopenic purpura, on the other hand, is another rare disorder of blood coagulation system. SLE patient with occurrence of TTP during its course is associated with greater morbidity and mortality.

Clinical Picture: We report a rare case of a 47 years old female with a 7 years history of ANA negative systemic lupus erythematosus, maintained on oral steroids with thrombotic thrombocytopenic purpura initially presented with bicytopenia and malar rash. SLE, despite negative ANA was diagnosed based on criteria established by American College of Rheumatology. Later in its course, patient developed pancytopenia, fever, change in sensorium, seizure, and renal failure, all consistent with clinical findings of thrombotic thrombocytopenic purpura. Due to progressive renal failure, renal biopsy was done which showed presence of thrombi. Immunofluoresce microscopy further showed presence of IgA, IgM and IgG with diffuse segmental glomerular basement membrane. Findings were consistent with thrombotic thrombocytopenic purpura and immune-complex mediated glomerulonephritis.

Outcome: The prognosis is guarded in patients with co-existing disease of SLE and TTP, with higher morbidity and mortality than either disease alone. Our patient was treated with steroids, antibiotics for concomitant infection and plasmapheresis. However, she failed to recover and died.

Conclusion: ANA negative SLE can be attributed to early treatment of steroids and presence of protenuria. Management of ANA negative SLE does not differ with ANA positive SLE. Moreover, early recognition and prompt treatment of plasmapheresis are important in management of TTP. However, despite proper management, higher percentage of relapse has been observed in cases with co-existing disease of SLE and TTP.

APLAR-0062

Hemolytic anemia and non-healing ulcer in a 27-year old female: case of SLE antiphospholipid antibody positive responsive to Cyclophosphamide therapy

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This is the case of a 27 year-old female with 7-month history of intermittent fever, rash and chronic non-healing right foot ulcer. The right foot ulcer did not improve with regular wound cleaning with Guava leaves and Hydrogen Peroxide. She later on had episodic dizziness, generalized body weakness and dyspnea on exertion. Consult done showed anemia and thrombocytopenia. Blood transfusions were done but later had ABO incompatibility. Few weeks after discharge, she had muscle and joint pains, discomfort in swallowing, productive coughing and fever with progressive shortness of breath and weight loss of 15 Kg over 2 months.

Patient was admitted with anemia of 5.6 mg/dL and thrombocytopenia of 90 000. Peripheral Blood Smear showed hypochromic anemia, slight anisocytosis, and few schistocytes. CoombÕs test Direct and Indirect were positive, C3 = 29.8 mg/dL, Anti dsDNA, Anti-Smith, Anti-RNP were strongly positive, ANCA IgM negative, SCL70 Antibody negative, Crossmatching was positive for warm auto-antibodies, both Lupus Anticoagulant and Antiocardiolipin Antibody IgG were positive and Duplex Scan of the right lower extremity was normal. She was started on Prednisone 20 mg/tab once daily and was later shifted to Hydrocortisone 40 mg IV once daily then to Pulse Therapy with Methylprednisolone. After 3 days of pulse steroid therapy, her symptoms of fever, muscle and joint pains, easy fatigability, shortness of breath and thrombocytopenia were improved however the anemia and the right foot ulcer persisted. Patient was started with Hydroxychloroquine 200 mg tab once daily, Prednisone 25 mg after breakfast and 20 mg after lunch and Cyclophosphamide 500 mg IV twice a month for 6 doses. Anemia was resolved after 3 doses of Cyclophosphamide and the right foot ulcer completely healed after 4 doses of Cyclophosphamide.

Conclusion: We presented an SLE Antiphospholipid Antibody Positive patient with Steroid Refractory Hemolytic Anemia and chronic non-healing ulcer on the right foot who responded to Pulse Cyclophosphamide therapy.

APLAR-0077

A case of adult-onset Stills disease associated with hemophagocytic lymphohistiocytosis

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Hemophagocytic lymphohistiocytosis(HLH) is an unusual syndrome thatÕs characterized by fever, elevated liver enzyme, cytopenias, hypertriglyceridemia, and pathologic finding of hemophagocytosis in the bone marrow and other tissues, but biopsies fail to demonstrate hemophagocytosis in approximately one-third of patients. Viral infection, underlying malignancy, such as malignant lymphoma, and autoimmune disease are known as the most common cause of hemophagocytic syndrome. We report of a case of adult-onset StillÕs disease(AOSD) associated with HLH. The patient initially manifested with fever, rash, arthralgia, and myalgia. The symptoms, leukocytosis (WBC 20200 cells/μL), and highly elevated ferritin level (>40000 ng/mL) were compatible with Yamaguchi criteria of adult-onset StillÕs disease(AOSD). Though a very few number of cells of hemophagocytosis were seen in the patientÕs bone marrow biopsy, the serum soluble IL-2 receptor level (4564 IU/mL) and AST (1503 mg/dL), ALT (148 mg/dL), bilirubin (9.25 mg/dL) level were highly elevated, which was also compatible with HLH, so we could diagnose the patient as AOSD with HLH. The patient was treated with prednisolone for 3 weeks, and then patientÕs symptom was subsided, and the abnormally elevated AST/ALT and bilirubin level was normalized.

APLAR-0105

Rhupus in a 40-year old Filipino with vaso-occlusive retinopathy: a case report

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Context: Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are consideredto be separate autoimmune diseases with defined criteria for diagnosis.However, recent genetic studies have identified various loci associated withincrease risk for both RA and SLE, hence called Rhupus syndrome. It occurs in 0.09 percent patients with SLE and little is known about the disease profile inthe local setting.

Objective: This study aims to present a case of a Rhupus syndrome in aforty-year old Filipino with severe vaso-occlusive retinopathy.

Clinicalpresentation: A 40-year old Filipino with vague abdominal pain for 2 months.The patient was a known case of rheumatoid arthritis (1998). The patient sought consultation for increase in intensity of abdominalpain associated with fever, easy fatigability, dry cough, palpitation,generalized body weakness and occasional shortness of breath. On review ofsystems, the patient had painless oral ulcer, hair fall, joint pain, stiffnessand limitation of motion in the morning over the hands, knees and feet.

Diagnostic testsshowed positive for anti-nuclear antibody (1:320 dilution with homogenousstaining pattern); antibodies to dsDNA, SS-A and SS-B were positive;proteinuria of 1,941 mgs/24 hour; and anemia. Transthoracic echocardiographyshowed minimal pericardial effusion; and bilateral pleural effusion on chest CTscan.

After completion ofMethyprednisolone pulse therapy, the patient had blurring of vision of the lefteye, which progressed to absence of light perception. Optical coherencetomography revealed extensive thickening of the retinal pigment epitheliumcompatible with retinal hemorrhages and edema of the left eye. Cyclophosphamidetherapy and intervitreal injection of Ranibizumab was done.

Diagnosis: Vaso-occlusive retinopathy of the left eye probably centralretinal vein occlusion secondary to vasculitis secondary to Rhupus syndrome.

Outcome: Despite completion of Methylprednisolone pulse therapy, two cycles ofCyclophosphamide, and intervitreal injection of Ranibizumab, the patientOsvisual acuity of the left eye persisted to absence to light perception.

APLAR-0115

Vena cava superior thrombosis and central nervous system involvement as initial manifestations in a patient with behcets disease

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Introduction: Beh*et's disease (BD) is a vasculitis with recurrent oral and genital aphthous ulcers, erythema nodosum and locomotor system involvement.This presentation reports a 31-year-old male patient diagnosed as BD with central nervous system involvement and accompanied by thrombosis in both vena cava superior and vena jugularis.

Case Report: 31 year old male patient applied to different doctors with complaints of face and neck swelling and headache about 2 month ago, however he did not get any results.The patient declared that he had recurrent oral and once genital aphthous ulcers, erythema nodosum, and acneiform skin lesions, as well as arthralgia nearly about 8 years. Laboratory tests were as follows; sedimentation: 39 mm/h, CRP:8.9 mg/dL. Doppler ultrasonographic image was compatible with acute thrombosis of the right internal jugular vein and the vena cava superior. Angiographic CT of thorax reported collateral vascular structures around the mediastinum, as well as superior vena cava and the right jugular vein thrombosis, the pulmonary artery was reported to be normal (Picture 2). Potential central nervous system involvement was evaluated with cranial angiographic MRI that reported a total of 4 hyperintensity in mm range at the level of centrum semiovale in the supratentorial sections at T2-weighted images and these hyperintensic images were compatible with vasculitis.Pathergy test was positive. The patient was diagnosed with BD according to the clinical, laboratory and radiological findings and treatment with cyclophospamide 1 g/month, corticosteroid 250 mg/3 days (continued by 1 mg/kg/day) and warfarin 5 mg/day was started. At the end of the first month, decrease in the compliants of the patient and normalization of the acute phase reactons were noticed in the control visit. Control Doppler USG showed slight signs of recanalization.

Conclusion: BD may be presented with different clinical manifestations. Thrombosis and/or arterial involvement observed in young men requires the exclusion of BD first of all.

APLAR-0116

Coexistence of systemic sclerosis and sarcoidosis: a case report

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Introduction: Sarcoidosis is a Th1-related multisystem granulomatous disease characterized by lymphadenopathy, skin lesions and various internal organ involvement. Systemic sclerosis is a chronic autoimmune disease characterized by skin thikness and fibrosis of various internal organs and vascular abnormality.

Case Report: 52-year-old female patient was complaining of Raynaud's phenomenon in hand finger joints about 6–7 years and she has not applied to any doctor. 2 years ago, she noticed brown-red color skin lesions on the right pretibial area and visited her Dermatologist, however she could not get any relief. Physical examination revealed telangiectasia on the face, reduction in mouth opening, sclerodactyly and pallor phase of Raynaud's phenomenon..Laboratory tests were as follows; ESR 38 mm/h, C-reactive protein: 3.5 mg/dL, RF was negative. Liver and kidney function tests were normal. Routine urine analysis was normal. Serological tests reported nucleon and homogeneous positive ANA, positive anti-Scl70, normal C3 and C4 complements, and anti-CCP, anti-Ro, anti-La, anti-Sm, anti-ribosomal P antibodies were negative. Serum ACE level was 65 U/L (normal values: 8–52 U/L). Skin biopsy was performed and non-caseating granulomas, granulomatous dermatitis consistent with sarcoidosis was determined.The patient was diagnosed as scleroderma and sarcoidosis according to the clinical, laboratory and histological findings. Therapy with corticosteroid 16 mg/day, hydroxychloroquine 200 mg/day and azathyoprine 150 mg/day was started. It was noticed on the follow-up pulmonary function tests and DLCO test that dyspnea on exercise was decreased and there was a significant regression in skin lesions. Clinical condition of the patient is stable at the moment and outpatient follow-up is continuing.

Conclusion: Coexistence of sarcoidosis with systemic sclerosis is a rare entity. Th1/Th2 paradigm is one of the most important reasons for this entity. Since each of these syndromes can do similar clinical presentation, the differentiation of actual overlap of syndromes is important in predicting prognosis and planning the treatment.

APLAR-0169

Rheumatoid arthritis of the knee with pus discharge that was diagnosed as a septic arthritis: case report

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Rheumatoid arthritis (RA) patient is susceptible to serious infection because of pathobiology of the disease itself, morbid condition and immunosuppressive treatment. Since clinical and laboratory features are resemble, it might be difficult to differentiate between RA relapse and septic arthritis (SA).

45 year-old woman with a 19-year history of RA, has been treated with Tacrolimus and prednisolone, has left knee swelling, redness, pain and recognized two subcutaneal masses at popliteal and lateral lesion of the knee 1 year ago. After then lateral mass was self-opened and the pus was discharged. A initially diagnosis of septic arthritis was established based on high CRP and accumulation of WBC at the home clinic. Several antibiotics were used but inflammation persisted. She consulted us 3 months after onset. Her laboratory data showed that WBC was 12500 and CRP was 6.3 and X-P or MRI showed high destructive change of knee joint, joint swelling, synovitis, and subcutaneal cysts. The pus was yellow and cloudy, the culture of pus was negative. Arthroscope was done and this showed fully synovitis and no bacterial colony was seen in histology. Successively synovectomy in the joint and debridement of subcutaneal cysts were performed. After operation the fistula was closed and local pain, swelling and inflammation were decreased. A diagnosis was established as RA relapse of the knee with fistula. TNF-α inhibitor disappeared her RA related symptoms and made no recurrence.

SA is an orthopedic emergency that can lead to joint destruction and significant morbidity and mortality. Then we must quickly diagnose and treat with proper method. In this case MRI findings (synovitis, no joint effusion, no soft tissue edema) were very useful to distinguish RA relapse and SA.

APLAR-0177

Patient with systemic lupus erythematosus presenting with painless massive ascites

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Presentation with massive ascites is rare in systemic lupus erythematosus(SLE).

A forty-year old woman presented with a 3 months' history of fatigue, weight loss and arthralgia. Swelling of the abdomen had occured one month before admission. On physical examination malar rash, massive painless ascites and decreased respiratory sounds were noted. There was no pretibial edema. The ESR was 51 mm/hour, the leukocyte was 2840 /mm3, lymphocyte 720/mm3, haematocrite 33%, and platelets 182000/mm3. Blood chemistry (including AST, ALT, GGT) and urine analysis were normal. The total protein and albumin levels were 4.7 and 1.8 g/dL, respectively. The serum-ascites albumin difference was lower than 1.1. Cultures remained sterile. There was no atypical cell. ANA and anti-dsDNA were positive. C3 and C4 levels were low. HBsAg, anti-HCV, anticardiolipin IgG, IgM and lupus anticoagulant were all negative. The GFR was 110 mL/min and proteinuria was 168 mg/day. The chest radiogram showed bilateral pleural effusion and echocardiogram revealed minimal pericardial effusion. EF was normal. Abdominal CT showed diffuse ascites. Gynecological examination was unremarkable. The patient was given 40 mg/d methyl prednisolone, 200 mg/d hydroxycloroquine, furosemide, sprinolactone and human albumine. Ascites regressed during the follow up, diuretic treatment and human albumin were discontinued. Due to the persitance of trace proteinuria and low levels of complements, a renal biopsy was performed, which showed class II lupus nephritis. Azathioprine was added. Ascited did not recur during the follow up. On the last outpatient visit, laboratory sudies were normal (total protein/albumin: 7.0 / 3.8 g/dL).

In SLE ascites may develop due to peritoneal involvement and it is usually painful. Painless ascites may also develop in chronic lupus peritonitis, however, it occurs gradually in months. Massive painless ascites developing in a short period of time is rare. This may be due to vascular pooling in the mesenteric vessels.

APLAR-0181

Septic arthritis of the left shoulder and both knees treated by local anesthetic procedure in a rheumatoid arthritis patient with intermittent pneumonia

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Septic arthritis should be diagnosed early and aggressive initiation of treatment is mandatory to prevent cartilage destruction and a subsequent crippling condition. We report a case of a 74-year-old female patient with rheumatoid arthritis, who suffered from bacterial infection of 3 joints(left shoulder and both knees) simultaneously. She had intermittent pneumonia and bleeding tendency. The former made it impossible to apply general anesthesia, and lumbar anesthesia was avoided to prevent epidural hematoma by venous injury. She visited our hospital with a high fever and pain of three joints, after 1 week hospitalization in another institute with repetitive percutaneous aspiration irrigation of the right knee and intravenous cephalosporin infusion. On the day of admission, both knees were irrigated arthroscopically, and the left shoulder was aspirated percutaneously and irrigated. All of these procedures were accomplished by lidocaine local anesthesia. After detection of gram positive cocci from synovial fluid of these three joints, intravenous linezolid with oral rifampicin and trimethoprim/sulfamethoxazole were prescribed for the purpose of infiltration of medicine into the inner region of biofilm, and risk of Health Care*Associated Methicillin-Resistant Staphylococcus aureus which was possible to be infected in former institute. Although the result of the culture told that causative bacteria was Methicilin- Susceptible Staphylococcus aureus, we continued to prescribe the same medicine, considering the possibility of existence of micro-abscess with biofilm and excellent penetrating ability of linezolid into bone, fat and muscle tissue over MIC. Arthroscopy revealed cartilage disappearance of the right knee. But the left knee and the shoulder had only rheumatoid arthritic change, and the cartilage was preserved. After 4 weeks of intoravenous and 6 weeks of oral antibiotic therapy, she could walk with 1crutch and was able to come home. There was no sign of recrudescence of septic arthritis 6 months later.

APLAR-0183

Acute polymyositis associated with severe subcutaneous edema and interstitial lung disease

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Inflammatory myopathy is characterized by symmetrical proximal muscle weakness of insidious onset. Although periorbital edema is a common manifestation of inflammatory myopathy, generalized subcutaneous edema is an uncommon manifestation of inflammatory myopathy. We describe a case of 47-year-old female patient who presented with severe generalized edema, proximal muscle weakness with dyspnea.

A 47-year-old woman admitted for severe generalized edema, dyspnea and proximal muscle weakness for a week. A physical examination revealed erythematous skin lesions with generalized nonpitting edema involving the entire body. Velcro rale was heard at lower lung zones. A neurological examination showed decreased muscle power of grade 4 in her shoulder and pelvic girdles. On laboratory test, muscle enzymes were elevated; creatinine kinase was 12 176 U/L, and myoglobin was >30 000 ng/mL. Her white blood cell count was 11 000/mm^3, erythrocyte sedimentation rate 103 mm/hour, C-reactive protein 6.91 mg/dL. Antinuclear antibody was positive (>1:2560, speckled type), but anti-Jo-1 antibody was negative. On high resolution computer tomography of chest, ground glass opacity with air space consolidation on both lower lung fields was seen. On magnetic resonance imaging of both thighs, diffuse subcutaneous tissue edema with multifocal muscle edema was seen. The diagnosis was confirmed as polymyositis based on the proximal muscles weakness, elevated levels of serum muscle enzymes, and electromyogram showing a myopathic pattern. She was treated with 60 mg/day of oral prednisone after methylprednisolone 1 g/d for 3 days. However, her muscle weakness was continued with esophageal involvement, and muscle enzymes were not decreased. After using intravenous immunoglobulin 2 g/d for 5 days, she was improved gradually in muscle weakness and subcutaneous edema showing decreased muscle enzymes. This case showed unusual features of inflammatory myositis with severe subcutaneous edema involving entire body and gound glass appearance on lower lung field. Conclusively, acute myositis can come with various and atypical symptoms.

APLAR-0206

A case of juvenile systemic lupus erythmatosis with aplastic anemia.

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Introduction: We report a case of systemic lupus erythmatosis with aplastic anemia who responded to combination therapy oral cyclosporine and cyclophosphamide pulse monthly therapy.

Case: 15-year-old girl was diagnosed as juvenile systemic lupus erythmatosis and performed methyl prednisolone pulse therapy and treated with prednisolone (1 mg/kg) and mycophenolate mofetil. As withdrawing of prednisolone, she presented thrombocytopenia instead of normal serum complement level. Thinking of the possibility of drug myelosuppression, we changed mycophenolate mofetil into azathioprine. On the course of prednisolone withdrawing, severe leukocytopenia and thrombocytopenia appeared, then we performed bone marrow aspiration and biopsy that revealed hypocellular marrow. She was diagnosed as aplastic anemia complicated with systemic lupus erythmatosis, and additional methyl prednisolone pulse therapy was performed. We changed azathioprine into cyclosporine. To intensity the immunosuppression therapy to systemic lupus erythmatosis, we introduced cyclophosphamide pulse monthly therapy.

Discussion: Aplastic anemia is a rare feature of systemic lupus erythmatosis. As previously reported, we performed immunosuppression therapy that is equivalent to treatment of systemic lupus erythmatosis. Aplastic anemia should be considered it we experienced systemic lupus erythmatosis patient with pancytopenia that is resistant to several therapy.

APLAR-0225

Bone infarction of talus in a patient with overlap syndrome of systemic sclerosis and Sjogrens syndrome

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Background: Overlap syndrome is defined as an entity that satisfies the diagnostic criteria of at least two connective tissue diseases. Although severe joint pain without the evidence of arthritis sometimes seen in these clinical syndromes, but bone infarction may rarely occur in association with disease of autoimmune connective tissue disease.

Case report: We described a 37-years-old female patient with Sjogren's syndrome and advanced systemic sclerosis (SSc) whose initial examination revealed pulmonary hypertension. After one year irregular corticosteroid therapy, she presented with severe pulsating pain of her left ankle and the distal extremity of left leg. There was no history of trauma or recent infection. After MRI evaluation, she has been diagnosed with bone infarction of left talus. A well-demarcated intramedullary lesion in left talus of high signal intensity on the fat suppressed PD/T2-w sequences is noted. It also showed avascular necrosis of the left tibia.

Discussion: SSc with Sjogren's syndrome are the most common combinations in overlap syndrome and in such cases the main musculoskeletal features are arthralgias and/or arthritis, but bone infarction is rare cause of musculoskeletal pain in patients with SSc or Sjogren's syndrome. Bone infarction is a clinical entity characterized by aseptic osteonecrosis occurring in the metaphysis and diaphysis of long bones, as a result of a compromised artery supply, mainly in the lower limbs. Even though the pathogenesis is not completely understood, it is known that many factors may induce bone ischemia and favour bone necrosis by intraluminal or extraluminal obliteration. For the early detection of medullary bone infarction, MRI appears to be the most sensitive imaging investigation. We should have an awareness of the probability of bone infarction in patients with connective tissue diseases.

APLAR-0233

Systemic sclerosis transformation to systemic lupus erythematosus complicated with lupus nephritis and pulmonary hemorrhage

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We present a rare case of systemic sclerosis with transformation to systemic lupus erythematosus who experienced acute renal failure, high blood pressure and pulmonary hemorrhage. Renal biopsy revealed lupus nephritis, class IV-G (A) rather than systemic renal crisis.

A 34-year-old woman had 7 years history of systemic sclerosis. Her clinical manifestations were Raynaud's phenomenon, proximal scleroderma, sclerodactyly and recurrent ischemic digital ulcers. ANA and anti-Scl-70 Ab were positive. Rapid deterioration of renal function (serum creatinine increased from 0.9 mg to 6.2 mg/dL), high blood pressure 190/130 mmHg, oliguria and lower legs pitting edema were noted. Renal biopsy revealed diffuse glomerulonephritis, endocapillary proliferation, hyaline thrombi/necrosis and cellular crescents, compatible with lupus nephritis, class IV-G (A). Laboratory tests showed WBC 3150/cumm, Hb 9.7 mg/dL, platelet 87000/cumm, low C3/C4 (28.9/3.8 mg/dL) and high titer anti-dsDNA 1956 IU/mL. She received methylprednisolone and cyclophosphamide pulse therapy. Bilateral lower legs edema subsided and renal function improved (serum creatinine declined to 4.2 mg/dL).

Three weeks later, sudden onset of hemoptysis, dyspnea with oxygen desaturation developed. Chest CT scan revealed multifocal ground glass opacity change, compatible with pulmonary hemorrhage. Laboratory tests showed negative anti-cardiolipin Ab, anti-beta2GPI Ab, c-ANCA, p-ANCA and anti-GBM Ab. Immediate plasma exchange, hemodialysis, methylprednisolone and cyclophosphamide pulse therapy were administered. Hemoptysis ceased, dyspnea and oxygen saturation improved. Anti-dsDNA titer decreased to 154 IU/mL.

It is very rare for systemic sclerosis with transformation to systemic lupus erythematosus. In addition to scleroderma renal crisis, overlapping systemic lupus erythematousu with lupus nephritis should be considered one of the differential diagnoses in systemic sclerosis patients with rapid deterioration of renal function.

APLAR-0236

Effective treatment with Rituximab in refractory antineutrophilic cytoplasmic antibody-associated vasculitis in a filipino male

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Background: Antineutrophilic cytoplasmic antibody (ANCA) – associated vasculitis presents as a generalized disease involving the upper and lower respiratory tracts, with necrotizing vasculitis of small and medium-sized blood vessels and necrotizing glomerulonephritis. While the standard regimen of cyclophosphamide and glucocorticoids have improved treatment outcomes, not all patients achieve remission. Rituximab, an anti-CD20 monoclonal antibody, is a promising remission-inducing agent in ANCA-associated vasculitis.

Objective: To present a case of ANCA-associated vasculitis in Filipino male refractory to treatment with cyclophosphamide, who then underwent treatment with rituximab.

Case: A 31-year old Filipino male, non-smoker, with no prior history of tuberculosis, was diagnosed with ANCA-associated vasculitis in October 2011 when he presented with weight loss, recurrent fever, eye redness, hemoptysis, hematuria, arthralgias, maculopapular rash, and positive antineutrophilic cytoplasmic antibodies. He was treated with pulse methylprednisolone 1 g for 3 doses followed by oral prednisone (1 mg/kg/day) and monthly cyclophosphamide 500 mg intravenously for 5 months with initial improvement in hemoptysis, dyspnea, oral ulcers and maculopapular rash. In March 2012, the hemoptysis, maculopapular rash and arthralgias recurred. High resolution CT scan of the chest revealed ground glass opacities, reticulonodular and fibrotic densities, and a cavity at the right lower lobe. Cyclophosphamide intravenous infusions were increased to 1 g every 2 weeks. There were increasing arthralgias, frequent hemoptysis, exertional dyspnea, and a large, necrotizing vasculitic ulcer. Rituximab was given at 325 mg/m^2 of body surface area weekly for four doses. The patient responded dramatically, with resolution of hemoptysis and arthralgia, markedly decreased dyspnea, granulation of the vasculitic ulcer, and resolution of infiltrates on radiographs. Three months after rituximab treatment the vasculitic ulcers has resolved completely. He remains stable on daily prednisone at 5 mg/day.

Conclusion: Rituximab may be effective in ANCA-associated vasculitis refractory to cyclophosphamide, with both clinical and radiographic improvement.

APLAR-0244

Endometrial tuberculosis causing amenorrhea and abnormal uterine bleeding in a lupus patient treated with cyclophosphamide

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Background: Amenorrhea may occur in patients with lupus treated with cyclophosphamide. This is commonly attributed toprimary ovarian failure leading to infertility, a possible complication of cyclophosphamide. Urogenital tuberculosis (TB) can be a rare cause of amenorrhea and infertility in lupus patients.

Objective: To present a case of endometrial TB causing amenorrhea and abnormal uterine bleeding in a patient with lupus nephritis treated with cyclophosphamide.

Case: A 32-year old Filipino female, who was diagnosed with lupus nephritis, was managed with high dose steroid and IV cyclophosphamide. SLE renal flare improved with treatment, but she subsequently developed amenorrhea and vaginal spotting for two months. Symptoms were initially attributed to premature ovarian failure due to cyclophosphamide.

Gynecologic ultrasound examination showed thickened endometrium, and normal ovaries and uterus. Dilatation and curettage was then performed. Histopathology of endometrial curetting revealed chronic granulomatous endometritis with Langhans giant cells. Endometrial tuberculosis (TB) was diagnosed and anti-KochÕs therapy was started. The patient showed a favourable response, with resumption of normal menstruation after only the first month of treatment.

Conclusion: It is important to consider a wide range of differential diagnosis for gynecologic symptoms in lupus patients. Tuberculosis should be considered in areas of high endemicity.

APLAR-0264

A case of bilateral elbow osteoarthritis

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Background: Osteoarthritis (OA) is the most common form of arthritis, and is strongly related to aging. It most commonly affects the knees, hands, feet, hips and spine. Elbow OA is uncommon, presenting in about 2–27% of the population in some studies.

Objective: To present a case of bilateral elbow osteoarthritis with olecranon bursitis.

Case: A 57-year old Filipino male working as a coffin-maker/designer presented with mild dull pain in both elbows, VAS 2/10, of 12 weeks duration, precipitated by repeated flexion-extension of the elbows, and temporarily relieved by rest and intake of NSAIDs. There was also note of soft, nontender, slightly fixed 3 × 3 cm cystic mass at both olecranon processes. Inflammatory markers were taken. X-ray of both elbows revealed spur formation at the coronoid process of both ulnar bones; Enthesophyte formation at the ulnar insertion sites of the triceps brachii bilaterally and; Linear lucencies on the spur with enthesophyte formation on the left. The joint spaces were maintained and no lytic lesions were noted. Upon inquiry of his work history, it was learned that he uses both elbows as a support to prop up the heavy horizontal bars of the coffins he makes. He was diagnosed with Bilateral Elbow OA with Olecranon bursitis at the PGH Rheumatology Clinic and given Celecoxib 200 mg BID for 2 weeks.

Conclusion: Osteoarthritis is a disease involving weight-bearing joints. The elbows are not commonly involved in weight-bearing hence the low incidence of OA in this part of the body. This stresses the importance of taking a good occupational history to be able to have a high index of suspicion in diagnosing the disease. Early and correct diagnosis will lead to proper advice on how to minimize stress on the joints and prevent further joint damage or disability.

APLAR-0281

A case of primary Sjogrens syndrome improved by the treatment of prolactinoma

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Primary SjogrenÖs syndrome (pSS) is an autoimmune disease characterized by dryness in the eyes and mouth due to destruction of the salivary and lacrimal glands. Several cases of prolactinoma have been reported accompanied by systemic lupus erythematosus (SLE). Those studies suggested that prolactin might play a role in the pathogenesis of some rheumatic disease. However, there is no report of prolactinoma with pSS, thus we report the first case of prolactinoma associated with pSS, which is improved by dopaminergic agonist.

We report a 36-year-old woman who developed pSS accompanied by prolactinoma. She visited our hospital with symptoms of dry eye and dry mouth ten years ago. The blood test showed positive results of ANA (1:320, speckeld and cytoplasmic pattern), anti-Ro/SSA, anti-La SSB, and anti thyroglobulin Ab (>4000 IU/mL). The Schirmer test was positive and Tc-99 m pertechnetate salivary scan showed decreased absorption in both parotid glands and submental glands. After 2 years, she suffered from galactorrhea and oligomenorrhea. The blood test showed an increase of prolactin to 221.9 ng/mL (normal range; 4.79–23.3 ng/mL) and sella magnetic resonance imaging revealed a hypodense mass in a pituitary gland. She was additionally diagnosed as prolactinoma and began taking dopaminergic agonist, bromocriptine mesylate. After taking bromocriptine, she felt that dry eye and dry mouth was improved with reduction of prolactin level (3.27 ng/mL). She had stoped taking bromocriptine for 2 weeks by herself, she suffered from severe mouth and eye dryness with re-increase of prolactin (60.57 ng/mL). These symptoms, however, were improved after re-starting of bromocriptine. Now, she has being followed for 6 months taking synthyroid and bromocriptine without recurrence of severe dryness.

APLAR-0282

Differential diagnosis between dermatomyositis and post-polio syndrome in patient with poliomyelitis

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Dermatomyositis(DM) is a rare idiopathic inflammatory myopathy characterized by chronic inflammation of proximal skeletal muscles and typical skin manifestations, resulting in symmetric muscle weakness. We experienced a case of DM in patient with previous poliomyelitis. Fifty three year-old man visited with skin rash and left leg weakness. He had a history of polymyelitis when he was one year old and the power of his left leg was only grade I. Initially, he was diagnosed as having post-polio syndrome (PPS) because of unilateral muscle weakness and pain which had a complication of previous poliomyelitis and the findings of electromyography (EMG). After 4 months with conservative therapy for PPS, bilateral upper arm weakness developed and the skin rash aggravated progressing in whole body. He was diagnosed as having dermatomyositis, based on elevated muscle enzyme levels, typical skin rashes such as GottronÖs papule, heliotrope rash and V sign, MRI finding which showed muscle inflammation, and EMG finding showing muscle disease. He was managed with high-dose steroid and methotrexate, and then the symptoms disappeared and muscle enzyme levels were normalized. When a patient with previous poliomyelitis has newly developed muscle weakness or pain, we should consider other causes other than PPS.

APLAR-0298

A case of a polyarthritis seronegative juvenile idiopathic arthritis patient

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Introduction: Abouthalfof children with polyarticular juvenile rheumatoid arthritis will have evidence of radiographic progression within two years after diagnosis. Newly diagnosed children are at high risk of substantial joint destruction and potential disability, emphasizing the need for prompt treatment.

Case: We report a 12 *year old boy suffered from recurrent pain on his fingers, knees, elbows since 10 months and worsen in 2 days . There was stiffness on his fingers and knees. Sometimes chest pain, dyspneu, tenderness in all part of his bodies, redness on his palmars and plantar feet. He had history of epilepsy . His aunty had rheumatic disease in young age. Had been diagnosed as Juvenile Idiopathic Arthritis for 10 months and treated with methotraxate (mtx) 10–15 mg/m^2/week and methyprednosolone (MP) 0.25 mg/bodyweight/ day for seven months then changed to subcutaneous mtx 20.7 mg/week. Extremities examination revealed tenderness, contracture on both metacarpophalangeal (MCP), proximal interphalank (PIP), metatarsophalangeal (MTP) joints, tenderness and flexi contracture on both of his knees. Tendernes along his legs. Chest examination was normal. Hand radiography revealed osteopenia juxta articular distal interphalank (DIP) and PIP joints. Chest, cervical, thoracal, lumbosacral radiography, echocardiography showed no abnormality. Electroenchephalography (EEG) examination showed low voltage. Laboratory examination revealed haemoglobine 13.1 g/dL, leucocyte 13.050/µL, thrombocyte 327.000/ µL. ESR: 6 mm/hour. Rheumatoid Factor 8 IU/mL, ANA 15.93 units, Anti double stranded-DNA 12.5 IU/mL, hs_CRP <5 mg/L, anti CCP (Cyclic-citrullinated Peptide): <3.0 RU/mL, microalbumin urin <5 mg/L. After treated with mtx 27.5 mg orally/ week, folic acid 1 tablet/week, MP 48 mg/day, hidroxychloroquin 125 mg/12 hours/day, ketorolac every 12 hours, tramadol 1–2 mg/kg BW for 2 weeks, pain, tenderness, and contracture on his hands disappeared, but hand pain and tenderness remain on both of his knees and legs

APLAR-0302

A Case of systemic lupus erythematosus with human immunodeficiency virus infection : a therapeutic problem

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Introduction: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with a wide clinical manifestations. Combined immunodeficiency disease due to HIV infection and autoimmune disease is a very rare find. The main problem in the management of this is the use of immunosuppressants. Giving immunosuppressants provision allowing for the emergence of opportunistic infection.Infection is the leading cause of death due to HIV infection.

Case: 35 years old Balinese female, a merchant, came to Sanglah with complaint of limp bodies from a week before admission, weight loss of about 5 kg, and intermittent fever. We found hair loss, alopecia, malar rash, anemia, and white patches on the tongue. It was found 4 criteria SLE according to the American College of Rheumatology (ACR) in 1997, a clinical malar rash, lymphopenia, anti-dsDNA the (+) and ANA test (+). HIV test results (+) either by ELISA or western blot method. Normal Chest X-ray. She was treated by injection of metilprednisolone 62.5 mg iv every 12 hours. Patients are allowed for outpatient with metylprednisolone tablet 1 mg/kg body weight. A week after the metylprednisolone, the patient developed fever accompanied by cough and phlegm. Thorax photo shown a picture of tuberculosis and sputum smear (AFB) results positive 3 times. She was treated by oral antituberculosis category I. Finally,she was well controlled by 32 mg metylprednisolone tablets, chloroquine and oral antituberculosis drug.

Summary: SLE cases with HIV infection is very rare. SLE diagnosis with HIV infection are also complicated due to the similarity of clinical and laboratory manifestations between them. Giving immunosuppressants should be very careful.

APLAR-0303

Henoch schonlein purpura associated with acute poststreptococcal glomerulonephritis: A case report

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Introduction: Acute poststreptococcal glomerulonephritis (APSGN) is one of the most common renal diseases resulting from a prior infection with group A beta hemolytic streptococcus (GAS). Henoch Schonlein Purpura (HSP) is a systemic disease with frequent renal involvement, characterized by IgA mesangial deposits, its etiology is still remain unknown but several infections have been described as trigger agents including GAS infection. The incidence of APSGN patients simultaneously presenting with HSP are rare and only five patients have been reported.

Case Presentation: We described a 4-year-10-month-old Balinese boy who developed severe proteinuria, hematuria, edema, hypertension and four fold increase of anti streptolysin-O (ASO) supporting APSGN diagnosis. In addition he had low serum levels of complement C3 fraction and normal C4 fraction. During hospitalization he developed non thrombocytopenic palpable purpura with lower limb predominance, abdominal pain and skin biopsy showed

leukocytoclastic vasculitis confirmed the HSP diagnosis. He responded to treament with steroids, ACE inhibitor and diuretic. It remained unclear to our setting whether the course of disease when initial presenting with APSGN followed by HSP or APSGN as a part of HSP.

Conclusion: We reported a case with APSGN and HSP appear concurrently after GAS infection. Either two diseases appear concurrently with respect to their own pathophysiology or it was a single entity remains unclear.

Keywods: APSGN, Henoch Schonlein Purpura, children, anti streptolysin O

APLAR-0319

Neuropsychiatric manifestations in patients with late diagnostic of systemic lupus erythematosus

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Introduction: Neuropsychiatric of systemic lupus erythematosus (NPSLE) manifestations could develop before the diagnosis of SLE. Seizures are one of the most serious neuropsychiatric manifestations of SLE. Here, we report a late diagnostic of SLE came with manifestation of seizure.

Case Report: A 36-years-old married woman presented to the emergency room with first ever generalized seizure. The patient appeared anxious and disorientation. Six month before admission patient had history of loss weight, chronic fever, and oral ulcer. Patient had visited physician but the symptom still persist. We found livedo reticularis on hand and feet. ANA was homogenous and speckled. Anti-dsDNA was elevated. CD4 and CD8 were low and anti HIV tested were negative. Brain CT Scan showed normal. Therefore we diagnosed her as NPSLE. She was given intravenous methylprednisolone pulses in the doses 1 g daily for 3 days and plan to tap down, than we added MMF in the dose of 500 mg twice daily. On the 5th day, her symptoms clinically improved.

Conclusion: We report a successfully treated case of NPSLE manifestation. Seizures are probably one of the most relevant clinical expressions of damage accrual in SLE. They can occur at anytime in the course of SLE and even before the diagnosis of lupus has been made. In fact, up to 11% NPSLE occur before the disease is diagnosed. High dose steroid is the mainstay of treatment in NPSLE.

Key words: Neuropsychiatric of systemic lupus erythematosus, seizure, late diagnostic

APLAR-0323

Ocular toxicity of chloroquine/Hydroxychloroquine:a report of 6 cases from a tertiary rheumatology referral institute from south India

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Introduction: Antimalarials are widely used in the rheumatolog y practice since decades and are known for their safety profile.But chloroquine induced occulotoxicity is one rare complication which needs frequent monitoring.Toxicity ranges from reversible pigmentation changes to irreversible retinopathy early recognition may prevent irrersible damage.Retinal toxicit reported incidence about 0.5% and recent study 4000 patients by Frederick Wolf et.al shown incidence of definitive toxicity is 6.5 per 1000 patients,and possible toxicity is 0.4 per 1000 patients.

Methods/Materials: Patients identified with Chloroquine retipathy during routine screening by ophthalmological evaluation from inpatient case records and outpatient follow up were analyzed. The definite or probable toxicity definitioned as cases with evidence for bull's eye damage on either retinal examination or in the visual field. Possbile cases defined as eye examination records indicating that the patient had any evidence of toxicity but for which drug related retinal changes could not be verified.

Results: Six patients identified as possible cases of chloroquine/hydroxychloroquine retinopathy .Three patients had Systemic lupus erythematosus, three patients had rheumatoid arthritis. All are female, Mean age 46.4 $\pm$ 7.02 years,Mean duration of the underlying disease was 84 $\pm$ 60.71 months, Mean duration of the drug usage 52 $\pm$ 23.9 months, Mean cumulative dose of Hydroxychloroquine 340.6 $\pm$ 68.5 g, one patient used chloroquine (cumulative dose of 97.5 g)followed by hydroxychloroquine. Five patients had Decreased visual acuity. All patients had Retinal pigmentary changes in Fundus examination, two patients had visual field defects. Only one patient had Significant co morbid conditions(Diabetes, but no diabetic retinopathy). None of the patients had severe underlying rheumatologic disease; all patients were having only mild disease activity. No patient was on other ocular toxic drugs.

Conclusions: Ocular toxicity with Chlorooquine is under reported .Toxicity may depends on the cumulative dose of the drug and duration of the drug usage.Early Diagnosis may prevent irreversible damage.

APLAR-0329

Multiple malignancies in a patient with ANCA-associated vasculitis

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Granulomatosis with polyangiitis(GPA) is a rare, systemic autoimmune disease with unknown etiology, characterized by pathologically granulomatous inflammation, systemic necrotizing vasculitis affecting predominantly small vessels. Several studies indicated a link between GPA and cancers and most of cancers reported have been attributed to exposure to immunosuppressive drugs such as cyclophosphamide. Only few reports have been reported about cancers in a patient with GPA after glucocorticoid alone treatment or before administration of immunosuppressive drugs. Thus, here we report a patient who had gasric adenocarcinoma and papillary thyroid cancer (PTC), and myelodysplastic syndrome (MDS) after diagnosis of GPA.

A 69-year-old man who has adenocarcinoma of stomach, papillary thyroid gland, and myelodysplastic syndrome (MDS) after diagnosis with GPA and treatment with glucocorticoid alone. He had been diagnosed with GPA involving large intestinal tract and mesenteric lymph nodes, presenting with abdominal pain and diarrhea. Symptoms were improved after prednisolone alone treatment. One year later, he was readmitted with unexplained anemia during the regular follow up. Esophagogastrofibroscopy was performed and a biopsy showed adenocarcinoma of stomach. He underwent subtotal gastrectomy. After gastric surgery, anemia was not improved. Therefore, bone marrow biopsy was performed and the result was consistent with myelodysplastic syndrome. On PET-CT, hot uptake was observed on left lobe of thyroid gland. The microscopic findings of thyroid biopsy specimens revealed papillary thyroid cancer. He underwent total thyroidectomy and has received outpatient chemotherapy treatment.

APLAR-0330

Calcinosis in Juvenile Dermatomyositis: a case of spontaneous resolution without treatment

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Calcinosis is reported in one third to half of cases of Juvenile Dermatomyositis (JDM) and is usually associated with prolong or inadequately treated disease[1,2]. Management can be difficult. Different treatment options were reported, including Pamidronate, Anti-TNF Inhibitor and surgical intervention, but responses vary. Here we report a case of spontaneous resolution of calcinosis in a JDM patient even without 'conventional' treatment.

PS first presented to us at the age of 7 years old with classical heliotrope rash, Gottron's papules, symmetrical proximal muscle weakness and raised muscle enzymes. Muscle biopsy demonstrated typical histological features of JDM. High dose Prednisolone and subcutaneous Methotrexate were commenced. He showed initial response but then became steroid dependent with recurrence of rash and weakness once the dose of Prednisolone was reduced. Cyclosporin was added in as steroid sparing agent. However his parents decided to stop western medicine and to try alternative therapies three years after the diagnosis. His disease grumbled with persistent skin rash and muscle weakness. He also developed calcinosis in multiple sites after stopping all medicine (Fig 1).

Despite the lack of supervised conventional treatment, his skin and muscle power improved gradually. Calcinosis also showed regression on subsequent follow up (Fig 2). Even it is considered as a damage, our case shows that calcinosis in children can regress if the disease is remitted.

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2. Cummulative organ damage and prognostic factors in juvenile dermatomyositis: a cross-sectional study median 16.8 years after symptom onset. Helga Sanner, Jan-Tore Gran, Ivar Sjaastad, Berit Flato. Rheumatology 2009;48:1541–47.

APLAR-0335

Ischemic cerebral infarction in a child with henoch schonlein purpura

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Background: Henoch schonlein purpura is a systemic vasculitis of small vessels affecting predominantly the skin, gastrointestinal tract, joints, and kidneys. Neurological involvement such ischemic cerebral infarction is uncommon manifestation in this disease.

Objective: To present a case of ischemic cerebral infarction in a child with henoch schonlein purpura.

Case Report: A 9 years old girl was reffered to Soetomo hospital because of abdominal pain, arthralgia, palpable purpura on her lower extremities and buttocks. Laboratory examination revealed increased on leucocyte and normal platelet. The patient was diagnosed as henoch schonlein purpura. Treatment were antibiotic, ibuprofen and oral steroid. She had seizure without fever on 8th days of admission. Ct-scan revealed ischemic cerebral infarction and electroencephalography were normal. There were also recurrent of abdominal pain and purpura that improved after methylprednisolone pulse and azathiophrine were given.

Summary: Neurological involvement such ischemic cerebral infarction in a child with henoch schonlein purpura as a systemic vasculitis disease is uncommon manifestation, but it can involve many organs such as neurologic system.

Keywords: Henoch schonlein purpura, neurological involvement, ischemic cerebral infarction.

APLAR-0376

Spondylitis accompanying to psoriasis – Its treatment with imfliximab

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A 46 year old male case had prevalent psoriasis that did not give response to classical treatments. He also had severe waist ache. In his routine laboratory exanimation; romatoid factor was negative, ESR and CRP were positive. Peripheral joint involvement was not observed in his examination made by the physical treatment and rehabilitation department. According to modified New York criterion, there were inflamatuar waist ache and deficiency in his waist movements. ÖBilateral grade 4 sacroiliitis' was observed in his radiographic examination. With these accompanying findings he was diagnosed spondylitis. Infliximab treatment was started: skin lesions decreased by 50% after after first infusion, after third infusion lesions were completely healed. BASDAI index was; six before infusion, three after first injection and 1.3 at third infusion.

In conclusion, infliximab treatment applied to spondylitis that is similar to ankylosing spondylitis in psoriasis had a beneficial effect both on skin and joint complaints.

APLAR-0378

Systemic lupus erythematosus in the view of erythematotelangiectatic rosacea

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A 45 year old female patient was defining a blushing on her face and sometimes redness attacks. She was also defining photosensitivity. It was learned that she was diagnosed rosacea at various health organizations she applied, she used various treatments and she did not get any response on these treatments. It was learned that she was endeavoring to keep away from triggering factors which were described to her. At the dermatologic examination erythema and telengiectasias were observed at forehead, cheeks and chin. Her eye examination was normal. Because she had photosensitivity, immunologic laboratuar investigation was requested in addition to routine investigations. ANA came positive. The patient had four criterion with respect to ARA criteria. It was consulted with the rheumatology clinique, she was diagnosed Ösystemic lupus erythematosusÖ.

Both rosacea and systemic lupus erythematosus stays in the range of diseases where photosensitivity is observed. In our patient, there were erythema and telengiectasias at cheeks and chin. In her anamnesis photosensitivity and sometimes erythema attacks were present without sun light contact. In this article, a systemic lupus erythematosus case that resembled to *erythematotelangiectatic rosacea* clinically was presented and literature was reviewed.

APLAR-0430

Lupus salpingitis in a young newly diagnosed systemic lupus erythematosus (SLE) patient: A case report

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Introduction: SLE is a multisystem autoimmune disease. We report a rare case of a newly diagnosed SLE patient with manifestation in the reproductive system.

Case: A previously healthy 16 year old female student had recurrent admissions for intolerable lower abdominal pain without bowel and urinary symptoms. She attained menarche at the age of 11, had regular menses cycle and was not sexually active. Ultrasound revealed right ovarian cyst measuring 4 × 3 cm and ascites. HPE from the first laparoscopic cystectomy and appendectomy showed benign right ovary cyst with chronic inflammation over the appendix without vasculitis. Exudative ascites was obtained from the second diagnostic laparoscopy. Infection was excluded. Both the omentum and fallopian tube HPE showed mild to moderate chronic active inflammation with no evidence of granuloma or malignancy. Laboratory investigations revealed pancytopenia with lymphopenia, direct CoombÖs test was 2 + with no evidence of hemolysis. ESR was 23 mm/H, CRP was not raised and both C3, C4 were low. She had bilateral basal pleural effusion and minimal posterior pericardial effusion. Infective screening excluded tuberculosis, hepatitis and retroviral disease. CT abdomen showed left lateral pelvic lymph nodes, largest was 1.2 cm with no other abnormalities. Colonoscopy was normal. Her ANA, anti-RNP, SSA, SSB were positive and anti-Smith Ab was equivocal. Anti-ds DNA and antiphospholipid antibody screen were negative. She was diagnosed to have SLE, started on prednisolone 1 mg/kg/day and her symptoms improved markedly.

Discussion: Female reproductive system involvement is rare in SLE. Only four reported cases were found of which three had biopsy proven ovarian vasculitis, two with both ovary and fallopian tube involvement. In this patient, there was presence of HPE proven right salpingitis although ovarian involvement was inconclusive. Involvement of the female genital tract as a target organ in SLE has been proposed. Although uncommon, this manifestation is possible in SLE patients who are not sexually active but present with symptoms suggestive of pelvic inflammatory disease provided tuberculosis is excluded.

APLAR-0463

Tuberculosis of the knee-a case report

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Extrapulmonary tuberculosis affecting the knee is rare in all form of tuberculosis (0.1–0.3%). This case highlights the uncommon but increasingly recognized presentation of tuberculosis arthritis of the joint. . Ourpatient had a history of chronic gouthy arthritis with recurrent attack. This condition confounded the diagnosis which causes delay in analysis. High level of suspicion and use of rapid and efficient microbiological diagnostic method can decrease the delay of the diagnosis.

A 58-year old man, known diabetic since 1 year, presented with pain and swelling of left knee for 4 months. He also had history of low grade fever for 1 month, and lost of body weight. He was initially treated as a case of acute gouthy artritis and has undergone joint aspiration from the knee in the previous hospital. Physical examination revealed painfull swelling of the left knee and the right ankle. Chest radiograph was normal. Radiograph of the right knee showed swelling of the soft tissue, and there was no evidence of erosion. Data on admission revealed hemoglobin 10.9 mg/dL, white cell count was 11.8 mm^3 with neutrophil of 75.9%. The ESR was 95 mm/hour. Joint fluid aspiration revealed yellow cloudly fluid, white blood cell count of 180 /µl with neuthropil of 83/µl and lymphocyte of 97/µl and no crystal. The immunoserologic test, a polymerase chain reaction, used to detect *Mycobacterium tuberculosis* was positif in the synovial fluid. The patient was given anti-tuberculosis therapy with rifampicin,isoniazid,ethambutol and pyrazinamide. There was gradual resolution of the knee effusion over the next 8 weeks. The patient also had resolution of fever and arthritis symptom, and increase 4 kg of the body weight.

Conclusion: Clinician should suspect TB synovitis in all patient with febril condition and arthritis especially in the diabetic patient, eventhough there is no evidence of pulmonary TB.

APLAR-0501

Peripheral artery occlusion in systemic lupus erythematosus related to antineutrophil cytoplasmic antibodies (ANCA): a case report

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Patients with systemic lupus erythematosus (SLE) may be found a vasculitis, but rarely 15–20% have corelation to an ANCA-associated vasculitis (AAV). The major link is with perinuclear-ANCA (pANCA) but not to cytoplasmic-ANCA (cANCA). Three main AAVs are Churg-Strauss syndome, microscopic polyangitis and Wegener's granulomatosis, all feature are small-vessel vasculitis. SLE and small sized vessel vascullitis are ussualy two distinguishable autoimmune disease. We report patient with overlapping syndrome SLE and AAV. This patient did not include fulfilling the criteria for SLE and AAV.

A 39 years old woman complaint with blackish on her hand and toes fingers since one month ago. It was begining in the fingertips and often feel pain, and they turing blue when exposed to cold, which then turns into a continues blackish, feel throbbing, without a sense of numbness or tingling. It was accompanied with a fever, and concomiant with skin redness and blisters on the upper arm, hand, thigh, calf, and foot, whitout pain, burning, or itching, and not seen pus or smells bad. She was complaint facial flushing when exposed to sun light. Wheight loss of 5 kg in the last 1 month. There were no complaints of hair loss, oral ulcer, or joint pain. No history of smoking, and she never had a miscarriage. Patient using birth control progesteron injection every three months.

Phisical examination found hypertension, gangrene on the fingertip. ABI (Ankle Brachial Index = 1:1), but not found lupus hair, oral ulcers or discoid lesions. Laboratory found anemia, lymphopenia, thrombocytopenia, ESR 89 mm/hour, CRP 29.4 mg/L (N < 10 mg/L), positive ANA with speckeld pola, positive anti dsDNA in ANA panel, positive pANCA, negative HbsAg, and negative anti HCV, and not found hypercoagulability. Doppler USG result was found good flow artery to distal of both legs and hand, there was no sign of critical limb ischemia or occlusion, supporting diagnosis of vasculitis.

Keywords: SLE, vasculitis, ANCA

APLAR-0137

Viral meningitis due to herpes simplex virus type 2 as a complication of treatment with etanercept for ankylosing spondylitis

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Inhibitors of tumor necrosis factor (TNF) *alpha represent important treatment advances in autoimmune disease. As the use of Inhibitors of tumor necrosis factor (TNF) *alpha for autoimmune disease, treatment adverse effects are increasing. Especially they have been associated with an increased risk of serious infections such as bacterial, fungal, viral infections. Viral meningitis is rare to be infected with herpes simplex virus type 2 and a polymerase chain reaction of cerebrospinal fluid allowed us diagnosis. We report the case of a 33-year-old man with viral meningitis due to herpes simplex virus type 2 as a complication of treatment with etanercept for ankylosing spondylitis.

APLAR-0249

Entecavir-associated myopathy: a case report and literature review

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Introduction: Entecavir, a nucleoside analogue (NA), has been shown effective in the treatment of chronic hepatitis B virus infections.

Methods: We first report a case of entecavir-associated myopathy, we also do a literature review and discussed myopathies associated with nucleoside analogues.

Results: A 44-year-old man presented with myalgia and progressive weakness of the lower extremities lasted for three months. He had an HBV infection and had received antiviral treatments with entecavir with a stable dosage of 0.5 mg per day for five years. Laboratory tests showed that serum creatine kinase (CK) levels were significantly elevated. Muscle histopathology demonstrated that the abundance of T lymphocytes infiltrated muscle fibers and there was no expression of HBV surface antigen and HBV core antigen in muscle fibers. Entecavir-associated myopathy was subsequently diagnosed and entecavir was finally withdrawn. Prednisone and other immunosuppressive agents were not recommended. The muscle weakness and laboratory findings improved after conservative care. His symptoms eventually resolved, and his serum CK levels went down rapidly after he stopped entecavir. Four months after he discharged from hospital, his HBV DNA load had increased to 1.1×10^8 copies/mL. He was prescribed antiviral treatment with lamivudine and adefovir. Then his HBV DNA load had decreased to 0.4×10^2 copies/mL. No myalgia or progressive weakness happened. He still takes lamivudine and adeforvir now.

Conclusion: We conducted the literature review on myopathies associated with nucleoside analogues. We found that patients who engage in NA therapy should be closely monitored for muscular side effects. Careful analysis of all clinical features and management techniques can aid an accurate diagnosis of myopathies associated with nucleoside analogues. The prognosis for myopathies associated with nucleoside analogues is good for patients who discontinue use of the relevant medication or switch to another NA.

APLAR-0250

Two times methylprednisolone pulse therapies in SLE patient with idiopathic orbital inflammatory pseudotumor

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Idiopathic orbital inflammatory pseudotumor (IOIP) is a nonspecific, nonneoplastic inflammatory reaction in the orbit which is the third most common cause of inflammation within the orbit. It presents with proptosis, unilateral pain, swelling, diplopia, and reduced vision. Ocular manifestations related to Systemic Lupus Erythematosus (SLE) have an incidence estimated between 3% and 30%. However the two times of methylprednisolone pulse therapies to inflammatory orbital in patients with SLE is extremely rare. We describe a case of IOIP within a background of SLE, and its successful treatment with two times methylprednisolone pulse therapies.

A 19-year-old woman had 1 month diplopia, right-side proptosis, right eyelid swelling, a restriction of movement and a reduction in vision in the right eye with a 4-year history of SLE. She had systemic symptoms like fever, headache, nausea and vomiting.

Ocular examination revealed lateral proptosis, swelling of the right eyelid. Intraocular pressure (IOP) was 12.9 mmHg OD and 12.7 mmHg OS. Magnetic resonance imaging (MRI) revealed a swelling and heterogeneously enhancing right eye muscle. Serum investigation indicated erythrocyte sedimentation rate (ESR) 118 mm/h, C-reactive protein (CRP) 1.33 mg/dL, serum ferritin 333.6 ng/mL, antinuclear antibodies (ANA) 1:320, double-stranded-DNA (dsDNA) 40 U/mL. A presumptive diagnosis of IOIP was made and the patient was treated with intravenous methylprednisolone (500 mg/day for 3 days). Her symptoms improved immediately, and steroid was gradually tapered. One week later, right-side proptosis, swelling appeared again. The patient was treated with intravenous methylprednisolone (500 mg/day for 3 days) second time. She showed rapid improvement in all ocular signs and symptoms. The ESR dropped to 7 mm/h and the CRP decreased to 0.247 mg/dL. In conclusion, IOIP in a patient with SEL is rare and presents a diagnostic dilemma as well as therapeutic challenge. In our case, intravenous methylprednisolone appears to be effective.