Autoimmunities in Patients Hyper IgM

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Introduction

Hyper-immunoglobulin M (HIGM) syndrome or class switch recombination defect (CSRD) is a rare inherited type of primary immunodeficiencies (PIDs), which is characterized by normal or elevated serum concentration of IgM, and absent or decreased IgG, IgE, and IgA serum levels.

Defects in class switch recombination, B cell signaling, and somatic hyper mutations (SHM) processes could be associated with HIGM. Several genes mutations have been identified to be implicated to the HiGM phenotype, including cluster of differentiation 40 ligand (*CD40L*), nuclear Factor-Kappa-B essential modulator (*NEMO/IKKγ*), *CD40*, and activation-induced cytidine deaminase (*AICDA*), *uracil-DNA glycosylase (UNG), inhibitor of kappa light chain gene enhancer in B cells, alpha (IκBα),* nuclear factor kappa-B subunit 1 (NKFB1), ataxia telangiectasia mutated (ATM), post meiotic segregation increased 2 (PMS2), MutS Homolog 6 (MSH6), MutS Homolog 2 (MSH2) and INO80.

HIGM syndrome can be inherited either as X-linked (X-HIGM) or autosomal trait. CD40L and NEMO defects are manifested in form of X-HIGM, while AICDA, UNG and CD40 deficiencies have an autosomal inheritance pattern.

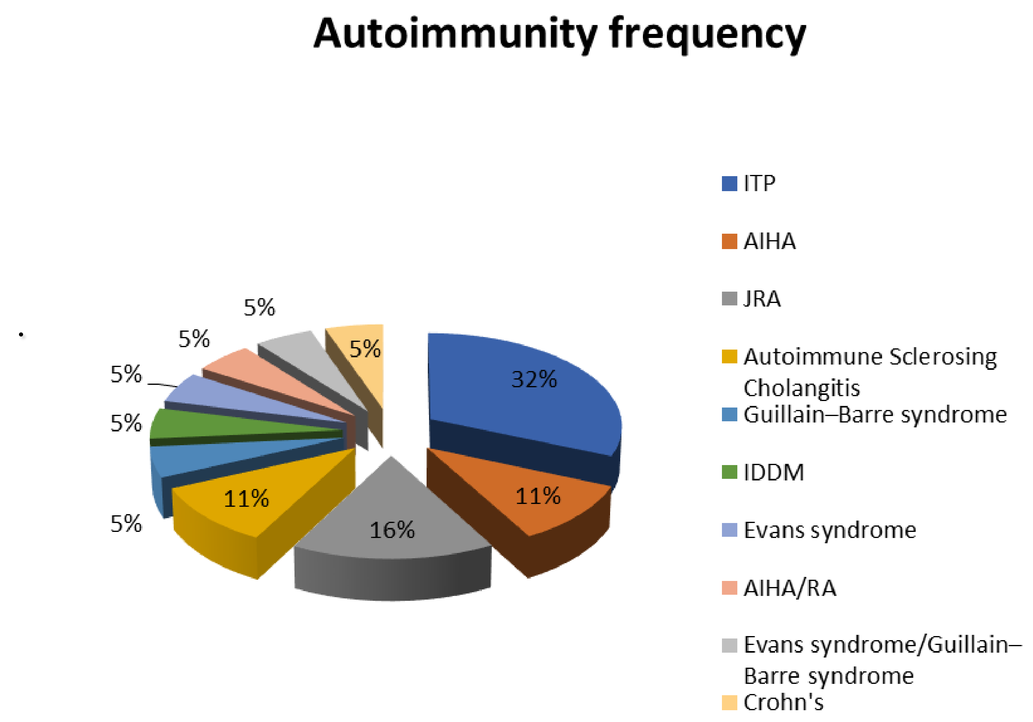
Accordingly, this study was conducted to assess demographic records, clinical presentations, and laboratory data of HIGM syndrome patients with or without autoimmune diseases.

Methods

Clinical features and immunological data were collected from the 79 Iranian HIGM patients' medical records diagnosed in Children's Medical Center in Iran. To compare clinical records and laboratory data, all HIGM patients were classified into two different groups of patients with autoimmune disease and patients without autoimmune diseases.

Results

A total of 79 patients (60 male and 19 female) with median (IQR) age at the time of the study of 12 (6-22.45**).** Forty-seven (59.5%) of the patients were born to consanguineous families. The positive family history of primary immunodeficiency was observed in 19 (24.1%) patients**.** The most common clinical manifestation among HIGM patients was Respiratory tract infection (78.5%). Autoimmunity diseases were seen in 19 patients (23.75% , 3 females and 16 males).
The most common autoimmune presentations among HIGM patients were ITP (32%), juvenile rheumatoid arthritis (16%) , AIHA (11%) and Sclerosing cholangitis (11%), Guillain-Barré syndrome, Evans syndrome, diabetes mellitus, chrohn's disease



Conclusions

management of autoimmunity in patients with PID requires special considerations because dysregulations and dysfunctions of the immune system along with persistent inflammation impair the process of diagnosis and treatment.

Reference

1.Yazdani, R., et al., *The hyper IgM syndromes: Epidemiology, pathogenesis, clinical manifestations, diagnosis and management.* 2018.
2. Abolhassani, H., et al., *Clinical implications of systematic phenotyping and exome sequencing in patients with primary antibody deficiency.* 2019. **21**(1): p. 243.