ASSOCIATION OF IP6K3 GENE SNP rs791903 AND HASHIMOTO'S THYROIDITIS IN A COHORT OF EGYPTIAN PATIENTS

Salah Ahmed Marzouk, Eman Saad Nassar, *Tamer Mohamed Abdelhamid El-Sherbiny, Hassan Ahmed Bachu

Department of Clinical and Chemical Pathology, *Department of Internal Medicine,
Faculty of Medicine, Alexandria University

Introduction

Hashimoto's thyroiditis (HT) is an autoimmune thyroid disorder (AITD) characterized by chronic lymphocytes infiltration and proliferation in the thyroid gland resulting in progressive damage of the gland with release of thyroid peroxidase and thyroglobulin immunoglobulin. Etiology of HT is multifactorial and still unclear. However, the probability of developing HT has both environmental and genetic influence with the latter been more prominent. The study on pathogenetic mechanics has revealed various genes involved in development of HT, such as those coding the Human Leukocyte Antigen (HLA) complex; commonly, HLA-B* 46:01, HLA-A* 02:07 and HLA-DRB4. There is emerging evidence on the role of single nucleotide polymorphisms (SNPs) in the predisposition to HT. A genome-wide association study (GWAS) done on Croatian population found rs791903 inside inositol hexakisphosphate kinase 3 (IP6K3) gene as a candidate for HT predisposition in caucasian population. There exist a few studies done on this gene in other nationalities besides Caucasians.

Aim of the work

The aim of this study is to investigate the association of IP6K3 gene SNPs variant rs791903 in Hashimoto's thyroiditis in a cohort of Egyptian subjects.

Subjects and Methodology

This is a cross-sectional study carried out in outpatient clinic of the Endocrine Clinic of Alexandria Main university hospital. It included 50 patients diagnosed with HT on follow-up and 50 healthy subjects who were matched in both sex and age. Participants below 18 years of age, with active diagnosis of other autoimmune disease or any cancer, and those on treatment like radiotherapy, chemotherapy or glucocorticoids were excluded from this study.

Informed consent taken from all participants enrolled in the study. A complete medical history and clinical examination was done. Blood samples for routine laboratory investigation such as thyroid function test; TSH, free T3,T4, anti- TPO/ anti-Tg as well as for lipid profile were taken from patients with HT. rs791903 polymorphism genotyping was done using TaqMan assay Real-Time PCR assay.

Results

There was a statistically significant difference in genotype distribution of rs791903 (IP6K3 gene) in HT cases than in Healthy control group (p=.012). There was an increased frequency of recessive homozygous (CC) in HT case; however, there were no significant difference in the allele distribution between the two study groups. We also observed a statistically significant difference in serum levels of anti-TPO in HT cases (p=.013) with an increased odd ratio of high serum level in the presence of CC genotype (OR = 4.947, 95% CI, p=.0189).

Conclusion

This study showed that there is a genotypic association between IP6K3 rs791930 recessive variant (CC) and occurrence of HT together with high anti-TPO antibodies. The location of IP6K3 gene on short arm of chromosome 6, near major histocompatibility complex (MHC) has been previously associated with with other autoimmune disorders such as rheumatoid arthritis, which is common in HT patients and Graves' disease pointing to the high candidacy of this gene in development of HT and autoimmunity.