Analysis of chosen polymorphisms rs2476601 A/G - PTPN22, rs1990760 C/T - IFIH1, rs179247 A/G - TSHR in pathogenesis of autoimmune Thyroid diseases in children

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Abstract

Introduction: Autoimmune Thyroid diseases are multi-factorial diseases with a genetic susceptibility and environmental factors. A potential role of the protein tyrosine phosphatase non-receptor type 22(PTPN22) gene, the interferon induced helicase domain 1 (IFIH1) gene, the Thyroid-stimulating hormone receptor (TSH-R) gene polymorphisms on autoimmune Thyroid diseases(AITDs) in children has not been established equivocally yet.

The underlying reason for reaction diseases is that the loss of immune tolerance to tissue-specific antigenic peptides that results in immunologic response directed against one's own body's cells. Still not fully understood, complex immune mechanisms together with the dysfunction of the immune system may be concerned within the autoimmune diseases pathological process. Among the foremost common chronic autoimmune endocrine disorders in kids, there are autoimmune thyroid diseases (AITDs) that include Graves' disease (GD) and Hashimoto's thyroiditis (HT) further as kind sort diabetes (T1D). In kids with autoimmune thyroiditis immune reactions are directed against the cells of the thyroid. In GD the thyrotrophin receptor (TSH-R) is activated with antibodies inflicting the over activity of the thyroid gland, whereas in HT body substance and cell-mediated thyroid injury end up in the destruction of thyroid cells and hypothyroidism as a consequence. In diabetic patients, an inappropriate immune response ends up in auto reactive T-cell infiltration and production of tissue-specific autoantibodies that cause the destruction and dysfunction of the hypoglycemic agent secreting pancreatic beta cells and hypoglycemic agent deficiency. The mechanisms resulting in the development of those diseases remain unknown, but various information indicates that except for the environmental factors there's a powerful genetic susceptibility to the response diseases. The connectedness of genetic factors is obvious from the agglomeration of AITDs or T1D among families, especially monozygotic and dizygotic twins. Several genes could be concerned within the modulation of the system and a few of them were recently found to influence response endocrine disorders development. Moreover, recent studies have incontestable that some genetic risk factors for pathology square measure shared between diseases, causative to the event of quite one autoimmune disease. Current publications showed an association between response diseases and body 10p15 region for IL2RA (interleukin 2 receptor-0), more than 2q33 region for CTLA-4 (cytotoxic T-lymphocyte antigen-4), and body 2q24 region for IFIH1 (interferon elicited with helicase C domain 1). The foremost frequent variety of human ordering variation is single ester polymorphisms (SNPs) providing powerful tools for a range of medical genetic studies. though bound polymorphic variants of genes cryptography IL2AR, CTLA-4, or IFIH1 are reportable to implicate T1D and AITDs development in adults, there square measure solely few studies that specialize in kids. Interleukin 2 (IL2) could be a lymphocyte protein taking part in a crucial role in modulation of immune physiological condition as a necessary self-tolerance regulator. Its action is mediated by a quaternary receptor signal advanced (IL2R) containing β, γ, and atypical receptors. The alpha subunit of the IL2 receptor, IL2Rα (also called CD25), encoded by the interleukin 2 receptor β cistron (IL2RA), plays a key role in mediating lymphokine 2 immunoregulatory operate. The expression of IL2RA has been represented at high levels on the surface of the regenerative T cells (Tregs), a population of T cells with a capability to inhibit auto reactive T cells. Additional studies indicated IL2RA's essential role in sensitizing lymph cells for elicited death that's crucial for his or her operate as a suppressor for T cell immune responses to auto-, alloantigens, further as tumor antigens and antigens account from pathogens. SNPs of genes influencing Treg to operate, like IL2RA, might cause associate degree accumulated risk of disease.

Aim: To estimate the association of polymorphisms of protein tyrosine phosphatase non-receptor type 22 genes, the interferon induced helicase domain 1 gene, Thyroid-stimulating hormone receptor gene with the predisposition to Graves' disease (GD) and Hashimoto's Thyroiditis (HT) in children.

Methods: The study was performed in 142 patients with GD, 57 with HT and 160 healthy volunteers. The three single nucleotide polymorphisms (SNPs): rs2476601 - PTPN22 in the protein tyrosine phosphatase non-receptor type 22 gene, rs1990760 - IFIH1 in the interferon induced helicase domain 1 gene, rs179247 - TSHR in the Thyroid-stimulating hormone receptor gene were genotyped by Taq-Man SNP genotyping assay using the real-time PCR. Furthermore, the interaction between rs1990760, rs2476601, rs179247 polymorphisms and the status of thyroglobulin antibody (TgAb), Thyroid peroxidase antibody (TPOAb) and TSH receptor antibody (TRAb) were analyzed.

Results: rs2476601: Our study revealed that rs2476601-A alleles were more frequent (18% in men and 20% in women) in GD patients in comparison to healthy subjects (11% in men and 10% in women). P-value=0.009 with OR=2.13 and 95% confidence interval for OR: 1.2–4.0, what means that risk for development of GD is over two times higher for A allele in comparison to G allele. Moreover rs2476601 A alleles were more frequent (25% in men and 21% in women) in HT patients in comparison to healthy subjects (11% in men and 10% in women). P-value=0.008 with OR=2.48 and 95% confidence interval for OR: 1.3–6.0, what means that risk for development of HT is two and a half times higher for A allele in comparison to G allele.

rs1990760: Rs1990760 T alleles were more frequent in GD male patients in comparison to healthy males (69% vs. 42%). P-value=0.003 with OR=3.00 and 95% confidence interval for OR: 1.5–6.2, what means that
risk for development of GD is three times higher for T allele in comparison to C allele, when considering male group. In case of HT patients rs1990760 T alleles were also more frequent in males compared to healthy subjects (85% vs. 42%). P-value=0.086 with OR=2.47 and 95% confidence interval for OR: 0.9–7.5, what means that risk for development of HT is nearly two and a half times higher for T allele in comparison to C allele. Results for female group were non-significant from the statistical point of view, hence are not discussed here.

rs179247: Our study revealed that rs179247 A alleles were more frequent (47% both in men and women) in GD patients in comparison to healthy subjects (37% in men and 38% in women). P-value=0.039 with OR=1.51 and 95% confidence interval for OR: 1.0–2.3, what means that risk for development of GD is over two times higher for A allele in comparison to G allele.

Conclusions: rs2476601: A/G polymorphism in protein tyrosine phosphatase non-receptor type 22 gene could contribute to development of AITDs in children and an allele is the main risk factor. rs1990760: C/T polymorphism in the interferon induced helicase domain 1 gene could contribute to development of AITDs in children and T allele is the main risk factor. rs179247: A/G polymorphism in Thyroid-stimulating hormone receptor gene could contribute to development of AITDs in children and an allele is the main risk factor.

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