Association of CTLA4, PADI4 and FTO polymorphisms with autoimmune thyroid diseases in male children

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OBJECTIVES

To identify the association between polymorphisms of CTLA4, PADI4 and FTO genes and Graves' disease (GD) and Hashimoto's thyroiditis (HT) prognosis in male children.

METHODS

The study was performed in 145 patients with GD, 57 with HT and 160 healthy volunteers. The three single nucleotide polymorphisms (SNPs): rs231775 – CTLA4, rs1748033 – PADI4 and rs6499640 - FTO were genotyped by TaqMan SNP genotyping assay using the real-time PCR.

RESULTS

Distribution of genotypes and alleles: rs6499640 - FTO in GD and controls

Group	Genotype/Allele	All	Male		Female
GD	A/A	51 (36%)	15 (45%)		36 (34%)
	A/G	74 (53%)	17 (52%)		57 (53%)
	G/G	15 (11%)	1 (3%)		14 (13%)
	A	176 (63%)	47 (71%)	*p=0.044 OR=1.95*	129 (60%)
	G	104 (37%)	19 (29%)		85 (40%)
Controls	A/A	23 (29%)	14 (27%)		9 (32%)
	A/G	47 (59%)	30 (58%)		17 (61%)
	G/G	10 (13%)	8 (15%)		2 (7%)
	A	93 (58%)	58 (56%)		35 (63%)
	G	67 (42%)	46 (44%)		21 (38%)

Rs6499640 A alleles were more frequent in GD male patients in comparison to healthy males (71% vs 56%).

A/A genotype was identified in 45% of GD male patients, whereas in healthy males only 27% was identified as a A/A genotype.

OR=1.95 means that risk for development of GD is 1.95 times higher for a A allele in comparison to a G allele.

Distribution of genotypes and alleles: rs231775 - CTLA4 in HT and controls

Group	Genotype/Allele	All	Male		Female
HT	A/A	24 (42%)	4 (40%)		20 (43%)
	A/G	19 (33%)	1 (10%)		18 (38%)
	G/G	14 (25%)	5 (50%)		9 (19%)
	A	67 (59%)	9 (45%)		58 (62%)
	G	47 (41%)	11 (55%)	*p=0.008 OR=2.90*	36 (38%)
Controls	A/A	25 (31%)	17 (33%)		8 (28%)
	A/G	44 (54%)	28 (54%)		16 (55%)
	G/G	12 (15%)	7 (13%)		5 (17%)
	A	94 (58%)	62 (60%)		32 (55%)
	G	68 (42%)	42 (40%)		26 (45%)

Rs231775 G alleles were more frequent in HT male patients in comparison to healthy males (55% vs 40%).

G/G genotype was identified in 50% of HT male patients, whereas in healthy males only 13% was identified as a G/G genotype.

OR=2.90 means that risk for development of HT is 2.90 times higher for a G allele in comparison to a A allele.

Distribution of genotypes and alleles: rs1748033 - PADI4 in HT and controls

Group	Genotype/Allele	All	Male		Female
HT	C/C	34 (67%)	16 (89%)		20 (62%)
	C/T	10 (20%)	0 (0%)		7 (24%)
	T/T	7 (14%)	3 (11%)		5 (14%)
	C	78 (76%)	32 (89%)	*p=0.032 OR=3.40*	47 (74%)
	T	24 (24%)	6 (11%)		17 (26%)
Controls	C/C	39 (51%)	23 (48%)		16 (55%)
	C/T	29 (38%)	20 (42%)		9 (31%)
	T/T	9 (12%)	5 (10%)		4 (14%)
	C	107 (69%)	66 (69%)		41 (71%)
	T	47 (31%)	30 (31%)		17 (29%)

Rs1748033 C alleles were more frequent in HT male patients in comparison to healthy males (89% vs 69%).

C/C genotype was identified in 89% of GD male patients, whereas in healthy males only 48% was identified as a C/C genotype.

OR=3.40 means that risk for development of GD is 3.40 times higher for a C allele in comparison to a G allele.

CONCLUSIONS

- Rs6499640 A/G polymorphism in FTO gene could contribute to development of Graves' disease in boys and A allele is the main risk factor.
- Rs231775 A/G polymorphism in CTLA4 gene could contribute to development of Hashimoto's thyroiditis in boys and G allele is the main risk factor.
- Rs1748033 C/T polymorphism in PADI4 gene could contribute to development of Hashimoto's thyroiditis in boys and C allele is the main risk factor.

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