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Clin Endocrinol (Oxf). 2019 Feb;90(2):320-327. doi: 10.1111/cen.13887. Epub 2018 Nov 15.

Paediatric-onset and adult-onset Graves' disease share multiple genetic risk factors.

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Abstract

BACKGROUND: Graves' disease (GD) is an autoimmune thyroid disease (AITD) with a peak incidence between 30 and 50 years of age. Although children and adolescents may also develop the disease, the genetic background of paediatric-onset GD (POGD) remains largely unknown. Here, we looked for similarities and differences in the genetic risk factors for POGD and adult-onset GD (AOGD) as well as for variants associated with age of GD onset.

MATERIALS AND METHODS: A total of 1267 GD patients and 1054 healthy controls were included in the study. Allele frequencies of 40 established and suggested GD/AITD genetic risk variants (39 SNPs and HLA-DRB1*03) were compared between POGD (N = 179), AOGD (N = 1088) and healthy controls. Subsequently, multiple linear regression was used to explore the relationship between age of GD onset and genotype for each locus.

RESULTS: We identified six POGD risk loci, all of them were also strongly associated with AOGD. Although for some of the analysed variants, including HCP5 (rs3094228), PRICKLE1 (rs4768412)

and SCGB3A2 (rs1368408), allele frequencies differed nominally between POGD and AOGD patients, these differences were not significant after applying multiple testing correction (P_{cor} = 0.05/40 = 1.25 × 10^{-3}). Regression analysis showed that patients with higher number of HCP5 risk alleles tend to have a significantly earlier onset of GD (P = 6.9 × 10^{-5}).

CONCLUSIONS: The results of our study revealed that POGD and AOGD share multiple common genetic risk variants. Moreover, we demonstrated for the first time that HCP5 polymorphism is associated with an earlier age of GD onset in a dose-dependent manner.

KEYWORDS: Graves' disease; HCP5; autoimmunity; children; genetics; single nucleotide polymorphism; thyroid

PMID: 30358895 DOI: 10.1111/cen.13887

Grant support

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