

Risk of other autoimmune diseases increased in people with Graves' disease or Hashimoto's thyroiditis relative to the general UK population

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Commentary on: **Boelaert K, Newby PR, Simmonds MJ, et al.** Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. *Am J Med* 2010;**123**:183.e1–9.

Autoimmune thyroid disease, including Grave's disease and Hashimoto's thyroiditis, is known to segregate within families presumably due to genetic factors.¹ Additionally, there is evidence that individuals with autoimmune thyroid disease are predisposed to other autoimmune diseases though historically this has not been well quantified.²

In this study, Boelaert and colleagues performed a cross-sectional analysis of a multicentre cohort of patients with autoimmune thyroid disease to determine the prevalence of other autoimmune diseases within this population, as well as parental history of thyroid disorders. The cohort consisted of 3286 Caucasian patients seen in UK hospital thyroid clinics. Of these, 2791 had Grave's disease and the remaining 495 had Hashimoto's thyroiditis. The authors also calculated the RR of other autoimmune diseases in this group by comparing to prevalence estimates for these diseases in the general UK population based on aggregated data from a number of other studies.

The study found that a substantial proportion of these participants with autoimmune thyroid disease had another coexisting autoimmune disease: 9.67% for those with Grave's disease and 14.3% for those with Hashimoto's thyroiditis. The most common coexisting autoimmune disease was rheumatoid arthritis followed by vitiligo, pernicious anaemia, type 1 diabetes, celiac disease, inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis and Addison's disease. The RRs for many of these were quite high and were particularly striking for some of the rare autoimmune diseases, presumably due in part to the rarity of these diseases in the general population. The study participants recalled a high prevalence of autoimmune thyroid disease, as well as other autoimmune diseases in their parents.

This study is a useful addition to the literature but, as with any investigation, it does have some limitations as explained below.

The sample population

The fact that the sample population consisted entirely of Caucasian participants limits our ability to generalise these data to other ethnic groups. It is also likely that the study sample was affected by selection bias since, as the authors' discussed, the participants were drawn from hospital-based thyroid specialty

clinics. The patients in these clinics may have had their thyroid disease discovered during evaluation for other autoimmune diseases resulting in referral to these thyroid clinics. This could have led to an overestimation of the prevalence of these diseases. One consequence of the method of sample selection was that although Hashimoto's thyroiditis is more common than Grave's disease in the general population, the study sample was heavily weighted toward Grave's. The authors address this issue by conducting all analyses separately for Grave's and Hashimoto's, but this highlights the fact that the sample size for those with Hashimoto's was fairly small and quite small for males.

Other methodologic considerations

The mean age at enrolment for participants with Grave's disease and Hashimoto's thyroiditis was approximately 47 years old. This has important implications for the prevalence estimates since some of the autoimmune diseases examined tend to occur early in life (ie, type 1 diabetes), while others tend to occur later (ie, rheumatoid arthritis and pernicious anaemia). It is likely that the reported prevalence of rheumatoid arthritis and other late-onset diseases in this cross-sectional analysis underestimates the lifetime risk of developing these problems in patients with autoimmune thyroid disease. This possibility was mentioned by the authors in their discussion, but one wonders if they might have been able to shed more light by performing a stratified-by-age analysis, particularly in the Grave's disease cohort which appears to have had a large enough sample size.

On the other hand, the reported RRs may have been exaggerated by limitations in the general population data extracted from other studies, which may under-report the prevalence of many of these autoimmune diseases. This appears to be the case in particular for the general population prevalence of autoimmune thyroid disease itself, which the author's report to be 0.65% for Grave's disease and 0.80% for Hashimoto's disease. These are much lower than reported in some population studies, particularly when 'sub-clinical' hypo- and hyperthyroidism are included.^{3 4} Additionally, it is not clear that the authors used statistical techniques to control for differences in age and other factors when comparing to general population estimates.

Conclusion

This study reinforces existing data which suggest that autoimmune thyroid disease demonstrates strong familial association and is associated with other autoimmune diseases. The actual reported prevalence and RR values should be viewed as estimates which are subjected to a number of methodologic limitations and lack generalisability to non-Caucasian populations. Nonetheless, it reinforces the fact that clinicians must be vigilant to the possibility of other autoimmune diseases, including rheumatoid arthritis, celiac disease and pernicious anaemia, existing or developing in their patients with autoimmune thyroid disease.

Competing interests None.

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