RESPONSE TO COMMENT ON MÄKIMATTILA ET AL.

Every Fifth Individual With Type 1 Diabetes Suffers From an Additional Autoimmune Disease: A Finnish Nationwide Study. Diabetes Care 2020;43:1041–1047

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We thank Bellastella et al. (1) for their interest in our study (2) on autoimmune diseases (ADs) in individuals with type 1 diabetes (T1D). We also thank them for bringing our attention to their observation of similar prevalence rates of additional ADs in an Italian cohort of individuals with T1D.

Bellastella et al. found that 18% of their young cohort had at least one additional AD compared with 22.8% in our older cohort. They also reported a considerably higher prevalence of two additional ADs, 13% vs. 3%, and concluded that the younger age and shorter diabetes duration in their cohort might explain the differences.

We agree that age might explain the diverging results. However, as we stated in our article, older age enables detection of accumulating ADs, but an age difference also inevitably results in a birth cohort effect. Considering that the age of their cohort was 28.6 ± 9.9 years (mean ± SD) compared with 51.5 ± 11.8 years in ours, their cohort reflects a 20-years-younger birth cohort. As the incidence rates of ADs have risen (3), stronger clustering of ADs might be found in more recent birth cohorts similar to that seen in the one of Bellastella et al.

In addition, there might be differences due to the age at onset of diabetes. The age at onset in our study was below 40 years, while the cohort of Bellastella et al. included only childhood-onset T1D. Therefore, we reconstructed a subsample from our Finnish Diabetic Nephropathy (FinnDiane) Study population mimicking their study: childhood-onset diabetes and birth year 1984 or later resulting in a mean age of 28.5 years ($n = 130$). In this subsample, the proportion of additional ADs was 19.2%, close to that of the Italian cohort. However, the proportion of two additional ADs was low (2.3%), similar to that of our entire FinnDiane cohort.

Interestingly, the presence of any kind of thyroidism was 16% in the young Italian cohort (1), whereas in our older cohort, 18.1% had hypothyroidism and 2.4% had hyperthyroidism. Of note, we found a linear relationship between the age of diabetes onset (1.7% by year) and age (1.3% by year) for hypothyreosis but not for hyperthyreosis (2).

In general, greater risk of an AD in individuals with T1D is conferred by female sex, older age, and longer duration of diabetes (2,4). However, the age at onset and peak incidence varies depending on the AD. The peak incidence of thyroid autoimmunity in the young occurs during puberty, while in adults the risk is the highest in middle-aged women. In children with genetic risk of T1D, thyroid autoantibodies peak around puberty, whereas in children with T1D, thyroid dysfunction may be present at the diagnosis of T1D or after several decades (5). Taken together, our findings and those of Bellastella et al. together with previous data suggest that thyroid and pancreatic autoimmunity may have different environmental and genetic triggers. In conclusion, we agree with Bellastella et al. that individuals with T1D, or those with genetic risk of T1D, should be screened throughout life for subclinical and clinical ADs.

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References

1. Bellastella G, Maiorino MI, Esposito K. Comment on Mäkimattila et al. Every fifth individual with type 1 diabetes suffers from an additional autoimmune disease: a Finnish nationwide study Diabetes Care 2020;43:1041–1047 (Letter). Diabetes Care 2020;43:e105. DOI: 10.2337/dc20-0565

2. Mäkimattila S, Harjutsalo V, Forsblom C, Groop P-H; FinnDiane Study Group. Every fifth individual with type 1 diabetes suffers from an additional autoimmune disease: a Finnish nationwide study. Diabetes Care 2020;43:1041–1047

3. Lerner A, Jeremias P, Matthias T. The world incidence and prevalence of autoimmune diseases is increasing. International Journal of Celiac Disease 2015;3:151–155

4. Warncke K, Fröhlich-Reiterer EE, Thon A, Hofer SE, Wiemann D, Holl RW; DPV Initiative of the German Working Group for Pediatric Diabetology; German BMBF Competence Network for Diabetes Mellitus. Polyendocrinopathy in children, adolescents, and young adults with type 1 diabetes: a multicenter analysis of 28,671 patients from the German/Austrian DPV-Wiss database. Diabetes Care 2010;33:2010–2012

5. Kordonouri O, Hartmann R, Deiss D, Wilms M, Grüters-Kieslich A. Natural course of autoimmune thyroiditis in type 1 diabetes: association with gender, age, diabetes duration, and puberty. Arch Dis Child 2005;90:411–414