

Autoimmune thyroid disease in children and adolescents with type 1 diabetes mellitus in Northwest Iran

To the Editor

I read with interest the article by Shiva and Behbahan¹ on autoimmune thyroid disease (ATD) in children and adolescents with type 1 diabetes mellitus (T1DM) in Northwest Iran. Epidemiological data have supported a shared genetic susceptibility to ATD and T1DM. Both diseases frequently occur within the same family, and in the same individual.² I have 2 comments considering the aforementioned study.

First, a contradiction exists considering the insignificant correlation of anti-thyroid markers with thyroid stimulating hormone (TSH) in the study and recommendations presented by the authors. The authors stated that in patients with ATD (seropositive for at least one antibody N=21), the mean serum TSH levels were 4.3 ± 3.8 μ IU/ml, and in patients without ATD (seropositive for both antibodies, N=155), the mean serum TSH levels were 2.9 ± 2 μ IU/ml ($p=0.103$), indicating that TSH level is not significantly higher in T1DM patients who are seropositive for ATD compared with seronegative ones. The authors also stated that there was no significant difference ($p=0.422$) between mean serum TSH levels of seropositive patients for both antibodies (4.1 ± 3.5 μ IU/ml) and those seropositive for only one antibody (3.1 ± 1.4 μ IU/ml). Despite that, the authors recommended serum TSH in those proved seropositive especially for both anti-thyroid peroxidase (a-TPO) and anti-thyroglobulin (a-Tg). Initiation of a thyroid autoimmunity manifested by proliferation of anti-thyroid antibodies is not necessarily accompanied by simultaneously elevated TSH and reduced thyroxin levels. It needs a considerable time before full-blown hypothyroidism is biochemically documented. In a recent Croatian study,³ the prevalence of hypothyroidism in diabetic patients with elevated serum thyroid antibodies was 52.2%. There were no diabetic patients who developed hypothyroidism in the absence of thyroid antibodies. Cumulative incidence of hypothyroidism in diabetic patients after 3 years from the moment of thyroid antibodies appearance was 55%. The mean interval between T1DM onset and hypothyroidism development was 3.3 ± 2.5 years, and between thyroid antibodies appearance and hypothyroidism development was 1.7 ± 1.2 years.

Second, early recognition of ATD in patients with T1DM is important for 3 reasons: 1. it alerts

pediatricians to consider other T1DM associated autoimmune diseases, 2. concomitant subclinical hypothyroidism influences metabolic control in children and adolescents with T1DM and is associated with an increased risk of symptomatic hypoglycemia,⁴ 3. it raises concerns regarding justification of routine screening for ATD in patients with T1DM. Identified by screening, the prevalence of ATD is reported to be up to 10-folds higher in young patients with T1DM than in healthy children.⁵ Annual laboratory determinations of anti-thyroid antibodies should be part of routine tests in the diabetic population, especially in girls, children with T1DM for >9 years, patients above 12 years of age, and those in whom T1DM is associated with another autoimmune disease.^{6,7} Until now, there are generally no uniform recommendations regarding standardized screening procedure, as well as the treatment of patients with clinically asymptomatic disorder and evidence of autoimmunity. However, the following factors must be considered in initiation and anticipating the successful applicability of comprehensive routine screening of ATD in patients with T1DM; 1. critical prevalence of ATD in patients with T1DM in a particular country, 2. anticipated high sensitivity and specificity of the adopted screening test, 3. availability of plausible consensus regarding the treatment protocol of ATD in patients with T1DM, even in subclinical cases, 4. adequacy of economic resources to fulfill the financial context of the screening test. Thus, the proposed screening ought to be country-specific.

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Reply from the Author

Thank you for providing us the opportunity that Saudi Medical Journal has considered for authors to respond to the comments of readers.

I would like to express our gratitude to Prof. Al-Mendalawi for his nice comments on our article: "Autoimmune thyroid disease in children and adolescents with type 1 diabetes mellitus in Northwest Iran."¹ As mentioned by Prof. Al-Mendalawi, the presence of ATD and T1DM variably correlate with each other depending on the patient's age, gender, and ethnic background. This may explain the significant difference between results yielded by various studies carried out worldwide in cases with different age groups, races, and gender distribution. Besides, the duration

of either diabetes or seropositivity for antithyroid autoantibodies play considerable roles in raising the level of TSH and development of ATD, and consequently hypothyroidism. The mean age of our patients was 8.3 years, and the mean duration of T1DM among them was 1.6 years, therefore, our finding of lower incidence of ATD and the absence of meaningful statistical difference in mean TSH level between our studied groups should not be considered to be contrary to other studies anywhere, but rather, it may have resulted from inevitable anthropologic differences between studied cases. Although the mean TSH level of seropositive patients was more than those of seronegative ones in our study, however, their difference was not shown to be statistically significant, and this might be due to the shortness of disease duration. However, the direct correlation between “diabetes duration” and the “TSH level” in seropositive patients was revealed clearly.

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