Brief report

Thyroid function and autoimmunity in children and adolescents with Type 1 Diabetes Mellitus

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A B S T R A C T

We evaluated 233 children and adolescents with T1 Diabetes to analyze the prevalence and characteristics of Autoimmune Thyroid Disease. AITD was found in 23%, the majority being female and patients older than 5 years of age. Screening is mandatory, and the best approach could be guided by gender and age.

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1. Background

The autoimmune etiology of Type 1 Diabetes Mellitus (T1D) is already well established, as well as its association with autoimmune thyroid disease (AITD) [1]. The American Diabetes Association (ADA) describes an AITD prevalence of 17–30% in T1D patients [1], similar to the International Society for Pediatric and Adolescence Diabetes (ISPAD)-29% of the patients in the first years after T1D diagnosis [2]. The presence of AITD increases the risk of thyroid dysfunction, which can affect glycemic control and clinical evolution [3–7].

Considering the pediatric age group and teenagers, there are few national studies evaluating the prevalence and characteristics of AITD in T1D patients. Therefore, the aim of this study was to evaluate the prevalence and characteristics of AITD in
this specific age group and discuss screening recommendations regarding our population.

2. Methods

This was a cross-sectional study with data from medical records of T1D children and adolescents, regularly followed-up in the Diabetes Outpatient Clinic, Pediatric Endocrinology Unit, of the Santa Casa School of Medicine of São Paulo, from June 2011 to June 2014. Were included patients with T1D, who had thyroid function and autoimmunity been evaluated before 20 years of age. Diagnosis of T1D was established according to ADA recommendations [1]. Laboratory analysis included antibodies against thyroperoxidase (anti-TPO) and thyroglobulin (anti-TG), chemiluminescence (IU/mL); serum free thyroxin (FT4) (ng/dL) and thyroid-stimulating hormone (TSH) (µIU/mL) immunofluorometric assay until 05/12/2011 and chemiluminescence from this date; glycated hemoglobin (HbA1c), turbidimetric immunoassay method (Ref. 4–6%). Patients with positive anti-TPO, and/or anti-TG, were considered as having AITD. Hypothyroidism was considered when TSH was above 10 µIU/mL. When TSH was between 5 µIU/mL and 10 µIU/mL, in AITD patients, TSH measurement was repeated each 6 months. If TSH levels were still elevated, they were considered as having hypothyroidism.

To analyze the impact of age at T1D diagnosis and the presence of AITD, the patients were subdivided in 3 groups according to age at onset of T1D: <5 years, 5–10 years and >10 years. For the statistical analysis, the variables were tested by the Shapiro–Wilk test and the Student’s t test was used to compare normally distributed data in different groups and comparison test of proportions (z test). Mann–Whitney Rank Sum Test was used when quantitative variables were not normally distributed. P-value <0.05 was considered statistically significant. Data were analyzed using SigmaStat software 3.5.

3. Results

We included 233 T1D patients, 131 females (56%), mean ± SD age at T1D diagnosis 7.7 ± 4.0 years; mean duration of T1D 12.4 ± 5.8 years. AITD was found in 49/233 (21%), 35/49 females (71.4%), mean age at diagnosis 11.9 ± 3.3 years and mean time between T1D diagnosis and AITD of 3.7 ± 3.1 years. Patients with <5 years of age at the time of T1D diagnosis took a longer time to present AITD (6.4 years, varying between 1.1 and 14). Patients with AITD tested positive to anti-TPO in 15/49 (30.6%), anti-TG in 19/49 (38.8%) and both in 15/49 (30.6%); 18/49 (37%) of them had hypothyroidism, 1/49 (2%) hyperthyroidism and 30/49 (61%) had normal thyroid function. In the AITD patients with normal thyroid function, 18/49 (37%) had TSH in normal levels throughout the reporting period. Temporary mild elevated titters of TSH (5–10 µIU/mL) on at least one occasion, with normal FT4 levels, occurred in 12/49 (24%) patients, all with subsequent normalization and maintenance (for a period of 4.4 ± 3.1 years) of TSH levels. The prevalence of hypothyroidism was 8.6% (20/233) and 65% of them (13/20) were female. There was no significant difference in diabetes control between patients with hypothyroidism and normal thyroid function (P = NS).

4. Discussion

In the present study, the prevalence of AITD was 21%, within the range found in other studies in the same age group, from 12.8% to 25.5% [8–14]. If we compare our data to other national studies on pediatric population, we found only one with a bigger number of patients, who studied 383 (9 months to 25 years of age) diabetic patients, in a different area of Brazil. This study has found a lower prevalence of positive anti-thyroid antibodies of 16.7% [15]. Similarly, to the current study, patients with longer duration of diabetes had higher incidence of thyroiditis.

Many studies in the literature have demonstrated a higher incidence of AITD in older T1D patients [11,12,16]. Our data demonstrated also a tendency of higher incidence in the older age group. Interestingly, there was a significant difference of time between the T1D diagnosis and AITD diagnosis: those patients with diabetes diagnosed before the age of 5 years took a longer time to develop AITD, when compared to patients older than 5 years. This data is compatible with other studies [11]. Also clinically relevant is that, in patients with AITD, TSH can increase temporally to values between 5 µU/mL and 10 µU/mL, and return to normal values spontaneously, without treatment.

Concerning screening recommendations, Ramos et al. [17] screened patients with thyroiditis using only anti-TPO, and encountered lower prevalence of AITD then Rodrigues [18], which assessed both antibodies (20.6% and 35.5%, respectively), suggesting that there is a loss of diagnosis of AITD when using only anti-TPO antibodies. In our study, if we only measured one antibody, we would have missed approximately one third of AITD.

Concluding, we observed that the prevalence of AITD in children and adolescents with T1D in our population is 21%. Important characteristics of this group are the higher prevalence in females and in older patients, and the longer time to develop AITD in patients with diagnosis of diabetes under 5 years of age. We also observed that if screening strategy includes antibodies, both anti-TPO and anti-TG should be measured. These features could suggest different approaches for screening of thyroid dysfunction in T1D patients, specifically related to the reduced risk of boys and younger patients.

Conflict of Interest

None.

REFERENCES


