RESEARCH ARTICLE

Autoimmune thyroid disease in children with diabetes and adolescents: A single center study from south Punjab

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Abstract

Objective: To evaluate the prevalence of autoimmune thyroid disease in children with diabetes.

Methods: The descriptive cross-sectional study was conducted from January to December 2019 at the Children Hospital and the Institute of Child Health, Multan, Pakistan, and comprised paediatric type 1 diabetes mellitus patients of both genders. Blood samples were obtained for detailed testing of thyroid functions tests. Data was analysed using SPSS 20.

Results: Of the 161 paediatric subjects, 83(51.6%) were boys. The overall mean age was 9.7±4.3 years. Thyroid peroxidase antibody was positive in 34(21.1%) patients and thyroglobulin antibody in 27(16.7%). Both antibodies were positive in 17(10.5%) patients. Six (3.7%) patients had evidence of subclinical hypothyroidism, 8(4.9%) had overt hypothyroidism and 1(0.62%) had hyperthyroidism.

Conclusion: The prevalence of autoimmune thyroid disease among children and adolescents with type 1 diabetes mellitus was 21%, with hypothyroidism being more prevalent compared to hyperthyroidism.

Keywords: Autoimmune thyroid disease, Anti-thyroid peroxidase antibody, Anti-thyroglobulin antibody, Diabetes mellitus type 1, Glycosylated haemoglobin. (JPMA 71: 1804; 2021)

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Introduction

Type 1 diabetes mellitus (T1DM) is caused by immune-mediated destruction of pancreatic beta cells.[1] It is associated with other autoimmune disorders, like Graves's disease, Hashimoto's thyroiditis, Addison's disease, Coeliac disease and pernicious anaemia.[2]

The prevalence of thyroid disease in children with diabetes and adolescents varies from 10% to 24%.[3,4] The appearance of thyroid peroxidase antibody (TPO-Ab) and thyroglobulin antibody (TG-Ab) in T1DM precedes thyroid dysfunction. Both these antibodies can be used as a diagnostic marker for autoimmune thyroid disease (AITD). Screening for anti-thyroid antibodies in T1DM may help in the early detection of autoimmune thyroid disorders. There is no consensus on screening for AITD in patients with T1DM.[5] It is also known that AITD increase with the advancement of age.[6]

Early detection of autoimmune thyroid disorders need screening for antibodies in T1DM. Clinically, thyroid dysfunction can cause metabolic disturbances and may undermine diabetes control. Hypothyroidism alters carbohydrate metabolism, while hyperthyroidism may worsen glycaemic control. Therefore, regular screening of T1DM subjects allows early detection and treatment of thyroid dysfunction.

The current study was planned to evaluate the prevalence of AITD in TIDM children and adolescents.

Subjects and Methods

The descriptive cross-sectional study was conducted from January to December 2019 at the Children Hospital and the Institute of Child Health, Multan, Pakistan. After approval from the institutional ethics review committee, the sample size was calculated on the basis of 17% prevalence of thyroid antibodies,[6] using the formula for single proportion with 95% confidence level and 6% margin of error. The sample was raised using consecutive sampling technique from among children and adolescents aged 2-15 years of either gender with T1DM. Those already on thyroid medication and with any acute febrile illness were excluded, and so were those with other autoimmune diseases or secondary diabetes mellitus.

After taking informed consent, detailed history of each patient was taken, including date of visit, name, age, gender, age at which T1DM was diagnosed and its duration. Symptoms suggestive of hypothyroidism, like coarse facies, lethargy, cold intolerance, swelling in front of neck, constipation, pubertal delay, and of hyperthyroidism, like palpitations, emotional liability, heat intolerance, weight-loss, exopthalmos etc., were

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specifically noted.

TIDM was diagnosed according to the criteria of American Diabetes Association (ADA).[7] Glycosylated haemoglobin (HbA1C) level was estimated by using high-performance liquid chromatography (HPLC) method. HbA1C was considered an indicator of glycaemic control; 6-7.9 = good control, 8-9.9 = fair control and >10 = poor control.[8] Thyroid function tests (TFTs) were done using chemiluminesence immunoassay. Normal values for TFT were free T4 (fT4) 0.89-1.76ng/dl and thyroid stimulating hormone (TSH) 0.7-6.4uIU/ml. TPO-Ab and TG-Ab ware estimated using enzyme immunoassay with normal values <35 IU/ml and <40 IU/ml respectively.

Patients were classified according to TFT results. Overt hypothyroidism was diagnosed as low fT4 with high TSH, subclinical hypothyroidism as normal fT4 with high TSH, hyperthyroidism as high fT4 with low TSH, and subclinical hyperthyroidism as normal fT4 and low TSH.[9]

Data was analysed using SPSS 20. Quantitative variables were presented as mean and standard deviation (SD), while qualitative variables were represented as frequencies and percentages. P<0.05 was taken as statistically significant.

Results

Of the 161 paediatric subjects, 83(51.6%) were boys. The overall mean age was 9.7±4.3 years. The most common age group was >10 years with 90(55.9%) subjects, followed by 5-10 years 49(30.5%) and <5 years 22(13.6%).

TPO-Ab was positive in 34(21.1%), TG-Ab 27(16.7%) and both antibodies were positive in 7(4.3%) subjects.

Table-1: Baseline characteristics and thyroid disorders of children with type 1 diabetes mellitus (n=161).

Age groups	
<5 years	22 (13.6%)
5-10 years	49 (30.5%)
>10 years	90 (55.9%)
Gender	
Male	83 (51.6%)
Female	78 (48.4%)
TPO-Ab	34 (21.1%)
TG-Ab	27 (16.7%)
Both TPO-Ab & TG-Ab	7 (4.3%)
Subclinical hypothyroidism	17 (10.5%)
Hypothyroidism	8 (4.9%)
Hyperthyroidism	1 (0.62%)

TPO-Ab: Thyroid peroxidase antibody.
TG-Ab: Thyroglobulin antibody.

Table-2: Prevalence of thyroid antibodies by age range in children with type 1 diabetes mellitus (n=161).

Antibodies Age groups	2-5 years	5-10 years	10-15 years
TPO-Ab (Total 34)	0	14 (41.2%)	20 (58.8%)
TG-Ab (Total 27)	0	10 (37%)	17 (63%)

TPO-Ab: Thyroid peroxidase antibody.
TG-Ab: Thyroglobulin antibody.

Table-3: Relationship between positivity of autoimmune thyroid disease (AITD) with duration of type 1 diabetes mellitus (T1DM).

Duration of Diabetes	< 5 years	> 5 years	P-value*
TPO-Ab (total no 34)	25 (73.5%)	9 (24.5%)	0.16
TG-Ab (total no 27)	22 (81.5%)	5 (18.5%)	0.038

* Chi-square test of significance.
TPO-Ab: Thyroid peroxidase antibody.
TG-Ab: Thyroglobulin antibody.

Table-4: Association of glycaemic control with thyroid antibodies in children with type 1 diabetes mellitus (T1DM) (n=161).

Diabetes Control	TPO-Ab positive	TPO-Ab negative	P value*	TG-Ab positive	TG-Ab negative	P value*
Good	7	33	0.052	5	26	0.17
Fair	9	53		8	57	
Poor	18	41		14	51	

* Chi-square test of significance.
TPO-Ab: Thyroid peroxidase antibody.
TG-Ab: Thyroglobulin antibody.

Subclinical hypothyroidism was found in 17(10.5%) subjects, hypothyroidism 8(4.9%) and hyperthyroidism in 1(0.62%) (Table-1).

Highest positivity of AITD was seen in subjects aged >10 years, while zero positivity wsa seen those aged <5 years (Table-2). Duration of diabetes was associated with AITD. TPO-Ab and TG-Ab were seen more in subjects with diabetes duration <5 years compared to those with >5 years (Table-3).

Strict glycaemic control was observed in 33(20.5%), fair control in 59(36.6%) and poor control in 69(42.8%) subjects (Table-4).

Discussion

To the best of our knowledge, this is the first study looking into prevalence of autoimmune thyroid disease in diabetic children and adolescents in Pakistan's southern Punjab region. The level of positivity of TPO-Ab, Tg-Ab and of the two antibodies together shown in the current

study are consistent with earlier studies.[10-13] It is not known whether these antibodies are directly responsible for the pathogenesis of thyroid disease or are the result of destruction mediated by T-cell infiltration in the thyroid. However, a study[14] observed that patients with an increase in TSH and auto antibodies progressed more frequently to thyroid disease.

One or more thyroid antibodies was positive in majority of diabetic patients, which was similar to other studies.[15,16] Thyroid antibodies are strongly associated with future risk of thyroid disease.[17] TSH level was high in 15.4% of patients and all were positive for thyroid auto antibodies. A study[18] reported clinical hypothyroidism in 2.8% T1DM children, while the current data showed it in 4.9%. The presence of subclinical hypothyroidism varies 3-11%[19] in literature. In the current study, it was on the higher side at 10.5%. The prevalence of hyperthyroidism reported in literature varies from 0.5% to 6%,[20] while in the current study it was 0.6%.

Autoimmune thyroid disease is also associated with age and duration of diabetes. It was more common in adolescent age group 10-15 years and <5 years' duration of diabetes, which is in line with literature.[21] Glycaemic control also affects the prevalence of AITD.[22]

One of the limitations of the current study is that thyroid antibodies were performed once with no interval levels. Children with negative thyroid antibodies may develop these over a period of time. Annual antibodies level in children with T1DM would reflect better prevalence of autoimmune thyroid disease. Being a cross-sectional research, the study also lacks information on thyroid autoimmunity before and between the diagnosis of T1DM, leading to failure in establishing the causal association.

Conclusion

There was a high prevalence of thyroid abnormalities in the current sample from southern Punjab. Hypothyroidism was more prevalent in children compared to hyperthyroidism. Thyroid function tests and thyroid antibodies in all children and adolescents with T1DM should be checked regularly.

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Conflict of Interest: None.

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