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Thyroid dysfunction in subjects with type 1 diabetes at a tertiary care unit of Karachi, Pakistan

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ABSTRACT

Background: Genetic factors are involved in the development of T1D and studies have shown that the development of T1D also increases the risk of development of other autoimmune diseases.
Objective: To assess the frequency of thyroid dysfunction in subjects with type 1 diabetes.
Methodology: This study was conducted at Baqai Institute of Diabetology and Endocrinology (BIDE), a tertiary care diabetes center of Karachi Pakistan from January 2005 to March 2017. Subject with type 1 diabetes (T1D) of all ages and both genders were included in the study. T1D was diagnosed on the basis of History, physical examination and relevant laboratory tests. The data of all registered patients was entered in a specially designed software. Thyroid stimulating hormone (TSH) was used as a screening test to assess thyroid dysfunction in subjects with type 1 diabetes. Further evaluation included FT4, T3 and thyroid antibodies where indicated. The data was analyzed on SPSS version 20.
Results: A total of 153 T1D subjects (67 male and 86 female) were included in the study. Out of 153 subjects, 23 (15.0%) had thyroid dysfunction of which 17 (11.1%) were found to have hypothyroidism (subclinical or clinical), 6 (3.9%) were hyperthyroid while 130(84.96%) subjects were having normal thyroid function. Statistical differences were found in body mass index and serum creatinine level among the different categories of thyroid dysfunction. The required dose of insulin was higher (but not significant) in subjects having hypothyroidism as compared to hyperthyroid or subjects with normal thyroid function.
Conclusion: High frequency of thyroid dysfunction was observed in subjects with T1D. Hypothyroidism was more common than hyperthyroidism. All subjects with T1D should be screened with TSH to evaluate for thyroid dysfunction.

1. Introduction

Type 1 diabetes is one of the most common endocrine disorder among children and adolescent worldwide.[1] There are significant differences in the incidence of T1D among different countries, highest rates reported from Finland and Sardinia (37 per 100000 people per year) and lowest rates reported from China and Venezuela (0–1 per 100000 people per year).[1]

In Pakistan, estimated 7.5 million people are affected with diabetes according to International Diabetes Federation (IDF).[2] The exact prevalence of T1D is largely unknown, however according to an old Pakistan based study, conducted in 2002, the prevalence of hyperthyroidism and subclinical hyperthyroidism was 5.1 and 5.8% respectively while the prevalence of hypothyroidism and subclinical hyperthyroidism was 4.1 and 5.4% respectively. Both hyperthyroidism and hypothyroidism had a female predominance.[3] The pathophysiology of T1D is associated with autoimmune destruction of pancreatic beta cells leading to absolute insulin deficiency. Additionally, genetic factors have also been postulated to be involved in the development of T1D and studies have shown that the development of T1D also increases the risk of development of other autoimmune diseases. The most frequent comorbid conditions in T1D include auto immune thyroid diseases[4–8] cardiac diseases (4–9%) pernicious anemia (5–10%), Addison's' disease (0.5%) and vitiligo (2–10%).[4,5]

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Autoimmune thyroid diseases (ATD) are the most common autoimmune manifestations in children and adolescents with T1D[6,7]. Several genetic risk factors have been associated with T1DM, ATD and other autoimmune disorders.[8] However, the prevalence varies according to age, sex and ethnic origin of subjects as well as duration of T1D.[9] There are multiple links between diabetes and thyroidal dysfunction. American diabetes association (ADA) currently recommends for screening TSH after stabilization at onset of T1D and every one to two years thereafter.[9]

There is scarcity of data regarding thyroid dysfunction and its association with type 1 diabetes in Pakistan. Therefore, the aim of this study was to assess the frequency of thyroid dysfunction in subjects with T1D attending a tertiary care unit of Karachi, Pakistan.

2. Methodology

It is a cross sectional retrospective study conducted at Baqai Institute of Diabetology and Endocrinology (BIDE), a tertiary care unit of Baqai Medical University from January 2010 to March 2017. We include the subjects with T1D, visiting the outpatient department of BIDE and electronic database were taken and analyzed without any breach of confidentiality regarding their identification. T1D was labeled with reference to the ADA guidelines 2017 by retrieving information from the subject's records. None of the subject was having any prior history of using thyroid medication.

Thyroid stimulating hormone (TSH), was used as a screening test to assess thyroid dysfunction in subjects with T1D. Anti-thyroid antibodies have been done in only few cases where it was a special requirement. Sample selection process was described in Fig. 1. TSH values of range 0.4–4.5 was taken as a standard as determined by immune analysis (ELISA). Subjects were divided into 3 groups i.e. with normal thyroid function, with hypothyroidism and with hyperthyroidism. The relationship of thyroid dysfunction with T1D was also assessed with subject age, gender, body mass index (BMI), glycated hemoglobin (HbA1c) and the dose of insulin required for all 3 groups.

2.1. Statistical analysis

The data was analyzed on SPSS version 20. Chi-square Test, Independent *t*-test and analysis of variance (ANOVA) were used, where appropriate, to test for any statistically significant differences. P-value of < 0.05 was considered to be statistically significant.

3. Results

The study included 153 subjects with type 1 diabetes, 67(43.8%) were males and 86(56.2%) were females. Baseline characteristics of studied subjects stratified by thyroid status is shown in Table 1. Most of the subjects had age of ≤ 20 years. Positive family history of diabetes was found in 36.6% subjects with mean body mass index was $19.83 \pm 5.3\,kg/m^2$. Mean serum creatinine and HbA1c level was 0.95 ± 0.58 mg/dl and 10.89 ± 2.72%, respectively. It was observed that hyperthyroid patients had significantly lower BMI and higher serum creatinine level than subjects with normal thyroid or hypothyroid (P-value < 0.05). However, no significant differences were seen in terms of age, gender, marital status, family history of diabetes, blood pressure, and HbA1c level.

Mean dose of insulin to control hyperglycemia was found to be higher in hypothyroid subjects as compare to hyperthyroid and normal thyroid subjects but this difference was not statistically significant (P-value > 0.05) as shown in Table 2.

Frequency of thyroid dysfunction as shown in Fig. 1. Twenty-three (15.0%) subjects had thyroid dysfunction, 17 (11.1%) subjects were found to have hypothyroidism (subclinical or clinical), 6 (3.9%) subjects were hyperthyroid while 130 (84.96%) subjects were having normal thyroid function.

4. Discussion

In this study thyroid dysfunction was observed in 23 (15%) subjects who suffer from T1D and associated with a higher level of HbA1c at presentation and required higher doses of insulin to control diabetes compared to subjects with TID who had normal thyroid function.

Prevalence of thyroid dysfunction in diabetics varies in different studies, a large clinic based study of 1310 type1 and type 2 diabetics in adults reported 13.4% thyroid dysfunction, 8.8% in men and 16.8% in women.[10] NHANES 111 reports the prevalence of hypothyroidism in 4.6% and hyperthyroidism in 1.3% in U.S population. Similarly another published study reported a frequency of thyroid dysfunction as 14.6% in both type 1 and type 2 subjects with diabetes. Additionally, in diabetics 13% subjects were found to have subclinical hypothyroidism.[11]

The largest reported study on thyroid dysfunction and subjects with type 1 diabetes has reported a prevalence of 9.5% among 7097 children and adolescents.[7] We observed similar trends in our study participants.

A small study from North India reported a prevalence of 17.4% hypothyroidism and 13.1% subclinical hypothyroidism, in girls with

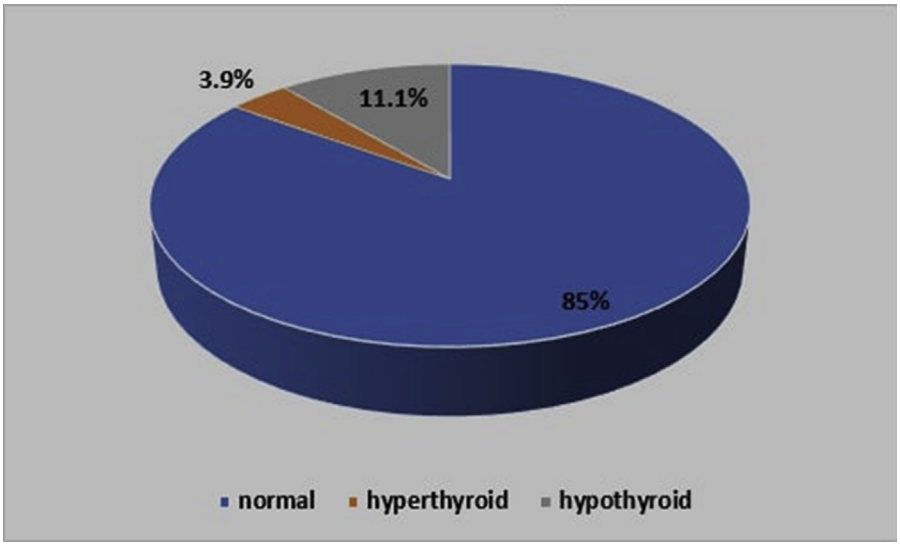

Fig. 1. Frequency of patient with hopothyroid and hyperthyroid.

Table 1
Thyroidal dysfunction with respect to baseline characteristics of patients.

Parameter	Thyroid-stimulating hormone (TSH)			P-value	Overall
	normal	hyperthyroid	Hypothyroid		
N	130(84.96%)	6(3.9%)	17(11.1%)	–	153
Age (years)					
≤20	74(56.9%)	4(66.7%)	10(58.9%)	0.889	88(57.5%)
> 20	56(43.1%)	2(33.3%)	7(41.2%)		65(42.5%)
Gender					
Male	60(46.2%)	1(16.7%)	6(35.3%)	0.274	67(43.8%)
Female	5(83.3%)	70(53.8%)	11(64.7%)		86(56.2%)
Marital Status					
Single	97(77.6%)	5(83.3%)	10(66.7%)	0.592	112(76.7%)
Married	28(22.4%)	1(16.7%)	5(33.3%)		34(23.3%)
Family history of diabetes					
No	83(63.8%)	5(83.3%)	9(52.9%)	0.399	97(63.4%)
Yes	47(36.2%)	1(16.7%)	8(47.1%)		56(36.6%)
BMI (kg/m^2)	19.51 ± 4.78	16.88 ± 3.25	22.88 ± 7.94	0.024	19.83 ± 5.3
Systolic BP (mmHg)	106.39 ± 15.63	100 ± 20	107.19 ± 12.64	0.644	106.26 ± 15.42
Diastolic BP (mmHg)	71.89 ± 9.48	69 ± 10.25	70 ± 9.13	0.623	71.58 ± 9.43
Serum Creatinine (mg/dl)	0.9 ± 0.44	1.9 ± 2.08	0.93 ± 0.28	0.003	0.95 ± 0.58
HbA1c (%)	11 ± 2.67	10.4 ± 4.22	10.15 ± 2.61	0.5	10.89 ± 2.72

Data presented as mean ± SD or n(%).
P-value < 0.05 was considered statistically significant.

Table 2
Insulin dose requirements with respect to thyroidal status.

Parameter	Thyroid-stimulating hormone (TSH)				
	Normal	Hyperthyroid	Hypothyroid	P-value	Overall
n	130	6	17	–	153
Total insulin dose per day	55.1 ± 28.22	55.6 ± 23.25	66.62 ± 26.12	0.180	56.40 ± 27.91

Data presented as mean ± SD.
P-value < 0.05 was considered statistically significant.

type 1 diabetes and 4.2% subclinical hypothyroidism in boys with type1 diabetes.[12]

Out of many reasons postulated for this high prevalence of autoimmune thyroid disease in T1D is common sharing of autoimmune etiology. Various genetic and environmental factors interact with each other to produce immune dysfunction in various susceptible organs including pancreas and thyroid. It has been reported that despite the presence of anti-thyroid antibodies in blood majority of patients do not present with symptoms of thyroid dysfunction.[13] Therefore, as per the guidelines of American Diabetes Association (ADA) and the international society of pediatrics and adolescent diabetes (ISPAD) assessment of thyroid function and thyroid antibodies in children with T1D should be performed at the time of diagnosis or if are normal the test should be repeated every two years or more frequently if symptoms of thyroid disorder appears.[9,14]

In this study hypothyroidism was associated with a more aggressive disease in pediatric subjects with TID, they had higher HbA1c levels and required higher insulin doses for achieving good glycemic control. In a study by Fatourechi et al., it was documented that children who had both TID and hypothyroidism had significantly higher HbA1c levels at enrollment, presented at younger age and most of them experienced DKA as the first presentation.[15] Balsamo et al., and Lin et al., also observed the association of severe metabolic derangement and impaired thyroid function in subjects with newly diagnosed TID.[6,16] There are many interpretations to explain the disease severity of T1D with thyroid dysfunction. The effect of hypothyroidism on increasing insulin resistance and glucose metabolism is well documented[17] as thyroid hormones stimulate glucose uptake into peripheral tissues and enhance the effect of insulin action on glucose transport in to cell.[4,17] In hypothyroid patients this mechanism is disrupted leading to higher glucose levels leading to various acute and chronic complications of diabetes.[5]

The strength of our study is the proper documentation of a large number of T1D subjects, however limitation of our study is that this is a single center study and antibody status was not checked in every subject due to financial constraints.

In this study we have observed association of thyroid dysfunction with type 1 diabetes, hypothyroidism (either clinical or subclinical) was found to be more common rather than hyperthyroidism with female predominance. Further long term studies are needed to validate our findings.

Authors contribution

N Sajid: Concept and design, Interpretation of data, wrote and reviewed the manuscript.

M Riaz: Concept and design, interpretation of data, edit and reviewed the manuscript.

A Fawwad: Interpretation of data, edit and reviewed the manuscript.

A Basit: Concept and design, edit and reviewed the manuscript.

Declaration of competing interests

Nothing to declare.

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