THYROID DYSFUNCTION IN PATIENTS WITH TYPE 1 DIABETES

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ABSTRACT

Objective: To determine the frequency of thyroid dysfunction in patients with type 1 diabetes mellitus using thyroid function tests.

Methodology: This was a descriptive study conducted from January 2017 to June 2017. All patients presenting with type 1 diabetes mellitus (DM) were included irrespective of their age and gender. Thyroid status was determined by screening patients with thyroid stimulating hormone (TSH), free T4 (FT4) and free T3 (FT3). Patients were categorised into five groups consisting of euthyroid, subclinical/overt hypothyroidism and subclinical/overt hyperthyroidism.

Results: One hundred and four patients comprising of 38 (36.5%) males and 66 (63.5%) females had an overall mean age of 20.5 ±4.4 years, mean body mass index (BMI) 24.9 ±1.6 and mean duration of diabetes of 3.7 ±1.4 years. The mean HBA1c was 7.9 ±0.71% and mean TSH was 5.4 ±4.4 m IU/mL. Twelve (11.5%) patients were hypothyroid, 16 (15.4%) had subclinical hypothyroidism and 76 (73.1%) were euthyroid. No case of hyperthyroidism was seen.

Conclusion: Thyroid dysfunction especially overt and subclinical hypothyroidism were commonly found in patients with type 1 diabetes mellitus.

Key Words: Type 1 diabetes mellitus, Hypothyroidism, Thyroid dysfunction

INTRODUCTION

Thyroid dysfunction is increasingly being reported in patients with diabetes mellitus (DM) and there is evidence that thyroid dysfunction whether overt or subclinical, affects the overall glycaemic control[1]. About 24.8% of patients with Type 1 (T1) DM have abnormal levels of thyroid autoantibodies while 12.3% of patients have overt hypothyroidism[2]. The overall prevalence of thyroid autoimmune disorders in T1DM is 60% while 40% have overt thyroid dysfunction[3].

The occurrence of thyroid dysfunction is higher in patients with T1DM as compared to the general population[4,5]. The prevalence of subclinical hypothyroidism is also greater than reported for the general population (15% versus 4.3%). The screening method of choice is the use of serum TSH and other thyroid hormone levels because despite frequent recommendations for other markers i.e. thyroid per oxidase (TPO) antibodies and thyroglobulin antibodies (TGAbs), it is difficult to screen all patients with diabetes. The reasons is the limited availability of these assays in peripheral areas of our country as well as the higher costs incurred by the patients[6,7]. Different studies have reported different levels for the prevalence of thyroid dysfunction with T1DM the range being 12-24% in female and up to 6% in male

patients[4]. Others have reported rates of up to 60% with association to various factors (female gender, increasing age and the presence of diabetic ketoacidosis)[3,8]. Various studies have reported positive TPO antibodies in up to 80% of patients with T1DM and it is shown that levels of these antibodies increases with increasing age[9,10]. Hypothyroidism of autoimmune origin is reported in lower ages as compared to previous studies and it is alarming[11]. It also necessitates to devise evidence based screening protocols so that earlier diagnosis can be made for better management. The prevalence of thyroid dysfunction in 15 to 30% of T1DM patients who show close association with the occurrence of TPO antibodies and thyroid stimulating antibodies (TSAbs). This is concurred by Severinski et al[12] who have shown 15% prevalence of thyroid dysfunction with higher occurrence in female population (21%).

In Pakistan, limited data is available to know about the association of the two diseases which are prevalent worldwide. Thyroid disorders, if untreated, result in deranged and aberrant blood glucose levels and unless screened it is difficult to know about this co existing illness. This study will help to know about the two associated illnesses and better awareness in the health professionals regarding its screening and timely treatment.

METHODOLOGY

This was a descriptive study of six months duration conducted in the Department of Diabetes and Endocrinology, Hayatabad Medical Complex, Peshawar from January 2017 to June 2017. Approval was taken from institutional research ethics committee. All patients were approached for informed consent before including in the study. We included all patients from both genders with T1DM using clinical features, need for insulin and C-peptide levels as needed. Patients with systemic illnesses, diagnosed thyroid disorders and patients taking medications were excluded on the basis of history and examination. Using consecutive sampling technique, all T1DM patients attending Outpatient Department (OPD) were screened and detailed history and physical examination was performed on all patients followed by 3cc blood samples taken for thyroid function tests. TSH was the main test for evaluating thyroid function with normal range of 0.5 to 5 mIU/ml which was supplemented by free thyroxin (FT4) and triiodothyronine (T3) levels. Thyroid function tests (TFTs) were done on Cobos 6000 machine (Roche) and electro-chem illuminescence immunoassay method was used. Patients were categorised into five groups;

i.   Those having overt hypothyroidism (TSH >5.0 mIU/ml, FT4 <10pmol/l and ft3 <4.0 pmol/l);

ii.   Those having subclinical hypothyroidism (normal FT4 and FT3 and TSH >5.0 mIU/ml);

iii.   Those having overt hyperthyroidism (TSH <0.5 mIU/mL, FT4 >20 pmol/l and FT3 >8 pmol/l);

iv.   Those having subclinical hyperthyroidism (normal FT4 and FT3, with TSH <0.5 mIU/ml);

v.   Those having normal levels of TFTs.

Data were entered and analyzed using SPSS version 22.0. The descriptive variables were presented as mean ± standard deviations (SD) while categorical variables were presented as frequencies and percentages. Chi-square test was used to compare categorical variables. Independent t-test was used to compare groups.

RESULTS

Total 104 patients comprising of 38 (36.5%) males and 66 (63.5%) females with an overall mean age of 20.5 ±4.4 years (range being 12-30 years) were included in the study. The mean BMI was 24.9 ±1.6 (range being 20.4-29) with a mean duration of diabetes of 3.7 ±1.4 years (range being 1-7 years).

The mean HBA1c was 7.9 ±0.71% (range: 6.6 to 10) and mean TSH was 5.4 ±4.4 mIU/ml (range: 1.3 to 16.3 mIU/ml). Twelve (11.5%) patients were hypothyroid, 16 (15.4%) had subclinical hypothyroidism and 76 (73.1%) were euthyroid (Table 1). We did not observe any cases of hyperthyroidism in our study.

There were significant mean differences for patients with hypothyroidism as compared to the rest of the sample in terms of TSH (MD: 7.7 mIU/ml, 95% CI: 5.5 to 9.9, p <0.0001), FT4 (MD: 9.7 pmol/L, 95% CI: 8.7-10.6, p <0.0001) and FT3 levels (MD: 10.8, 95% CI: 9.4 to 12.1, p <0.0001). There were no significant mean differences for age, duration of diabetes, random blood sugar (RBS) and HbA1c. On the other hand, there was significant difference for mean TSH (MD: 8.3 mIU/ml, 95% CI: 6.6 to 10.1, p <0.0001) while no difference for the FT4 and FT3 when the data was analysed for subclinical hypothyroidism (Table 1). Similarly on chi-square analysis no difference was noted regarding age (p= 0.35), and gender (p= 0.63).

Table 1: Comparison of various clinical variables for the three groups according to thyroid function status

Variable	Hypothyroid (Overt) (n = 12)	Subclinical (n = 16)	Euthyroid (n = 76)
Age (years)	20.5 ± 3.8	19.8 ± 4.3	20.7 ± 4.5
Duration of DM	3.7 ± 1.7	3.6 ± 1.4	3.7 ± 1.4
BMI	25.8 ± 1.5	25.6 ± 1.2	24.6 ± 1.6
TSH (mIU/ml)	12.4 ± 1.3	12.5 ± 2.1	2.9 ± 0.6
FT4 (pmol/l)	4.7 ± 0.83	14.5 ± 1.2	14.4± 1.5
FT3 (pmol/l)	2.2 ± 0.89	12.8 ± 2.7	12.9 ± 2.4
HbA1c (%)	7.8 ± 0.63	8.1 ± 0.64	7.9 ± 0.74
RBS (mg/dl)	227.0 ± 27.3	224.6 ± 32.7	219.1 ± 32.9

DISCUSSION

The study results provided important information regarding the frequency of thyroid dysfunction in T1DM patients. No association of gender (p= 0.63) was observed as described in other studies[13]. However TSH, FT4 and FT3 levels were significantly different between hypothyroid patients and rest of the patients which is also in agreement with other studies[13,14]. The overall frequency was 11.5% for hypothyroidism and 15.4% for subclinical hypothyroidism, with a cumulative frequency of 26.9% for thyroid related disorders in our study. Thyroid dysfunction increases with increasing age and especially in patients with positive serum thyroid antibodies[3]. In a large survey with a sample of 17353 subjects from the USA it was reported that 4.6% overall prevalence of hypothyroidismexisted[15]. Umpierrez et al[14] has concluded that patients with positive TPO antibodies are 17 times more likely to develop hypothyroidism as compared to patients with negative TPO antibodies.

The association between type 1 diabetes mellitus and thyroid disease has been described in many studies. However there are wide differences in the stated rates for development of thyroid dysfunction[16-18]. Some studies have identified increased risk for women (12–24%) as compared to men (6%)[4,19,20]. However, we did not observe any gender association despite the fact that there were more women (63.5%) in this study.

Studies have shown that mutations in human leukocyte antigen (HLA) associated genes are dominant in patients with T1DM which lead to overall increase in autoimmune diseases such as thyroid dysfunction, celiac disease and Addison's disease[21,22]. Recently, Ikegami et al. has shown that polymorphism in HLA associated genes is also associated with autoimmune diseases and there are 10 genes in T1DM patients which are non-HLA associated[23]. They have shown that polymorphism in the CTLA4 is common for both T1DM patients and in those who develop autoimmune thyroid dysfunction[24]. It has provided proof of the close association between T1DM and autoimmune thyroid dysfunction on the basis of genetic abnormalities in HLA regions of the human genome.

Mohn et al[19] has shown that the presence of subclinical hypothyroidism is associated with higher episodes of hypoglycaemia which is improved with introduction of substitution therapy. Furthermore, hypothyroidism is also being shown to be responsible for insulin resistance in patients with diabetes[24]. Similarly, Donner et al[20] has also shown that genetic susceptibility may also be associated with higher incidence of Grave's disease in T1DM patients. In our study however, we did not find any significant differences for HBA1C values and random blood sugar readings.

LIMITATIONS

This study has the weakness of a cross-sectional study where definitive conclusion between associations and correlations are difficult to obtain. Future studies with long-term longitudinal design as well as inclusion of screening methods involving thyroid autoantibodies are needed, because these studies will provide answers for the natural history of thyroid disorders in patients with T1DM.

CONCLUSION

Thyroid dysfunction especially hypothyroidism and subclinical hypothyroidism are commonly found in patients with type 1 diabetes mellitus. The most important tool is the use of thyroid stimulating hormone levels and other hormonal markers of thyroid function.

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