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Prevalence of Thyroid Dysfunction and Thyroid Autoimmunity in Patients with Type 1 Diabetes Mellitus attending Tertiary Care Hospital in Madurai, South India

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Abstract: ***Objectives: To assess the prevalence of thyroid dysfunction and antithyroid peroxidase (Anti –TPO) positivity in patients with type 1 diabetes mellitus attending tertiary care centre in Madurai. Research Design & Methods: This was a cross sectional observational study among subjects with type 1 Diabetes mellitus attending Department of Endocrinology, Madurai Medical College, Madurai. Thyroid function tests (TFT) and antithyroid peroxidase (Anti –TPO) were measured using the electro chemiluminiscence method. Results: A total of 177 patients (M: F, 92:85) were recruited and mean age was 11.58 ± 3.65 years (Range 2-18 years). Mean age at diagnosis and mean duration of diabetes mellitus was 9.5 ± 3.64 and 3.56 ± 3.1 years respectively. The prevalence of antithyroid peroxidase (Anti –TPO) positivity was 29.9 % and the prevalence of overt, subclinical hypothyroidism and Graves' disease were 14.6%, 5.6% and 1.1% respectively. Significantly higher proportion of female has autoimmune positivity than males (71.7% vs 28.3%, respectively, P =0.005). Conclusion: Our study demonstrated that autoimmune hypothyroidism is highly prevalent among patients with type 1 diabetes mellitus. Screening for hypothyroidism and thyroid autoimmunity should be undertaken in all Type 1 Diabetes mellitus at diagnosis and periodic intervals.***

Keywords: Thyroid autoimmune prevalence · Type 1 diabetes · Thyroid dysfunction · Anti-thyroid peroxidase antibody

1. Introduction

Autoimmune thyroid disease (AITD) is commonly associated with Type 1 diabetes mellitus (T1DM) with varying prevalence depending on the methodology of the study and patients characteristics like age, sex and ethnicity[1]. Hashimoto's disease is the most common AITD seen in patients with T1DM, and antithyroid peroxidase antibody (Anti TPO) is the most common associated antibody in overt and subclinical hypothyroidism[2]. American Diabetes Association (ADA) guidelines recommends screening for Anti TPO and thyroid function tests (TFT) soon after diagnosis of T1DM and rechecking every 1–2 years[3].

Untreated hypothyroidism leads to significant morbidities such as disturbances in growth and development in children, delayed puberty, menstrual irregularity in females and impairment in quality of life[4]. Few studies have shown that an increased risk of symptomatic hypoglycaemia in patients with hypothyroidism. Although the prevalence of AITD in patients with T1DM has been well described in the literature, there is a dearth of information regarding the prevalence and clinical profile of such patients in South India[5,6]. Therefore we planned to assess the prevalence of thyroid dysfunction and Anti –TPO positivity in patients with type 1 diabetes mellitus attending tertiary care centre in Madurai, South India.

2. Research Design and Methods

This was a cross-sectional observational study to evaluate the prevalence of thyroid dysfunction and antithyroid peroxidase (Anti –TPO) positivity in patients with type 1 diabetes mellitus (T1DM). All subjects with T1DM patients attended the Diabetes and endocrine clinic of Government Rajaji Hospital, Madurai Medical College over a period of two years from January 2017 to December 2018 were included in the study. Government Rajaji Hospital is a 2500 bed tertiary referral hospital for south Tamilnadu located in Madurai.

All Subjects with T1DM with or without any previously history or symptoms of thyroid dysfunction were included in the study. Criteria for diagnosis of T1DM were as per the standard American Diabetes Association guidelines either previous history of diabetic ketoacidosis or GAD 65 antibody positivity. Diabetes classified as other than T1DM like Type 2 diabetes, secondary form of diabetes, monogenic diabetes and syndromic diabetes were excluded. Participants were excluded if they were pregnant or had any acute or chronic systemic illnesses that could interfere with thyroid function tests. Informed consent was obtained from all patients or their guardians and assent from those younger than 18 years. The study was approved by the Institute Ethics committee of Madurai Medical College.

Patients were evaluated with detailed history; age of diagnosis of T1DM; duration of T1DM; and anthropometric data like height, weight, and body mass index (BMI); general and systemic examination (including goitre, features of target organ damage, other endocrinological abnormalities) findings were recorded. Biochemical evaluation was conducted on serum obtained after an overnight fast. HbA1c was measured using HbA1c—high performance liquid chromatography (HPLC) (BioRad Variant D10); Other biochemical parameters including fasting and prandial plasma glucose, urine ketones, serum

electrolytes, fasting C-peptide level, thyroid profile, anti-TPO antibody were recorded. All the tests were done on chemiluminescence method (TSH, FT4, anti-TPO antibody) using Maglumi 800 chemiluminescence analyzer.

Primary hypothyroidism was diagnosed based on raised thyroid stimulating hormone (TSH >5.5 mIU/mL) and low FT4 (<0.89 ng/dL) levels. Anti-TPO levels >60 IU/mL were defined as positive. Goiter was examined and graded as per the WHO grading system[7]. GAD 65 antibody was estimated by ELISA method.

3. Results

The study sample consisted of 177 patients; out of them, 92 were male (51.97 %) and male:female ratio was 1.1:1. Age of the study participants ranged from 3 to 18 years with a mean of 11.58 ± 3.65 years. Age at the diagnosis of T1DM ranged from 2 to 18 years with a mean of 9.5 ± 3.64 years. The duration of diabetes at the time of data collection was 0–12 years with a mean of 3.76 ± 2.18 years. The demographic parameters did not differ significantly in males and females [Table 1]. The prevalence of antithyroid peroxidase (Anti –TPO) positivity was 29.9 % and the prevalence of overt, subclinical hypothyroidism and Graves' disease were 14.6%, 5.6% and 1.1% respectively. Significantly higher proportion of female has autoimmune positivity than males (71.7% vs 28.3%, respectively, P =0.005) [Table 2]

4. Discussion

In the present study we showed that prevalence of thyroid dysfunction and thyroid autoimmunity is higher in T1DM compared with general population reported in literature[2]. T1DM is a common endocrine disorder of the childhood and adolescent age group. Among various autoimmune disorders, autoimmune hypothyroidism is the most common endocrine abnormality in T1DM patients[8]. The other autoimmune disorders associated with T1DM are celiac disease, Grave's disease, and primary adrenal insufficiency[8]. Our finding is similar to the observation from other reported literature from India[5,6]. Worldwide, the prevalence of autoimmune hypothyroidism in T1DM varies widely and ranges from 10% to 50%[2].

While a recently published review and a meta-analysis reported a much higher rate of 7–30% for the prevalence of hypothyroidism in patients with T1DM[9]. The heterogeneity in the reported prevalence of hypothyroidism in these studies could be due to the variable population characteristics including age and ethnicity of patients, the differences in study design including the cut-off levels, assay method and classification of the disease with different definitions including autoimmune, subclinical, and clinical hypothyroidism[1].

Recent studies have revealed some genes that might be responsible for the joint susceptibility to T1DM and autoimmune thyroid dysfunction. HLA class II loci, CTLA4, INS, PTPN2 and FOXP3 are among the identified genes[10]. These genes have been recognized as the key role players in the regulation of the immune response. Untreated hypothyroidism leads to significant morbidities such as disturbances in growth and development in children, delayed puberty, menstrual irregularity in females and impairment in quality of life [4,11]

Among Type 1 DM, the prevalence estimates range from 7 to 20% compared with 1 to 10% in the general population. Hyperthyroidism is also more common in people with Type 1 diabetes (3 to 6%) vs. 0.1 to 2.0% in the population without diabetes[12]. The strength of our study is largest number of Type 1 diabetes populations are included in the study among South India. Limitations are other autoimmune markers were not studied and metabolic assessment in special reference to levothyroxine supplementation was not studied.

5. Conclusion

Our study demonstrated that autoimmune hypothyroidism is highly prevalent among patients with type 1 diabetes mellitus. Screening for hypothyroidism and thyroid autoimmunity should be undertaken in all Type 1 Diabetes mellitus at diagnosis and periodic intervals.

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Table 1: Demographics of the 177 subjects with Type 1 Diabetes Mellitus

	All	Male	Females
Number	177	92	85
Age	3 – 18 Years	10.92 ± 3.45	12.01 ± 3.42
Duration of T1DM	0-15 Years	3.7 ± 1.6	3.4 ± 2.6
GAD 65 Positivity	98	55	43
Previous Diabetic Ketoacidosis	79	42	37
HbA1C	10.60%	10.20%	11.20%

Table 2: The prevalence of Thyroid dysfunction and thyroid autoimmunity

	No (%)	Male	Females
Anti TPO Positivity	53 (29.9 %)	15	38
Overt Hypothyroidism	26 (14.6%)	8	18
Subclinical Hypothyroidism	10 (5.6%)	4	6
Graves' Disease	2 (1.1%)	1	1