

Study on the Prevalence of Thyroid Disorders and Thyroid Autoimmunity among Type 1 Diabetics.

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Abstract

Introduction: Type 1 Diabetes is a common autoimmune endocrine disease in children and adolescents. The presence of auto antibodies targeted against β -cell antigens represents the autoimmune character of Type 1 Diabetes. Due to this autoimmune basis, individuals with Type 1 Diabetes are at increased risk for the development of additional autoimmune disorders compared with the general population. **Material & Methods**A cross sectional observational study to analyse the prevalence of thyroid disorders and thyroid autoimmunity among Type 1 Diabetes in Department of General medicine, Government General Hospital, Guntur Medical College, Guntur. Established cases of Type 1 Diabetes, diagnosed based on standard criteria were included. **Results:** Out of the 64 study population, total number of hypothyroid patients were 8 (12.5%). Majority (7 out of 8 cases) were having subclinical hypothyroidism. With regards to thyroid autoimmunity status, total number of patients positive for Thyroid Peroxidase Antibodies (TPOA) were 12 (18.75%). Total number of TPOA patients with hypothyroidism were 58% (7 out of 12) and total number of hypothyroid patients with TPOA were 87.5% (7 out of 8). **Conclusions:** Study confirms the association between autoimmune hypothyroidism and type 1 diabetes and suggests that all subjects with type 1 diabetes, particularly those with positive Thyroid Peroxidase antibodies, should undergo annual screening by serum Thyroid Stimulating Hormone measurement to detect asymptomatic thyroid dysfunction.

Keywords: type 1 diabetes, thyroid disorders, thyroid auto immunity, correlate

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I. Introduction

Type 1 Diabetes is a common autoimmune endocrine disease in children and adolescents. It is a clinical syndrome in which the destruction of the pancreatic islet β -cells leads to progressive insulin deficiency and hyperglycaemia, which in turn gives rise to micro vascular complications such as retinopathy, nephropathy, and neuropathy as well as macro vascular complications.¹

The presence of auto antibodies targeted against β -cell antigens represents the autoimmune character of Type 1 Diabetes. Due to this autoimmune basis, individuals with Type 1 Diabetes are at increased risk for the development of additional autoimmune disorders compared with the general population². Commonly coexisting immune-mediated disorders are Autoimmune Thyroid Disease, Coeliac Disease, Addison's Disease and pernicious anaemia.^[1,2,3,4]

These diseases are associated with organ-specific autoantibodies: Thyroid peroxidase, thyroglobulin, Thyroid stimulating hormone receptor autoantibodies with Autoimmune Thyroid Disease endomysial autoantibodies and transglutaminase autoantibodies with Coeliac Disease, and 21-hydroxylase autoantibodies with Addison's Disease. Using these autoantibodies, organ-specific autoimmunity may be detected before the development of autoimmune clinical disease.^[3]

The most prevalent among these is thyroid autoimmunity.^[3,5,6,7] Its prevalence varies from 8 to 50% depending on the age, sex, and ethnic origin of the subjects. In the general population, thyroid autoimmunity is more frequent in female subjects and prevalence increases with age. In diabetic patients, age and sex distributions are similar, but the prevalence is higher and increases with duration of the disease.⁸

Most patients with thyroid autoimmunity are asymptomatic⁹. Even if symptomatic; symptoms may be attributed to diabetes. So, the diagnosis of thyroid dysfunction in diabetic patients based solely on clinical manifestations can be difficult¹⁰. Though not clinically evident, underlying hypothyroidism has its own impact on morbidity particularly by exacerbating the coexisting dyslipidaemia commonly found in type 1 diabetes and thus increases the risk of cardiovascular diseases.

Because of this high prevalence, lack of clinical features and the impact on morbidity, most investigators recommend screening children and adolescents with type 1 diabetes for autoimmune thyroid disease. Early detection has the potential to prevent significant morbidity related to unrecognized disease.

Objectives of the present study were to determine the prevalence and pattern of thyroid disorders and thyroid autoimmune status in Type 1 Diabetic patients and to correlate thyroid autoimmunity with thyroid dysfunction

II. Material & Methods

A cross sectional observational study to analyse the prevalence of thyroid disorders and thyroid autoimmunity among Type 1 Diabetes in Department of General medicine, Government General Hospital, Guntur Medical College, Guntur.

Study population:

Patients were enrolled from the patient population who attended the Department of general Medicine between November 2017 to December 2018. 64 patients among them satisfied criteria for inclusion into the study. Patient list did not include paediatric group since they were not attending our hospital.

No. of patients enrolled: 71

No. of patients included: 64

No. of patients excluded: 07

Inclusion criteria:

Established cases of Type 1 Diabetes, diagnosed based on standard criteria [Symptoms of diabetes and a casual plasma glucose ≥ 200 mg/dl (11.1 mmol/l) or Fasting plasma Glucose ≥ 126 mg/dl (7.0 mmol/l) or 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l)] and insulin dependence proved by C peptide level of < 1 ng/ml.

Exclusion criteria:

- Pregnancy
- Evidence of other autoimmune diseases like Addison's disease, vitiligo, autoimmune hepatitis, rheumatoid arthritis, Systemic Lupus Erythematosus.
- Multinodular goitre, known thyroid disease with negative thyroid autoimmunity.
- Past history of thyroid surgery or radioiodine therapy.

Consent:

The study was approved by the Institutional ethical committee. Patients were informed about the details of the test performed and blood sample collected with consent.

Sample collection:

Venous blood sample collected in 8 hrs fasting state. serum separation, sample was sent for analysis.

Method of testing:

T3, T4, TSH	-- Radio Immuno Assay
Thyroid peroxidase	-- Enzyme Linked Immuno
Antibodies	-- Sorbent Assay

Normal ranges:

T3	0.8 – 1.4 ng/ml
T4	4.2 – 11 μ g/dl
TSH	0.5 – 5 mIU/ml
TPOA	up to 40 IU/ml

Result interpretations:

- ¾ Any T3 /T4 value above the upper limit of normal along with a low TSH < 0.5 mIU/ml is considered as hyperthyroidism.
- ¾ Any T3 /T4 value below the lower limit of normal along with an elevated TSH > 5 mIU/ml is considered as hypothyroidism.
- ¾ TSH > 5 mIU/ml along with normal range T3, T4 is considered as subclinical hypothyroidism.
- ¾ TSH < 0.5 mIU/ml along with normal range T3, T4 is considered as subclinical hyperthyroidism.
- ¾ Thyroid autoimmunity is considered to exist if Thyroid Peroxidase Antibody level is > 40 IU/ml and not to exist if it is lesser.

Statistical analysis:

Statistical analysis was done using standard formulae SPSS (Statistical Package for Social Sciences) in windows Dos version. The significance of difference between means in two groups was calculated using student t test and the significance of difference in proportions using chi-square test. Fisher exact test was used when any one of the values was less than 5 in chi-square test. Statistical significance at 5% levels was taken for p value < 0.05.

III. Observation And Results

Total number of patients in the present study were 64 out of whom 51.6% (n=33) were females and 48.4% (n=31) males. Mean age of the study population was 20.2±5.16 years.

Out of the 64 study population, total number of hypothyroid patients were 8 (12.5%), out of whom 2 were male and 6 females. Majority (7 out of 8 cases) were having subclinical hypothyroidism and only 1 case had overt hypothyroidism. There were no hyperthyroid patients in the present study.

With regards to thyroid autoimmunity status, total number of patients positive for Thyroid Peroxidase Antibodies (TPOA) were 12 (18.75%). Out of those 12, 4 were male and 8 female. Total number of TPOA patients with hypothyroidism were 58% (7 out of 12) and total number of hypothyroid patients with TPOA were 87.5% (7 out of 8).

TABLE 1 : Thyroid status in relation to Gender.

THYROID STATUS	TOTAL NO. (IN%)	GENDER	
		MALE	FEMALE
EUTHYROID	56(87.5%)	29(45.3%)	27(42.2%)
HYPOTHYROID	8(12.5%)	2(3.1%)	6(9.4%)
HYPERTHYROID	nil		

On comparing the female : male 3:1 ratio by chi square test , the p value is 0.1573 which is > 0.05 . So, the association between gender and hypothyroidism is not significant indicating that there is no significant gender difference among hypothyroid and euthyroid type 1 diabetics as per this study.

TABLE 2: Thyroid Autoimmunity Status in relation to Gender.

THYROID AUTOIMMUNITY	TOTAL (IN %)	Gender	
		Male	Female
TPOA NEGATIVE	52(81.25%)	27(42.25%)	25(39%)
TPOA POSITIVE	12(18.75%)	4(6.25%)	8(12.5%)

On comparing the female : male ratio 2:1 by chi square test , the p value is 0.2482 which is > 0.05 . So, the association between gender and thyroid autoimmunity is not significant indicating that there is no significant gender difference among those who are positive for Thyroid peroxidase antibody and those who are negative for the same in type 1 diabetics as per this study.

TABLE 3 : Correlation Between Thyroid Function and Autoimmunity.

CATEGORY	HYPOTHYROID	EUTHYROID	TOTAL
TPOA NEGATIVE	7(58%)	5(42%)	12
TPOA POSITIVE	1(2%)	51(98%)	52
TOTAL	8	56	64

Values in brackets represent row percentage. 58% of Thyroid peroxidase antibody positive patients are hypothyroid whereas only 2% of Thyroid peroxidase antibody negative patients are hypothyroid. 87.5% of hypothyroid patients are Thyroid peroxidase antibody positive whereas 12.5% of them are Thyroid peroxidase antibody negative. On comparing these two values by chi square test , the p value is 0.001 which is statistically significant at 1% levels. So, the association between thyroid autoimmunity and hypothyroidism is significant indicating that hypothyroidism is more prevalent among Thyroid peroxidase antibody positive individuals than in Thyroid peroxidase antibody negative individuals.

On assessing Thyroid Peroxidase Antibody status as a predictor for development of thyroid dysfunction, the positive predictive value is 58% and the negative predictive value is 98%.

TABLE 4: Thyroid Autoimmunity in relation to duration of diabetes.

AUTOIMMUNE STATUS	MEAN DURATION OF DIABETES IN YEARS
TPOA POSITIVE	4.5 ± 3.5
TPOA NEGATIVE	3.2 ± 1.9

On comparing the two means by student t test, the p value is 0.081 which is > 0.05 . So, the association between thyroid autoimmunity and duration of diabetes is not significant indicating that prevalence of Autoimmune Thyroid Disease is not related to duration of diabetes as per this study.

TABLE 5: Thyroid Autoimmunity in relation to age of the patients.

THYROID AUTOIMMUNITY	MEAN AGE IN YEARS \pm SD
TPOA POSITIVE	21.2 \pm 5.6
TPOA NEGATIVE	20 \pm 5

On comparing the two means by student t test, the p value is 0.478 . So, the association between prevalence of thyroid autoimmunity and age of diabetics is not significant, indicating that prevalence of Autoimmune Thyroid Disease is not related to age of the patients as per this study.

IV. Discussion

Prevalence: Present study confirmed the high prevalence of a second organ-specific autoimmune manifestation in individuals with type 1 diabetes. By cross – sectional analysis the prevalence of thyroid autoimmunity in study population is 18.75%. (12 out of 64).

This is in concordance with many other similar studies from various parts of the world. Most of the studies state the prevalence to be between 15 to 30%. Roldan MB et al⁵ -17.6%; Prazny M¹¹ - 22%, McCanlies E¹²-26.6% , Maugendre D et al⁷ -17%

In an observational cross-sectional study by Palma et al¹³ the prevalence of anti- Thyroid Peroxidase Anti bodies was 10.8%. Forty-four (11.2%) new cases of Thyroid Dysfunction were diagnosed during the clinical evaluation.

Guillermo E. Umpierrez et al¹⁴ showed a prevalence of thyroid dysfunction to be 33%. All patients had hypothyroidism mostly subclinical. None had hyperthyroidism. 80% of them were positive for Thyroid Peroxidase antibodies. Among the Thyroid Peroxidase Anti body positive individuals, 83% of females and 51% of males developed hypothyroidism on follow up.

In their study, Thyroid Peroxidase Anti body positivity as a predictor for development of thyroid dysfunction was assessed and they found out 67% positive predictive value and a 90% negative predictive value. As per their study, patients who were Thyroid Peroxidase positive were 17.91 times as likely to develop hypothyroidism as patients who were Thyroid Peroxidase negative (95% CI 3.89–82.54).Our study is comparable to this study in all terms except that this study was a longitudinal study, where they did assessment for Thyroid Peroxidase Anti body every 4 years and thyroid function on yearly basis.

Thyroid autoimmunity in relation to gender:

In present study, though the actual number of females was high, with a F: M ratio of 2:1, it was not of statistical significance. This may be due to two reasons. 1. Actual prevalence being equal; 2. Smaller study population.

Gemma C et al⁸ reported female preponderance. 18.3% females had Autoimmune Thyroid Disease whereas it was 7% in males. Olga Kordonouri et al¹⁵ showed a similar female preponderance and they had 63% of Autoimmune Thyroid Disease patients as females.

Thyroid autoimmunity in relation to age:

Many studies have shown that the prevalence of thyroid autoimmunity is high among older patients than younger patients. But in our study we didn't find a significant age difference between Thyroid Peroxidase Anti body positive and Thyroid Peroxidase Anti body negative individuals. This may be because of the reason that we included only patients of age >12 . But there are reports, where presence of Thyroid Peroxidase Anti body is not influenced by age .

Olga Kordonouri et al¹⁵ states that the prevalence of significant thyroid antibody titers increases with increasing age of patients and reached its maximum in the 15- to 20-year age group. Holl RW et al¹⁶ found the prevalence of Autoimmune Thyroid Disease to increase dramatically with age. O Kordonouri R, Hartmann et al¹⁷ reports the prevalence to be high in > 12 years age group.

Jennifer M. Barker et al¹⁸Czerniawska E et al⁹ agree the higher prevalence in older age.

Thyroid autoimmunity in relation to duration of diabetes:

According to many prospective studies incidence of thyroid autoimmunity increases as years pass by since the diagnosis of diabetes. The net result would be a higher prevalence of Autoimmune Thyroid Disease among patients with longer duration of diabetes than the newly diagnosed cases.

But in our study there is no significant difference in duration of diabetes between, Thyroid Peroxidase Anti body positive and Thyroid Peroxidase Anti body negative persons. This has also been confirmed in many longitudinal as well as cross-sectional studies.

D Hansen et al¹⁹, Maugendre D et al⁷ showed that the duration of diabetes doesn't influence development of Autoimmune Thyroid Disease. The Indian study by Menon PS. et al²⁰ also observed that the thyroid autoimmunity did not change with duration.

V. Conclusions

Present study confirms the association between autoimmune hypothyroidism and type 1 diabetes and suggests that all subjects with type 1 diabetes, particularly those with positive Thyroid Peroxidase antibodies, should undergo annual screening by serum Thyroid Stimulating Hormone measurement to detect asymptomatic thyroid dysfunction.

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