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STUDY OF THYROID FUNCTION ABNORMALITIES IN DIABETIC PATIENTS.

Endocrinology

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ABSTRACT

Objectives: To find out the prevalence of various types of thyroid dysfunction in diabetic patients and to correlate Diabetes mellitus and Thyroid dysfunction by estimating fT3, fT4, and TSH in diabetic patients. **Materials And Methods:** This cross sectional observational study was done on a total of 150 diabetic subjects over a period of 12 months at Government General Hospital, Kadapa. Estimation of BMI, serum TSH, free T3,free T4 FBS, PPBS, HbA1c,serum total cholesterol, HDL Cholesterol, LDL cholesterol and serum triglycerides was done in the study population. **Statistical Analysis:** It was done by using S.P.S.S. version 20.0.For all the statistical tests of significance, a P-Value of <0.05 was considered to reject the null hypothesis. For continuous variables, the Student "t" test was done to test the difference in means. For categorical nominal variables, the Chi-square test was done to test the association between the variables. ANOVA test was done to test the difference in means between more than two groups. **Results:** Among the 150 diabetic patients studied, 66.6% had normal thyroid profile (euthyroid), and 33.3% had thyroid dysfunction out of which 23.3% had subclinical hypothyroidism, 8% had clinical hypothyroidism, 2% had clinical hyperthyroidism while no one had subclinical hyperthyroidism. **Conclusions:** This study showed a higher prevalence of hypothyroidism in diabetic patients compared to the general population. It was also observed that diabetics with thyroid dysfunction had abnormal lipid profile compared to the diabetics with normal thyroid profile.

KEYWORDS

Thyroid dysfunction, Diabetes mellitus, Hypothyroidism, Subclinical hypothyroidism, Hyperthyroidism

INTRODUCTION

Diabetes mellitus is a major non communicable disease that causes hyperglycemia. The mechanisms of hyperglycemia are genetic, acquired, or environmental. This leads to decreased insulin secretion from the pancreas, reduced glucose utilization in the peripheral tissue, and increased hepatic glucose production. Thyroid diseases in Diabetic patients are regularly encountered .Thyroid hormones are critical for growth, neuronal development, reproduction, and regulation of energy metabolism. Hypothyroidism and hyperthyroidism are common conditions with variable prevalence among different populations with potentially devastating health consequences. The prevalence of thyroid diseases in the general population varies from 6.6% to 13.4%.[1,2]This is due to the difference in the degree of iodine consumption among various regions, the difference in sensitivity of the TSH assays, and the large population diversity.[3]

The relationship between the two diseases is more commonly recognized. Several studies reported thyroid dysfunction in the diabetic population ranging from 2.2% to 17 %.[4] However, some studies showed even higher prevalence. Study by Udoing et al. in Nigeria showed a prevalence of 46.5%, Gurjeet Singh et al. reported a prevalence of 30% in Punjabi population, Celani et al. reported a prevalence of 31.4% in Italy .[5,6,7]Thyroid disorders were more common in subjects with type 1 diabetes than those with type 2 diabetes. Some genetic factors might be responsible for the co-occurrence of autoimmune thyroid diseases (A.I.T.D.) and type 1 diabetes.[8]

Diabetes mellitus influences thyroid function at the level of hypothalamic control of TSH release and the conversion of T4 to T3 in the peripheral tissue. Marked hyperglycemia causes a reversible reduction of the activity and hepatic concentration of T4-5 deiodinase. It leads to low concentration of serum T3, elevated levels of reverse T3 and low, normal or high levels of T4.90 Uncontrolled DM both Type 1 and Type 2, may induce a "Low T3 state" characterized by low serum total T3 and free T3 levels and an elevation in reverse T3 (rT3) but normal serum T4 and serum TSH concentrations. Decreased serum T3 is due to reduced peripheral conversion of thyroxine (T4) to tri-iodothyronine (T3) via a 5"monodeiodination reaction. In euthyroid diabetic patient serum, levels of T3, and basal TSH levels in response to TRH is influenced by the glycemic status of the patient, and poorly controlled diabetes may induce reversible "low T3 state".[9,10] Studies indicate that it might be the long term diabetic control that determines the plasma T3 levels. Uncontrolled diabetes may also result in impaired TSH response to TRH or loss of expected nocturnal TSH peak. TSH response and "low T3 state" may become normal with improvement in glycemic status, but even with reasonable diabetes control, the normal nocturnal TSH peak may not be restored in C-peptide negative patients, i.e., those with completely absent pancreatic beta-cell function. Diabetes mellitus affects the assessment of thyrotoxicosis by falsely lowering the blood levels of thyroxine(T4) and triiodothyronine(T3) during severely uncontrolled hyperglycemia. T4 (total and free) and T3 concentrations may be inappropriately normal when hyperthyroidism is present in the patient with poor diabetic control, making some diagnostic difficulties which are supported by suppressed serum basal TSH or an absolutely flat response to TRH.[11] On the other hand, Thyroid hormones are insulin antagonists. High levels of thyroid hormones act as diabetogenic. In contrast, low levels of thyroid hormones inhibit the development of Diabetes.

In India, data is inadequate on thyroid diseases in diabetes patients. Our study is proposed to evaluate the prevalence of thyroid dysfunction among diabetes mellitus patients residing in Andhra Pradesh. An attempt was made to compare and correlate these two metabolic disorders by taking into account various biochemical parameters.

- **Primary Objectives:** To find out the prevalence of various types of thyroid dysfunction in diabetic patients and to correlate Diabetes mellitus and Thyroid dysfunction by estimating fT3, fT4, and TSH in diabetic patients.
- **Secondary Objectives:** 1) To determine the association between HbA1c levels, BMI and the presence of various types of thyroid dysfunction in diabetic patients. 2) To determine the association between lipid parameters and the presence of various types of thyroid dysfunction in Diabetic Mellitus patients

Materials And Methods

The present study was conducted from 1st November 2020 to 1st November 2021 at Government General Hospital in India over a period of 12 months. The study was done on a total of 150 diabetic subjects.

Inclusion Criteria

All those patients more than 14 years of age who were diagnosed as either T1DM or T2DM based on the A.D.A. guidelines with the duration of diabetes for at least six months attending the outpatient clinic at the Department of General Medicine, Government General Hospital, Kadapa, were included.

These patients are being treated with either oral hypoglycemic agents or parenteral insulin.

Exclusion Criteria

1. Patients with pancreatitis and drug-induced diabetes were excluded.
2. All those who have a proven thyroid disorder and are on treatment were excluded.
3. Patients on amiodarone and other drugs altering thyroid function.
4. Patients with co morbidities like HIV and Tuberculosis.
5. Gestational diabetes mellitus.
6. Patients who have undergone previous thyroid surgeries were excluded.
7. Patients suffering from liver diseases, renal disease, cardiac failure, cancer patients, and very sick patients were excluded.

Written consent was obtained from each patient after explaining the objectives as well as the methodology of the study. A detailed history of duration and severity of the disease, clinical symptoms, and also family history, personal history, and drug history, and Co morbid diseases was also obtained. A thorough physical examination was done to look for local and systemic features to rule out thyroid disease. Measurement of weight, height and blood pressure were done. The Body Mass Index was determined by weight and height calculations using the following equation: BMI = Weight in Kg / Square of height in meters. According to Indian guidelines, a BMI - 23 to 24.9 is defined as overweight, a BMI- ≥ 25 is moderate obesity, and a BMI ≥ 30 is severe obesity.

Biochemical Investigations

Estimation of serum TSH, free T3,free T4 was done by a chemiluminescent method in Access 2 immunoassay systems analyzer developed by Beckmann coulter diagnostics.FBS, PPBS, HbA1c,serum total cholesterol, HDL Cholesterol, LDL CHOLESTEROL and serum triglycerides were estimated using AU480 Beckmann coulter analyzer.

Statistical Analysis

Statistical analysis was done by using S.P.S.S. version 20.0. Descriptive statistics were calculated as frequency, percentage, mean and standard deviation. For all the statistical tests of significance, a P-Value of <0.05 was considered to reject the null hypothesis. After the normality tests (Kolmogorov-Smirnov and Shapiro-Wilk) showed normal distribution of continuous variables, the Student "t" test was done to test the difference in means. For categorical nominal variables, the Chi-square test was done to test the association between the variables. ANOVA test was done to test the difference in means between more than two groups

OBSERVATIONS AND RESULTS

In the present study 27.3% of the diabetic subjects were in the age group of 41-50 years while 25.3% were aged 51-60 years and 17.9% were above 60 years. Out of 150 patients 23 patients were type 1 diabetes and 127 patients were type 2 diabetes. The majority of the diabetic subjects were 54.66% males while the remaining 45.33% were females. Among the study subjects 54.66% were obese and 17.33% were overweight.

The mean of the study group is 47.36. The BMI of the females in the study population is significantly higher than that of males. Please see Table 1 and Table 2 for the mean values of various biochemical parameters

In the present study, out of 150 patients, 8 patients had low free T3, Low free T4 levels and high TSH Levels; 4 patients had low Free T4 levels, Normal Free T3 Levels and high TSH levels (clinical hypothyroidism-8%) whereas 2 patients had high Free T3 levels , high Free T4 Levels and low TSH levels whereas 1 patient had high Free T4 levels , normal free T3 level and low TSH level. (clinical hyperthyroidism-2%).In this study 35 patients had high TSH levels , normal Free T3 and Free T4 levels (subclinical hypothyroidism-23.3%) whereas 100 patients had normal TSH levels , Free T3 and Free T4 levels.(euthyroidism-66.6%). See Table 3

Table 1:mean Values Of Various Biochemical Parameters In The Study Group

	MEAN±SD
AGE	47.36±14.26
FBS	160.16±79.3
PPBS	252.66±113.9
HbA1c	7.214±1.66
Free T3	2.448±0.93
Free T4	1.394±0.46
TSH	4.964±6.54
Serum total cholesterol	190.45±42.11
Serum Triglycerides	146.24±59.2
Serum LDL Cholesterol	110.6±27.1
Serum HDL Cholesterol	44.6±8.45

Table 2: Comparison Of Various Biochemical Parameters In Male And Female Diabetic Subjects

	FEMALES Mean±SD (Standard deviation)	MALES Mean±SD (Standard deviation)	STUDENT T TEST P-VALUE
AGE	48.26±13.14	46.6±15.16	0.481
FBS	155.6±72.4	163.89±84.35	0.527
PPBS	242.5±110.4	261.07±116.7	0.322
HbA1C	7.17±1.6	7.24±1.71	0.817
B.M.I.	26.60±2.93	23.8±2.74	<0.001**
FT3	2.58±1.2	2.33±0.58	0.093
FT4	1.39±0.57	1.39±0.34	0.974
TSH	5.69±6.85	4.38±6.24	0.221
Total Cholesterol	195.11±42.27	186.58±41.84	0.217
Triglycerides	159.22±59.51	135.4±57.08	0.014**
LDL Cholesterol	112.9±28.88	109.32±25.59	0.412
HDL Cholesterol	46.23±9.07	43.36±7.71	0.038**

Table3: Distribution Of Various Thyroid Parameters In The Study Group

Thyroid biochemical parameters		Diabetic group (N=150)	
		n	%
Free T3 (pg/ml)	Low (<1.4)	8	5.3%
	Normal (1.4 to 4.2)	140	93.3%
	High (>4.2)	2	1.3%
Free T4 (ng/ml)	Low (<0.8)	12	8%
	Normal (0.8 to 2)	135	90%
	High (>2)	3	2.0%
TSH (µU/L)	Low (<0.3)	3	2.0%
	Normal (0.3 to 5.6)	100	66.6%
	High (>5.6)	47	31.3%

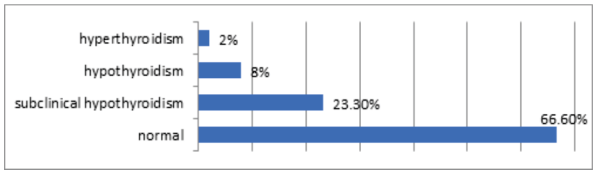

Figure 1: Bar Chart Showing The Prevalence Of Various Types Of Thyroid Dysfunction In The Study Population

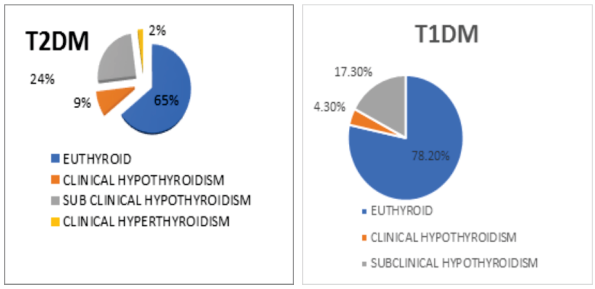

Figure 2: Pie Charts Showing The Prevalence Of Various Types Of Thyroid Dysfunction According To The Type Of Diabetes

DISCUSSION

The prevalence of thyroid dysfunction varies among different populations. The present study concluded that 33.3% of diabetic subjects had thyroid dysfunction .Overall the most common type of thyroid dysfunction found among patients was subclinical hypothyroidism (23.3%), followed by clinical hypothyroidism (8%), and then patients with clinical hyperthyroidism (2%) while

subclinical hyperthyroidism was not detected. See Figure 1. In the present study, out of 23 patients with T1DM, 4 had subclinical hypothyroidism, and one patient had overt hypothyroidism. The prevalence is 21.7%, in which all cases were of hypothyroidism. No cases of hyperthyroidism were seen. This may be due to the small size of the T1DM patients studied.

In the present study, out of a total of 150 diabetic patients, we had 116 patients who are <60 years (in adolescent, adult, and middle age group) and 34 patients who are elderly (≥60 years of age). Out of the patients < 60 Years, 24 had subclinical hypothyroidism,10 had hypothyroidism, and two patients were hyperthyroid. The overall prevalence of thyroid dysfunction for patients less than 60 years was 31.03%. Out of the elderly patients (≥ 60 years), 11 had subclinical hypothyroidism, 2 had overt hypothyroidism, and 1 had hyperthyroidism. The overall prevalence of 61 thyroid dysfunction in the elderly population was 41.17%, which is more than that of the patients who were in the age group of <60 years. The prevalence of subclinical hypothyroidism in the elderly group was 32.3%, which is more than that of the middle age, adult, and adolescent group, which is 20.6%

In the present study, the prevalence of Thyroid dysfunction was 46.9% in female and 22% in male diabetic patients. The prevalence of thyroid dysfunction was more in females as compared to males in this study and this was statistically significant(P-Value=0.006); similar results were found in other studies.

In the present study, the mean serum TSH is significantly higher in the study population. These are in agreement with the number of reports on TSH levels in type 1 and type 2 diabetes mellitus, and many studies have reported elevated TSH levels such as Gray et al.[12], Perros et al.[4], Flatau et al.[13], Ditta et al.[14],Elmenshawi IM etal.[15] In the present study there was no statistically significant difference in the mean HbA1c, mean BMI between the diabetics with abnormal thyroid profile and normal thyroid profile.

In the present study, we have observed that there is a worsening of the lipid parameters in diabetic patients with co-existing thyroid dysfunction. We have noticed elevated levels of triglycerides(p=0.02), LDL cholesterol(p=0.008), and reduced HDL levels(p=0.003) in people with diabetes with abnormal thyroid profile compared to euthyroid diabetics. Among the study subjects, those with abnormal thyroid profile have higher mean values of Triglycerides and LDL-Cholesterol and reduced mean HDL Cholesterol compared to diabetics with normal thyroid profile and this was statistically significant(P-Value<0.05).

CONCLUSION

Our study has showed 33.3% prevalence of thyroid dysfunction in diabetic patients, the most prevalent form being 23.3% of subclinical hypothyroidism followed by 8% of clinical hypothyroidism and 2% of hyperthyroidism. The increased prevalence of subclinical hypothyroidism in Diabetes mellitus patients in our study is consistent with many previous studies. Our results demonstrate that detection of thyroid dysfunction level, especially subclinical hypothyroidism and its association with biochemical abnormalities like poor glycemic control, dyslipidemia, early will enable better treatment and prevention or delay the onset of complications. A recent finding shows that subclinical hypothyroidism and DM add to significant problems such as retinopathy and neuropathy. Unrevealed thyroid dysfunction may harmfully impact Diabetes & its complications. Failure to recognize the presence of thyroid dysfunction among DM patients may be a primary cause of poor management of diabetes. We recommend universal screening, regular monitoring and treatment of thyroid dysfunction in DM patients.

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