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Research Article

A CROSS-SECTIONAL STUDY OF THYROID DISORDER IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: The objectives of the study were to assess thyroid function in diabetes mellitus by estimating free T3, free T4, and TSH in type 2 diabetic subjects, and the correlation between TSH and HbA1c.

Methods: It was a cross-sectional study. The study was conducted at the Sapthagiri Institute of Medical Science in Bengaluru, Karnataka, and a total of 75 newly diagnosed type 2 diabetes mellitus patients were enrolled for this study from January 2020 to January 2021.

Results: The prevalence of thyroid disorder among type 2 diabetes mellitus patients was 14.7% (11). Out of 11 cases, 4 (5.4%) cases belonged to hypothyroidism, 1 (1.3%) case was hyperthyroidism, 6 (8.0%) cases were subclinical hypothyroidism, and subclinical hyperthyroidism cases were not found in this study. Normal thyroid function was found in 64 (85.3%) cases.

Conclusion: Thyroid disorders are more prevalent in people with type 2 diabetes. Female diabetics are more likely to have this finding. Subclinical hypothyroidism is the most frequent thyroid disorder. Thyroid disorders are more commonly associated with diabetes among people with diabetes who have poor metabolic control.

Keywords: Type 2 diabetes mellitus, Hypothyroidism, Subclinical hypothyroidism.

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INTRODUCTION

Diabetes is rapidly approaching the position of a possible epidemic in India, with over 62 million diabetics now diagnosed [1,2]. According to Wild *et al.* [3], the global prevalence of diabetes is anticipated to quadruple from 171 million in 2000 to 366 million in 2030, with India experiencing the highest growth. Many factors influence the incidence of sickness across a country, and recognizing those factors is critical to assisting change while addressing health challenges.

Coller and Huggins investigated the role of hyperthyroidism in diabetes in 1927, establishing a link between hyperthyroidism and diabetes progression. It was discovered that surgical removal of parts of the thyroid gland had a beneficial effect on the restoration of glucose tolerance in hyperthyroid patients with concurrent diabetes [4].

Glucose metabolism is also influenced by several distinct pathways in hypothyroidism. Hypothyroidism is characterized by a lowered rate of hepatic glucose production [5], which explains why hypothyroid diabetes patients have lower insulin requirements [6].

It has been proposed that the increased FFA release could be explained in part by an increase in catecholamine-stimulated lipolysis caused by excess thyroid hormones. Furthermore, hyperthyroidism accelerates non-oxidative glucose elimination, resulting in excess lactate production, which enters the Cori cycle and encourages further hepatic gluconeogenesis. Hyperthyroidism causes an increase in GH, glucagon, and catecholamine levels, which impairs glucose tolerance by increasing insulin resistance [7].

Because there is research in this area in India, a cross-sectional study was undertaken at Sapthagiri Institute of Medical Sciences in Bengaluru to investigate thyroid disorders in patients with type 2 diabetes mellitus in a tertiary care hospital.

Aim

This study aims to assess thyroid function in diabetes mellitus by estimating free T3, free T4, and TSH in type 2 diabetic subjects.

METHODS

Study design

This was a cross-sectional study.

Study period

The study period was 12 months.

Place of study

The study was conducted in the Department of General Medicine, Sapthagiri Hospital.

Sample size

75.

Sampling technique

All type 2 diabetes mellitus patients fulfilling inclusion and exclusion criteria during the study period.

Sample size calculation.

$$n = (Z\alpha)^2 pq/d^2$$

The prevalence of diabetes in the urban Karnataka population is 11.1% (13)

p=Prevalence
q=100-p
d=Allowable error
Zα-1.96 (95% CI)=75

Inclusion and exclusion criteria

Inclusion criteria

The following criteria were included in the study:

- All known case of type 2 diabetes mellitus patients and newly diagnosed type 2 diabetes mellitus based on HbA1C, FBS, and PPBS
- All type 2 diabetes mellitus cases who are on hypoglycemic drugs (insulin and oral hypoglycemic drugs).

Exclusion criteria

The following criteria were excluded from the study:

- Gestational diabetes
- Patients who were previously diagnosed with thyroid disorders.

Methods of collection of data

Methodology

After obtaining approval and clearance from the ethical committee, a detailed history and clinical examination were carried out on all the subjects who gave informed consent to participate in the study, and necessary investigations were done as follows:

- FREE T3 (normal range: 4.26–8.10 pmol/l)
- FREE T4 (normal range: 6.4–20.6 pmol/L)
- TSH (normal range: 0.46–4.68 μIU/L).

According to the American Diabetic Association guideline (2021)

Result	Fasting plasma glucose (FPG)
Normal	<100 mg/dl
Pre-diabetes	100–125 mg/dl
Diabetes	126 mg/dl or higher

Result	HbA1C
Normal	<5.7%
Pre-diabetes	5.7–6.4%
Diabetes	6.5% or higher

All participants were questioned using a standardized questionnaire that had been pre-tested. We collected demographic data as well as other pertinent information. The thyroid gland in the neck was checked for enlargement. Routine examinations for diabetic problems were also performed. A fundoscopy was performed with the help of an ophthalmologist. A tuning fork (vibration sense) and a tendon hammer were used to test the individuals for peripheral neuropathy (deep tendon reflex). Weight and height were obtained as anthropometric measures.

Diagnosis criteria for thyroid dysfunction

Participants with high TSH and low fT3 and fT4 were diagnosed with primary hypothyroidism, whereas those with high TSH but normal fT3 and fT4 were diagnosed with subclinical hypothyroidism [8,9]. Those with low TSH and high fT3 and fT4 were considered to have primary hyperthyroidism, while those with low TSH but normal fT3 and fT4 were considered to have subclinical hyperthyroidism (39–41). Subjects with normal or low TSH but low fT3 and fT4 were considered to have secondary hypothyroidism [10].

Thyroid function assay procedure

T2DM participants' and controls' frozen sera were thawed and allowed to reach room temperature. The samples were tested for free T3, free T4, and TSH in three runs, each on a separate day, in batches. Each run of the analyses was evaluated using the control samples given in the reagents kits, according to the manufacturer's instructions.

Analytical statistics

The Statistical Package for the Social Sciences (SPSS) IBM version 23 was used to analyze the study's data. The mean and SD was used to compare quantitative variables such as weight, height, blood pressure, serum TSH, and serum T3, and correlation and coefficient were also analyzed to compare the proportions. A statistically significant value was defined as $p<0.05$.

RESULTS

Age distribution among type 2 diabetes mellitus patients, we have found a majority of the cases belonged to the 41–50 years of age group, that is, 20 (26.7%). The next most common age group was 20–30 years. Eighteen (24%) cases belonged to this age group. In the 31–40 years of age group, patients consisted of 16 (21.3%), another 13 (17.3%) and 8 (10.7%) cases were found in the 51–60 years and above 60 years of age group, respectively. The mean age was 42.44 years (Table 1).

Sex distribution among the study population female cases was predominantly higher than male cases, female cases were 53 (70.7%) and male cases were 22 (29.3%), respectively. The male and female ratio was 1:2.40 (Table 2).

We have found in anthropometric measurement among type 2 diabetes mellitus patients, that the mean height was 162.16 cm, mean weight was 64.70 cm, and mean BMI was 24.86 kg/m^2 (Table 3).

Maximum no. of the cases was suffering from diabetes >5 years, that is, 47 (62.6%) cases. Twenty-three (30.7%) cases had diabetes during 1–5 years. Only 5 (6.7%) cases had diabetes during <1 year, respectively. The mean duration of diabetes among the study population was 6.40 years (Table 4).

Table 1: Age distribution among type 2 diabetes mellitus patients (n=75)

Age in year	No. of cases	Percentage
20–30	18	24.0
31–40	16	21.3
41–50	20	26.7
51–60	13	17.3
Above 60	08	10.7
Total	75	100.0

Table 2: Sex distribution among type 2 diabetes mellitus patients (n=75)

Sex	No. Of cases	Percentage
Male	22	29.3
Female	53	70.7
Total	75	100.0
M: f	Ratio – 1:2.40	

Table 3: Anthropometric measurement among type 2 DM patients (n=75)

Anthropometric measurement	Type 2 DM patients
	Mean±SD
Height (cm)	162.16±7.05
Weight (kg)	64.70±10.43
BMI (kg/m^2)	24.86±4.65

Table 4: Duration of the diabetes among the study population (n=75)

Duration	No. of cases	Percentage
<1 year	05	6.7
1–5 years	23	30.7
>5 years	47	62.6
Total	75	100.0
Mean±SD	6.40±3.41	

Our study participant's mean blood sugar (F) was 146.70 mg/dl. Blood sugar (PP) was 256.84 mg/dl and mean HbA1c was 8.13%, respectively (Table 5).

The prevalence of thyroid disorder among type 2 diabetes mellitus patients was 14.7% (11). Out of 11 cases, 4 (5.4%) cases belonged to hypothyroidism, 1 (1.3%) case was hyperthyroidism, 6 (8.0%) cases were subclinical hypothyroidism, and subclinical hyperthyroidism cases were not found in this study. Normal thyroid function was found in 64 (85.3%) cases (Table 6).

In hypothyroidism cases, the mean value of FT3 was 2.85 pmol/L, FT4 was 2.32 pmol/L, and TSH was 17.87 µIU/l. We have found in hyperthyroidism cases, the mean value of FT3 was 9.96 pmol/L, FT4 was 23.40 pmol/L, and TSH was 0.015 µIU/l. In subclinical hypothyroidism cases, the mean value of FT3 was 5.61 pmol/L, FT4 was 18.65 pmol/L, and TSH was 10.55 µIU/l, respectively (Table 7).

The mean FT3 was 5.73 pmol/L, FT4 was 15.28 pmol/L, and TSH was 2.20 µIU/l found in euthyroid cases.

We have found a positive correlation between sugar (F) and TSH in type 2 diabetes mellitus patients. Correlation factor was 0.330* and p=0.047 (Table 8).

We have found a positive correlation between sugar (PP) and TSH in type 2 diabetes mellitus patients. Correlation factor was 0.297* and p=0.010 (Table 9).

We have found a positive correlation between HbA1c and TSH in type 2 diabetes mellitus patients. Correlation factor was 0.262* and p=0.023 (Table 10).

DISCUSSION

The study included 75 type 2 diabetic patients between the ages of 25 and >60 who were all shown at the Medicine Department OPD at Sapthagiri Institute of Medical Sciences in Bengaluru. Based on history and biochemical studies, all of the patients were examined and diagnosed with type 2 diabetes mellitus.

In this study, the prevalence of thyroid disorder among type 2 diabetes mellitus patients was 14.7% (11). Out of 11 cases, 4 (5.4%) cases belonged to hypothyroidism, 1 (1.3%) case was hyperthyroidism, 6 (8.0%) cases were subclinical hypothyroidism, and subclinical hyperthyroidism cases were not found in this study. Normal thyroid function was found in 64 (85.3%) cases.

These findings show a high incidence of abnormal thyroid hormone levels in the diabetic population, which is supported by various studies [11].

About 89% of patients in a study by Moghetti *et al*. [12] had hypothyroidism, while 11% had hyperthyroidism. Celani *et al*. [11] & Udiong *et al*. [13] also found that subclinical hypothyroidism was the most common followed by hypothyroidism (23.1%).

In this study, age distribution among type 2 diabetes mellitus patients, we have found the majority of the cases belonged to the 41–50 years of age group, that is, 20 (26.7%). The next most common age group was 20–30 years; 18 (24%) cases belonged to this age group. In the 31–40 years of age group, patients consisted of 16 (21.3%), another 13 (17.3%), and 8 (10.7%) cases were found in the 51–60 years and above 60 years of age group, respectively. The mean age was 42.44 years.

The mean age of type 2 DM patients in this study was 57.5 years. This may be because the prevalence of type 2 DM increases with age [14].

This reflects the pattern observed by Chinenye *et al.* (57.1) in a multicenter study involving DM patients [15].

Ofoegbu *et al.* reported a mean age of 59.2 years in Enugu in a study that evaluated the body composition of Nigerians with DM [16].

Table 5: Distribution of BSF, BSPP, and HbA1C of type 2 DM patients (n=75)

Variables	Type 2 DM patients
	Mean±SD
BSF (mg/dl)	146.70±35.76
BSPP (mg/dl)	259.84±65.88
HbA1c (%)	8.13±1.65

Table 6: Prevalence of thyroid disorder among type 2 diabetes mellitus patients (n=75)

Thyroid disorder	No. of cases	Percentage
Hypothyroidism	4	5.4
Hyperthyroidism	1	1.3
Subclinical hypothyroidism	6	8.0
Subclinical hyperthyroidism	00	0.0
Euthyroid	64	85.3
Total	75	100

Table 7: Mean±SD value of FT3, FT4, and TSH in thyroid disorder cases among type 2 diabetes mellitus patients (n=75)

Thyroid disorder	FT3 (pmol/L)	FT4 (pmol/L)	TSH (µIU/l)
Hypothyroidism	2.85±0.57	2.32±1.63	17.87±3.91
Hyperthyroidism	9.96±0.00	23.40±0.00	0.015±0.00
Subclinical hypothyroidism	5.61±1.32	18.65±5.27	10.55±0.96
Euthyroid	5.73±1.38	15.28±2.90	2.20±0.69

Table 8: Correlations between blood sugar (F) and TSH

	FBS	TSH
FBS		
Pearson correlation	1	0.230*
p value		0.047
No. of cases	75	75

*Correlation is significant at the 0.05 level (two tailed)

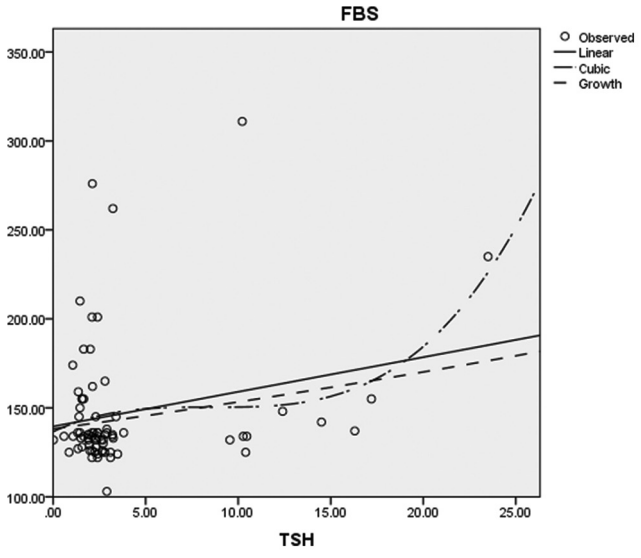


Table 9: Correlations between blood sugar (PP) and TSH

	PPBS	TSH
PPBS		
Pearson correlation	1	0.297*
p value		0.010
No. of cases	75	75

*Correlation is significant at the 0.05 level (two tailed)

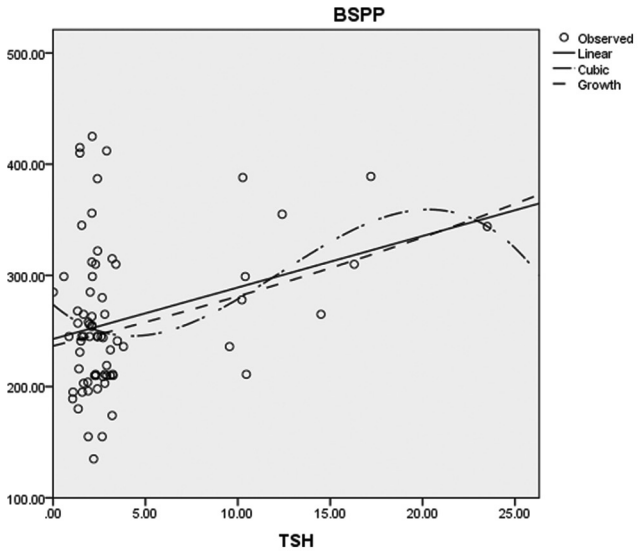
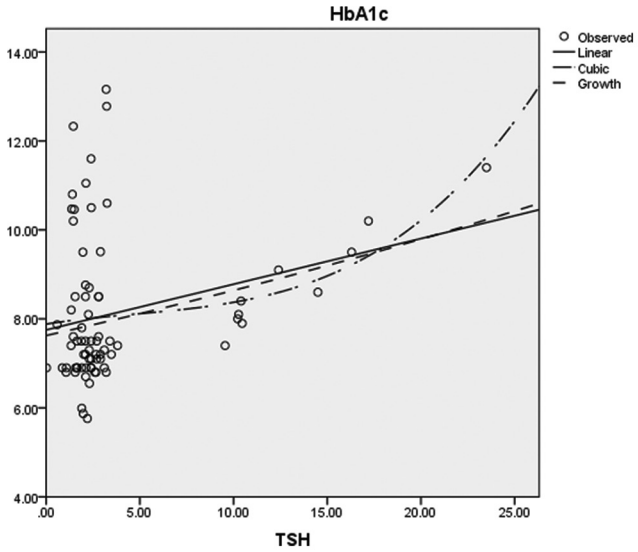


Table 10: Correlations between blood HbA1c and TSH

	HbA1c	TSH
HbA1c		
Pearson correlation	1	0.262*
p value		0.023
No. of cases	75	75

*Correlation is significant at the 0.05 level (two tailed)



Okafor *et al.* in Enugu reported 55.7 years as the mean age of type 2 DM patients they evaluated for cardiometabolic risk factors [17].

In this study, sex distribution among the study population female cases was predominantly higher than the male case, female cases were 53 (70.7%) and male cases were 22 (29.3%), respectively. The male and female ratio was 1:2.40.

Females with type 2 diabetes were 3.8 times more likely than males to suffer thyroid dysfunction, according to Telwani *et al.* [18]. This is in line with the findings of an Indian study, which found that ladies were more likely than males to suffer from thyroid issues (69% vs. 31%). These findings are also in line with those of some other studies. As a result, the female gender has an impact on the occurrence of thyroid diseases in diabetic patients [19].

Anthropometric measurement among type 2 diabetes mellitus patients, the mean height was 162.16 cm, mean weight was 64.70 cm, and mean BMI was 24.86 kg/m^2.

Thyroid dysfunction was found to be linked with central obesity (abnormal waist circumference) (OR=2.5, 95% CI=1.5–5.2, p=0.001). This is comparable to the findings of Udenze *et al.* in Lagos, Nigeria, who found a link between waist circumference and thyroid dysfunction [20]. Thyroid dysfunction and obesity were also linked with metabolic syndrome, according to Biondi *et al.* [21]. This could be since obesity and leptin are linked. Leptin regulates TRH gene expression in the paraventricular nucleus, making it an essential neuroendocrine regulator of the hypothalamic-pituitary-thyroid axis [22]. Other theories proposed to explain the link between increased TSH, obesity, and subclinical hypothyroidism in some groups include iodine deficiency, autoimmune thyroiditis, and mutations in the TSH receptor genes [22].

Duration of diabetes of type 2 DM patients data is presented in Table 4. Maximum no. of the cases was suffering from diabetes >5 years, that is, 47 (62.6%) cases. Twenty-three (30.7%) cases had diabetes during 1–5 years. Only 5 (6.7%) cases had diabetes during <1 year, respectively. The mean duration of diabetes among the study population was 6.40 years.

Stanley *et al.* [23] study observed female gender, central obesity, and duration of DM >5 years.

The distribution of BSF, BSPP, and HbA1C of type 2 DM patients' data is presented in Table 7. We have found in thyroid disorder cases; all variables were much higher than those who had normal thyroid in type 2 diabetic patients.

In hypothyroidism cases, the mean value of FT3 was 2.85 pmol/L, FT4 was 2.32 pmol/L, and TSH was 17.87 μIU/l. We have found in hyperthyroidism cases, the mean value of FT3 was 9.96 pmol/L, FT4 was 23.40 pmol/L, and TSH was 0.015 μIU/l. In subclinical hypothyroidism cases, the mean value of FT3 was 5.61 pmol/L, FT4 was 18.65 pmol/L, and TSH was 10.55 μIU/l, respectively.

The mean FT3 was 5.73 pmol/L, FT4 was 15.28 pmol/L, and TSH was 2.20 μIU/l found in euthyroid cases.

Our study participant's mean blood sugar (F) was 146.70 mg/dl. Blood sugar (PP) was 256.84 mg/dl and mean HbA1c was 8.13%, respectively.

Elevated HbA1c (poor glycemic control) has been linked to chronic DM problems. According to this study, type 2 diabetes patients with high HbA1c were 4.3 times more likely to have thyroid dysfunction than those with good glycemic control (HbA1c 7%). This could be attributed to chronic hyperglycemia's negative effects on the hypothalamic-pituitary axis, where it reduces or eliminates the nocturnal TSH peak [24]. Clinical and subclinical hypothyroidisms have both been classified as insulin-resistant conditions in prior research. In his study, Bazrafshan *et al.* [25]

discovered a substantial association between HbA1c levels and TSH levels, which are consistent with our findings. Ardekani *et al.* [26] found that HbA1c levels were considerably higher in diabetic patients with thyroid problems, which is consistent with our findings.

Hyperglycemia also reduces the activities of thyroxine deiodinase, which decreases the peripheral deiodination of T4 to T3 (8). In their study, Schlienger *et al.* [27] titled "Effect of diabetic management on the level of circulating thyroid hormones," Schlienger *et al.* discovered that poor diabetes control (glycosylated hemoglobin 12%) is linked to a low T3 syndrome due to impaired T4 to T3 conversion.

We have found positive correlation between sugar (F) (PP) and HbA1c versus TSH in type 2 diabetes mellitus patients. Correlation factor was sugar (F) versus TSH 0.330* and p=0.047. Sugar (PP) versus TSH was 0.297* and p=0.010. HbA1c versus TSH was 0.262* and p=0.023, respectively.

The correlation between HbA1c and TSH is consistent with Velija-Asimi and Karamehic findings [28]. They looked at the impact of treating hypothyroidism on metabolic regulation and hyperinsulinemia and found a positive and significant association between TSH and HbA1c. The findings contradict those of Celani *et al.* and Smithson who found different amounts of thyroid hormones in diabetic patients [11].

CONCLUSION

Thyroid disorders are more prevalent in people with type 2 diabetes. Female diabetics are more likely to have this finding. Subclinical hypothyroidism is the most frequent thyroid disorder. Thyroid disorders are more commonly associated with diabetes among diabetics who have poor metabolic control. Thyroid hormones affect glycosylated hemoglobin levels as well. In light of the high yield reported in this investigation, as well as the possibility of thyroid disease symptoms being hidden by the diabetes condition and thyroid exacerbating the diabetic image, biochemical thyroid disease screening in diabetic patients is recommended.

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AUTHORS' CONTRIBUTIONS

H.O.D. was involved in the study's design and coordination, as well as helping to draft the manuscript and doing the statistical analysis.

CONFLICTS OF INTEREST

I declare that there was no business or financial relationships that may be considered as a potential conflict of interest during the research.

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