



## Original Article

# To Study the Frequency of Thyroid Disorders in Patients with Type II Diabetes Mellitus

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## Abstract

**Introduction:** Type II diabetes and thyroid disorder are the two most commonly encountered endocrine disorders in our community. The presence of thyroid disorder in patients with diabetes deteriorates the glycemic control and hence increases the incidence of complications. Hence the prevalence of thyroid disorder in patients with T2DM needs to be investigated.

**Aims and Objectives:** The present study is done to study the frequency of thyroid disorders in patients with type 2 Diabetes mellitus patients and to determine the subtypes of thyroid disorders in patients with type 2 diabetes mellitus.

**Materials and Methods:** In this cross sectional study, data of 110 type II diabetes mellitus patients visiting the OPD and IPD of the department of general medicine of Sri Siddhartha Medical College hospital, Tumkur are included. Inclusion criteria are all patients with T2dm with onset of diabetes  $\geq 30$  years with duration of diabetes  $\geq 6$  months. Exclusion criteria are patients with T1DM, gestational DM, pancreatitis, & steroid induced diabetes.

**Results:** Out of the 110 diabetic patients 43(39.1%) are males and 67(60.9%) are females; 73 (66.4%) are euthyroid, 24 (21.8 %) have sub-clinical hypothyroidism (5 males & 19 females), 8 (7.3%) have clinical hypothyroidism (7 females and 1 male), 3 (2.9%) have clinical hyperthyroidism (2 male & 1 female) & 2 (1.8%) have subclinical hyperthyroidism (both females).

- BMI was significantly higher in T2DM patients with thyroid dysfunction ( $p=0.027$ ) especially in patients with subclinical hypothyroidism ( $p=0.034$ ).
- The incidence of thyroid dysfunction was higher in female T2DM patient's than their male counterparts ( $p=0.008$ ).
- The incidence of hypertension was higher among T2DM patients with thyroid dysfunction than the euthyroid T2DM patients ( $p=0.035$ ).
- Mean FBS & PPBS was significantly higher in T2DM patient's with thyroid dysfunction when compared to T2DM patient's without thyroid dysfunction ( $p < 0.001$  &  $p < 0.001$  respectively).
- Poor achievement of the guideline recommended target of FBS & PPBS was seen in T2DM patients ( $p < 0.001$  &  $p < 0.001$  respectively) with thyroid dysfunction, especially in patients with sub-clinical hypothyroidism ( $p < 0.001$  &  $p = 0.001$  respectively).
- FBS & PPBS were significantly higher in patients with higher BMI. ( $p=0.014$  &  $p=0.027$  respectively.)

**Conclusions:** *There is an increased frequency of thyroid disorders in patients with T2DM, especially in female diabetics & in diabetics with higher BMI. The glycemic control was also poor in T2DM patients with thyroid dysfunction, especially among the Sub-clinical hypothyroid patients. There was also higher incidence of hypertension among T2DM patients with thyroid dysfunction. Hence, routine screening for thyroid dysfunction in type 2 diabetes mellitus patients may be justified especially in females and in patients with higher BMI.*

**Keywords:** *Type 2 diabetes mellitus, hypothyroidism, subclinical hypothyroidism, hyperthyroidism, subclinical hyperthyroidism, BMI.*

**MeSH Terms:** *Diabetes Mellitus, Type II Type 2 Diabetes, Type 2 Diabetes Mellitus.*

## Introduction

Type II diabetes and thyroid disorder are the most commonly encountered endocrine disorders in our community. T2DM is the predominant form of diabetes worldwide, accounting for 91% of cases worldwide<sup>1</sup>. Thyroid diseases are also a common endocrinopathy seen in the adult population. Insulin and triiodothyronine both closely participate in cellular metabolisms. Thus excess or deficiency of either insulin or thyroid hormones could result in the functional derangement of the cellular metabolism.

Diabetes mellitus involves multiple organ systems and leads to significant morbidity and mortality due to accompanying microvascular and macrovascular complications. Diabetes mellitus has been defined as "A metabolic syndrome characterized by chronic hyperglycemia and disturbance of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency in insulin secretion and or insulin action".

Hypothyroidism causes reduced renal clearance of insulin<sup>2</sup> and hence diabetic patients on insulin may suffer from recurrent episodes of hypoglycaemia. Hypothyroidism is also known to cause weight gain and insulin resistance. Abnormalities in leptin metabolism may be responsible for the above pathology. Leptin is a product of ob gene secreted by the adipocytes.<sup>3</sup> Increased leptin levels decreases appetite and increases energy expenditure. Inactivating mutations in leptin or leptin receptor causes early onset obesity.<sup>3</sup>

The presence of thyrotoxicosis in patients with diabetes deteriorates the glycemic control. Poor control of diabetes may play a role in occurrence of thyroid dysfunction, as high glucose levels results in decreased TSH secretion and the

nocturnal peak of TSH is impaired in all the patients of diabetes mellitus regardless of their blood glucose control and HbA1c.

If a patient with diabetes mellitus is also suffering from clinical or subclinical hypothyroidism then the risk of him developing diabetic retinopathy and diabetic nephropathy increases many fold. Not just the frequency but also the severity of diabetic retinopathy is increased in such patients<sup>4</sup>.

A plethora of studies have evidenced an array of complex intertwining biochemical, genetic and hormonal malfunctions mirroring the pathophysiological association between diabetes mellitus and thyroid dysfunction.

Hence if the patients in our community with type II diabetes mellitus truly have a higher incidence of thyroid disorders, then a routine thyroid function test in all these patients can be justified because early detection of thyroid disorders and its prompt correction helps substantially in achieving glycemic control and thus helps in preventing the complications of diabetes mellitus and ameliorating the quality of life of patients suffering from type II dm. Correcting the underlying thyroid disorder even if subclinical, will help in achieving the target HbA1c.

The present work is a modest attempt to study the prevalence of thyroid disorders in patients with type 2 diabetes mellitus.

## Materials and Methods

The present study titled "To Study the Frequency of Thyroid disorders in patients with Type II Diabetes Mellitus" was carried out in the department of general medicine in Sri Siddhartha Medical College & Research Centre, Agalkote, Tumkur.

**Source of Data:** The study group includes all type II diabetes mellitus patients visiting the OPD and IPD of the department of general medicine of Sri Siddhartha Medical College hospital, Tumkur.

**Study Design:** Cross sectional study

#### Inclusion criteria

1. All patients with type ii diabetes:
  - With onset of diabetes at an age  $\geq 30$  years
  - With duration of diabetes for  $\geq 6$  months.
2. All type II diabetes mellitus patients regardless of their glycemic control.
3. All type II diabetes mellitus patients regardless of their treatment (oral anti-diabetic agents/insulin).

#### Exclusion criteria

1. Type I DM
2. Patients with:
  - a) Gestational diabetes mellitus.
  - b) Pancreatitis
  - c) Steroid induced diabetes
  - d) History of thyroidectomy
  - e) History of radioactive iodine

#### Sample size

Sample size has been calculated using the formula

$$N = z^2 \times p(1-p) / d^2$$

N – minimum sample size required

Z = confidence interval at 95% (standard value of 1.96)

P = 29% (estimated from a prospective study of thyroid-dysfunction in patients with type 2 diabetes in general population from ravishankar et al. Imedpub journals 2013, vol.5 no. 1:2)

D=margin of error (0.09)

$$D = z \times \sqrt{p(1-p)} / 100 = 1.96 \times \sqrt{0.29(1-0.29)} / 100 = 0.09$$

$$N = (1.96)^2 \times 0.29(1-0.29) / (0.09)^2 = 98$$

The minimum sample size for this study is 98 patients with type 2 diabetes. To cater for hemolysed and lipemic samples, data will be collected from 110 subjects.

#### Methods of collection of data

Pretested structured questionnaire was prepared first. Collection of data was started once clearance was obtained from Ethical clearance committee of Sri Siddhartha Medical College, Tumkur. After taking informed consent from the patients, the type II diabetes mellitus patients attending OPD and IPD of the department of general medicine of Sri Siddhartha Medical College Hospital during the January 2017 to October 2018 who satisfied the inclusion criteria and those who did not come under the exclusion criteria were screened for thyroid function (t3, t4 and TSH) and were studied according to the proforma.

#### Materials

Questionnaire, Body mass index, Blood pressure, Fasting blood sugar, Post prandial blood sugar, Thyroid profile (fT3, fT4, TSH) and Fundus examination.

The patients for the study were selected without any bias for sex, severity or control of diabetes. Complete history was recorded with particular emphasis on symptoms of thyroid dysfunction. The presence of associated illness like hypertension were noted. Family history regarding diabetes mellitus and treatment history of oral hypoglycemics or insulin along with duration was also included.

A thorough general and systemic examination was carried. The fundus examination for diagnosis of diabetic retinopathy was also done.

#### BMI calculation

Body mass index (BMI) is calculated with height and weight of the subject using the following formula - BMI = weight (kg) / height (m)<sup>2</sup>.

#### Blood sugar

Both fasting and postprandial blood sugar are estimated by trinder's (glucose oxidase) method and read at 505/670 nm.

#### Thyroid profile

Estimation done in fasting serum sample.

Laboratory estimation of serum ft3, ft4 and tsh levels will be done by ultrasensitive sandwich Chemi-Lumiscence Immuno Assay (C.L.I.A.)

Method for which 2 ml of venous blood will be drawn from the patient and centrifuged and the serum (500µml) collected from that will be incubated for 1 hour at room temperature after adding the reagent (separately for ft3, ft4 &tsh). Instrument used: advia centaur.

Normal readings are:

- Thyroid stimulating hormone (tsh): 0.30 – 5.5 µIu/ml
- Free t4: 0.70 – 1.80 ng/dl
- Free t3: 1.7 – 4.2 pg/dl

### 5.11 Data management and Analysis:

Data was entered into Microsoft excel and was compared with data on the hard copy forms to ensure accuracy. Inconsistencies were detected by running simple frequencies and correlations and those identified were addressed before data analysis began.

Data was summarized using tables, pie charts and bar charts. Continuous data e.g.age, duration of Diabetes mellitus, blood pressure, weight, height, BMI, FBS, PPBS, TSH, fT3 and fT4were summarized using measures of central tendency (Means, Medians, mode, minimum, maximum and standard deviations). Nominal variables e.g. gender, marital status, education level, types of medication used, family history of diabetes and patterns of thyroid dysfunction were summarized using counts, frequencies and proportions. Analysis was done using SPSS version 23.0.

For Categorical variables based on distribution Pearson Chi-Square test was used to compare groups. In cross tabs bigger than 2 x 2, if more than 20% of the cells had an expected count less than 5 then likelihood ratio was taken into consideration. In 2 x 2 cross tabs if all 4 cells had an expected count of >10 than Pearson Chi-Square test was used and if any of the cells had an expected count of < 10 than Fisher's Exact test was used.

For continuous variables Student's t-test (Independent samples t-test) was used.

Independent samples Kruskal-Wallis test was used for non-parametric analysis.

### Results

The study sample included 110 patients with type 2 diabetic mellitus visiting the outpatient department and also those in the inpatient department. Each patient was assessed clinically and by laboratory investigations as per the proforma.

Following observations regarding thyroid profile in patients with type 2 diabetes mellitus were made in the study:

- In the present study, 33.63% (37) of the total 110 patients with T2 diabetes mellitus had an abnormal thyroid profile.
- Sub-clinical hypothyroidism being the most common type of thyroid dysfunction accounted for 21.8% of the patients (24/110). 7.3% of the patients (8/110) had clinical hypothyroidism which was the 2<sup>nd</sup> most common type of thyroid dysfunction. 2.7% (3/110) had clinical hyperthyroidism and 1.8 % (2/110) had sub-clinical hyperthyroidism.
- There is a statistically significant correlation between thyroid dysfunction and gender, systemic hypertension, BMI, mean and target FBS & PPBS.
- However, there was no correlation between thyroid dysfunction and age, duration of diabetes, type of treatment, family history of diabetes.
- The frequency of thyroid dysfunction among the T2DM patients studied is33.63%. Sub-clinical hypothyroidism being the most common type of thyroid dysfunction accounted for 21.8% of the patients.
- The thyroid dysfunction is more common in female patients (78.4%) with type 2 DM than their male (21.6%) counterparts. (p=0.008)
- There is an increased incidence of hypertension in T2 DM patients with thyroid dysfunction. (p=0.035)
- BMI was significantly higher in T2DM patients with thyroid dysfunction

(p=0.027) especially in patients with subclinical hypothyroidism.(p=0.034)

- Mean FBS & PPBS is significantly higher in patients with thyroid dysfunction. (p<0.001 & p<0.001 respectively)
- Poor achievement of the guideline recommended target of FBS & PPBS was seen in T2DM patients with thyroid

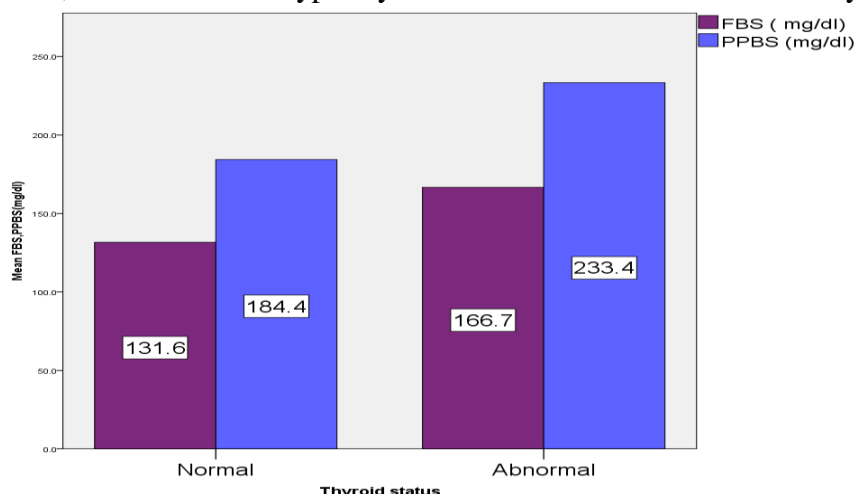
dysfunction (p<0.001 & p<0.001 respectively) especially in patients with sub-clinical hypothyroidism.(p<0.001 & p=0.001 respectively)

- FBS & PPBS were significantly higher in patients with higher BMI. (p=0.014 & p=0.027 respectively).

**Table 12:** Distribution of cases among different categories of thyroid function

		Number of cases	Percentage
Diagnosis	Clinical hyperthyroidism	3	2.7%
	Clinical hypothyroidism	8	7.3%
	Euthyroid	73	66.4%
	Subclinical hyperthyroidism	2	1.8%
	Subclinical hypothyroidism	24	21.8%
	<b>Total</b>	<b>110</b>	<b>100.0%</b>

Among the study group 66.4% had normal thyroid profile, 7.3% had overt hypothyroidism, 21.8% had subclinical hypothyroidism, 2.7% had overt hyperthyroidism and 1.8% had subclinical hyperthyroidism.



Mean FBS & PPBS in patients with normal thyroid function 131.6 mg/dl and 184.4 mg/dl respectively whereas mean FBS & PPBS in patients with thyroid dysfunction are 166.7 mg/dl and 233.4 mg/dl respectively.

**Discussion**

In the present study, 21.8% of the patients (24/110) had sub-clinical hypothyroidism, 7.3% of the patients (8/110) had clinical hypothyroidism and 2.7% (3/110) had clinical hyperthyroidism and 1.8 % (2/110) had sub-clinical hyperthyroidism. Similar findings were observed in a study by Pramanik et al<sup>5</sup> done in 100 T2 diabetes mellitus patients in Eastern India in which 23 % (23/100) patients had sub-clinical hypothyroidism and 3%(3/100) had clinical hypothyroidism.

Out of 37 patients with abnormal thyroid status 14 patients (37.8%) were of age between 31-40 years, 8 patients (21.6%) were between 41-50 years, 6 patients (16.2%) were between 51-60 years, 8 patients (21.6%) were between the age group of 61-70 years, and 1 patient (2.7%) was between the age group of 71-80 years. Compared with normal thyroid profile group it has no statistical significance. (p=0.274). The present study is similar to Papazafiropoulou et al who found age did not correlate with altered thyroid profile in diabetic patients.<sup>6</sup>

Out of 37 T2DM patients with abnormal thyroid status 8 patients (21.6%) were males and 29 patients (78.4%) were females whereas out of 73 patients with thyroid dysfunction 35 patients (47.9%) were males and 38 patients (52.1%) were females. It is statistically significant. Hence there is a higher incidence of thyroid dysfunction in female diabetics than their male counterparts. ( $p = 0.008$ ). This finding is similar to the study by Papazafiropoulou et al who found in their study that thyroid dysfunction was significantly more among females than male diabetic patients.<sup>6</sup>

Out of 37 patients with abnormal thyroid status 14 patients (37.8%) had diabetes for 1-5 years, 17 patients (45.9%) had diabetes for 6-10 years and 3 patients (8.1%) had diabetes for 11-15 years and another 3 patients (8.1%) had diabetes for 16-20 years. When compare with normal thyroid profile group it is of no statistical significance. ( $p=0.572$ ). The findings of our study are similar to that by Al-Wazzan et al<sup>7</sup> who did not find any correlation between duration of diabetes mellitus and subsequent development of thyroid dysfunction.

Out of 37 T2DM patients with thyroid dysfunction only 10 patients (27%) had no systemic hypertension and 27 patients (73%) had systemic hypertension whereas out of 73 T2DM patients with normal thyroid function 38 patients (52.1%) had systemic hypertension and 35 patients (47.9%) were normotensives. It is statistically significant. Hence there is a higher incidence of hypertension in T2DM patients with abnormal thyroid status. ( $p = 0.035$ ). However, it is not known to what degree the effect of thyroid dysfunction has with regards to development of hypertension due to other variables like age and hyperlipidemia. In contrast, Shanmugam S et al, Chubb et al and Papazafiropoulou et al who in their study found that there was no significant association of altered thyroid profile with systemic hypertension.<sup>8,9,6</sup>

Out of the 37 T2DM patients with thyroid dysfunction 4 patients (10.8%) had normal BMI, 6 patients (16.2%) were at risk, 13 patients (35.1%) had Class I obesity, 14 patients (37.8%) had Class

II obesity whereas out of the 73 patients with normal thyroid function, 8 (11%) had normal BMI, 27 patients (37%) were at risk of obesity, another 27 patients (37%) had class I obesity and 11 patients (15.1%) had class II obesity. Thus it was observed that BMI was significantly higher in T2DM patients with thyroid dysfunction ( $p=0.027$ ) especially in patients with subclinical hypothyroidism ( $p=0.034$ ). Similar findings were reported by Telwani AA et al and Papazafiropoulou et al who found in their study that type 2 diabetic patients with thyroid dysfunction had significantly higher BMI compared to type 2 diabetic patients without thyroid dysfunction.<sup>10,6</sup>

Mean FBS & PPBS in patients with normal thyroid function is 131.6 mg/dl and 184.4 mg/dl respectively whereas mean FBS & PPBS in patients with thyroid dysfunction are 166.7 mg/dl and 233.4 mg/dl respectively. It is statistically significant. Thus mean FBS & PPBS is significantly higher in patients with thyroid dysfunction ( $p<0.001$  &  $P<0.001$ ).

Among 73 patients with normal thyroid function 75.3% had FBS  $\leq$  130 mg/dl and 42.9% had FBS  $>$  130mg/dl, whereas among 37 patients with thyroid dysfunction only 35.1% had FBS  $\leq$  130mg/dl and 64.9% had FBS  $>$  130mg/dl, which is statistically significant. Hence there is an association between thyroid status and achieving target FBS ( $p<0.001$ ). Among 24 Type 2DM patients with Sub-Clinical Hypothyroidism 6 (25%) had FBS  $\leq$  130mg/dl and 18 (75%) had FBS  $>$  130 mg/dl and when compared to the Type 2 DM patients of other categories of thyroid spectrum it is statistically significant indicating poor achievement of guideline recommended FBS target in T2 DM patients with sub-clinical hypothyroidism ( $p<0.001$ ). Also Among 73 patients with normal thyroid function 72.6% had PPBS  $\leq$  180 mg/dl and 27.4% had PPBS  $>$  180mg/dl, whereas among 37 patients with thyroid dysfunction only 37.8% had PPBS  $\leq$  180mg/dl and 62.2% had PPBS  $>$  180mg/dl, which is statistically significant. Hence there is an

association between thyroid status and achieving of guideline recommended target PPBS ( $P < 0.001$ ). Among 24 Type 2DM patients with Sub-Clinical Hypothyroidism, 7 (29.2%) had PPBS  $\leq 180$ mg/dl and 17 (70.8%) had PPBS  $> 180$ mg/dl and when compared to the Type 2 DM patients of other categories of thyroid spectrum it is statistically significant indicating poor achievement of guideline recommended PPBS target in T2DM patients with sub-clinical hypothyroidism ( $p = 0.001$ ). Studies by Jain G et al, Shanmungam S and Singh T et al et al also made similar observations and that the glycemic control was poor among diabetic patients with thyroid dysfunction.<sup>11,8,12</sup>

In our study we found that there is a statistically significant difference in the distribution of FBS & PPBS across different categories of weight with FBS & PPBS being higher in patients with higher BMI. ( $p = 0.014$  &  $p = 0.027$  respectively). Similar findings were reported in a study by McLarty et al who reported that prevalence of IGT in subjects of all age group increased with rising BMI.<sup>14</sup> Yongik et al reported that the prevalence of diabetes mellitus and IGT increased with rising BMI and with increase in waist-hip ratio.<sup>13</sup>

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