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The Pattern of Thyroid Dysfunction in Women with Type 2 Diabetes Mellitus - A Cross-Sectional, Observational Study

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Abstract

Introduction/Background:

There has been a linear relationship between blood sugar levels and thyroid dysfunction proven before by various studies. There is a positive association between HbA1c/FBS levels with TSH found in previous studies. Diabetes and thyroid are the most common endocrine disorders in the world. Female gender is a risk factor for the development of thyroid dysfunction. Thyroid and diabetes are closely interrelated due to various biochemical and hormonal changes in the body. In our study, we studied the multiple patterns of thyroid dysfunction in female diabetic patients and the prevalence of diabetes in them, and we correlated various thyroid and diabetic parameters.

Aim of the study:

"To study the pattern of thyroid dysfunction in women with type 2 diabetes mellitus."

Materials and methods:

A Cross-sectional study is done on ninety-eight women who are type 2 diabetic patients visiting the department of general medicine in a tertiary medical centre in Tumkur, Karnataka, for one and half years [2021 and 2022]. Ethical clearance from the institution and consent from the patient is obtained.

Results:

A spearman's correlation analysis is conducted among all the diabetic parameters, FBS, PPBS, HbA1c, Thyroid Parameters, T3, T4, and TSH. The correlation matrix shows that TSH is positively correlated [r value is +] to FBS, PPBS, and HbA1c. The result is tested with a p-value, which is statistically significant as 'the p-value is <0.05. On the other hand, thyroid parameters T3 & T4 are negatively correlated to FBS, PPBS, and HbA1c and tested by p-value, which is statistically significant.

Conclusion:

The study shows that the prevalence of hypothyroidism and subclinical hypothyroidism are considerably high. It is essential to do thyroid function tests in all diabetic women. The study emphasises the need for strict and regular monitoring of blood sugars in diabetic patients who have co-existing hypothyroidism or subclinical hypothyroidism to prevent further diabetic complications, as uncontrolled sugars were significantly noted among these groups.

Keywords: Type 2 Diabetes, Thyroid dysfunction, Hypothyroidism, TSH, T3, T4, FBS, HbA1c.

Introduction

Diabetes mellitus and thyroid disorders are the most common endocrine disorders among the world population. According to International Diabetes Federation[IDF] Atlas, the prevalence of diabetes mellitus in the world population is estimated to be rising to 10.2% affecting 578 million by 2030, and 10.9% affecting 700 million by 2045. Also, 134 million Indians will have diabetes mellitus by 2045.[1]

Thyroid diseases are the next common endocrine disorders to diabetes mellitus, worldwide. According to a projection from various studies on thyroid diseases, it has been estimated that in India, thyroid disorders are present in around 42 million people.[2] The prevalence of thyroid disorders is higher in diabetic individuals when compared with non-diabetic individuals ranging from 15 to 40%.[3] Female diabetes mellitus patients are more prone to get thyroid disorders when compared to male diabetic patients.[4]

However, further research has to be done to know about the degrees of thyroid dysfunction in type 2 diabetes mellitus women, with or without other associated risk factors. There is not enough literature or studies conducted to know the pattern of thyroid dysfunction exclusively in type 2 diabetes women. Type 2 Diabetes mellitus patients are associated with more risk of developing subclinical hypothyroidism when compared with the healthy population, and if not detected and treated early, subclinical hypothyroidism may be associated with increased complications like diabetic nephropathy, and cardiovascular diseases, and can aggravate hypertension and dyslipidemia.[5]

The significant association of any pattern of thyroid dysfunction in type 2 diabetes women can enable physicians to decide on early or mandatory testing of thyroid hormone levels for every diagnosed type 2 diabetic woman [subjects of our study] to prevent complications.

The varying trends of thyroid dysfunction with diabetes help physicians to streamline the treatment for both diabetes mellitus and thyroid dysfunction. [Few drugs like pioglitazone are not given in graves/hyperthyroidism.] Studies show that type 2 diabetes mellitus can be aggravated by hyperthyroidism, whereas type 2 diabetes women are more associated with hypothyroidism[6]

However, there is a lack of enough data about the association of thyroid dysfunction, specifically in women with type 2 diabetes. This study exclusively focuses on the pattern of thyroid dysfunction in female diabetic [type 2] patients with more than 5 years of duration of diabetes.

Aim of the study:

"To study the pattern of thyroid dysfunction in women with type 2 diabetes mellitus"

Objectives:

1. To determine the pattern of thyroid dysfunction in women with Type 2 Diabetes mellitus women.

2. To correlate diabetic parameters with thyroid values in various thyroid disorders.

Methodology:

A Cross-sectional study is done on ninety-eight women who are type 2 diabetic patients visiting the department of general medicine in a tertiary medical centre in Tumkur, Karnataka, for one and half years [2021 and 2022]. Ethical clearance from the institution and consent from the patient is obtained.

Inclusion and Exclusion criteria:

Female patients from age 30 to 70 years are included in the study who are known diabetics for the duration of five years or more. ICU-admitted patients and patients with significant comorbidities were excluded from the study. Known patients of thyroid dysfunction who are on thyroid medications, pregnant women and lactating women were also excluded from the study.

A detailed history was taken, and a clinical examination is conducted. Informed written consent is obtained from the patient. Taking all the aseptic precautions, a fasting venous blood sample of 5ml is collected from the patients. FBS [Fasting Blood sugar] levels and HbA1c [Glycated haemoglobin] levels were measured. The serum levels of T3, T4, and thyroid stimulating hormone (TSH)] were measured.

Statistical Analysis

All the data were presented in tables. The pattern of thyroid dysfunction among the subject population was expressed as percentages and prevalence. Mean ± SD is calculated for all the variables. Histograms

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and Pie diagrams were put where ever applicable. Spearman's correlation was used to know the correlation coefficient and to compare all the thyroid and diabetic parameters. Spearman's correlation coefficient is the "r" Value; a positive value indicates a positive correlation, a zero value indicates no correlation, and a negative value indicates a negative correlation. The p-value was determined to know the statistical significance of the results. "p" value is the probability of knowing the statistical significance If <0.05, is significant, >0.05 is not significant. Excel spreadsheet was used to enter the data, and Epi software 3.5.4 is used to do the statistical analysis.

The study protocol was presented to the Institutional Research Committee and the Ethical Committee. Ethical clearance was granted for the study

Results:

Overall Thyroid Status distribution among the study subjects:

Among all the diabetic women prevalence of thyroid dysfunction was

34.7%

Number of cases with thyroid dysfunction X 100

Total number of cases

34 X 100 = 34.7% = 98

Among all the 98 study subjects, the prevalence of euthyroid status was 65.3% [64/98], the prevalence of Hypothyroidism was 24.5%[24/100], the prevalence of subclinical hypothyroidism was 6.1%[6/98], the prevalence of subclinical hyperthyroidism was 4.1%[4/98]. There was no clinical hyperthyroid status noted in the study subjects. The data is depicted in Table 1.

Table: 1 Various thyroid dysfunction among the Subjects

Thyroid status	No. of cases	Percentage
Euthyroid	64	65.3%
Hypothyroid	24	24.5%
Hyperthyroid	0	0%
Subclinical Hypothyroidism	6	6.1%
Subclinical Hyperthyroidism	4	4.1%
Total	98	100%

Comparison of diabetic parameters among various thyroid dysfunction:

High FBS levels[>130mg/dl] are noted prominently in Hypothyroid and subclinical hypothyroid patients that, constitute 87% and 100%, respectively, in contrast to 42% in euthyroid individuals and 25% in subclinical hyperthyroid individuals, as shown in Table 2.

Table 2: FBS values Comparison in various Thyroid status

Thyroid dysfunction	FBS >130	FBS ≤ 130	….. Total no. of cases

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Euthyroid	27[42%]	37[56%]	64
Hypothyroid	21[87%]	3[13%]	24
Subclinical Hyperthyroid	1[25%]	3[75%]	4
Subclinical Hypothyroid	6[100%]	0 [0%]	6
Total	**55**	**43**	**98**

High PPBS levels[>180mg/dl] are noted prominently in Hypothyroid and subclinical hypothyroid patients, constituting 41.7% and 66.7%, respectively, in contrast to 15% in euthyroid individuals. All subclinical Hyperthyroid patients have normal PPBS levels, as shown in Table 3.

Table 3: PPBS values Comparison in various Thyroid dysfunction:

Thyroid dysfunction	PPBS >180	PPBS ≤180	Total no. of cases
Euthyroid	15[23.4%]	49[76.6%]	64
Hypothyroid	10[41.7%]	14[58.3%]	24
Subclinical Hyperthyroid	0[0%]	4[100%]	4
Subclinical Hypothyroid	4[66.7%]	2[33.3%]	6
Grand Total	**29**	**69**	**98**

High HbA1c levels[>6.5%] are noted in all the patients ie; 100% of Hypothyroid[24/24], and Subclinical Hypothyroid[6/6] patients. 78% of Euthyroid patients also have high HbA1c levels. All subclinical Hyperthyroid patients have normal HbA1c, as shown in Table 4

Table 4: HbA1c values Comparison in various Thyroid Status:

Thyroid dysfunction	HbA1c >6.5	HbA1c≤6.5	Total no. of cases
Euthyroid	50[78%]	14[22%]	64
Hypothyroid	24[100%]	0[0%]	24
Subclinical Hyperthyroid	0[0%]	4[100%]	4
Subclinical Hypothyroid	6[100%]	0[0%]	6
Hyperthyroid	0[0%]	0[0%]	0
Grand Total	**80**	**18**	**98**

A spearman's correlation analysis is conducted among all the diabetic parameters, FBS, PPBS, HbA1c, Thyroid Parameters, T3, T4, TSH, and BMI. Results are shown in Fig1.

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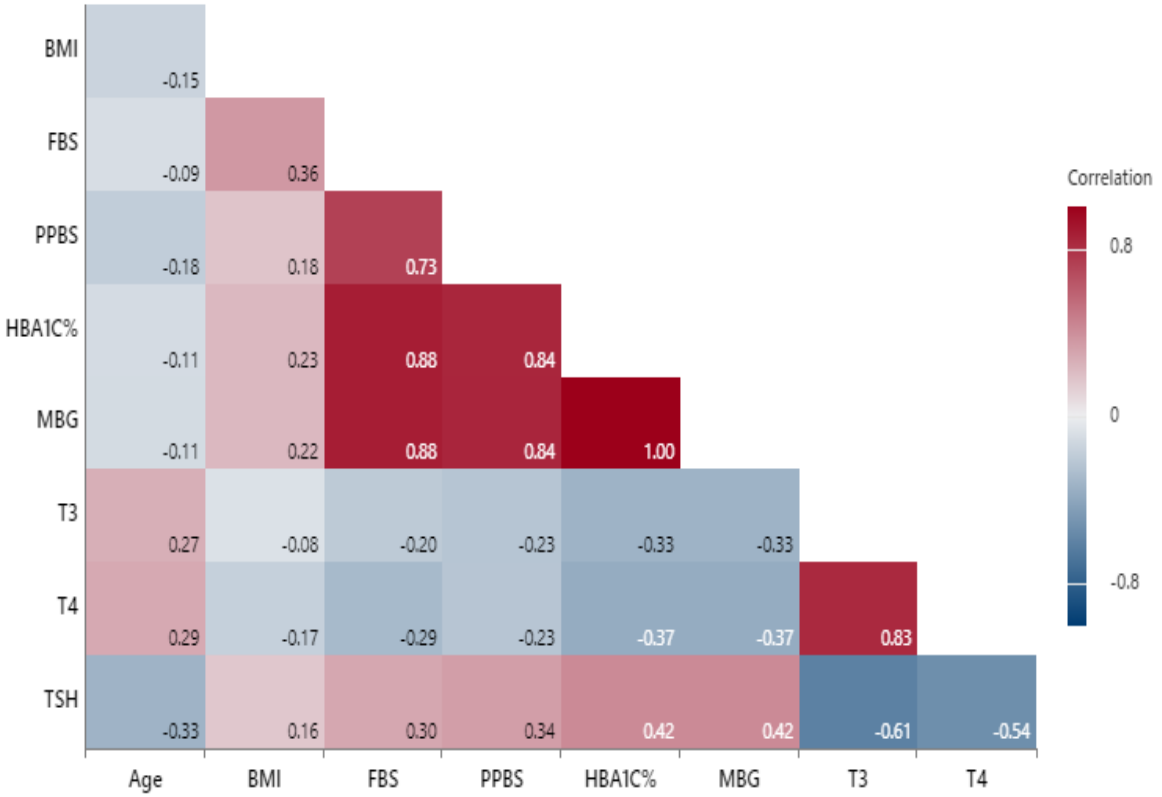
Fig 1 Correlation Coefficient r values between the variables:



Correlation of thyroid hormonal values with diabetic parameters:

The correlation matrix shows that TSH is positively correlated[r value is +] to FBS, PPBS, and HbA1c, and the result is tested with 'p-value, and it is statistically significant as 'p-value is <0.05 as shown in Table 5

Table 5: Correlation between TSH and Diabetic parameters

Diabetes Parameters	r Value	p-value
FBS	0.39	8.74E-05
PPBS	0.43	1.18E-05
HbA1C	0.45	3.65E-06
Mean Blood Glucose	0.45	3.65E-06

It is found that T3 is negatively correlated to all diabetic parameters FBS, PPBS, HbA1c and Mean blood glucose, and the result is statistically highly significant, as shown in Table 6.

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Table: 6 Correlation between T3 and Diabetic parameters

Diabetes Parameters	r Value	p-value
FBS	-0.24	0.015
PPBS	-0.30	0.003
HbA1C	-0.34	0.006
Mean Blood Glucose	-0.34	0.006

It is found that T4 is negatively correlated to all diabetic parameters FBS, PPBS, HbA1c and Mean blood glucose, and the result is statistically highly significant, as shown in Table 7.

Table 7: Correlation between T4 and Diabetic parameters

Diabetes Parameters	R-Value	P value
FBS	-0.33	0.001
PPBS	-0.30	0.003
HbA1C	-0.28	0.001
Mean Blood Glucose	-0.28	0.001

Table 8: Diagnostic criteria used in our study for categorisation of Thyroid status:

The pattern of Thyroid disorders	TSH [Normal Range = 0.465 to 4.68 µIU/mL	T3 [Normal Range = <1.49 to 2.6 nmol/I	T4 [Normal Range = 71 to 141 nmol/I
Clinical Hypothyroidism	> 10 µIU/mL	↓	↓

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Sub Clinical Hypothyroidism	4.68 to 10 µIU/mL	Normal Range	**Normal Range**
Normal- thyroid	Normal Range	Normal Range	**Normal Range**
Sub Clinical Hyper thyroidism	0.1 to 0.465 µIU/mL	Normal Range	**Normal Range**
Clinical Hyperthyroidism	**< 0.1 mIU/mL**	↑	↑

Discussion:

In our study, age distribution varied from 31 – 70 years, the majority ie; 53% (52/ 98), were between 41-50 years, 41% (40/98) were between 51 to 60 years, 4.% (04/98) among 31-40 years and 2% (02/98) among 61-70 years. The Mean Age ± SD is 49.4 ± 5.04 years. In our study 61-70 kg constituted 49%(48/ 98) , 51-60 kg constituted 24.4% (24/98) , 71-80 kg constituted 17.3%(17/ 98), and 81-90 kg constituted 9.18%(09/ 98). The Mean ± SD weight is 66.5 ± 8.33 kgs. In our study, 39.7%(39/ 98) cases had a height distribution of 161-165cm,25.5 %(25/ 98) cases had a height of 156-160cm, and 10.2 %(10/ 98) cases had a height of 150-155cm. The mean ± SD is 162 ± 4.64 cm.

Reference values for diabetic parameters used in our study are, FBS> 130 mg/dl as high/uncontrolled. PPBS > 180mg/dl as uncontrolled/high. HbA1c >6.5% is taken as uncontrolled diabetes. In the present study, FBS >130mg/dl was noted in 59.2% (58/98) cases, and FBS <130mg/dl was noted in 40.8% of cases (40/98). In the present study, PPBS <180 mg/dl was noted in 71.4% (70/98) cases, and PPBS >180 mg /dl was noted in 28.5% of cases (28/98). In the present study, HbA1c >6.5% was noted in 85.7% (84/98) cases, and HbA1c 5.7-6.4% is noted in 14.2% cases (14/98) cases. The mean ± SD is 7.60 ± 1.09%.

The Reference values of Thyroid disorders are based on diagnostic criteria mentioned in Table 8. In the present study, the normal range of T3 is noted as 1.49 to 2.6nmol/l. 62.3% [61/98] patients have T3 <1.49 nmol/I, 33.7% [33/98] have T3 in the range of <1.49 to 2.6 nmol/I, and 4% have T3 >2.6 nmol/l. Mean ± SD 1.38 ± 0.54 nmol/I. In the present study, T4 of 71-141 nmol/I was noted in 62.2% (61/98) cases which is in the normal range, <71 nmol/I was noted in 33.7% cases (33/98), and, >141 nmol/I was noted in 4.1% cases (04/98). Mean ± SD 82.54 ± 28.78 is 82.54 ± 28.78 nmol/I. In the present study, TSH of <0.465 µIU/mL is seen in 4.1% [4/98] patients, TSH of 0.465-4.68 µIU/mL is seen in 65.3% [64/98] patients, TSH of >4.68 µIU/mL is seen in 30.6% [30/98] patients. The mean ± SD is 5.98 ± 6.59 µIU/mL.

Prevalence Of Thyroid Dysfunction Compared To Previous Studies:

In our study, the prevalence of thyroid dysfunction among type 2 diabetic female subjects is 34.7%[36/98]. Euthyroid status was found in 65.3% [64/98], the prevalence of Hypothyroidism was found in 24.5%[24/100], the prevalence of subclinical hypothyroidism was found in 6.1%[6/98], the prevalence of subclinical hyperthyroidism was found in 4.1%[4/98]. There was no clinical hyperthyroid status noted in the study subjects.

In a study conducted by Ganie MA et al[7,] the prevalence of thyroid dysfunction was 33.2%, among which 24.1% had subclinical hypothyroidism, 6.8% had overt hypothyroidism, Subclinical hyperthyroidism and 0.9% had overt hyperthyroidism. In a study conducted by Kumar DR et al[8], the prevalence of thyroid dysfunction was 24%, out of which subclinical hypothyroidism was 11.25%, overt hypothyroidism in 12% and hyperthyroidism in 0.75%. Thyroid dysfunction was present in 13% of 200 non-diabetic controls. In a study conducted by Gurunath S et al [9,] the prevalence of thyroid disorders among type 2 diabetic females is 36.7% [61 out 166 female Type 2 diabetic patients had thyroid dysfunction].

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In a cross-sectional study conducted by Ozair M et al [10] prevalence of thyroid dysfunction (28%) was observed in type 2 diabetic patients with subclinical hypothyroidism (18.8%) as the commonest thyroid disorder. A case–control study was conducted by Khassawneh AH et al[11], the prevalence of thyroid disorders was found to be 26.7% in type 2 diabetes mellitus patients, which is significantly higher than among the controls. In Carmona CA et al study[12] prevalence of thyroid dysfunction was 19%, of which 5.1% corresponded to subclinical hypothyroidism, 1.3% to subclinical hyperthyroidism, and 0.8% to hyperthyroidism.

A study conducted in 2019 in southeast Nigeria comparing 354 diabetic and 118 non-diabetic persons concluded that risk factors of thyroid dysfunction in patients with type 2 Diabetes mellitus are female gender, obesity, DM nephropathy, HbA1c (≥7%), duration of diabetes mellitus(>5 years).[13] Bharadiya Amit et al in 2014 studied the thyroid dysfunction prevalence in patients with uncontrolled diabetes, and it was 53.3%, and it was more in females and elderly patients.[14] In a study conducted by Cátia Cristina et al in 2013, the prevalence of thyroid dysfunction in diabetics was 14.7% The prevalence of subclinical hypothyroidism in type 2 diabetes patients was 12%.[15]

In a study conducted by Sriram Shanmugam1 et al, the prevalence of thyroid dysfunction was 21.5% among diabetic patients, 12.4% were subclinical hypothyroid patients in that, 6.5% were subclinical hyperthyroid patients among them, and 2.7% were having clinical hypothyroidism.[16] In a study conducted by Mahesh Dave et al, 13% have thyroid dysfunction among type 2 diabetes. 9.25% have subclinical hypothyroidism, 1.9% have clinical hypothyroidism, and 1.9% have subclinical hyperthyroidism. Thyroid dysfunction was found more in females compared to males.[17]

Association Of Diabetic And Thyroid Parameters In Previous Studies:

High FBS levels[>130mg/dl] are noted prominently in Hypothyroid and subclinical hypothyroid patients that, constituting 87% and 100%, respectively, in contrast to 42% in euthyroid individuals and 25% in subclinical hyperthyroid individuals. High PPBS levels[>180mg/dl] are noted prominently in Hypothyroid and subclinical hypothyroid patients, constituting 41.7% and 66.7%, respectively, in contrast to 15% in euthyroid individuals. All subclinical Hyperthyroid patients have normal PPBS levels. High HbA1c levels[>6.5%] are noted in all the patients ie; 100% of hypothyroid[24/24], and Subclinical Hypothyroid[6/6] patients. 78% of Euthyroid patients also have high HbA1c levels. All subclinical Hyperthyroid patients have normal HbA1c.

In a study conducted by Vamshidhar et al [18], a continuous positive correlation of TSH with FBS and HbA1c was found. In a study conducted by Uppal V et al[14] significant negative correlation between glycosylated haemoglobin and serum T3 levels, and between glycosylated haemoglobin and serum T4 levels, there was a positive correlation between glycosylated haemoglobin and serum TSH levels. In a study conducted by Maaz Ozair et al[19], thyroid dysfunction was more in the poor glycemic control group with HbA1c more than >7%. The present study aimed to determine the pattern of thyroid dysfunction among the study subjects whom were type 2 diabetic women diagnosed as having type 2 diabetes for more than or equal to 5 years. The prevalence of thyroid dysfunction in our study was 34.7%, the prevalence of hypothyroidism was 24.5%, subclinical hypothyroidism was 6.1%, and subclinical hyperthyroidism was 4.1% among the study subjects. No cases of clinical hyperthyroidism were detected among the study subjects.

When compared to studies done to know the thyroid status in non-diabetic subjects, and in the general population, the prevalence of thyroid dysfunction is much higher in our study done on type 2 diabetes women [34.7%], and it is even more important because previously diagnosed thyroid dysfunction patients are excluded from the study. The secondary objective of our study was to evaluate the glycemic status among various thyroid dysfunction. The prevalence of uncontrolled or high FBS, PPBS and HbA1c levels was noted in hypothyroid and subclinical hypothyroid patients when compared to euthyroid and subclinical hyperthyroid patients in our study. The correlation between various diabetic parameters [FBS, PPBS, and HbA1c], and thyroid parameters [T3, T4, TSH] is also evaluated as a part of the study. The results showed that TSH is associated positively with FBS, PPBS, and HbA1c,

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and T3 and T4 are negatively correlated to diabetic parameters.

Conclusion:

As our study shows that the prevalence of hypothyroidism and subclinical hypothyroidism are considerably high, it is important to do thyroid function tests in all diabetic women, especially in type 2 diabetes women, irrespective of whether they present with symptoms of thyroid dysfunction or not. The early diagnosis and control of thyroid dysfunction also helps to the better control of blood sugars in diabetic patients and prevents the morbidity and complications that arise due to undiagnosed thyroid disorders. The study emphasizes the need for strict and regular monitoring of blood sugars in diabetic patients who have co-existing hypothyroidism or subclinical hypothyroidism, to prevent further diabetic complications, as the uncontrolled sugars were significant.

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