Study of association between Thyroid Dysfunction and BMI in women with type 2 Diabetes Mellitus

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Abstract

Introduction/Background: Thyroid illness is more common in women and it can increase the risk of cardiovascular diseases and can have an influence on bone health and on fertility as well. Hypothyroidism, whether it is subclinical or clinical/overt have got association with insulin resistance and variation in BMI. **Aim of the study:** To determine the association between thyroid dysfunction and BMI in women with type 2 diabetes mellitus . **Materials and methods**: A Cross -sectional study done in the department of general medicine at Sri Siddhartha Medical College & Hospital, Tumkur in female type 2 diabetic patients for duration of 18 months between January 2021 to July 2022. **Results** : Hypothyroidism cases constitute 15.3% cases, Subclinical Hypothyroidism cases constitute 1.02% cases and Hyperthyroidism cases constitute 4.08% in the BMI range of 22-25 kg/m^2 (normal). Hypothyroidism cases constitute 6.2% cases and subclinical hypothyroidism cases consitiute 4.08% in the BMI range of 26-29 kg/m^2 (over weight). Hypothyroidism cases constitute 2.04% cases and Subclinical hypothyroidism cases constitute 3.25% in BMI range of >30 kg/m^2(obese). **Conclusion**: In our study done on female type 2 diabetic patients, we conclude that Thyroid Stimulating Hormone [TSH] is positively correlated to BMI, but T3 and T4 thyroid hormones are negatively correlated to BMI .

Key words : Overt hypothyroidism, sub-clinical hypothyroidism, BMI, TSH, Diabetes.

Introduction

Thyroid dysfunction and diabetes mellitus are the most frequently occurring endocrinopathies with a large impact on cardiovascular health. A high prevalence of Thyroid dyfunction is seen among both type 1 (T1DM) and type 2 (T2DM) diabetes mellitus patients[1]. Thyroid diseases, after diabetes are the second most prevalent metabolic disorders in the world. Many factors including biological and geographical factors affect thyroid dysfunction prevalence rates.

The prevalence of obesity in the world has increased with the change in lifestyle and food habits over the time. In 2015, obesity and overweight are known to have caused 4 million deaths and 120 million DALYs [Disability-adjusted life-years]. Females are at higher risk of becoming obese compared to males by 12% worldwide. [2,3]

Weight gain, Overweight and Obesity can affect various hormonal changes in the body that can cause temporary or permanent changes in the bodily functions at cellular level. Studies have been conducted and published previously to know the association between weight,

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blood sugars and thyroid hormones. Few studies have shown inconsistent results about the correlation between thyroid hormone levels and BMI, and few other research studies showed decrease in TSH levels with BMI.[4]

Most of the studies have documented the relation between TSH and BMI, but very few studies were done to know the relation between thyroid hormonal levels [T3, T4] and BMI, the results were controversial. Studies documented showed negative correlation of BMI with T3, and positive correlation or no association with T4.[5]

Diabetes, due to inadequate insulin has effect on various hormones including thyroid hormone levels. The coversion from T4 to T3 is disturbed in diabetes mellitus leading to decrease in T3 levels, though this change is not noticed in all cases. The factors that contribute to the development of hypothyroidism in patients with type 2 diabetes mellitus are female sex, co-existing autoimmune diseases, days spent in hospital, obesity, and old age.[6]

The glucose metabolism is altered in patients with thyroid dysfunction. Subclinical hypothyroidism is commonly associated with increasing age, increase in sugar levels and more associated with females than males.[7]

Studies showed that females with type 2 diabetes mellitus over the age of 60 yrs have more prevalence of subclinical hypothyroidism. A cross-sectional study done in India on 1,508 Type 2 diabetes mellitus patients have more hypothyroidism cases in the age group of above 65 years, and more incidence in females than males.[8] This shows thyroid dysfunction, type 2 diabetes, BMI, sex hormones, female gender, age, and BMI are closely related.

In diabetic patients who have normal thyroid levels, the normal circadian pattern of increase in TSH levels in the night is absent, and the TSH –TRH response cycle is also disturbed. Thyroid hormone level variation is seen with insulin resistance, hyperinsulinemia, and long term hyperglycemia. Diabetic ketoacidosis and other systemic diseases can cause decrease in T3, T4 levels as well. Thyroid gland proliferation can happen as a consequence of long term hyperinsulinemia, and can cause goiter formation.[9]

Aim of the study

The aim of the study is to determine the association between thyroid dysfunction and BMI in women with type 2 diabetes mellitus

Objectives

1. To determine the pattern of thyroid dysfunction and BMI in women with Type 2 Diabetes Mellitus women.
2. To assess the glycemic status in relation to various TSH levels in Type 2 Diabetes Mellitus women.

Materials and methods

Ethical clearance was taken from institutional ethical committee. Informed consent was obtained from each patient included in the study. A cross-sectional study done in the department of general medicine at Sri Siddhartha Medical College & Hospital, Tumkur in female Type 2 diabetic patients for duration of 18 months between January 2021 to July 2022.

Inclusion criteria

- Patients willing to participate in the study
- Age distribution of 30-70 years
- Female patients with more than 5 years of duration of diabetes [type 2]

Exclusion criteria

- Seriously ill patients
- Known hypo/hyperthyroid patients on treatment
- Pregnant and Lactating women
- Patients taking drugs known to alter thyroid dysfunction.
- T2DM patients taking drugs that alter thyroid levels like amiodarone or immunomodulators.
- Severely ill T2DM patients with complications of diabetes mellitus.

Methodology

The patients attending OPD of Department of Medicine and inpatients admitted in the medicine wards & ICU at Sri Siddhartha Medical College & Hospital, Tumkur were selected randomly and included in the study .

Thorough clinical history was taken in a prestructured proforma and demographic characteristics like age, gender, height, weight, BMI, occupation, residence

were included. History of weight gain or loss, palpitations, heat intolerance, warm moist skin, cold intolerance, dry skin, loss of hair, irregular periods were also noted. Past history of DM/HTN/ Cirrhosis of liver/ Chronic kidney disease/Bronchial asthma were included. Treatment history was taken. Family history of type2 diabetes mellitus and thyroid disorders was also noted in our study. Personal history such as diet, sleep, appetite, bowel & bladder habits, history of smoking, alcohol and any drug abuse was noted. All the patient's vitals were noted, and a thorough general examination and systemic examination was conducted.

All the patients were asked for feasible routine investigations including CBP (Complete blood picture), Fasting glucose levels, Post prandial blood glucose levels, HbA1c, Serum T3 levels, Serum T4 levels and Serum TSH levels.

Plasma glucose levels were measured using a hexokinase enzymatic reference method and the reference values mentioned as g/dl.[10] Thyroid hormone levels were measured by chemiluminiscence method[11] The normal thyroid hormone levels range in our laboratory were, T4 – 71 to 141 nmol/L, T3 – 1.49 to 2.6 nmol/L and TSH was 0.465 – 4.68 µIU/L.

Sub clinical hypothyroidism is defined as normal T4 and T3 and TSH >4.5 µIU/L and <10 µ IU/L. HbA1c in venous blood samples was measured using high-performance liquid chromatography (HPLC) (BioRad VARIANT II haemoglobin analyser) and less than 7% is taken as normal or under control.

Body measurements: Weight was measured in kg. Height was measured in cm. BMI was expressed in units of kg/m^2. Normal BMI range was taken as 22 to 25 kg/m^2. Overweight was considered as BMI ranging from 26 to 29.9 kg/m^2. Obesity was defined for any BMI of 30 kg/m^2 and above 12.

Statistical analysis

The data obtained from the patients with regard to clinical and laboratory investigations is presented in tabulated forms. The numbers are expressed in percentages, mean, median and standard deviation. The qualitative variables are expressed as frequency and percentages. Association between categorical variables is tested using chi-square test. Relation between glycemic status and thyroid hormone levels is tested using spearman's Correlation Coefficient. Data entry is done using Excel spread sheet, and statistical analysis is carried out using Epi.info. software version 3.5.3. 'p' value less than 0.05 was considered significant .

Results

In our study age distribution varied from 31 – 70 years. Among 31- 40 years age group, 4.08% participated, among 41-50 years age group, 57.14% participated, among 51 to 60 years age group, 36.73% participated, and among 61-70 years age group, 2.04% participated. The Mean Age was 49.4 ± 5.04 years.

In our study, weight distribution of 61-70 kg constituted 48.9%, 51-60 kg constituted 24.4%, 71-80 kg constituted 17.3% and 81-90 kg constituted 9.18%. The Mean weight was 66.5 ± 8.33 kg. In our study, 39.7 % cases had height distribution of 161-165cm, 25.5 % cases had height of 156-160cm, 10.2 % cases had height of 150-155cm. The Mean height was 162 ± 4.64cm.

Table 1: BMI distribution of Cases in our study

BMI distribution	No. of cases	Percentage
22-25 (Normal)	64	65.2
26-29 (Over weight)	25	25.5
>30 (Obese)	09	9.18
Mean ± SD	25.3 ± 2.80	
Total	98	99.9%

As shown in Table 1; In the present study, BMI of 22-25 kg/m^2 noted among 65.2% cases , BMI of 26-29 kg/m^2 noted among 25.5% cases, BMI >30 kg/m^2 noted among 9.18% cases. The Mean BMI was 25.3 ± 2.80 kg/m^2.

Diabetic parameter distribution: HbA1c of >6.5% noted in 85.7% cases and 5.7-6.4% noted in 14.2% cases. Mean HbA1c was 7.60 ± 1.09%. FBS >130mg/dl was noted in 59.1% cases and <130mg/dl noted in 40.8% cases.The Mean FBS was 134 ± 13.6mg/dl. PPBS of <180 mg/dl noted in 71.4% cases and >180 mg /dl noted in 28.5% cases. The Mean PPBS was 179 ± 36.5mg/dl.

Thyroid hormone levels: T3 hormone levels of 0.92-2.7 nmol/l noted in 77.5% cases and <0.92 nmol/l noted in 22.4% cases. The Mean T3 level was 1.38 ± 0.544 nmol/l. T4 hormone levels of 75-155 nmol/l is noted in 52.0% cases and <75 nmol/l was noted in 45.9% cases and >155 nmol/l noted in 2.1% cases. The Mean T4

level was 82.5 ± 28.8 nmol/l. TSH of 0.5-5.0 µIU/mL was noted in 74.4% cases and > 5.0 µIU/ml was noted in 25.2% cases and < 5.0 µIU/ml was noted in 1.02% cases. The Mean TSH was 5.98 ± 6.59 µIU/ml.

Known Hypertensive cases in the study were 13.2%, and they were on treatment, and 85% of the cases were not known hypertensives.

Table 2: BMI distribution and thyroid dysfunction in our study

BMI distribution	Hypothyroidism	Subclinical hypothyroidism	Hyperthyroidsim	Euthyroid	Total
22-25 (normal) (64)	15 (15.3 %)	01 (1.02 %)	04 (4.08%)	44 (44.8 %)	64 (65.2%)
26-29 (over weight) (25)	06 (6.1%)	04 (4.08%)	Nil	15 (15.3 %)	25 (25.5%)
>30 (Obese) (9)	02 (2.04 %)	03 (3.15 %)	-	04 (4.08%)	09 (9.18%)
Total	23 (23.4%)	08 (8.16 %)	04 (4.08 %)	63 (64.2%)	98 (99.9%)

Spearman's correlation, r Value, P <0.05,* = significant, >0.05 = not significant

As shown in Table 2; Hypothyroidism cases constitue 15.3% cases, Subclinical Hypothyroidism cases constitute 1.02% cases & Hyperthyroidism cases constitute 4.08% in the BMI range of of 22-25 kg/m^2 (normal). Hypothyroidism cases constitute 6.2% cases and subclinical hypothyroidism cases consitiute 4.08% in the BMI range of 26-29 kg/m^2 (over weight). Hypothyroidism cases constitute 2.04% cases and Subclinical hypothyroidism cases constitute 3.25% in BMI range of >30 kg/m^2 (obese).

Table 3 : Correlation between BMI, TSH and Diabetes

Diabetes Parameters	r Value	P value
BMI	0.05	0.626
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**

As shown in Table 3; It is found that TSH is positively correlated to FBS, PPBS, HbA1c and Mean blood glucose and is statistically highly significant. TSH is positively correlated to BMI which is not significant.

Table 4 : Correlation between BMI, T3 and Diabetes

Diabetes Parameters	R Value	P value
BMI	**-0.08**	**0.417**
FBS	-0.24	**0.015**
PPBS	-0.30	**0.003**
HbA1C	-0.34	**0.006**
Mean Blood Glucose	-0.34	**0.006**

Spearman's correlation, r Value, P <0.05,* = significant, >0.05 = not significant

As shown in Table 4; It is found that T3 is negatively correlated to BMI, FBS, PPBS, HbA1c and Mean blood glucose and is statistically highly significant.

Table 5 : Correlation between BMI ,T4 and Diabetes

Diabetes Parameters	R Value	P value
BMI	**-0.08**	**0.427**
FBS	-0.33	**0.001**
PPBS	-0.30	**0.003**
HbA1C	-0.28	**0.001**
Mean Blood Glucose	-0.28	**0.001**

Spearman's correlation, r Value, P <0.05,* = significant, >0.05 = not significant

As shown in Table 5; It is found that T4 is negatively correlated to BMI, FBS, PPBS, HbA1c and Mean blood glucose and is statistically highly significant.

Table 6: Correlation between BMI and Diabetes

Diabetes Parameters	R Value	P value
FBS	0.25	**0.015**
PPBS	0.14	0.166
HbA1C	0.15	0.137
Mean Blood Glucose	0.15	0.137

Spearman's correlation, r Value, P <0.05,* = significant, >0.05 = not significant

As shown in Table 6; It is found that according to Spearman's correlation, BMI is positively correlated to all diabetic parameters FBS, PPBS, HbA1c and Mean blood glucose but, statistically significantly correlated to only to FBS.

As shown in Table 7, According to chi square test, there was no statistical significant association between various BMI groups and thyroid abnormalities.

Discussion

The Mean Age group in our study was 49.4 ± 5.04 years. The prevalence of thyroid disorders was found to be highest in the age group of < 50 years. This when evaluated was statistically significant with p value of 0.028. The results of our study were compared with the previous studies. In Ogbonna et al study[13] where the mean age of type 2 DM patients was 57.5 years. This may be due to the fact that the prevalence of type 2 DM increases with age. In Muhammed et al[14] study done to know the relation between thyroid dysfunction and type 2 diabetes, the mean age of the diabetic group was 51.38 ± 7.42 years, and that of the control group was 50 ± 7.55 years.

The Mean BMI in our study was 25.3 ± 2.80 kg/m^2. In Obead M et al study[15] the mean BMI was 32.12 ± 4.89. (P < 0.05). In Bhujanga Shetty et al[16] study, 51% of the subjects were overweight and 29% were obese. In Ogbonna et al[13] study it was observed that T2DM patients had higher mean BMI than the controls (27.6 ± 5.0 vs. 26.2 ± 3.8). This difference was statistically significant. In Vadivelan Mehalingam et al study[17], the prevalence of thyroid dysfunction is 17.5% in patients with type 2 diabetes mellitus and there was significant association with BMI and thyroid disorders. In Awad et al study[18], no significant differences were found between thyroid levels and age, sex-distribution, BMI, systolic, diastolic BP, cholesterol and HDL. In this study 60% of diabetic patients were eldery above 60 years of age. 11% were having thyroid dysfunction above 60 years. 77 diabetic and 54 thyroid patients were found obese. In Al Mohareb study[19], the mean BMI was

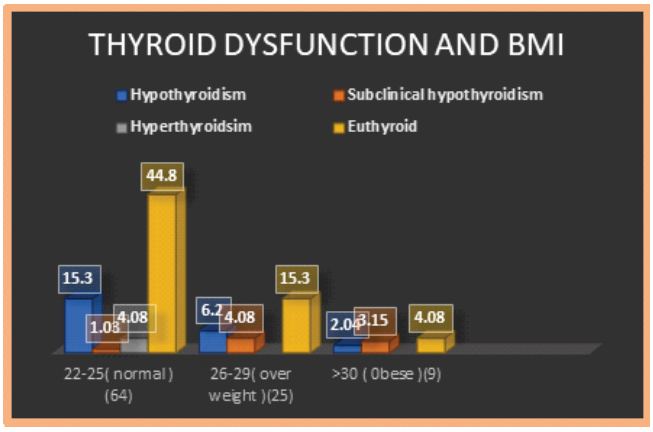
Table 7: Correlation between BMI and Thyroid abnormalities

BMI distribution	Hypothyroidism/subclinical hypothyroidism / Hyperthyroidism	Euthyroid	dF Value	P value*
22-25 (normal) (64)	16	44	3.715, 2	0.1561 ns
26-29 (over weight) (25)	10	15		
>30 (Obese) (9)	05	04		
Total	23	63		

Chi square test, P <0.05, = significant, >0.05 = not significant

45.6±1.5kg/m^2 and 23.2±0.5kg/m^2, for the obese and non-obese subjects, respectively with p value<0.001.

In our study, the Mean T3 level was 1.38 ± 0.544 nmol/l. The Mean T4 level was 82.5 ± 28.8 nmol/l. The Mean TSH was 5.98 ± 6.59 µIU/ml. In Al Mohareb et al study[19], the mean TSH was significantly higher in the obese group compared to the non-obese controls, 2.7 ±0.8 versus 1.7±0.13, P value 0.014, respectively. T3 was significantly lower in the obese group compared to the non-obese controls, 3.9±0.1 versus 5.0±0.1, respectively, P value was 0.001, however, T4 was similar in the two groups, P>0.05. In the whole group (N=107), there was a positive correlation between serum TSH and both body weight (r, 0.35, P value 0.001) and BMI (r, 0.34, P value 0.001). T4 and BMI were not associated, where as BMI was negatively correlated with T3. In Mohmmed jasim et al[14] study the mean thyroid-stimulating hormone (TSH) levels in people with diabetes with thyroid dysfunction was 11.88 ± 5.62 while that in euthyroid diabetics was 2.66 ± 1.04.



In the present study, Hypothyroidism was noted in 24.4% cases (24/98). Euthyroid status in 75.7% (74/98) cases. Subclinical hypothyroidism was noted in 6.1% cases (06/98). Hyperthyroidism was noted in 4.08% cases (04/98). In Bhujanga Shetty[16] study, thyroid dysfunction was found in 42% of the subjects, where 36% had subclinical hypothyroidism and 6% had overt hypothyroidism. No cases of hyperthyroidism were noted.

In our study, HBA1c of >6.5% is noted in 85.7% (84/98) cases and 5.7-6.4% is noted in 14.2% cases (14/98). The Mean HBA1c was 7.60 ± 1.09. In Mohmmed jasim et al[14] study the HbA1c levels which reflect the glycemic control in patients who had thyroid dysfunction were found to be 10.33 ± 2.37 while that of euthyroid diabetics was 7.16 ± 1.04 and that of control population is in the range of 4%–6. In Al Mohareb et al[19] mean HbA1c in overweight was 5.58 ± 0.55**. Mean HbA1c in obese was 5.77 ± 0.78**.

In the present study according to Spearman's correlation there was no significant association between thyroid dysfunction and BMI. The correlation matrix shows that thyroid parameters T3, T4 are negatively correlated to BMI which is highly statistically significant and TSH is positively correlated to BMI which is not significant.

In Obead M et al[15] study, one of the risk factors for the development of insulin resistance is hypothyroidism which is associated with weight gain and concomitant changes to the other components that comprise metabolic syndrome. Bhujanga Shetty[16] et al didn't find a significant association between thyroid dysfunction and the age, duration of diabetes and BMI in their study population. In Ranran Xu et al[20] study the results showed there was no association with BMI and TSH. Free T4 showed negative correlation with BMI. Free T3, and TSH levels were positively correlated with BMI. Some studies show positive correlation between TSH and insulin and HOMA-IR[21]. In He J et al[22] study, in patient group with subclinical hypothyroidism, BMI and systolic blood pressure were significantly high. In patient group with overt hypothyroidism, HDL Cholesterol and systolic blood pressure were high. Blood pressure, Cholesterol, and BMI values are increased in women of subclinical hypothyroidism group when compared to women of euthyroid group.

Thyroid dysfunction especially, subclinical hypothyroidism is closely associated with alteration of glucose metabolism[23]. In hypothyroid metabolic syndrome females; high TSH levels have been found to be associated with dyslipidemia. Insulin resistance also plays causative role in the development of Metabolic syndrome.

Conclusion

In our study we found out that there was a positive association between TSH and BMI, and negative association between T3, T4 levels and BMI in female type 2 diabetes patients.

Hence it is important to do thyroid function tests in all

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overweight and obese diabetic patients irrespective of age, especially in females as female sex itself is a risk factor for the development of thyoid diseases.

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