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Original Research Article

EVALUATION OF THYROID FUNCTION ABNORMALITIES IN TYPE 2 DIABETES MELLITUS: A COMPARATIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance as well as progressive pancreatic beta-cell dysfunction. Persistent hyperglycemia and inflammation associated with T2DM is associated with various endocrine complications including thyroid dysfunction. Altered glucose metabolism, insulin resistance as well as chronic inflammation in T2DM may predispose patients to thyroid hormone imbalances.

Materials and Methods: In this comparative observational study, 50 T2DM patients and 50 age-matched healthy controls were evaluated for thyroid function. Demographic data, diabetes duration, and glycaemic control (HbA1c) were recorded. Thyroid function tests (T3, T4, and TSH) were performed for all participants. Individuals were classified into euthyroid and patients with thyroid function abnormalities. Statistical analysis was conducted using the chi-square test for categorical variables and independent t-test for continuous variables. P values less than 0.05 was taken as statistically significant.

Results: Gender and age distributions were comparable between the groups. In the T2DM group 64% were euthyroid whereas 34% patients were found to have hypothyroidism (24% subclinical, 10% overt) and 2% had subclinical hyperthyroidism compared to 86% euthyroid and 14% hypothyroid (10% subclinical, 4% overt) among controls (P = 0.019). Mean T3 and T4 levels were significantly lower in T2DM patients (2.88 ± 0.42 pg/mL and 1.10 ± 0.27 ng/dL, respectively) than controls (3.10 ± 0.38 pg/mL and 1.31 ± 0.38 ng/dL; P = 0.0072 and 0.0019, respectively), while TSH levels were significantly higher in T2DM (5.18 ± 1.44 mIU/L vs. 3.07 ± 0.74 mIU/L; P < 0.0001). Furthermore, thyroid dysfunction was significantly associated with poor glycaemic control (HbA1c > 7%) (P = 0.0016).

Conclusion: Thyroid dysfunction is more prevalent in T2DM patients compared to healthy individuals and is significantly associated with poor glycaemic control. Routine thyroid screening in T2DM may facilitate early detection and management of thyroid abnormalities, potentially improving metabolic outcomes.

Key Words: Thyroid Dysfunction, Type 2 Diabetes Mellitus, Glycaemic Control, Subclinical Hypothyroidism, TSH.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance as well as progressive pancreatic beta-cell dysfunction.[1] Impaired glucose uptake by peripheral tissues as well as increased hepatic glucose production and lipid metabolism dysregulation is the hallmark of T2DM. Insulin resistance in muscle and adipose tissue is main reason for hyperglycemia. Additionally chronic low-grade inflammation and oxidative stress further exacerbate the disease progression.[2] Persistent hyperglycemia seen in

T2DM leads to beta-cell exhaustion thereby reducing insulin secretion and worsening glycaemic control. The incidence of T2DM is increasing globally because of factors such as sedentary lifestyles, increasing Body mass index and intake of high-calorie processed foods. The other factors for increasing incidence of T2Dm include rapid urbanization and economic development leading to work condition requiring reduced physical work.[3]

Uncontrolled diabetes has detrimental effects on various endocrine glands, including adrenal, pituitary as well as thyroid glands. Chronic hyperglycemia, insulin resistance and systemic inflammation which is hallmark of T2DM contribute to hormonal dysregulation.[4] The thyroid gland is one of the most vulnerable glands and is significantly influenced by diabetes because of its shared biochemical and physiological pathways with glucose metabolism. Oxidative stress and chronic inflammation associated with T2DM have been implicated in the development of thyroid dysfunction. These disruptions are known to affect thyroid hormone levels which in turn influence insulin sensitivity and glucose metabolism thereby creating a bidirectional relationship between diabetes and thyroid dysfunction.[5]

The presence of diabetes has been associated with an increased prevalence of subclinical and overt thyroid dysfunction, including primary hypothyroidism, subclinical hypothyroidism and less commonly hyperthyroidism. Insulin resistance and hyperinsulinemia influence thyroid hormone synthesis, conversion as well as metabolism often resulting in a decrease in triiodothyronine (T3) levels and an increase in thyroid-stimulating hormone (TSH) levels.[6] Conversely, thyroid hormones also play a critical role in glucose metabolism by influencing hepatic glucose production, and insulin sensitivity. Hypothyroidism is known to increase insulin resistance and dyslipidemia thereby further complicating hyperglycemia in T2DM. Moreover hyperthyroidism increases insulin clearance thereby leading to worsening hyperglycemia and poor glycaemic control.[7]

Routine screening of thyroid function in patients with T2DM is of significant importance given the high prevalence of thyroid dysfunction in diabetic patients.[8] Many patients with diabetes have subclinical thyroid dysfunction which in many instances remain undiagnosed due to absence of overt symptoms. If left untreated subclinical hypothyroidism can lead to worsening dyslipidemia, increased cardiovascular risk and poor glycaemic control.[9] Screening for thyroid dysfunction in diabetes patients is crucial for early identification and management of hormonal imbalances. One of the important aspect of thyroid dysfunction in cases of T2Dm is that thyroid function abnormalities in diabetes patients may mimic symptoms of poor glycaemic control and it is important to differentiate between the two for appropriate clinical management.[10]

We undertook this comparative analysis of thyroid dysfunction in T2DM patients to identify the prevalence and patterns of thyroid abnormalities in patients having T2DM and to compare their prevalence with those of healthy individuals

MATERIALS AND METHODS

This was a comparative observational study conducted in the Department of Endocrinology at a tertiary care medical college located in a rural area. The study aimed to evaluate thyroid function abnormalities among patients with Type 2 Diabetes Mellitus (T2DM) in comparison to healthy individuals. 50 individuals known to be having T2DM were included in this study on the basis of a predefined inclusion and exclusion criteria. 50 age matched healthy individuals were also included as a control group. Sample size was calculated on the basis of a pilot study examining the prevalence of thyroid dysfunction in T2DM. Using OpenEpi software (version 3) and assuming a 90% power with a 95% confidence interval, the required minimum sample size was 45 patients in each group. To account for potential dropouts, 50 patients with T2DM and 50 age-matched healthy individuals were enrolled in each group.

Group A (Cases): 50 patients diagnosed with T2DM
Group B (Controls): 50 healthy age-matched individuals

Demographic details such as age, gender, residential address, occupation, height, weight, and BMI were recorded. In the T2DM group, the duration of diabetes, details of current treatment (oral hypoglycaemic agents or insulin) and presence of any other systemic illnesses (e.g., hypertension, chronic obstructive pulmonary disease) were noted. A detailed history was taken particularly with respect to signs and symptoms suggestive of thyroid dysfunction. Medication history was carefully reviewed to exclude individuals taking drugs known to interfere with thyroid hormone metabolism.

All participants underwent a comprehensive general and systemic examination. The presence of diabetes-related end-organ involvement was assessed through renal function tests and fundoscopy.

Laboratory investigations included fasting blood sugar (FBS), postprandial blood sugar (PPBS), and glycosylated hemoglobin (HbA1c) were measured in both groups. A complete blood count (CBC) and lipid profile were performed to assess haematological and metabolic status. Renal function tests (RFT), including blood urea and serum creatinine were done in all cases. Thyroid function tests (TFT) were carried out by measuring serum T3 , T4 and Thyroid Stimulating Hormone (TSH) levels in all participants. Based on TFT results, patients were categorized into different thyroid dysfunction groups using established reference ranges: T3 (0.9–2.4 ng/dL), T4 (5.5–12.4 g/dL), and TSH (0.6–5.5 IU/mL).

Data were entered into Microsoft Excel and then exported to SPSS software (version 23.0) for analysis. Quantitative variables (e.g., TSH, T3, T4, fasting blood sugar, postprandial blood sugar, HbA1c) were expressed as mean ± standard deviation (SD). Qualitative variables (e.g., presence of thyroid dysfunction, co-morbid conditions) were expressed as frequency and percentages. For comparisons between the two groups (T2DM vs. healthy controls), the chi-square test was used for categorical variables, and an independent t-test was applied for continuous variables. A p-value <0.05 was considered statistically significant.

Inclusion Criteria

1. Patients with Type 2 Diabetes Mellitus (FBS >140 mg/dL and PPBS >200 mg/dL on at least two separate occasions).
2. Age between 18 and 60 years.
3. Ready to provide informed written consent.
4. Equal number of healthy individuals matched for age and sex enrolled as control group.

Exclusion Criteria

1. Refusal to give written informed consent.
2. Patients on medications known to alter thyroid hormone levels (e.g., lithium, amiodarone, interferon, aminoglutethimide).
3. Previously diagnosed thyroid disorders.
4. Presence of autoimmune diseases.
5. Patients with uncontrolled hypertension or severe chronic obstructive pulmonary disease.
6. Age <18 years or >60 years.

RESULTS

The analysis of gender distribution among the studied groups showed that in Group A (patients with diabetes mellitus), males were more prevalent, accounting for 29 cases (58%), while females constituted 21 cases (42%). Similarly, in Group B (healthy individuals), males made up 27 cases (54%), while females accounted for 23 cases (46%). The overall gender distribution was comparable between both groups (P= 0.8405). [Table 1]

Table 1: Gender distribution of studied cases

Group	Males		Females		Total	
	No of cases	Percentage	No of cases	Percentage	No of cases	Percentage
Group A (Diabetes Mellitus)	29	58 %	21	42 %	50	100 %
Group B (Healthy Individuals)	27	54 %	23	46 %	50	100 %
P= 0.8405						

The analysis of age distribution among the studied groups showed that in Group A (patients with diabetes mellitus), the majority of cases were in the 51-60 years age group (40%) followed by the 46-50 years (34%). In Group B (healthy individuals) the highest proportion was also in the 51-60 years (36%), followed by the 46-50 years age group (30%). The mean age in Group A was 47.8 ± 8.68 years, while in Group B, it was 45.12 ± 9.02 years. There was no statistically significant difference in the mean age of patients in both the groups. [Table 2]

Table 2: Age groups of the studied cases

Age Group	Group A (patients with diabetes mellitus)		Group B (Healthy individuals)	
	No of Patients	Percentage	No of Patients	Percentage
19-40 years	7	14.0%	9	18.0%
41-45 years	6	12.0%	8	16.0%
46-50 years	17	34.0%	15	30.0%
51-60 years	20	40.0%	18	36.0%
Mean Age	47.8 +/- 8.68 years		45.12 +/- 9.02 years	
P= 0.1333				

The analysis of the distribution of signs and symptoms (though not solely attributable to thyroid dysfunction) among the studied patients showed that the most common symptom was generalized weakness, observed in 32 cases (64%), followed closely by fatigue and lethargy in 31 cases (62%). Thinning of hair/hair fall was also highly prevalent, reported in 27 cases (54%). Other frequently noted symptoms included constipation in 20 cases (40%) and dry skin with pigmentation changes in 14 cases (28%). Unexplained weight gain was present in 14 cases (28%), while mood swings or anxiety, menstrual disturbances, facial puffiness, and joint pain with muscle stiffness were reported in fewer cases, ranging from 5 (10%) to 9 (18%). [Figure 1]

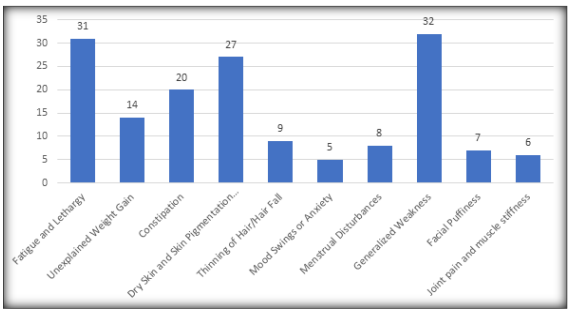

Figure 1: Signs and Symptoms of the studied cases

The analysis of thyroid status among the studied groups showed that in Group A, the majority were euthyroid (64%), while 17 cases (34%) had

hypothyroidism, including 12 cases (24%) of subclinical hypothyroidism and 5 cases (10%) of overt hypothyroidism. Hyperthyroidism was observed in 1 case (2%) in the form of subclinical hyperthyroidism, with no cases of overt hyperthyroidism. In Group B (healthy individuals), euthyroid status was observed in 43 cases (86%), while hypothyroidism was present in 7 cases (14%), comprising 5 cases (10%) of subclinical hypothyroidism and 2 cases (4%) of overt hypothyroidism. There were no cases of hyperthyroidism in this group. There was a statistically significant difference in thyroid function status between patients with T2DM and healthy individuals (P=0.019). [Table 3]

Table 3: Comparison of thyroid function abnormalities in studied cases

Thyroid Status	Group A		Group B		P Value
	No of Patients	Percentage	No of Patients	Percentage	
Euthyroid	32	64.0%	43	86.0%	0.019
Subclinical Hypothyroidism	12	24.0%	5	10.0%	
Overt Hypothyroidism	5	10.0%	2	4.0%	
Subclinical Hyperthyroidism	1	2.0%	0	0.0%	
Overt Hyperthyroidism	0	0.0%	0	0.0%	
Total	50	100%	50	100%	

The analysis of thyroid function parameters among the studied groups showed that T3 levels were lower in Group A (patients with diabetes mellitus) with a mean of 2.88 ± 0.42 pg/mL compared to 3.10 ± 0.38 pg/mL in Group B (healthy individuals), and this difference was statistically significant (P = 0.0072). Similarly, T4 levels were significantly reduced in Group A (1.10 ± 0.27 ng/dL) compared to Group B (1.31 ± 0.38 ng/dL) with a P-value of 0.001. On the other hand, TSH levels were notably higher in Group A (5.18 ± 1.44 mIU/L) compared to Group B (3.07 ± 0.74 mIU/L), and this difference was highly statistically significant (P < 0.0001). [Table 4]

Table 4: Mean T3, T4 and TSH levels in studied groups

Parameter	Group A - Mean ± SD	Group B - Mean ± SD	P Value
T3 Levels (pg/mL)	2.88 ± 0.42	3.10 ± 0.38	0.0072
T4 Levels (ng/dL)	1.10 ± 0.27	1.31 ± 0.38	0.0019
TSH Levels (mIU/L)	5.18 ± 1.44	3.07 ± 0.74	< 0.0001

Table 5: Correlation between HbA1c and thyroid function abnormalities in T2DM cases

HbA1c Category	HbA1c (%)	No Of cases	glycaemic Control	Thyroid Function Abnormalities
Good Control	<7	32	Good	6
Suboptimal/poor Control	> 7	18	Suboptimal	12
P =0.0016 (Significant) *				

The analysis of HbA1c levels and their association with thyroid function abnormalities showed that among the 32 patients with good glycaemic control (HbA1c < 7%), thyroid function abnormalities were observed in 6 cases. In contrast, among the 18 patients with suboptimal or poor glycaemic control (HbA1c > 7%), thyroid dysfunction was noted in 12 cases. There was a strong association between poor glycaemic control and the presence of thyroid function abnormalities in patients with T2DM (P =0.0016). [Table 5]

DISCUSSIONS

Thyroid dysfunction in Type 2 Diabetes Mellitus (T2DM) has emerged as a significant area of research due to its implications on overall disease management.[11] Previous studies suggest that chronic hyperglycemia, insulin resistance and systemic inflammation in T2DM may contribute to the development of thyroid abnormalities.[12] Prolonged metabolic disturbances can affect thyroid hormone synthesis and peripheral conversion potentially exacerbating the metabolic complications of diabetes. Furthermore, the inflammatory environment often observed in T2DM may predispose individuals to autoimmune thyroid disorders, compounding the risk of dysfunction.[13] Our study evaluated thyroid function abnormalities in patients with type 2 diabetes mellitus (Group A) as compared to healthy individuals (Group B). Demographic analysis revealed a comparable gender distribution between the groups with males representing 58% in the diabetic cohort and 54% in the healthy group (P = 0.8405). Similarly, the age distribution was comparable with a mean age of 47.8 ± 8.68 years in Group A versus 45.12 ± 9.02 years in Group B (P = 0.1333). In our study majority of diabetic patients were euthyroid (64%). However, a significant proportion demonstrated thyroid dysfunction. 34% had hypothyroidism (with 24% exhibiting subclinical hypothyroidism and 10% overt hypothyroidism) and 2% had subclinical hyperthyroidism. In contrast, only 14% of healthy

individuals had evidence of hypothyroidism, with no cases of hyperthyroidism recorded. The difference in the prevalence of thyroid dysfunction between diabetic patients and healthy controls was statistically significant (P = 0.019).

Telwani AH et al conducted a study to find out the prevalence of thyroid disorders in patients with type 2 diabetes mellitus.[14] For this purpose, the authors undertook a study comprising of 100 diabetic patients and 100 controls. The study found thyroid dysfunctions to be more common in diabetic patients as compared to controls (P-value <0.001). The most common thyroid dysfunction in diabetic patients was subclinical hypothyroidism (seen in 16%), while the least common was hyperthyroidism (1%). Serum T3 and T4 levels were significantly lower, whereas serum TSH levels were significantly higher in the diabetic group compared to the control group. The prevalence of thyroid disorders in diabetics was significantly higher in patients aged ≥50 years, more in females, more in patients with BMI ≥30, and more in patients with a duration of diabetes ≥5 years. On the basis of these findings, the authors concluded that there was a high prevalence of thyroid dysfunctions in diabetic patients. They recommended routine screening for thyroid dysfunction among diabetic patients to allow early recognition of these disorders. Similar thyroid function abnormalities in cases of diabetes were also reported by the authors such as Demitrost L et al,[15] and Papazafiropoulou A et al.[16]

Dr Kalra et al conducted a a comprehensive review of the interrelationship between type 2 diabetes mellitus (T2DM) and thyroid dysfunction (TD), highlighting their bidirectional influence on metabolic and endocrine functions. The review analysed existing literature, and guidelines to assess prevalence, and screening recommendations for thyroid dysfunction in T2DM. The review found that there was lack of standardized guidelines for thyroid screening in T2DM. The authors advocated for an evidence-based and systematic approach for assessing thyroid functions in diabetic patients.[17]

In our study there was a strong positive correlation between HbA1c level and thyroid function abnormalities. among the 32 patients with good glycaemic control (HbA1c < 7%), thyroid function abnormalities were observed in 6 cases. In contrast, among the 18 patients with suboptimal or poor glycaemic control (HbA1c > 7%), thyroid dysfunction was noted in 12 cases. Elgazar E et al conducted a cross-sectional study to determine the prevalence of thyroid dysfunction in diabetic patients and its relation to glycaemic control.[18] For this purpose, the authors undertook a study comprising 200 patients with type 2 diabetes mellitus (DM) and 200 apparently healthy controls. Each participant was tested for fasting and 2-hour postprandial blood glucose, glycated hemoglobin (HbA1c), thyroid function tests (TSH, FT3, FT4), serum total cholesterol and triglycerides, and thyroid antibodies (anti-TPO and anti-Tg for hypothyroidism). The study found that serum TSH and T3 levels were significantly higher in diabetics compared to controls (P < 0.001, P = 0.001, respectively). Thyroid dysfunction was significantly more prevalent in patients with HbA1c ≥ 8% (P = 0.0001) and in those with a longer duration of diabetes (P < 0.001). On the basis of these findings, the authors concluded that thyroid dysfunction was more prevalent in patients with type 2 DM, and its prevalence increased with higher HbA1c levels. The correlation between higher HbA1c levels and thyroid dysfunction seen in this study was similar to our study. The authors such as Biondi B et al,[19] and Bhattacharjee R et al,[20] also reported similar correlation between HbA1c levels and thyroid dysfunction.

CONCLUSION

We found a significant association between Type 2 Diabetes Mellitus (T2DM) and thyroid dysfunction. Additionally, Poor glycaemic control (HbA1c > 7%) was found to have a strong positive correlation with thyroid function abnormalities. Therefor early detection and effective management of glycaemic levels is important to decrease risk of thyroid dysfunction in T2DM patients. Integrating regular thyroid function assessments into diabetes care will have an important role in improving overall patient outcomes.

Conflict of Interest: None.

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