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Original Research Article

Thyroid dysfunction in type 2 diabetes mellitus patients attending diabetic clinic in a tertiary care centre: a cross-sectional study

Bithika Jamatia^{1*}, Rajesh K. Debbarma², Tapan Majumdar³

¹Indira Gandhi Memorial Hospital, Agartala, Tripura, India

²Department of Medicine, ³Department of Microbiology, Agartala Government Medical College and G. B. Pant hospital, Agartala, Tripura, India

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*Correspondence:

Dr. Bithika Jamatia,

Email: bithikajamatia@gmail.com

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ABSTRACT

Background: Thyroid disease and type 2 diabetes mellitus are two common co-existing endocrinopathies found in the general population. Since thyroid dysfunction complicates the metabolic derangement observed in diabetes, its treatment is necessary in order to achieve stability of metabolic control. Therefore, the aim of the present investigation was to estimate the functional thyroid disorders and the associated factors in type 2 diabetes patients.

Methods: In 230 diabetic patients, the blood sugar level and thyroid function tests were performed and compared. Most of the patients were in the age group of 51-60 years (36.08%).

Results: The prevalence of thyroid dysfunction in diabetic patients was 15.21% with a higher rate in female patients. Subclinical hypothyroidism (12.17%) was the commonest thyroid dysfunction.

Conclusions: The data suggest that subclinical hypothyroidism was more prevalent in type 2 diabetes mellitus, and may confer a greater risk of diabetic complications. It is therefore important to diagnose thyroid dysfunction in diabetic patients and the practice should be inculcated in diabetic care.

Keywords: Type 2 diabetes, Hyperthyroidism, Hypothyroidism, OPD

INTRODUCTION

Diabetes mellitus refers to a group of common metabolic disorders that shares the phenotype of hyperglycemia. Factors such as sedentary lifestyle, dietary indiscretions, ethnicity, hypertension and obesity are the major contributors to diabetes mellitus.¹⁻³ The World health organization has projected that the global prevalence of diabetes will rise to 300 million (7.8%) by 2030.⁴ In India, diabetes mellitus is a common rising disorder and has reached approximately 20% in urban populations and approximately 10% in the rural population.⁵ The influence of some endocrine and non-endocrine organs other than the pancreas on diabetes mellitus is

documented.⁶ Prevalence of thyroid dysfunction in 30% (22% hypothyroidism and 8% hyperthyroidism) type 2 diabetes patients was reported.⁷ Diabetic women are more frequently affected than men, and hypothyroidism is more common than hyperthyroidism.⁸ Thyroid hormones are insulin antagonists, both insulin and thyroid hormones are involved in cellular metabolism. Excess or deficit of any one can result in functional derangement of the other.⁹ In euthyroid individuals with diabetes mellitus, glycemic status influences serum tri-iodothyronine (T3) levels, basal thyroid-stimulating hormone (TSH) levels and TSH response to thyrotropin-releasing hormone (TRH).¹⁰ Poorly controlled diabetes, both type 1 and type 2, may induce a low total serum and free T3 levels, an

increase in reverse T3, but near normal serum T4 and TSH concentrations by a reduction in the peripheral conversion of thyroxine (T4) to T3 via 5'-monodeiodination reaction.¹¹ Studies have shown that long-term diabetic control can determine plasma T3 levels. Poorly controlled diabetes may result in impaired TSH response to TRH or loss of normal nocturnal TSH peak. TSH responses and "low T3 state" may normalize with improvement in glycemic status, however even with good diabetes control, the normal nocturnal TSH peak may not be restored in patients with totally absent pancreatic beta-cell function.¹²

Grave's disease is the commonest cause of hyperthyroidism. Variable glucose intolerance has been noted in up to 50% of patients with Grave's disease and in 2-3% of patients with frank diabetes, when hyperthyroidism develops in previously euglycemic individuals. In known diabetic patients, the development of hyperthyroidism results in deterioration of diabetic control. Varied metabolic changes tend to occur as a result of hyperthyroidism which contributes to the deterioration of glycemic control.¹¹ Changes include accelerated gastric emptying, enhanced intestinal glucose absorption and increase in portal venous blood flow in the gastrointestinal system.¹¹ With regards to insulin secretion; hyperthyroidism may cause decreased insulin secretion or normal or increased levels of insulin in the peripheral and portal circulation.^{12,13} There could be masking of increased insulin secretion due to increased degradation of insulin. In hyperthyroidism, the insulin clearance rate is reported to be increased by about 40%. Long-term thyrotoxicosis has been shown to cause beta-cell dysfunction resulting in reduced pancreatic insulin content, poor insulin response to glucose and decreased rate of insulin secretion. Thyroid hormones cause beta-cell apoptosis which contributes to deterioration in glucose control in patients with thyrotoxicosis.¹⁴ Hypothyroidism results in impaired or decreased liver glucose output thereby compensating for insulin resistance present in peripheral tissues and accounting for the diminished insulin requirement for glycemic control in hypothyroid diabetic patients. As regards to beta-cell function, normal or reduced basal plasma insulin levels have been described in hypothyroidism hence the attenuated endogenous glucose production in the hypothyroid state. On the other hand, increased glucose-stimulated insulin secretion has been recently described as a response to elevated whole-body insulin resistance increasing the demand on beta cells.¹⁵ The rate of hepatic glucose output is decreased probably due to reduced gluconeogenesis. A post-receptor defect has been proposed to explain the decrease in insulin-stimulated glucose utilization in peripheral tissues. The net effect is an increased risk of recurrent hypoglycemia in a diabetic individual.¹⁶ Although most of these observations apply to overt hypothyroidism, insulin resistance has been also reported in subclinical hypothyroidism.¹⁷ Unrecognized thyroid dysfunction may impair metabolic controls in patients with diabetes and in addition, may amplify

existing cardio-vascular risk. Recognition and treatment of thyroid dysfunction in diabetic patients will benefit glycemic control, attenuate cardiovascular risk, and improve general well-being.¹⁸ Therefore, diabetes patients need to be screened for thyroid dysfunction. The present study is intended to study the thyroid hormone dysfunction with the diabetic process. We focused to estimate the proportion of thyroid dysfunction and identifying the functional thyroid disorders in type 2 diabetes mellitus patients. Moreover, we studied the factors associated with functional thyroid disorders in type 2 diabetes mellitus patients namely age, sex, BMI, smoking and family history of thyroid disease.

METHODS

Study design

A cross-sectional study was conducted in the diabetic clinic of Agartala government medical college (AGMC) and GB Pant Hospital, Agartala, West Tripura, India from January 2017 to June 2018. Systematic random sampling was adopted and every 3rd patient was selected on every alternate day in Medicine and Endocrinology OPD of the hospital till the sample size was achieved. Patients with known thyroid disease, acute illness and chronic liver disease were excluded from the study. Data regarding age and duration of diabetes were noted in the proforma of the study subjects. Assessment of body mass index (BMI) was done in all the study participants. Body weight was measured using an electronic scale to the nearest 0.1 kg. Subjects were asked to stand straight and relaxed with minimum clothing. Height was measured to the nearest 0.1 cm by using the wall-mounted stadiometer. The height of the subjects was taken in the standing position, without footwear keeping head in the Frankfurt plane. BMI was subsequently calculated dividing body weight in kilogram by the square of height in meters. BMI between 25-29.9 kg/m² was taken as overweight while BMI above 30 kg/m² was taken as obesity for the purpose of this study. Blood pressure (BP) was measured in the study subjects with the help of a digital BP instrument. Subjects with BP 140/90 mmHg to $\geq$ 140/90 mmHg were considered hypertensive.

Diagnosis of diabetes

The diagnosis of diabetes mellitus is based on the American diabetes association (ADA) criteria for type 2 diabetes mellitus: symptoms of diabetes plus random plasma glucose concentration $\geq$ 200mg/dl or fasting plasma glucose level $\geq$ 126 mg/dl or (c) HbA1C $\geq$ 6.5% or (d) 2 hours plasma glucose level $\geq$ 200 mg/dl during an oral glucose tolerance test.

Diagnosis of thyroid dysfunction

The guidelines for the detection of thyroid dysfunction were considered as given below.¹⁹ Normal: when T3, T4, FT3, FT4 and TSH are within the normal range. Primary

hypothyroidism: when TSH is more than 5.0 mU/l and T3, T4, FT3 and FT4 is less than the normal value. Primary hyperthyroidism: when TSH is less than 0.5 mU/l and T3, T4, FT3 and FT4 is more than the normal values. Subclinical hypothyroidism: when TSH is more than 5.0 mU/L and T3, T4, FT3 and FT4 is within the normal range. Subclinical hyperthyroidism: when TSH is less than 0.5 mU/L and T3, T4, FT3 and FT4 is within the normal range.

Eligibility criteria

All diagnosed cases of type 2 diabetes mellitus were included in the study except patients with type 1 and gestational diabetes mellitus, patients who were on medication that are known to modify the thyroid functions, e.g. lithium, amiodarone, etc., who had undergone surgery of the thyroid gland, on drug-induced hyperglycemia, e.g. high dose steroids, pentamidine, diazoxide, etc and not willing to participate in the study were excluded from the study.

Informed consent

Informed consent was obtained from all participants and detailed history was taken regarding diabetes and thyroid dysfunction. Data regarding age, sex, height, weight, blood glucose level, thyroid function test were collected from the participants. Body mass index (BMI) was calculated to assess overweight/obesity BMI=weight in kilograms/ height in meters).²

Biochemical analysis

Glucose estimation was done by GOD- POD method²⁰⁻²⁴. Thyroid function test was done using VIDAS TSH, VIDAS T3, VIDAS T4, VIDAS FT3, VIDAS FT4 technique.²⁵⁻²⁸ Glycosylated hemoglobin was done in all study subjects by high performance liquid chromatography (HPLC) technique in the laboratory. The normal reference values of thyroid hormones are given below.²⁰⁻²⁴ Total T3: 0.92-2.33 nmol/l, total T4 : 60.0-120.0 nmol/l, TSH: 0.25- 5 μ IU/ml, FT4 : 10.6-19.4 pmol/l and FT3: 4-8.3 pmol/l.

Statistical analysis

Data on continuous variables like age, duration of diabetes, BMI, and HbA1c were entered in the master chart and expressed as mean with standard deviation. Data were analyzed using Epi info version 7.0. Statistical analysis was done using the Pearson Chi-square test, Fishers exact test and unpaired t test. All statistical analysis was carried out at 5% level of significance and p value of ≤ 0.05 was considered significant.

RESULTS

A total of 230 participants having type 2 diabetes mellitus were included in the final analysis. The baseline

characteristics of the study subjects are given in (Table 1). The mean duration of diabetes was 7.1 ± 2.45 years and the mean glycosylated hemoglobin (HbA1c) was 7.87 ± 2.54 among the study subjects. The maximum number of diabetic patients included in this study were in the age group of 32-80 years. The age, gender and BMI of the study subjects are given in (Table 2).

Table 1: Baseline characteristics of study participants.

Parameter	Mean $\pm$ SD
Age (years)	56.99 $\pm$ 9.97
BMI (kg/m ²)	27.28 $\pm$ 3.92
Duration of diabetes (years)	7.87 $\pm$ 2.54
HbA1c (%)	9.4 $\pm$ 2.54

Table 2: Age, gender and BMI distribution of study participants (n=230).

Demographic variables	N (%)
Gender	
Male	123 (53.48)
Female	107 (46.52)
Age group (years)	
30-40	16 (6.95)
41-50	50 (21.73)
51-60	83 (36.08)
61-70	68 (29.56)
>70	13 (5.65)
BMI	
Underweight	2 (0.86)
Normal weight	64 (27.82)
Overweight	95 (41.30)
Obese	69 (30)

The result of thyroid function test in the study subjects according to gender is shown in (Table 3-4). The prevalence of thyroid dysfunction in type 2 diabetes mellitus was found to be 15.21%. Thyroid dysfunction was more common in females (71.42%) as compared to males (28.57) and the difference was statistically significant ($p < 0.05$).

Table 3: Thyroid function test results of the study participants.

Thyroid function test	N (%)
Normal	195 (84.78)
Abnormal	35 (15.21)
Hypothyroidism	5 (2.17)
Hyperthyroidism	2 (0.86)
Sub-clinical hypothyroidism	28 (12.17)
Sub-clinical hyperthyroidism	0

Thyroid dysfunction occurs significantly more in patients with positive family history of thyroid dysfunction ($p < 0.05$) is shown in (Table 5). This shows that there is association of family history and thyroid dysfunction. Majority of the patients with thyroid dysfunction were in

the larger age group. Increased incidence of sub-clinical hypothyroidism is seen with increasing age (Table 6). Using Fishers exact test (>0.05) which is statistically insignificant ($p=0.76$).

Table 4: Thyroid function test in study subjects according to gender.

Gender	Thyroid function test N (%)		P value
	Normal	Abnormal	
Female	82 (76.63)	25 (23.36)	0.05
Male	113 (91.86)	10 (8.13)	

*Chi square test, $p<0.05$ taken as a significant.

Table 5: Distribution of the study participants according to family history of thyroid dysfunction and cross tabulation with thyroid function test.

Family history of thyroid dysfunction	Thyroid function test N (%)		P value
	Normal	Abnormal	
No	193 (86.55)	29 (13)	0.05
Yes	01 (14.29)	6 (85.71)	

*Fishers exact test, $p<0.05$ taken as a significant.

Table 6: Age distribution of patients having thyroid and differential thyroid dysfunction.

Age (years)	N	Thyroid dysfunction N (%)				P value
		Hypothyroidism	Hyperthyroidism	Sub-clinical hypothyroidism	Sub-clinical hyperthyroidism	
30-40	3 (8.57)	1 (3)	0	2 (6)	0	0.76
41-50	4 (11.42)	0	0	4 (11)	0	
51-60	10 (28.57)	1 (3)	1 (3)	8 (23)	0	
61-70	15 (42.85)	2 (6)	1 (3)	12 (34)	0	
>70	3 (8.57)	1 (3)	0	2 (6)	0	

*Fishers exact test, $p<0.05$ taken as a significant

In the present study, the prevalence of thyroid dysfunction in type 2 diabetes mellitus was found to be 15.21%, which is higher than the previous studies reporting 8.6%, 8.4%, 13.7%, 12.5% and 12.3%.^{8,29-31} However, some earlier investigations reported a higher prevalence of thyroid dysfunction in diabetic patients than our study like 27.8%, 32.4%, 16%, and 29%.³²⁻³⁵

Table 7: Thyroid dysfunction in study subjects according to duration of diabetes.

Duration of diabetes (years)	Hypothyroidism	Hyperthyroidism
<1	3	1
1-5	12	4
5-10	8	-
>10	7	-

There are many risk factors known to be associated with thyroid dysfunction in the general population, including

This shows that there is no association of age and thyroid dysfunction. In the present study, majority of the patients with thyroid dysfunction were overweight and obese. There is increased incidence of thyroid dysfunction with increased BMI (Table 10). The correlation of smoking with thyroid dysfunction in the study participants using Chi square test (>0.05) is shown in (Table 11). It was observed that there is no significant association of smoking and thyroid dysfunction ($p=0.21$).

DISCUSSION

Diabetes is a leading cause of morbidity and mortality worldwide. Thyroid disorders are also very common endocrine disorders in the general population. The associations between diabetes and thyroid disorders have long been reported and they have been shown to mutually influence each other.¹² The objective of our study was to estimate the proportion of thyroid dysfunction in type 2 diabetes mellitus patients, to identify the functional thyroid disorders in type 2 diabetes mellitus patients and to study the factors associated with functional thyroid disorders in type 2 diabetes mellitus patients namely age, sex, BMI, smoking and family history of thyroid disease.

age, gender, BMI, family history of thyroid disease and smoking. In our study, most thyroid dysfunction was seen in female patients (25 patients, 23.36%) compared to male patients (10 patients, 8.13%).

Table 8: Thyroid function test in study subjects according to glycemic status.

HbA1c (%)	Hypothyroidism	Hyperthyroidism
6.5-7	2	1
7.1-8	5	2
8.1-9	7	2
>9	12	4

Table 9: Correlation of thyroid dysfunction with cardiovascular disease.

Parameter	Hypo-thyroidism	Hyper-thyroidism	P value
Normal ECG	21 (60)	8 (23)	0.32
Abnormal ECG	4 (11)	2 (6)	

There is a statistically significant difference between thyroid function test and gender, which means there is the association of thyroid dysfunction and gender. Previous studies also reported more prevalence of thyroid

disorders in females as compared to males.^{8,35-38} Thus, the prevalence of thyroid disorders in diabetic patients is influenced by female gender.

Table 10: BMI distribution of patients having thyroid dysfunction and correlation of thyroid dysfunction with BMI.

BMI category	N	Thyroid dysfunction N (%)				P value
		Hypothyroidism	Hyperthyroidism	Sub-clinical hypothyroidism	Sub-clinical hyperthyroidism	
Underweight	2 (5.71)	0 (0)	2 (100)	0 (0)	0 (0)	0.05
Normal	2 (5.71)	0 (0)	0 (0)	2 (100)	0 (0)	
Overweight	17 (48.57)	5 (29.41)	0 (0)	12 (70.58)	0 (0)	
Obese	14 (40)	0 (0)	0 (0)	14 (100)	0 (0)	

Most of our patients with family history of thyroid dysfunction (06 patients, 85.71%) had abnormal thyroid function test. Diabetic patients with a positive family history of thyroid disease had a higher chance of developing thyroid dysfunction, while a family history of diabetes did not increase the risk for thyroid dysfunction which is the same observation reported earlier.³⁹ Among Saudi type 2 diabetic patients of more than 25 years of age, positive family history of thyroid disease is the most prominent risk factor for thyroid dysfunction, as is also shown in Caucasians.^{40,41}

Table 11: Cross tabulation between thyroid function test and smoking.

Smoking	Thyroid function test		P value
	Normal	Abnormal	
No	145 (82.85)	30 (17.14)	0.21
Yes	50 (90.91)	5 (9.09)	

*Chi square test, p<0.05 taken as a significant.

In the present study, the total number of patients examined comprised 123 males (53.47%) and 107 females (46.52%). In earlier studies, more male patients were reported than the females, for example, 64% vs 36% and 53% vs. 47%.^{32,42} However, one study reported a greater number of female patients (52.9%) than male patients (47.1%).³¹ Regarding age, most of the patients in the present study were in the age group 51-60 (36.08%), followed by 61-70 years (29.56%) and 41-50 years age group (21.73%) with a mean age of the patients was 56.99 years and the age range from 32 to 81 years. In an earlier study, most of the patients were above the age group of ≥50 years (66%) and the mean age of the study population was 54.63 years.⁴³ In one more investigation, the mean age of the patients was 50.4 and the age range was 26-85 years.³¹

In our study, most of the patients were overweight (95 patients, 41.30%) and obese (65 patients, 28.26%) followed by normal weight or healthy (64 patients, 27.82%) and underweight (02 patients, 0.86%) with the mean BMI 27.12. A previous study recorded the

prevalence of thyroid disorders in diabetics more in patients with BMI ≥30 as compared to patients with BMI<30 (51.7% versus 48.3%).³⁵ Similar results were reported by other studies.^{8,43} Most of the smoker patients enrolled in our study had normal thyroid function test (55 patients, 90.91%). It may be noted that smoking has no effect on thyroid dysfunction among type 2 diabetic patients.⁴⁰ Also, a very low prevalence was noticed among Saudi females for cultural reasons.⁴⁴ Smoking has been reported to be a risk for thyroid dysfunction, where higher T4 levels and lower TSH levels were reported among smokers but not among nonsmokers or former smokers. This may be explained by the toxicological effect of smoking on increasing levels of thyroxin binding globulin among smokers.⁴⁵ In our study, most common thyroid dysfunction among type 2 diabetic patients is sub-clinical hypothyroidism (28 patients/12.17%) followed by hypothyroidism (5 patients/2.17%) and hyperthyroidism (2 patients, 0.86%).

Thyroid dysfunction is more common in female patients, age more than 50 years and with increased BMI. In agreement with this, previous study recorded subclinical hypothyroidism (15.2%) as the most common thyroid dysfunction followed by hypothyroidism 10.6%.³² Another study reported subclinical hypothyroidism (12%) in patients with type 2 diabetes, thyroid disorders seen more in the age group of 40-58 years and patients with BMI >25 were at increased risk of having thyroid disorder.³¹

CONCLUSION

Diabetes mellitus patients and subclinical hypothyroidism may confer a greater risk of diabetic complications. It is therefore important to diagnose thyroid dysfunction in diabetic patients and this practice should be inculcated in diabetic care.

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