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Research Article

Spectrum of thyroid disorders among patients with type 2 diabetes mellitus

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Abstract

***Background and objectives*:** Thyroid disorders (TD) are common among patients with type 2 diabetes mellitus (T2DM). Information on types of functional and structural TDs among Bangladeshi patients with T2DM is scarce in the literature. The present study aimed to determine the magnitude and characteristics of different TDs among Bangladeshi diabetic patients attending an urban healthcare center in Dhaka.

***Material and methods*:** The study included patients with T2DM who attended an urban Endocrinology Outpatient consultation center in Dhaka over a period of two years. Diagnosis of TDs was based either on previous medical records or on investigational results of thyroid functions/gland during the first visit. Standard criteria were used to diagnose TDs.

***Results*:** Total 1424 patients with T2DM were enrolled in the study. The mean age of the study population was 48.8 ± 12.9years and 45.2% and 54.8% were male and female respectively. Among 1424 participants 217 (15.2%) had functional and/or structural abnormalities of thyroid gland. For those with abnormal thyroid function (14.3%), the most common was clinical hypothyroidism (10.5%), followed by subclinical hypothyroidism (2.6%), and clinical thyrotoxicosis (1.3%). Except for one, all patients with overt hypothyroidism had primary hypothyroidism. Among patients with overt thyrotoxicosis, Graves' disease was the most common entity (50%). Multinodular goiter was the most frequent diagnosis among structural abnormalities (7 out of 13). Female sex (OR: 3.0, 95%CI: 1.5, 6.1, p=0.003) and obesity (OR: 2.3, 95%CI: 1.1, 5.0, p=0.039) had higher odds of having a diagnosis of overt hypothyroidism among patients with T2DM. Hypertension, dyslipidemia and obesity were significantly ($p < 0.05$) higher in diabetic patients with overt hypothyroidism.

***Conclusion*:** TDs especially hypothyroidism are common among female Bangladeshi patients with T2DM. Dyslipidemia and obesity are significantly more in overt hypothyroidism among patients with T2DM.

Introduction

Diabetes mellitus (DM) and thyroid disorders (TDs) are the two most commonly encountered endocrine disorders in day-to-day endocrinology practice [1]. Worldwide 1 in 10 adults (20-79 years) are living with DM with an estimated

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number of 537 million, and approximately 200 million people have been suffering from TD [2-3]. The prevalence of TDs varies in different age groups and geographical regions based on their iodine nutrition and autoimmune status [4-7]. Thyroid dysfunction affects blood glucose control by altering insulin sensitivity, secretion, and peripheral glucose utilization [8]. Very high blood glucose may also affect the thyroid hormone concentration [9]. Moreover, anti-diabetic drugs have also been reported to affect the thyroid function status [8]. TDs are very common in the general population with a prevalence ranging from 6.6% to 13.4% [10-11]. Many observational studies reported a relatively higher prevalence of TDs ranging from 10% to 24% in type 2 diabetes mellitus (T2DM) patients compared to non-diabetic counterparts [11,12]. Studies from Bangladesh have also very similar findings [13,14]. However, studies from Bangladesh had small sample sizes and inappropriately defined the clinical hypothyroidism and subclinical hypothyroidism affecting the overall prevalence [13]. All studies in diabetic patients reported only the functional status of the thyroid gland, omitting equally important structural disorders namely thyroid nodule, thyroid malignancy and multinodular goiter. Also, no published article from Bangladesh categorized types of hyperthyroidism based on the etiology. In view of the above, the present study aimed to determine the prevalence and associated clinical features of different TDs among Bangladeshi patients with T2DM.

Materials and methods

The study was conducted at an Endocrinology Outpatient consultation center in Dhaka, Bangladesh. The study was approved by the Institutional Ethical committee of the Medical College for Women and Hospital, Uttara, Dhaka. Study participants' identities were kept confidential and anonymous at all times.

***Study population*:** All consecutive non-pregnant T2DM patients, attending Endocrinology Outpatient consultation center from August 2022 to September 2024 were primarily selected for the study. T2DM patients with pregnancy/gestational diabetes, secondary, and other types of diabetic patients were excluded from the study. Patients' clinical and demographic information were maintained in a prescription writing software database (Zilsoft Pro, Version 7.0). Clinical and demographic information of the study population were converted to an Excel document from the software database and imported to SPSS version 25.0 for statistical analysis.

***Diagnosis of TDs and other conditions*:** Diagnosis of TDs was based either on previous medical records or on investigational results of thyroid functions/gland during the first visit. The majority of the patients with TDs was previously diagnosed and came for routine follow-up for dose adjustment of existing medication. Functional TDs were diagnosed by symptoms suggestive of TDs, thyroid function tests namely serum thyroid stimulating hormone (TSH) and free thyroxine (FT4) tests. Estimation of TSH and FT4 was carried out by an indirect chemiluminescence method. Thyroid ultrasonogram findings were used to diagnose structural thyroid disease in suspected cases. In hyperthyroid patients, TSH receptor antibody (TRAb), thyroid scan, and radioactive iodine uptake tests were carried out to differentiate Graves' disease from other causes of thyrotoxicosis. Following criteria were used to diagnose different types of TDs:

a. For non-pregnant adults, a TSH range between 0.35 & 5.5μIU/mL and an FT4 range between 0.78 & 2.19 ng/dL, were considered normal based on laboratory cut-offs.

b. Subclinical hypothyroidism (SCH): FT4= 0.78 – 2.19 ng/dL and TSH=5.5 to <20.0 μIU/m.

c. Primary hypothyroidism: FT4< 0.78 ng/dL and TSH ≥20.0 μIU/mL

d. Secondary hypothyroidism: FT4< 0.78 ng/dL and TSH= undetectable to <20.0 μIU/mL

e. Subclinical thyrotoxicosis: FT4= 0.78 - 2.19 ng/dL and TSH <0.35 μIU/mL

f. Primary thyrotoxicosis: FT4> 2.19 ng/dL and TSH <0.35 μIU/m.

Solitary thyroid nodule and multinodular goiter were diagnosed based on ultrasonogram and thyroid scan findings while thyroid malignancy was

diagnosed by histopathology. Clinical hypothyroid includes both primary and secondary hypothyroidism.

Diabetes mellitus was diagnosed based on HbA1C and plasma glucose levels and classic symptoms of hyperglycemia or hyperglycemic crisis [15]. Hypertension was defined as systolic and diastolic blood pressure ≥140 and ≥90 mmHg respectively. A body mass index (BMI) over 30 kg/m^2 was considered as obese (WHO, 2004).

***Statistical analysis*:** Continuous variables are expressed as the mean ± standard deviation (SD), or median with interquartile range (IQR) depending on their distribution. Categorical variables are presented as frequency (number) and the percent. The association of baseline characteristics with different thyroid dysfunctions was analyzed by Chi-square tests and post hoc from adjusted residuals. Multivariable binary logistic regression was used to see the predictive association of baseline characteristics for overt hypothyroidism. Any value of <0.05 was used for statistical significance.

Results

Total 1424 patients with T2DM were enrolled in the study. The mean age of the study population was 48.8 ± 12.9 years. Majority (77.5%) was above 40 years of age and 45.2% and 54.8% were male and female respectively. Mean BMI of the participants was 29.2 ± 4.3 kg/ m^2 while 24.9% was obese. Detail profile of the study participants is shown in Table-1. Overall prevalence of thyroid disorders was present in 217 (15.2%) T2DM cases. Of the total study population, 1220 DM patients were euthyroid (Table-1). Types of thyroid disorders in patients with DM are shown in Table-2. Out of 217 patients with TDs, 204 (14.3%) and 13 (0.9%) had functional and other structural diseases respectively. The most common functional abnormality was overt hypothyroidism (10.5%), followed by subclinical hypothyroidism (2.6%), and overt thyrotoxicosis (1.3%). All except one had primary hypothyroidism. There were no cases of subclinical thyrotoxicosis. Graves' disease was the most common (9/18) cause of thyrotoxicosis. Of the total study population, 13 (0.9%) euthyroid cases had morphological abnormalities which included papillary thyroid carcinoma and goiters (Table-2).

Table-1: *Distribution of age, gender and clinical status of thyroid gland of the study population (N=1424)*

Variables	Values
Age, Mean ± SD Yrs	48.8 ± 12.9
<40 years, n (%)	321 (22.5)
≥40 years, n (%)	1103 (77.5)
Sex	
Male, n (%)	643 (45.2)
Female, n (%)	781 (54.8)
Physical findings, Mean ± SD	
SBP, mm-Hg,	130.3 ± 21.6
DBP, mm-Hg	78.7 ± 13.5
BMI, kg/m^2 (n=354)	29.2 ± 4.3
Comorbidities	
Hypertension	
Yes, n (%)	731 (51.3)
No, n (%)	693 (48.7)
Dyslipidemia	
Yes, n (%)	661 (46.4)
No, n (%)	763 (53.6)
Obesity present	
Yes, n (%)	354 (24.9)
No, n (%)	1070 (75.1)
Status of Thyroid gland	
Euthyroid, n (%)	1220 (85.7)
Thyroid disorders present, n %)	217 (15.2)
Thyroid disorders absent, n (%)	1207 (84.8)

Table-2: *Types of thyroid disorders in patients with T2DM (n= 1424)*

Types of TDs	N (%)
Overt Hypothyroidism	
Primary hypothyroidism	148 (10.4)
Secondary hypothyroidism	1 (0.1)
Total	**149** (10.5)
Subclinical thyroid disease	
Subclinical hypothyroid	37 (2.6)
Subclinical thyrotoxicosis	0
Total	**37** (2.6)
Thyrotoxicosis	
Graves' disease	9 (0.6)
Toxic multinodular goiter	6 (0.4)
Sub-acute thyroiditis & others*	3 (0.2)
Total	**18** (1.3)
Euthyroid goiter and nodules	
Papillary thyroid carcinoma	3 (0.2)
Multinodular goiter	7 (0.5)
Simple diffuse goiter	1 (0.1)
Benign solitary thyroid nodule	2 (0.1)
Total	**13** (0.9)

**Diagnosis was not confirmed.*

Significant ($p < 0.05$) differences in the frequency of sex distribution were observed in overt hypothyroidism and euthyroidism cases (Table-3). There was an overall significant ($p < 0.05$) association of different thyroid disorders with both dyslipidemia and hypertension. Significantly ($p < 0.05$) more cases of overt hypothyroidism had hypertension, dyslipidemia and obesity while it was opposite for diabetic patients with subclinical hypothyroidism and overt thyrotoxicosis. BMI was significantly (p=0.001) higher among those with overt hypothyroidism than euthyroidism (p=0.001).

A multivariable binary logistic regression model showed higher odds for female and obese individuals to have a diagnosis of clinical hypothyroidism than euthyroidism among people with DM (Table-4).

Table-3: *Characteristics of diabetic patients with thyroid functional disorders (n= 1424)*

Variables	Number	Thyroid function status				
		Overt hypothyroidism [N= 149]	**Subclinical hypothyroidism [N = 37]**	**Overt thyrotoxicosis [N=18]**	**Euthyroidism [N=1220]**	**p-value**
Age						
Mean ± SD yrs		50.1 ± 11.5	46.3 ± 12.8	46.8 ± 11.4	49.5 ± 12.9	0.330
<40 years, n (%)	321	29 (9.0)	13 (4.0)	5 (1.6)	274 (85.4)	0.216
≥40 years, n (%)	1103	120 (10.9)	24 (2.2)	13 (1.2)	946 (85.4)	
		p > 0.05	p > 0.05	p > 0.05	p > 0.05	
Sex, n (%)						
Male	643	30 (4.7)	11 (1.7)	5 (0.8)	597 (92.8)	**<0.001**
Female	781	119 (15.2)	26 (3.3)	13 (1.7)	623 (79.8)	
		p < 0.05	p > 0.05	p > 0.05	p < 0.05	
Hypertension, n (%)						
Yes	731	88 (12.0)	11 (1.5)	5 (0.7)	627 (85.8)	**0.002**
No	693	61 (8.8)	26 (3.8)	13 (1.9)	593 (85.6)	
		p < 0.05	p < 0.05	p < 0.05	p > 0.05	
Dyslipidemia, n (%)						
Yes	661	81 (12.3)	11 (1.7)	4 (0.6)	565 (85.5)	**0.007**
No	763	68 (8.9)	26 (3.4)	14 (1.8)	655 (85.8)	
		p < 0.05	p < 0.05	p < 0.05	p > 0.05	
****Obesity,** n (%)						
Yes	215	35 (16.3)	7 (3.3)	2 (0.9)	171 (79.5)	—*
No	139	9 (6.5)	5 (3.6)	2 (1.4)	123 (88.5)	
		p < 0.05	p > 0.05	p > 0.05	p < 0.05	
Physical findings, Mean ± SD						
Systolic BP, mm-Hg	1424	134 ± 18.3	128.2 ± 16.9	128.1 ± 11.5	131.0 ± 39.6	0.751
Diastolic BP, mm-Hg	1424	79.8±12.6	80.1±9.0	75.0±6.6	80.0±25.6	0.857
BMI, kg/m^2	354	31.7±5.8	28.8±4.5	27.5±2.5	28.7±4.5	**0.001**

*Note: ** Data of total 354 cases were analyzed. One-way ANOVA with post hoc HSD Tukey test or Pearson's chi-square test with post hoc analysis from adjusted residuals (AR) was done as appropriate. *Pearson's chi-square test could not be done due to >20% of cells' expected count <5.*

Table-4: *Predictors of overt hypothyroidism (vs. euthyroidism) among people with DM (n=338)*

Independent variables	Reference category	Odds ratio (95% CI)	p-value
Age ≥40 years	<40 years	1.7 (0.8 – 3.3)	0.157
Female sex	Male	3.0 (1.5 – 6.1)	**0.003**
Obesity (BMI ≥27.5 kg/m^2)	No-obesity (<27.5 kg/m^2)	2.3 (1.1 – 5.0)	**0.039**
Constant		0.03	<0.001

Note: Multivariable binary logistic regression analysis was done

Discussion

In the present study, the overall TDs among T2DM patients were 15.2%.The most common form of thyroid dysfunction was overt hypothyroidism (10.5%), followed by subclinical hypothyroidism (2.6%), and overt thyrotoxicosis (1.3%). Female diabetics were more commonly affected compared to males in all types of thyroid dysfunctions. Female sex and obesity were found to be independent predictors of overt hypothyroidism in diabetes. Overt hypothyroidism was seen more commonly in the elderly population aged above 40 years though it was not statistically significant. Among the structural thyroid disorders, euthyroid multinodular goiter was most prevalent among the study group. Thyroid dysfunctions among DM patients were observed with almost similar frequency in studies from Oman (12.6%), India (13.7%), and from Brazil (14%) [16-18]. However, many studies reported a relatively higher prevalence of thyroid dysfunctions among T2DM patients from Bangladesh (23.5%), India (23.6%), Jordan (26.7%), and Saudi Arabia (28.5%) [14,19-21]. A recent systematic review and meta-analysis also reported a higher prevalence (20.24%) of TDs among T2DM patients [22].

The variation in the prevalence of thyroid dysfunction among diabetics may be related to the study design and sampling technique. Most of the patients in our study were previously diagnosed cases of thyroid dysfunction, and further thyroid function tests were only done in the presence of suggestive symptoms and risk factors of thyroid disease. This could contribute to a relatively low frequency of subclinical hypothyroidism in our study (2.6%). Structural thyroid disorders were not routinely screened among our patients. Diagnosis of structural thyroid disorders was only attempted if the patient presented with suggestive problems. Therefore, routine screening of structural thyroid disease could yield higher frequency in our study as had been seen in a large-scale retrospective study from China. They found the overall prevalence rate of thyroid nodule was 38.3% on thyroid ultrasonogram. Increasing age of the study participants and the presence of diabetes had significant and positive co-relation with the thyroid nodule and goiter [23].

In our study, the majority of thyroid dysfunctions were previously diagnosed. During the study period, only patients with suggestive symptoms of TDs were screened for possible thyroid dysfunction. So, overt hypothyroid cases constituted a large proportion in our study group. Subclinical thyroid disorders were seen as less prevalent as routine screening for thyroid dysfunction was not advised in asymptomatic patients. Many cross-sectional studies reported a high prevalence of subclinical hypothyroid cases in diabetics, which was not seen in our study. This could be attributed to the study design. Antibody status was not tested and therefore, type 1 DM could not be identified and excluded. Besides, this was a single-center study and hence not a true representative of entire country. Despite having these limitations, a large sample size provided the true representation of TDs in T2DM patients. Inclusion of structural TDs and biochemical indices in TDs in diabetic patients provided further valuable clinical information to the existing evidence.

The observed frequency of thyroid dysfunction among T2DM patients was very high in our study, and females were more prone to develop thyroid dysfunctions. Females with obesity in the presence of T2DM should be routinely screened for clinical and subclinical hypothyroidism.

Conflict of Interest

The authors have no conflicts of interest to declare.

Fund

None.

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