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Thyroid Dysfunction in Adults with Newly Detected Type 2 Diabetes Mellitus: A Study in a Tertiary Care Hospital, Dhaka, Bangladesh

MD Mahbub Hossain Khan[1*], Nusrat Zarin[2], AFM Helal Uddin[3], MD Lutfar Rahman[4], MD Abdul Alim[5], Shams-El-Arefin[6], Kamrun Nahar[7], Mohammad Mahabub Hossain[8]

[*1]Assistant Registrar, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: mahabubssmc@gmail.com
Orcid ID: 0000-0002-1467-591X
[2]Assistant Professor, Department of Endocrinology, BIHS General Hospital, Dhaka, Bangladesh.
Email: mahabubssmc@gmail.com
Orcid ID: 0000-0003-0657-5318
[3]Associate Professor, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: dr.helal.uddin@gmail.com
Orcid ID: 0000-0002-9157-8195
[4]Medical Officer, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: lutfarssmc@gmail.com
Orcid ID: 0000-0002-6000-8333
[5]Registrar, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: alimssmc30@gmail.com
Orcid ID: 0000-0001-6833-2739
[6]Medical Officer, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: arefinshetu18@gmail.com
Orcid ID: 0000-0001-9644-2580
[7]Medical Officer, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: nahardmc18@gmail.com
Orcid ID: 0000-0002-5149-0113
[8]Assistant Professor, Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh.
Email: mahrinssmc@yahoo.com
Orcid ID: 0000-0002-1467-591X

*Corresponding author

Abstract

Background: Thyroid disorders and diabetes mellitus are common endocrine disorders that often coexist and can significantly impact each other's management. The American Diabetes Association recommends that people with diabetes be periodically screened for thyroid dysfunction due to the strong link between the two conditions. It is important for individuals to be aware of the risk factors for both conditions and to seek appropriate medical care if necessary, and for healthcare providers to consider testing for thyroid dysfunction in adults with newly detected type 2 diabetes mellitus. The aim of the study was to find out thyroid dysfunction in adults with newly detected type 2 diabetes mellitus. **Material & Methods:** This cross-sectional, descriptive study was conducted at the Departments of Medicine and Endocrinology at Sir Salimullah Medical College and Mitford Hospital in Dhaka. The study period lasted six months, from May to October 2019. A total of 102 adult patients (above 20 years old) with newly diagnosed type 2 diabetes mellitus who were attending the Endocrinology and Medicine Outpatient Department participated in the study. **Results:** Out of 102 adults with newly detected type 2 diabetes mellitus, the majority (86.3%) had normal thyroid function (euthyroid), while a smaller number (13.7%) had thyroid dysfunction. The most common subgroup of thyroid dysfunction was subclinical hypothyroidism (7.8%), followed by hypothyroidism (3.9%), subclinical thyrotoxicosis (1.0%), and hyperthyroidism (1.0%). The majority of the study population was male (66%) and from urban areas (88%), with a mean age of 45.1 years, a mean BMI of 25.0 kg/m2, and a mean waist circumference of 98.4 cm. About 45% had a family history of diabetes mellitus and 37% were smokers. The blood pressure of the study population was within normal limits. A minority (30%) had co-morbidities such as hypertension, dyslipidemia, and ischemic heart disease. The predictors of thyroid dysfunction were observed Age (OR=0.785), F/H of thyroid disorder (OR=0.495) BMI (OR=1.059), Anti-TPO Ab(OR= 0.021). **Conclusion:** Thyroid dysfunction and diabetes are commonly associated with each other and can impact clinical presentation and laboratory results. It is important to routinely screen for thyroid function in all patients with type 2 diabetes mellitus to detect, treat, and prevent complications of both these conditions.

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INTRODUCTION

Thyroid diseases and diabetes mellitus are two common endocrine disorders that often coexist and can significantly impact each other's management. The American Diabetes Association (ADA) recommends that people with diabetes be periodically screened for thyroid dysfunction due to the strong link between the two conditions.[1] Studies have shown that thyroid disease can affect glucose metabolism and uncontrolled thyroid dysfunction can affect the management of diabetes.[2,3] The global burden of diabetes is substantial, with the International Diabetes Federation estimating that 425 million people had diabetes in 2017 and this number is expected to rise to 529 million by 2045.[4] Diabetes is a leading cause of premature death, accounting for over 80% of all non-communicable disease deaths in 2015.[5] In 2017, there were 4.0 million deaths due to diabetes (age 20-79 years) and total healthcare expenditures for diabetes were estimated at USD 727 billion, which is projected to reach USD 776 billion by 2045.[4] The North American and Caribbean regions have the highest prevalence of diabetes (20-79 years) in the world at 11.0% in 2017. South East Asia, which includes Bangladesh, ranked third in the world and was home to one-fifth of the total number of people with diabetes. Bangladesh had the second highest prevalence of diabetes in South East Asia, with an estimated 7,349,526 diabetic patients, or 1 in 15 people.[4] The national prevalence of diabetes in Bangladesh was 6.8% (age-adjusted prevalence 8.3%), with 108530 diabetes-related deaths in 2017. By 2045, Bangladesh is expected to rank ninth in the top 10 countries with estimated 13.7 million diabetic patients.[4] There have been several studies documenting a higher-than-normal prevalence of thyroid function abnormalities in patients with diabetes mellitus. For example, Papazafiropoulou et al. found a prevalence of thyroid dysfunction of 12.3% among Greek type 2 diabetic patients, with a higher proportion of females affected.[6] In a study of young type 2 diabetic patients, Mukherjee found subclinical hypothyroidism in 43.33% of cases, overt hypothyroidism in 9.2%, subclinical hyperthyroidism in 8.3%, and clinical hyperthyroidism in 5%.[7] Vithiavathi et al. found that the most prevalent thyroid dysfunction among newly diagnosed type 2 diabetic patients was subclinical hypothyroidism (21%), followed by overt hypothyroidism (7%), with a higher prevalence of the dysfunction in females.[8] In a study of type 2 diabetic patients in India, Gupta et al. found a prevalence of thyroid dysfunction of 18.8%, with the most common dysfunction being subclinical hypothyroidism.[9] There is also evidence of an increased prevalence of diabetes in individuals with thyroid disorders. For example, a meta-analysis of 15 observational studies found that individuals with autoimmune thyroiditis had a significantly increased risk of developing type 2 diabetes.[10]

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Another study found that subclinical hypothyroidism was associated with an increased risk of type 2 diabetes, especially in individuals with a high body mass index.[11] A systematic review and meta-analysis of observational studies found that subclinical hypothyroidism was associated with an increased risk of developing type 2 diabetes, independent of other risk factors.[12] There is a strong link between thyroid disorders and diabetes mellitus, with both conditions often coexisting and impacting each other's management. The high prevalence of these conditions highlights the importance of effective management and prevention. It is important for individuals to be aware of the risk factors for both conditions and to seek appropriate medical care if necessary, and for healthcare providers to consider testing for thyroid dysfunction in adults with newly detected type 2 diabetes mellitus.

MATERIAL AND METHODS

This cross-sectional, descriptive study was conducted at the Departments of Medicine and Endocrinology at Sir Salimullah Medical College and Mitford Hospital in Dhaka. The study period lasted six months, from May to October 2019. A total of 102 adult patients (above 20 years old) with newly diagnosed type 2 diabetes mellitus who were attending the Endocrinology and Medicine Outpatient Department participated in the study. A purposive sampling method was used to select the participants, with the sample being carefully chosen based on specific criteria and characteristics rather than being drawn randomly from the population. Written informed consent was obtained from the study subjects prior to data collection. The data were collected with a pre structured questionnaire. The collected data were edited and cleaned. The clean data were input into SPSS software, Version 23.0 and analyzed. Chi-square tests were performed to observed the association between the study variables where $p<0.05$ considered the level of significance with 95%CI. The observed significant variables were further analyzed with logistic regression for the prediction of thyroid dysfunction. The ethical clearance of this study was obtained from the Institutional Review Board (IRB) of Sir Salimullah Medical College and Mitford Hospital. The inclusion and exclusion criteria were as follows:

Inclusion Criteria

- Adults aged 20 years or older
- newly detected patients with type 2 diabetes mellitus, irrespective of gender.
- Willing to participate.

Exclusion Criteria

- Patients with a thyroid disorder or on treatment.
- Patients with severe illness (sepsis, acute MI, severe heart failure, recent ICU admission).
- Patients with drug-induced hyperglycemia (high-dose steroids, pentamidine, diazoxide, etc.)
- Patients with type-1 diabetes mellitus.

RESULTS

Among the participant's cases, the average age was 45.1±7.4 years mean ± SD, BMI was 25.0±3.8 kg/m2 mean±SD, and mean WC was 98.4±8.6 cm mean ±SD among the study patients. Around 66% of patients were male, the majority of them were from urban areas (88%) and nearly

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half of them were businessmen (45%). 45% of patients had a family history of diabetes mellitus while 6.0% had a family history of thyroid disorder. Their blood pressure was within normal limits (mean SBP =135.5±10.2 mmHg and mean DBP=70.2±7.3 mmHg mean ± SD). 37% of patients were smokers and 30% of patients presented with multiple co-morbidities like hypertension, dyslipidemia, ischemic heart disease, stroke, etc. [Table 1]

Table 1: Distribution of the participants by characteristics of the study population (n=102).

Characteristics	**Frequency n (%)**	**Mean±SD**
Age (year)		45.1±7.4
BMI (kg/m^2)		25.0±3.8
SBP (mmHg)		135.5±10.2
DBP (mmHg)		70.2±7.3
WC (cm)		98.4±8.6
Gender		
Male	67 (65.69)	
Female	35 (34.31)	
Area of residence		
Urban	90 (88.24)	
Rural	12 (11.76)	
Occupation		
Service	30 (29.4)	
Business	46 (45.1)	
Housewife	24 (23.5)	
Others	2 (2.0)	
Smoking status		
Smoker	38 (37.2)	
Non-smoker	64 (62.8)	
F/H of Diabetes Mellitus		
Yes	46 (45.1)	
No	56 (54.9)	
Yes	31 (30.4)	
No	96 (94.1)	
Comorbidities		
Yes	31 (30.4)	
No	71 (69.6)	

Table 2: Distribution of the Risk factor of the study population (n=102).

Risk factor	**Frequency n (%)**
F/H of Diabetes Mellitus	46 (45.1)
F/H of Thyroid Disorder	6 (5.9)
Comorbidities	31 (30.4)

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Among the cases, the prevalence of certain risk factors among a group of individuals. The table indicates that 45.1% of the group has a family or personal history of diabetes mellitus, 5.9% has a family or personal history of thyroid disorder, and 30.4% has other medical conditions (co-morbidities).

Table 3: Thyroid functional status among the study population (n=102).

Thyroid functional status	Number (n)	Percentage (%)
Euthyroid	88	86.3
Thyroid dysfunction	14	13.7
Total	102	100

According to the table, most of the individuals in the group (88 individuals or 86.3%) have euthyroid thyroid function. A smaller number of individuals (14 individuals or 13.7%) have thyroid dysfunction. The total number of individuals in the group is also provided (102 individuals or 100%). This table suggests that the majority of individuals in the group have normal thyroid function, with a small minority experiencing thyroid dysfunction.

Table 4: Subgroups of thyroid dysfunction among the study population (n=102)

Categories of dysfunction	Number of patients	Frequency (%) (95% CI)
Hypothyroidism	4	3.9 (0.9-6.1)
Subclinical hypothyroidism	8	7.8 (6.5-8.9)
Hyperthyroidism	1	1.0 (0.2-2.4)
Subclinical thyrotoxicosis	1	1.0 (0.3-2.3)
Total	14	13.7 (8.1-16.8)

According to the table, there are a total of 14 patients with thyroid dysfunction, representing 13.7% of the total number of patients. Of these, 4 patients have hypothyroidism (3.9%), 8 patients have subclinical hypothyroidism (7.8%), 1 patient has hyperthyroidism (1.0%), and 1 patient has subclinical thyrotoxicosis (1.0%). The confidence intervals provided in the table indicate the range within which the true percentage is likely to fall, based on the sample of patients included in the study. This table suggests that the majority of patients in the group have normal thyroid function, with a small minority experiencing various forms of thyroid dysfunction.

Table 5: Comparison of family history of thyroid dysfunction with thyroid functional status among the study population (n=102)

F/H of thyroid dysfunction	Thyroid dysfunction		P value
	Yes n (%)	No n (%)	
Yes	1 (7.1)	5 (5.7)	0.829
No	13 (92.9)	83 (94.3)	

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According to the table, individuals in the group with a family history of thyroid dysfunction have thyroid dysfunction, representing 7.1% of this group. A total of 88 individuals in the group without a family history of thyroid dysfunction have thyroid dysfunction, representing 92.9% of this group. The p-value of 0.829 suggests that there is no statistically significant difference between the two groups in terms of the prevalence of thyroid dysfunction.

Table 6: Frequency of Anti-TPO Antibody among Study Population (n=102).

Thyroid functional status	**Anti-TPO Antibody**		**Total**
	Positive n (%)	**Negative n(%)**	
Euthyroid	4 (4.5)	84 (95.5)	88
Hypothyroidism	3 (75.0)	1(25.0)	4
Subclinical hypothyroidism	6 (75.0)	2 (25.0)	8
Hyperthyroidism	0	1 (100)	1
Subclinical Hyperthyroidism	0	1 (100)	1
Total n (%)	13 (12.7)	89 (87.3)	102 (100)

Among the cases, narrates the frequency of anti-thyroid antibodies among the functional groups of thyroids showing 13(12.7%) patients were anti-thyroid antibody (Anti-TPO) positive. Among different subgroups of thyroid functional status, most of the overt hypothyroidism (75%) and subclinical hypothyroidism (75%) were positive for anti-thyroid antibodies though the number of subjects was smaller. On the contrary, euthyroid and hyperthyroid patients were antibody-negative (Cent percent).

Table 7: Comparison of Anti-TPO Antibody Status with Thyroid Function among Study Population (n=102)

Thyroid Functional Status	**Positive n (%)**	**Negative n (%)**	**P value**
Euthyroid	4 (4.5)	84 (95.5)	<0.001
Hypothyroidism Subclinical	3 (75)	1(25)	
Hypothyroidism	6 (75)	2(25)	
Hyperthyroidism	0	1 (100)	
Subclinical Hyperthyroidism	0	1 (100)	

Among the cases, displays the comparison of Anti-TPO with different thyroid functional statuses among the study population, showing the comparison is statistically significant.

Table 8: Comparison between anti-TPO Antibody status with different levels of TSH among the study population (n=102).

TSH µIU/mL	**Anti-TPO Antibody**		**Total n (%)**	**P value**
	n (%)	**n (%)**		
<5	4 (4.4)	86 (95.6)	90 (100)	<0.001
(5-10)	5 (71.4)	2 (28.6)	7 (100)	<0.001
>10	4 (80.0)	1 (20.0)	5 (100)	<0.001

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Among the cases, anti-thyroid antibodies in light of the different levels of TSH, the highest frequency for positive anti-thyroid antibody (80%, 4/5) was observed in the group having TSH ≥10 µIU/mL followed by 71.4% (5/7) in the group having TSH (5-10) µ IU/mL, while only 4.4% (4/90) in the group having TSH <5 µIU/mL (p<0.001).

Table 9: Logistic regression analysis showing predictors of thyroid dysfunction (n=102)

Variables	OR	S.E	P value
Age	0.785	0.048	0.654
F/H of thyroid disorder	0.495	1.025	0.450
BMI	1.059	0.074	0.537
Anti-TPO Ab	0.021	0.654	<0.001

Among the cases, highlights Logistic regression analysis for predictive values over thyroid dysfunction in diabetes revealed that Anti-TPO antibody is independently related to thyroid dysfunction in patients with diabetes mellitus (p<0.001).

DISCUSSION

This study investigated thyroid dysfunction in patients with newly detected diabetes mellitus in the OPD of a tertiary-level hospital. It was observed that about 13.7% of the newly diagnosed patients with diabetes mellitus have thyroid dysfunction with a higher frequency for subclinical hypothyroidism followed by overt hypothyroidism, and an equal proportion of subclinical hyperthyroidism and hyperthyroidism. Anti-thyroid (Anti-TPO) antibody was also found to be positive in 12.7% of patients with the highest frequency in subclinical hypothyroidism and overt hypothyroidism subgroups. However, 4.5% of euthyroid patients were also positive for the anti-TPO antibody. The frequency of positive anti-TPO antibodies was found to be more with the TSH level between 5-10 mIU/L. However, there were no particular correlations of glucose level with thyroid hormones and anti-TPO antibody is an independent predictor for thyroid dysfunction. Similar findings were observed by other investigators like Papazafiropoulou et al. in 2010,[6] Norbe et al. in 2008,[13] and Aljabri in 2019,[14] in different populations. As there is an uprising global trend of occurring diabetes and observing autoimmunity among the diabetic population by many investigators, it may be imperative in the future to include testing for thyroid function tests and autoimmunity while diagnosing diabetes. In the present study,[9] (13.7%) patients had thyroid dysfunction and 88 (86.3%) were found to be euthyroid. Similar findings were observed by the investigators in Greek,[6] Portuguese,[13] Saudi Arabian,[14] Brazillian,[9] and Indian,[11,15] populations although the study populations were different in terms of geographic and ethnic origins. It was found that subclinical hypothyroidism was the commonest dysfunction occurring in 7.8%, followed by overt hypothyroidism in 3.9%, subclinical hyperthyroidism in 1.0%, and hyperthyroidism in 1.0% study population. These results are in concordance with the results from studies conducted in Norway (HUNT Study) by Fleiner et al,[16] a systematic review and meta-analysis in China by Han et al,[17] and in Portugal by

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Nobre et el,[12] and in India by Khurana et el,[11] Sreelatha et el.[15] This relationship cannot be explained as causal to diabetes but needs to keep in consideration while diagnosing any newly detected diabetic patients in terms of giving the importance of testing for thyroid dysfunction.[18] In an attempt to find out the status of anti-thyroid antibodies concerning thyroid functional status, 13(12.7%) patients were anti-TPO antibody positive and among the different subgroups, most of the overt hypothyroidism (3 out of 4, 75%) and subclinical hypothyroidism (6 out of 8,75%) were positive for the anti-TPO antibody. On the other hand, most of the euthyroid (95.5%) and all hyperthyroid (100%) patients were antibody negative. The presence of a significantly higher frequency of anti-TPO antibodies in patients with type-2 diabetes mellitus indicates the important role of autoimmunity in the development of thyroid dysfunction among type-2 diabetes mellitus patients. Alternatively, the two diseases are prevailing simultaneously in the same population and apparently, there seems to be an association though practically it may be co-occurrence in the same person. Thus, unless followed for a substantial period and investigated for a causal relationship between the two diseases, it cannot be concluded regarding the co-occurrence of the conditions. Nevertheless, it does not necessarily mean the presence of one disease in the event of another but warrants for the need of searching the presence of one of the other is detected. In Ghana, a case-control study [19] involving 302 types 2 diabetes patients and 310 nondiabetic controls aged 40–80 years revealed the prevalence of thyroid autoimmunity was significantly higher among Type 2 diabetic patients (12.2% vs. 3.9%, p= 0.0004) which has similar prevalence like the current study. Another study in India led by S Mukherjee (2015),[7] it was revealed that,[20] patients with diabetes mellitus out of 79 with thyroid dysfunction were positive for anti-TPO antibodies (27.84% of total thyroid abnormality) which were much higher than the frequency detected in the present study. On the other hand, as observed by them, 7 patients without any thyroid dysfunction showed anti-TPO antibody positivity (17.07%) which was 4.5% found by this study. Therefore, the presence of thyroid dysfunction and the positivity of anti-thyroid antibody is neither the obligatory association nor mutually exclusive events. With diabetes that could better be accomplished by thinking about the need for testing for hormonal abnormality and anti-thyroid antibody status in patients with newly detected diabetes mellitus. Therefore, assessing the status of thyroid dysfunction in the diabetic population will need investigation on a mass scale involving a larger sample size. In one study accomplished by Khurana et al. (2015), out of 32 diabetic patients who had thyroid disorders, 25 (78.12%) had no family history of thyroid disorders and 7 (21.87%) had a family history of thyroid disorder.[11] These findings were similar to a study done by Khurana et al. (2015), where out of 32 diabetic patients who had thyroid disorders, 7 (21.87%) had a BMI < 25, 6 (18.75%) had a BMI between 25 - 30 and 19 (59.37%) had BMI > 3016. Though apparently, it seems that BMI is related to thyroid dysfunction, it can also be explained by the fact that hypothyroid patients gain weight and conversely hyperthyroid patients lose weight which ultimately caused a significant difference in BMI among various thyroid functional statuses. The long-term impact of this

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observation and its consequences need further studies. In conclusion, the present study observed that about 13.7% of newly diagnosed patients with type-2 DM have thyroid dysfunction with a higher frequency for subclinical hypothyroidism. However, background hazards, if any in the environment related to iodine status or universal iodization of salt need to be considered before any clear inference.[21]

Limitations of the Study

The study was done on 102 cases only due to time and resource constraints. A study with a larger sample size is needed.

CONCLUSIONS

Thyroid dysfunction and diabetes are closely associated with each other through multidirectional pathways. The co-occurrence of these common endocrine conditions impacts clinical presentation and laboratory results while influencing screening, diagnostic and therapeutic strategies. A high index of suspicion should be kept for thyroid dysfunction in diabetes, especially difficult- to treat diabetes, and for diabetes in thyroid dysfunction, especially difficult-to-manage cases. The results of the present study suggest that thyroid dysfunction is likely to be more common in newly diagnosed patients with type-2 DM. This is following other studies. Furthermore, thyroid autoimmunity is one of the predictors for increased risk of thyroid dysfunction in this population group. No correlation appeared to be found between glycemic profile and thyroid functional status. In addition, patients with subclinical hypothyroidism had higher BMI than those with normal thyroid function. The treatment of hypothyroidism in the diabetic population helps in better control of other associated conditions. Based on these results, for any patient presenting to an outpatient department with type 2 diabetes mellitus, it is worthwhile to perform a thyroid function test to evaluate the thyroid status. This study necessitates a routine screening for thyroid function in all patients with type 2 diabetes mellitus to detect, treat and prevent a diverse range of complications of both these conditions.

Recommendation

A larger study involving a greater sample size of the study can improve the statistical power, which means that it is more likely to detect a true effect if one exists. A larger sample size can also increase the precision of the results, which means that the estimates of the effect will be more precise and narrower. However, it is important to consider the feasibility and cost of conducting a larger study, as well as the potential for biases in the sample. It may also be necessary to consider the appropriate sample size for the research question and the expected effect size. It is generally recommended to use sample size calculation methods to determine the appropriate sample size for a study.

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