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Association of Thyroid Disorders with Glycemic and Lipid Profiles in Subjects with Type 2 Diabetes Mellitus

Amrita Bhowmik[1], Shahnaj Begum[2]*, Muhammad Saiedullah[3]

[1]Department of Applied Laboratory Sciences, Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh
[2]Assistant Professor and Head, Department of Applied Laboratory Sciences, Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh
[3]Department of Physiology and Molecular Biology, Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh

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***Corresponding author:** Shahnaj Begum
Assistant Professor and Head, Department of Applied Laboratory Sciences, Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh

Abstract

Type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) share an underlying pathology with thyroid dysfunction, affecting glycemic and lipid profiles, particularly in rapidly transitioning populations. This study, conducted at a tertiary care hospital in Dhaka, Bangladesh, explored the association of thyroid disorders with glycemic and lipid profiles in subjects with T2DM. Blood samples from 172 subjects (75% male and 25% female) were analyzed for fasting plasma glucose (FPG), plasma glucose after breakfast (PGABF), glycated hemoglobin (%HbA1c), lipid profiles, and thyroid-stimulating hormone (TSH) levels. Subjects were categorized as euthyroid, hypothyroid and hyperthyroid groups according to TSH levels. The euthyroid group had FPG 6.1±0.8 mmol/L, PGABF 7.5±1.3 mmol/L, and HbA1c 6.2±0.5%, while higher FPG was observed in hypothyroid [10.3±4.2 ($p < 0.001$)] and hyperthyroid [10.3±4.6 ($p = 0.001$)] groups, along with increased PGABF and HbA1c levels. The euthyroid group presented with 52% elevated total cholesterol, 45% elevated triglycerides, 41% low high-density lipoprotein (HDL) cholesterol, and 51% elevated low-density lipoprotein (LDL) cholesterol. Notably, the hyperthyroid group showed 87% elevated serum triglycerides ($p < 0.001$), whereas the hypothyroid group had 23% elevated serum total cholesterol ($p < 0.001$). Findings indicate thyroid disorders are linked to elevated plasma glucose and HbA1c, with hyperthyroidism potentially elevating triglycerides in T2DM.

Keywords: Hypothyroidism, hyperthyroidism, hyperglycemia, dyslipidemia.

INTRODUCTION

Diabetes mellitus and thyroid dysfunction are the most common, interrelated and frequently occurring endocrinopathies that play an adversarial role on cardiovascular health (Mohammed Hussein *et al*., 2021; Sarfo-Kantanka *et al*., 2018). The prevalence of hypothyroidism and hyperthyroidism in the developed world is about 4-5% and 0.2-1.3% (Hollowell *et al*., 2002). In the people of Bangladesh though the actual prevalence and burden of thyroid dysfunction is unknown (Selim and Kamrul-Hasan, 2023), it is reported to be present in higher percentages (20%) of the general people (Paul *et al*., 2006). A community-based study conducted in the Khulna district identified a 20.43% thyroid disorder with 4.97% hypothyroidism, 6.59% subclinical hypothyroidism, 0.86% hyperthyroidism and 0.65% subclinical hyperthyroidism among 925 individuals (Paul *et al*., 2006). However, another study conducted in Dhaka city found a high prevalence of thyroid dysfunction (10.03%) with a higher prevalence of subclinical hypothyroidism (2.46%), hypothyroidism (3.8%) and subclinical hyperthyroidism (1.73%), hyperthyroidism (1.04%) (Das *et al*., 2010). A recent study observed a 7.0% prevalence of hypothyroidism in Dhaka which shows an increasing rate (Sayeed *et al*., 2020). In all the studies, females had a higher prevalence of hypothyroidism and subclinical hypothyroidism than males (Paul *et al*., 2006, Das *et al*., 2010, Sayeed *et al*., 2020).

The co-existence of T2DM and thyroid dysfunctions is notably high (Biondi *et al*., 2019). In subjects with T2DM, thyroid dysfunction has been found in 28% of the North Indians (Ozir *et al*., 2018), 23.5% in people of Bangladesh (Khan *et al*., 2017) and 36.9% in people of Pakistan (Bukhari *et al*., 2022). An underlying relationship between thyroid disorders and T2DM has been reported. Meta-analysis suggests that

hyperthyroidism increases the risk of T2DM (Rong *et al*., 2021). Since the thyroid hormones control all three metabolic tempi i.e., carbohydrate, lipid and protein metabolism, thyroid disorders (both hyperthyroidism and hypothyroidism) prompt poor glycemic control as evidenced by elevated HbA1c (Ogbonna *et al*., 2019) and higher cardiovascular risk factors as evidenced by higher insulin resistance (Roos *et al*., 2007) and disorders in lipid metabolism (Rizos *et al*., 2011). The biosynthesis of cholesterol, upregulation of low-density lipoprotein (LDL) receptor expression, exchange of cholesterol esters and triglycerides (TG) between the high-density lipoprotein (HDL) and very-low-density lipoprotein (VLDL), catabolism of the TG-rich lipoproteins, hepatic conversion of HDL2 to HDL3 particles and the overall lipid dynamics in the circulatory system and intracellular milieu are under the tight control of the thyroid hormones (Rizos *et al*., 2011), therefore, thyroid disorders strongly influence lipidemic status. Though DM is one of the strong predictors of cardiovascular diseases (CVD), the addition of thyroid disorders in DM enhances the risk of CVD events. In people of Bangladesh, atherosclerotic CVD (ASCVD) occurrence is higher with increasing trends over the last few decades that are possibly linked to changes in lifestyle and economic transitions leading to imposing extra health burden (Islam *et al*., 2017; Chowdhury *et al*., 2018). Thus, it is important to evaluate the impact of thyroid disorders on glycemic and lipid profiles in subjects with T2DM in our population.

MATERIAL AND METHODS

Study Subjects: A group of 172 subjects was randomly selected from a tertiary care hospital for this study.

Blood Sample Collection: Approximately 5.0 ml of venous blood was drawn from individual subjects in a clotting activator tube for assessment of fasting glucose, HbA1c%, lipid profiles and TSH analysis.

Biochemical measurements:

Serum glucose was measured by Glucose Oxidase (GOD-PAP) method; HbA1c% by dedicated high-performance liquid chromatography (HPLC); total cholesterol, triglyceride (TG), HDL cholesterol and LDL-cholesterol by enzymatic colourimetric method using autoanalyzer. TSH was measured by immunoassay.

Subjects were divided according to TSH cut-off values as euthyroid (0.4 to 4.0 mIU/L), hypothyroid (>4.1 mIU/L) and hyperthyroid (<0.3 mIU/L) (Luongo *et al*., 2021). Dyslipidemia was determined according to the NCEP-ATPIII (adult treatment panel III, 2001).

Statistical Analysis

The data were expressed as mean ± SD (Standard deviation). The statistical significance of differences between the values was assessed by independent sample t-test, Fisher's exact test using Statistical Package for Social Science (SPSS) version 22.

RESULTS

In this study total of 172 subjects were randomly included, among them 75% were male and 25% were female. The Mean±SD of age was 45±16 years. The age distribution of the study subjects is presented in Table 1. Most of the study subjects were fall between the age range of 21 – 50 years.

Table 1: Distribution of subjects according to age

Age	Frequency (%)
< 20 yrs	17 (10%)
21-50 yrs	123 (72%)
> 50 yrs	32 (18%)

Data are expressed as numbers (percentage)

The mean±SD of serum TSH in euthyroid, hyperthyroid and hypothyroid subjects is presented in Table 2. The highest proportion was observed in the euthyroid group (54%), followed by hypothyroidism (33%) and hyperthyroidism (13%).

Table 2: TSH status in the study subjects

Group	Mean±SD	Frequency
Normal (0.4 to 4.0 mIU/L)	2.4±1.1	92 (54%)
Hypothyroidism (>4.1 mIU/L)	8.7±7.1	57 (33%)
Hyperthyroidism (<0.3 mIU/L)	0.3±0.2	23 (13%)

Data are expressed as mean ± standard deviation (SD) and number (percentage).

Table 3 shows the glycemic status in the study subjects according to thyroid level. It was found that fasting glucose, after breakfast plasma glucose and HbA1c levels were significantly higher in hyperthyroid and hypothyroid groups compared to the euthyroid group (Table 3). The mean±SD value of serum total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and percentages of dyslipidemia are presented in Table 4. No significant differences in lipid levels were observed in the hyperthyroid and hypothyroid groups compared to the euthyroid group except for total cholesterol in the hypothyroid group

which exhibited significantly lower levels of serum total cholesterol compared to euthyroid (Table 4).

Table 3: Glycemic status in the study subjects according to thyroid level

TSH level (mIU/L)	Mean±SD		
	F (mmol/L)	ABF (mmol/L)	HbA1c (%)
Normal (0.4 to 4.0 mIU/L)	6.1±0.8	7.5±1.3	6.2±0.5
Hypothyroidism (>4.1 mIU/L)	10.3±4.2*	13.9±5.5*	8.9±2.2*
Hyperthyroidism (<0.3 mIU/L)	10.3±4.6**	15.1±6.5*	9.7±2.1*

Results are presented as mean ± standard deviation (SD). Data were compared using the Independent Sample t-test. The mean difference is significant at the 0.05 level. *P<0.001, **p=0.001.

Table 4: Lipid profiles in the study subjects according to thyroid status

Lipid parameters	Euthyroid	Hypothyroid	Hyperthyroid
Total cholesterol (mg/dL)	199±42	171±36 p = 0.028	201±55 p = 0.883
Elevated total cholesterol (>200 mg/dL)	48 (52%)	13 (23%) p < 0.001	11 (48%) p = 0.817
HDL cholesterol (mg/dL)	42±11	46±15 p = 0.272	41±10 p = 0.613
HDL cholesterol (<40 mg/dL)	38 (41%)	17 (30%) p = 0.167	10 (43%) p = 1.00
LDL cholesterol (mg/dL)	153±56	125±52 p = 0.090	142±79 p = 0.641
Elevated LDL cholesterol (> 130 mg/dL)	47 (51%)	21 (37%) p = 0.630	7 (30%) p = 0.102
Triglycerides (mg/dL)	153±70	149±74 p = 0.310	187±47 p = 0.216
Elevated Triglycerides (>150mg/dL)	42 (45%)	21 (37%) p = 0.536	20 (87%)* p < 0.001

Results are presented as mean ± standard deviation (SD) and number (percentage), data in hypothyroid and hyperthyroid groups were compared with the euthyroid group using the Independent sample t-test and Fisher's exact test.

Subjects were classified as elevated TG (>150 mg/dL), elevated total cholesterol (>200 mg/dL), elevated LDL cholesterol (>130 mg/dL) and Low HDL cholesterol (<40 mg/dL) according to their cut of values. A significantly higher proportion of elevated triglycerides was found in the group hyperthyroid in comparison to euthyroid ($p < 0.001$) but the proportion of elevated cholesterol was also found in hypothyroid in comparison to euthyroid ($p < 0.001$) respectively. Low HDL and elevated LDL cholesterol showed no significant difference in thyroid disorders compared to euthyroid (Table 4).

DISCUSSION

The glycemic and lipidemic status in thyroid disorders are evaluated in a group of T2DM subjects. In this study, we observed that thyroid disorders are present in 46% of the subjects with T2DM and thyroid disorders (both hypo- and hypothyroidism) are associated with poor glycemic status as evidenced by elevated plasma glucose and HbA1c. Though lipid levels were similar in subjects with thyroid disorders to the euthyroid subjects with T2DM, a higher percentage of subjects (87%) showed elevated serum triglycerides in hyperthyroid subjects.

The higher occurrence of thyroid disorders (23.5%) in subjects with T2DM has been reported in previous studies conducted in people of Bangladesh (Khan *et al*., 2017). Another Hospital-based small study indicated that 63.2% of subjects with T2DM had thyroid dysfunction (Biswas *et al*., 2020) but a lower prevalence (10%) has also been reported in another tertiary hospital-based cross-sectional study conducted in Jurain, Dhaka (Moslem *et al*., 2015). Poor glycemic control has been found to be associated with hypothyroidism in a group of subjects with T2DM in people of Bangladesh (Alo *et al*., 2020). Uncontrolled diabetic subjects exhibited a higher prevalence of thyroid disorder (Jali *et al*., 2017) and thyroid disorders were reported to be associated with a higher prevalence of dyslipidemia (Ozir *et al*., 2018). In our study, hypothyroid subjects with T2DM exhibited a lower occurrence of elevated LDL cholesterol and lower levels of serum total cholesterol compared to euthyroid subjects. This is consistent with the underlying mechanism of the reduction of hepatic cholesterol biosynthesis in hypothyroidism (Choi *et al*., 2000).

Various studies have been undertaken to understand the role and importance, and due to the higher prevalence of thyroid disorders in subjects with T2DM, emphasis is given to the assessment of thyroid functions in the patients of T2DM (Perros *et al*., 1995). Uncontrolled diabetes mellitus is often related to insulin resistance which promotes the growth of the thyroid tissues or thyroid dysfunctions may arise from the negative effect of some antidiabetic agents used for the management of diabetes mellitus (Kalra *et al*., 2019). Thus it is important to include the assessment and management of thyroid functions in T2DM particularly those who have uncontrolled glycemic profiles. Systematic and prospective studies are recommended on T2DM in our population.

CONCLUSION

Thyroid disorders are associated with poor glycemic control and hyperthyroidism may be an important factor for elevating triglycerides in T2DM.

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