Magnitude and Determinants of Hypothyroidism among Dyslipidemic Patients in Bangladesh: A Hospital-Based Cross-Sectional Study

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Keywords

Dyslipidemia · Hypothyroidism · Thyroid-stimulating hormone

Abstract

Background: Dyslipidemia is one of the most commonly experienced metabolic disorders, and it is strongly related to atherosclerotic cardiovascular disease. Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones. Several studies from developed countries provide evidence that the rate of hypothyroidism in dyslipidemic patients is higher, but there is a scarcity of data from Bangladesh. **Objectives:** The aim of this study was to evaluate the prevalence and determinants of hypothyroidism in the adult dyslipidemic Bangladeshi population. **Method:** We examined the thyroid function of outpatients who were advised for fasting lipid profile and who were found to be dyslipidemic at a tertiary care hospital in Savar, Bangladesh, by a cross-sectional study conducted from July 2016 to June 2017. A total of 200 outpatients aged 20–65 years were enrolled in this study. A standard questionnaire was used to take record of sociodemographic, socioeconomic, and behavioral features. Body mass index (BMI) and blood pressure were examined with standard procedures. Biochemical parameters, such as fasting lipid profile and thyroid function

markers, thyroid-stimulating hormone (TSH) and free thyroxine (fT4), were determined using standard assay methods. A p value <0.05 was considered to be statistically significant. **Results:** Among the participants, 56% were male and 44% were female. 11.5% of the dyslipidemic subjects had hypothyroidism, among which 9.5% had subclinical hypothyroidism and only 2% had overt hypothyroidism. We also found that serum mean $\pm$ SD levels of TSH were significantly higher in the obese group of patients ($p = 0.02$). There was a significantly positive association of BMI and diastolic blood pressure with serum levels of TSH ($p < 0.01$) and fT4 ($p = 0.02$), respectively. **Conclusion:** Dyslipidemic patients should have more regular checkups. The findings of this study might be helpful in setting up the clinical management of dyslipidemias with or without normal thyroid function.

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Introduction

Dyslipidemia, which refers to abnormal levels of lipids or fats in the blood, encompassing changes in the levels of triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), has been widely established as an in-

dependent major risk factor for chronic heart disease (CHD) and might even be a prerequisite, occurring before other major risk factors come into play [1, 2]. The term “dyslipidemia” is gradually becoming more popular to describe abnormal changes in the lipid profile, which represent an elevation of plasma total cholesterol (TC), known as hypercholesterolemia, or TGs, known as hypertriglyceridemia, or both, which contributes to the development of atherosclerosis. Low concentrations of HDL-C and high concentrations of TGs have been identified as possible independent predictors of CHD [3, 4], and combinations of those 2 conditions have been defined as atherogenic dyslipidemia [5]. It is well known that the composition and transport of lipoproteins may be changed owing to alterations in thyroid function [6, 7]. In general, hypothyroidism is associated with hypercholesterolemia mainly due to elevation of LDL-C concentrations, whereas HDL-C concentrations are usually normal or even elevated [7], whereas hyperthyroidism is accompanied by a decrease in serum levels of TC, LDL-C, and HDL-C [8]. The above changes are explained by the regulatory effects of thyroid hormones on the activity of some enzymes of lipoprotein metabolism [9–11]. Hypothyroidism has been reported to be present in 1.4–13% of hyperlipidemic patients [12]. Overt hypothyroidism is one of the secondary causes of hyperlipidemia and associated with coronary artery disease [13]. In overt hypothyroidism, thyroid-stimulating hormone (TSH) levels are high and free thyroxine (fT4) levels are low. Subclinical thyroid dysfunction refers to patients who have an abnormal TSH level and a normal fT4 level [6]. Several reviews suggested a TSH upper-limit cutoff value close to 4.5 or 5.0 mU/L [6] for subclinical hypothyroidism, and a TSH lower-limit cutoff value close to 0.3 or 0.5 mU/L was proposed to consider subclinical hyperthyroidism. In a recent study, an independent association of TSH level with serum TC level was found, and routine screening of thyroid function was suggested for the management of CHD patients [14]. The prevalence of subclinical hypothyroidism has been reported to be 4.3% in adults, while it is 0.7% in case of subclinical hyperthyroidism and higher in older men and women [15]. Data published on the relationship between subclinical hypothyroidism and CHD events are conflicting [16].

Many studies were done to assess the lipid profile status of hypothyroid patients. But no studies have focused on investigating the status of thyroid hormone in dyslipidemic subjects. We have conducted this study in a Bangladeshi adult population for the evaluation of thy-

roid function in dyslipidemic subjects, which might be helpful for the clinical management of dyslipidemic patients with hypothyroidism prevailing in the Bangladeshi adult population.

Materials and Methods

This was a cross-sectional study in which 200 adult male and female subjects diagnosed with dyslipidemia and who were advised for fasting serum lipid profile from the outpatient department of a tertiary care hospital in Savar, Bangladesh, were enrolled over a 1-year period (July 2016 to June 2017). Following the determination of the fasting lipid profile, fasting cholesterol oxidase, HDL, LDL, and TG were measured. TSH and fT4 were measured to detect hypothyroidism in these dyslipidemic patients. The sample size was calculated by using an estimated proportion of 13%. According to this, our sample size was 173, but we tried to enroll as many patients as possible and, finally, were able to get 200 samples from the hospital. Inclusion criteria included adult males and females with diagnosed dyslipidemia and able to communicate. Our exclusion criteria included pregnant or lactating women, patients with liver cirrhosis, chronic obstructive pulmonary diseases, chronic kidney disease, malignancy, and any other major illnesses which caused hospitalization.

Data Collection and Measurements

Dyslipidemic subjects were interviewed face to face by the researcher herself with a questionnaire evaluating socioeconomic and sociodemographic characteristics as well as lifestyle- and health-related habits. Height and weight were measured twice using a height-weight scale by a trained and experienced nurse, which had been calibrated before subjects stood with bare feet and wore light clothing, and then the averages were calculated. Body mass index (BMI) was calculated as weight in kilogram divided by height in meter squared. Overnight fasting (8–10 h) venous blood was collected between 8:00 and 9:00 a.m. Fasting blood samples were collected into plain tubes and allowed to clot for 30 min, and serum was separated by centrifugation for 10 min at 3,000 rpm using a refrigerated centrifuge for biochemical analyses. Serum TC was measured by the enzymatic endpoint (cholesterol oxidase/peroxidase) method. HDL, LDL, and TG were determined by the enzymatic color test of quantitative determination in human serum and plasma in the Beckman Coulter AU480 analyzer. Serum TSH and T4 were measured in a fully automated chemiluminescence immunoassay analyzer (Maglumi). Blood pressure measurement was carried out on the right arm of seated subjects, using a mercury sphygmomanometer (Diamond 2009, precision 2 mm Hg). Three measurements were consecutively taken with 5-min intervals by a physician. If a person's systolic blood pressure (SBP) is consistently equal to or above 140 mm Hg and/or a diastolic blood pressure (DBP) is equal to or above 90 mm Hg, the blood pressure is considered to be raised or is regarded as high blood pressure [17, 18].

Definitions of Variables

Dyslipidemia was diagnosed according to the criteria set by the National Cholesterol Education (Program Adult Treatment Panel III): TC >200 mg/dL, TG >150 mg/dL, LDL-C >165 mg/dL. Thyroid status was defined based on serum levels of TSH and fT4: (a)

Fig. 1. Thyroid function status of the dyslipidemic subjects.

euthyroid: serum TSH = 0.34–5.60 μ IU/mL and fT4 = 0.65–1.74 ng/dL; (b) overt hypothyroidism: serum TSH >5.6 μ IU/mL and fT4 <0.65 ng/dL; and (c) subclinical hypothyroidism: serum TSH >5.6 μ IU/mL and fT4 = 0.65–1.74 ng/dL. According to the guideline of the World Health Organization, underweight was defined as BMI <18.5 kg/m², normal weight as 18.5–24.9 kg/m², overweight as 25.0–29.9 kg/m², and obese as >30.0 kg/m². SBP >120 mm Hg and DBP >80 mm Hg after 3 measurements were defined as hypertensive. Regular physical activity was defined as participation in moderate or vigorous activity for $\geq$ 30 min/day at least 5 days per week.

Statistical Analysis

The data for this study were analyzed using Statistical Package for the Social Sciences (SPSS) software version 17. To explore if the BMI status of the study subjects was influenced by the thyroid function markers, serum mean $\pm$ SD levels of TSH and fT4 were compared and analyzed using one-way ANOVA followed by a post hoc least significant difference test. To examine the association of BMI, blood pressure, and lipid profile of the study subjects with their serum levels of thyroid function markers, TSH and fT4, correlation analysis was performed. To explore if differences in the BMI, blood pressure, fasting lipid profile, and thyroid function markers of the study subjects were influenced by gender, their mean $\pm$ SD levels were compared and analyzed statistically using Student's *t* test. A *p* value <0.05 was considered statistically significant.

Result

To understand the thyroid function status of dyslipidemic subjects, their serum levels of TSH and fT4 were analyzed. Of the total participants (*n* = 200), 88.5% of the dyslipidemic subjects were euthyroid, 9.5% were subclinically hypothyroid, and 2% were overtly hypothyroid (Fig. 1). Demographic characteristics of the subjects (*n* = 200) in this cross-sectional study showed that the prevalence of dyslipidemia in the 36–45 years age group was higher (52.5%) than in the 20–35 years age group (21%) and in the 46–65 years age group (26.5%). There was a

Table 1. Characteristics of study participants (*n* = 200) with dyslipidemia

Characteristics	<i>n</i>	%
Gender		
Male	112	56.0
Female	88	44.0
Age group		
20–35 years	42	21.0
36–45 years	105	52.5
46–65 years	53	26.5
Socioeconomic status		
Low income	40	20.0
Medium income	84	42.0
High income	76	38.0
Habit of physical exercise		
No physical exercise	145	72.5
Regular physical exercise	55	27.5
BMI status		
Underweight	4	2.0
Normal weight	48	24.0
Overweight	105	52.5
Obese	43	21.5
Blood pressure status		
Normal	82	41.0
Hypertensive	118	59.0

higher prevalence of dyslipidemia in the male outpatients (56%) than in the female ones (44%). Socioeconomic status of the study subjects based on their monthly income showed a higher prevalence of dyslipidemia in the middle-income group (42%) compared to the low- (20%) and high-income (38%) groups. Behavioral characteristics revealed that a higher prevalence of dyslipidemia was present in subjects without the habit of regular physical exercise (72.5%). The highest prevalence of dyslipidemia was found in the overweight group (52.5%), followed by the normal weight (24%), obese (21.5%), and underweight (2%) groups. Blood pressure status of the study subjects showed a higher prevalence of dyslipidemia in the hypertensive group of outpatients (59%) than in the normotensive group (41%) (Table 1).

Our study found that female patients had a higher BMI than male patients, which was statistically significant (*p* < 0.01). However, differences in SBP and DBP between male and female patients were statistically insignificant (*p* = 0.16 and *p* = 0.34). For the fasting lipid profile, it was found that only HDL-C in female patients was significantly higher than in male patients (*p* < 0.01) (Table 2).

Our study found that serum levels of TSH were significantly higher in the obese group of patients than in the

Table 2. Comparisons of BMI, blood pressure, fasting lipid profile, and thyroid function markers between male and female dyslipidemic subjects

	Gender		<i>p</i> value ^a
	male (<i>n</i> = 112)	female (<i>n</i> = 88)	
BMI	25.76±3.67	28.99±5.44	<0.01
SBP	87.95±14.01	85.28±12.58	0.16
DBP	136.96±23.75	133.98±19.57	0.34
TC	235.51±44.44	240.51±45.61	0.44
HDL-C	37.34±8.05	43.15±9.32	<0.01
LDL-C	135.7±48.41	141.15±46.37	0.42
TG	318.59±192.65	294.84±227.07	0.42
TSH	3.39±10.24	5.67±13.15	0.17
fT4	1.23±0.23	1.19±0.23	0.21

Values are means ± SD. Italics indicate statistical significance.
^a Significance: 2-tailed, *t* test.

Table 3. Comparisons of thyroid function markers between dyslipidemic subjects with different BMI status

	Thyroid function markers	
	TSH, mU/L	fT4, ng/dL
<i>Status of BMI</i>		
UW (<i>n</i> = 4)	2.60±0.90	1.13±0.13
NW (<i>n</i> = 48)	4.53±15.49	1.22±0.28
OW (<i>n</i> = 105)	3.03±2.97	1.22±0.2
OB (<i>n</i> = 43)	7.74±18.27	1.18±0.25
<i>Multiple comparisons</i>		
	LSD level of significance (<i>p</i> value)	
UW vs. NW	0.75	0.44
UW vs. OW	0.94	0.43
UW vs. OB	0.39	0.69
NW vs. OW	0.46	0.99
NW vs. OB	0.19	0.36
OW vs. OB	>0.02	0.29

Values of thyroid function markers are means ± SD. Italics indicate statistical significance. UW, underweight (BMI <18.5); NW, normal weight (BMI 18.5–24.9); OW, overweight (BMI 25.0–29.9); OB, obese (BMI >30.0); LSD, least significant difference.

overweight group. Differences in fT4 levels were not observed between patients with different BMI status (Table 3). BMI was significantly higher only in the subclinical hypothyroid group than in the euthyroid group (*p* = 0.04). All other groups showed no difference (Table 4). There were significantly positive correlations of BMI and DBP in the study subjects with serum levels of TSH (*p* <

0.01) and fT4 (*p* = 0.03), respectively (Table 5). There were also significantly positive correlations of serum TSH levels with serum levels of TC (*p* = 0.04) and of LDL-C (*p* = 0.04), respectively. On the other hand, a significantly negative correlation was observed for serum fT4 with HDL-C (*p* = 0.01) in the study subjects (Table 6).

Discussion

The prevalence of hypothyroidism in our study was 11.5% (2% overt and 9.5% subclinical). The prevalence of hypothyroidism in the general population was estimated to be 4.6% (0.3% overt and 4.3% subclinical) in the United States (NHANES III) [19]. On the other hand, the prevalence of hypothyroidism in the population with dyslipidemia was reported to be 1.4–13.3% [20–25]. Diekman et al. [23] performed a retrospective study in 1,509 consecutive referrals for severe dyslipidemia in the Netherlands, where the prevalence of hypothyroidism was 2.6% (0.7% overt and 1.9% subclinical). There are some other studies on a smaller number of patients with dyslipidemia, and these reported a prevalence of 6.8% (2.2% overt and 4.6% subclinical) in the United Kingdom [21], 7.8% (2.5% overt and 5.3% subclinical) in the United States [23], and 7.2% (2.8% overt and 4.4% subclinical) in Greece [24]. Thus, the proportion of subclinical hypothyroidism and overt hypothyroidism in our study is strongly supported by those studies. Higher serum cholesterol levels were found in subjects with high-normal TSH levels in studies conducted by Pirich et al. [25] and Michalopoulou et al. [26]. Another study found a significantly positive correlation of serum TSH level with serum TC and LDL-C levels in men and women [27]. Our study is relevant concerning those findings. We found a significantly positive correlation of serum TSH level with serum levels of TC (*p* = 0.04) and LDL-C (*p* = 0.04), respectively. On the other hand, a significantly negative correlation of serum fT4 with HDL-C (*p* < 0.01) was observed in the study subjects.

In Bangladesh, Savar is a suburban area where many people come from rural areas to improve the circumstances of their life. Urbanization confronts people with a number of challenges; imbalanced diets, physical inactivity, long working hours, and other urban stress factors, making them vulnerable to noncommunicable diseases. In this study, dyslipidemia was more frequent (52.5%) in subjects in the middle age group (36–45 years) than in the younger age group (20–35 years; 21%) and in the older age group (46–65 years; 26.5%); it was also higher in males (56%) than in females (44%) [28]. The higher prev-

Table 4. Comparisons of BMI and blood pressure between dyslipidemic subjects with different thyroid function status

	Parameters		
	BMI	SBP, mm Hg	DBP, mm Hg
<i>Thyroid function status</i>			
Euthyroid (<i>n</i> = 177)	26.89±4.45	86.21±13.38	135.17±21.05
Overt hypothyroid (<i>n</i> = 4)	29.77±7.45	92.5±18.93	135±20.82
Subclinical hypothyroid (<i>n</i> = 19)	29.31±6.70	90.79±12.50	140.26±30.39
Multiple comparisons			
LSD level of significance (<i>p</i> value)			
Euthyroid vs. overt hypothyroid	0.23	0.35	0.98
Euthyroid vs. subclinical hypothyroid	>0.03	0.16	0.34
Overt hypothyroid vs. subclinical hypothyroid	0.85	0.82	0.66

Values of parameters are means ± SD. Italics indicate statistical significance. Euthyroid: serum TSH = 0.34–5.60 µIU/mL and fT4 = 0.65–1.74 ng/dL. Subclinical hypothyroidism: serum TSH >5.6 µIU/mL and fT4 = 0.65–1.74 ng/dL. Overt hypothyroidism: serum TSH >5.6 µIU/mL and fT4 <0.65 ng/dL. LSD, least significant difference.

Table 5. Correlation of BMI and blood pressure with thyroid function markers

Parameters	TSH		fT4	
	Pearson correlation (<i>r</i>)	Significance (2-tailed), <i>p</i> value	Pearson correlation (<i>r</i>)	Significance (2-tailed), <i>p</i> value
BMI	0.18	<0.01	0.01	0.96
SBP	0.03	0.68	0.06	0.35
DBP	–0.03	0.68	0.16	>0.03

Italics indicate statistical significance.

Table 6. Correlation of lipid profile with thyroid function markers

	TSH		fT4	
	Pearson correlation (<i>r</i>)	Significance (2-tailed), <i>p</i> value	Pearson correlation (<i>r</i>)	Significance (2-tailed), <i>p</i> value
<i>Fasting serum lipid profile</i>				
TC	0.14	>0.04	–0.01	0.96
HDL-C	0.04	0.59	–0.22	>0.01
LDL-C	0.14	>0.04	0.02	0.72
TG	–0.06	0.37	0.04	0.59

Italics indicate statistical significance.

alence of dyslipidemia in the middle age group might have several reasons. First of all, the rapid urbanization might cause the middle age population to change their eating habits and to reduce physical activity due to a lack of recreational facilities [29], which may cause dyslipidemia. Another reason might be the several stressors related to an unstable job and to maintaining increasing living expenditures. In Bangladesh, males are still playing a vital role and are taking the major responsibility for the family and society, so that they are faced with many challenges in everyday life [30]. Those factors might have contributed to an increased prevalence of dyslipidemia in males compared to females.

We found a significantly positive association of BMI with only TSH ($p < 0.01$), but there was no association of BMI with fT4 ($p = 0.96$). Serum TSH levels were also sig-

nificantly higher in the obese group of dyslipidemic subjects ($p = 0.02$). Altogether, these findings show a relationship of subclinical hypothyroidism with obesity in the study of a Bangladeshi population of dyslipidemic subjects, indicating a role of thyroid hormones and involvement of thyroid dysfunction in the development of generalized obesity, which is supported by previous studies [31, 32].

There was no gender variation in thyroid function markers. TSH and fT4 were statistically insignificantly different between the groups without physical exercise and with regular physical exercise. TSH and fT4 were also insignificantly different between the different age groups of dyslipidemic subjects (data not shown). BMI was significantly higher in subjects belonging to the 36–45 years ($p < 0.01$) age group compared to the 46–65 years age group. BMI was significantly higher in the female dyslip-

idemic subjects than in the male ones ($p < 0.01$). These findings perhaps indicate the nature of the suburban population of hospital outpatients living in the surrounding areas of Savar investigated in this study and may be related to gender, socioeconomic status, as well as behavioral factors at different stages of life.

We found that the frequency of dyslipidemia was higher in the hypertensive subjects (59%) than in the normotensive subjects (41%). In addition, our study revealed a significantly positive association of DBP with fT4 ($p = 0.03$) in the dyslipidemic subjects. However, there was no association between SBP and thyroid function status. The changes in DBP from the thyrotoxic state to the hypothyroid and euthyroid states were highly significant by analysis of variance ($p < 0.01$). However, there were significant correlations between DBPs during hyperthyroidism and hypothyroidism ($r = 0.576$, $p < 0.01$), during hyperthyroidism and euthyroidism ($r = 0.476$, $p < 0.05$), and during hypothyroidism and euthyroidism ($r = 0.653$, $p < 0.01$); a previous study found similar results and supports our results [33, 34].

Limitation

This study was carried out in a relatively small sample of dyslipidemic subjects by a cross-sectional approach. Also, the study was conducted in 1 tertiary level hospital. So, large-scale multicenter studies are needed to characterize the lipid abnormalities connected with hypothyroidism. But the area investigated represents the unique characteristics of a combination of urban, semi-urban, and rural areas of Bangladesh. However, in future, we intend to conduct this type of study involving several tertiary level hospitals from all areas of Bangladesh, which will represent the whole country.

Conclusion

As the prevalence of hypothyroidism in a dyslipidemic adult population in Bangladesh is high, this group of patients should be involved in physical activities and health screening on a regular basis. Thus, they will be protected from several comorbidities and, subsequently, there will be a reduction of premature mortality. Two important indicators of dyslipidemia are TC and LDL-C, which had a positive association with TSH in this study. It is necessary to evaluate thyroid function before starting antilipemic agents in patients with dyslipidemia, taking into consideration the large population of dyslipidemic patients, because many of them have no specific clinical complaints or

signs of hypothyroidism. A misdiagnosed hypothyroidism may increase the risks of treatment with antilipemic agents in dyslipidemic patients, which could be a further reason to diagnose hypothyroidism early in these patients. The findings of this study might be helpful in setting up the clinical management of dyslipidemia in a Bangladeshi population with or without normal thyroid function.

Statement of Ethics

The study was approved by the ethical review committee of the Department of Public Health, North South University. Approval was also obtained from the authority of Enam Medical College Hospital. Informed written consent was obtained from the participants before data collection.

Disclosure Statement

All authors have read and approved the manuscript for publication and have declared that there are no financial and scientific conflicts of interest.

Author Contributions

R.R. planned and implemented the study procedure, S.Z. analyzed the data and revised the final draft of the manuscript, A.B.C. designed the data collection tools, M.H.N. supervised the data collection procedure and prepared the first draft, and M.D.H.H. overall supervised the study and finalized the manuscript.

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