Original Article

Biochemistry

Thyroid Hormone And Its Correlation With Age, Sex And Serum Lipid Levels In Hypothyroid And Euthyroid Sylheti Populations In Bangladesh

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ABSTRACT

Background: Hypothyroidism is defined as a deficiency of the thyroid hormone and an increase in the thyroid stimulating hormone (TSH) levels in patients, which has been associated with elevated levels of serum cholesterol in some populations. Sylhet has been described as the one of the wealthiest cities in Bangladesh and its population leads a life of relative luxury than in most other parts of the country. Lifestyle plays an important role in obesity, lipid profile, and thyroid profile related diseases, but no data are available regarding the thyroid status and the lipid profile in this Sylheti population. The aim of the present study was to assess whether hypothyroidism which was associated with abnormal lipid levels in the population of Sylhet, Bangladesh.

Materials and Methods: The data from adults older than 25 years, who did not previously have a diagnosis of hypothyroidism or those who were not taking thyroid replacement medication, were analyzed at the Women's Medical College and Hospital, Sylhet. Thyroid stimulating hormone (TSH), thyroxine (T4), serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL) and triglyceride (TG) levels were measured.

Results: In this study, it was found that hypothyroidism was more common in women (p=0.039) and in the advanced age group (p=0.038). The persons who met the criteria for hypothyroidism had higher mean cholesterol levels (209.89 vs. 191.49 mg/dl, p=0.038) and higher rates of elevated cholesterol levels (60.5% vs. 40.4%, p=0.024) than the euthyroid control group, but there were no significant differences in their LDL or HDL levels. The mean TG levels (186.04 vs. 231.47 mg/dl, p=0.013) and the rates of the elevated TG levels (50.6% vs. 68.4%) were higher in the hypothyroid group.

Conclusion: Hypothyroidism appears to be associated with abnormalities in the serum cholesterol or triglyceride levels in the Sylheti population. There might be a potential link between hypothyroidism and cardiovascular diseases such as atherosclerosis.

Key Words: Thyroid stimulating hormone, Hypothyroidism, Euthyroidism, Atherosclerosis

INTRODUCTION

The thyroid is one of the largest endocrine glands of the body. The process of thyroid hormone synthesis begins in the hypothalamus. The hypothalamus releases the thyrotropin releasing hormone (TRH). The TRH travels through the bloodstream to the pituitary gland. The pituitary gland then releases the thyroid-stimulating hormone (TSH) into the blood. The TSH stimulates the thyroid gland to produce the two main thyroid hormones, thyroxine (T4) and triiodothyronine (T3).

It is well known that alterations in the thyroid function can result in changes in the composition and in the transport of lipoproteins [1]. Specifically, the thyroid hormone stimulates the hepatic de novo cholesterol synthesis by inducing the HMG-CoA reductase that catalyzes the conversion of HMG-CoA to Mevalonate, which is the first step in the biosynthesis of cholesterol [2]. This results in an enhanced intracellular cholesterol concentration in hyperthyroidism and a decreased one in hypothyroidism. Additionally, thyroid hormones activate the LDL receptors. The promoter of the LDL receptor gene contains a thyroid hormone responsive element (TRE) which allows T3 to upregulate the gene expression of the LDL receptor. Moreover, thyroid hormones stimulate the cholesteryl ester transfer protein (CETP), an enzyme which transports cholesteryl esters from HDL2 to the very low density lipoproteins (VLDL) and triglycerides in the opposite direction. Finally, thyroid hormones stimulate the lipoprotein lipase (LPL) which catabolizes the triglyceride-rich lipoproteins and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 [3].

There is a substantial evidence that overt hypothyroidism alters several of the traditional risk factors for cardiovascular disease. Hypercholesterolaemia in hypothyroidism, characterized by elevated levels of LDL-C and Apo B, is caused by a decreased catabolism of LDL due to a reduction in the number of LDL receptors on the liver cell surfaces [1]. Hypothyroidism can also increase cardiovascular risk by causing diastolic hypertension. The potential mechanisms for reversible diastolic and systolic hypertension in hypothyroidism include increases in the peripheral vascular resistance [4] and arterial stiffness [5], respectively.

Studies have shown that 70% of the community in Sylhet relies on the remittance which is sent from relatives abroad and thus, the population leads a relatively luxurious lifestyle than in other parts of the country. However, to the best of our knowledge, no studies have examined whether a relationship exists between thyroid profile and lipid profile in this Sylheti population. The purpose of the present study was to explore the association between the thyroid hormones and the abnormal lipid profile, including that in cardiovascular diseases.

MATERIALS AND METHODS

This study was conducted at the Women's Medical College and Hospital, Sylhet during December 2009 to May 2010. Samples were

collected from a total of 204 patients, including 38 hypothyroid and 166 euthyroid individuals and control individuals. Out of the 204 patients, 41.2% were males and 58.8% were females. The study was pre-approved by the ethical committee of the institution's review board.

Exclusion criteria:

Persons having overt hypothyroidism or those taking medications which affected the thyroid function, such as thyroxine and anti-thyroid drugs and whose age were less than 25 years were excluded.

Sample collection and storage:

Blood samples were collected with a record of age and sex, from all of the subjects who came for the determination of hormones and the lipid profile. About 7-8 ml of peripheral blood was collected from each individual with the help of an expert. After the centrifugation of the collected blood, the serum samples were collected in microcentrifuge tubes and stored at -20° C. For long term storage, the serum samples were stored in a -80° C freezer. For each sample, the TSH, T4, total cholesterol (TC), TG, HDL and LDL levels were measured.

Thyroid Profile:

TSH and T4 were measured by using a direct ELISA method. TSH levels >4.20 µIU/mol and T4 levels <4.5 µg/dl were considered suggestive of hypothyroid.

Lipid Profile:

TC was measured by an enzymatic endpoint method (cholesterol oxidase/ peroxidase method). TG and HDL were measured by enzymatic colourimetric (GPO-POD) methods. The LDL levels were calculated by using Friedewald's formula.

Statistical analysis:

The results were expressed as frequency (percentages) and mean ± SD (standard deviation). The data analyses were carried out by using the Statistical Package for Social Sciences (SPSS) (version 16.0 for Windows, SPSS Inc., Chicago, USA). For these two groups, the descriptive statistics were computed and bivariate comparisons by using Chi-square analysis and the F test for mean were made. The differences were considered as significant, with a p value which was < 0.05.

RESULTS

Of the 204 respondents included in the study, 38 (18.6%) were found to fit the criteria for hypothyroidism. The study was conducted on two groups of subjects: the hypothyroid group (n=38) and the euthyroid group (n= 166) [Table/Fig 1].

Data are presented as frequency (percentage) and mean ± SD for parametric value. Pearson Chi-Square-test was performed to analyze data. *p<0.05 is considered significant. n = Number of study population; TC = total cholesterol; TG = triglyceride; HDL = High density lipoprotein; LDL = Low density lipoprotein.

Out of the 38 hypothyroid subjects, 10 (26.3%) were males and 28 (73.7%) were females. On the other hand, out of the 166 euthyroid subjects, 74 (44.6%) subjects were males and 92 (55.4%) were females. There was a significant difference (p=0.039) in sex between these hypothyroid and euthyroid groups. Hypothyroidism was more common in women. In the hypothyroid group, 8 (21.1%), 12(31.6%) and 18(47.4%) respondents and in the euthyroid group, 61(36.7%), 60(36.1%) and 45(27.1%) respondents were found to be in the young, middle aged and the elderly groups respectively. There was a significant difference (p=0.038) in age between these hypothyroid and euthyroid groups. Subclinical hypothyroidism was more common in the elderly.

Characteristic / Parameters		Hypothyroid (n = 38);	Euthyroid (n=166);	p value
Sex	Male	10 (26.3%)	74 (44.6%)	*0.039
	Female	28 (73.7%)	92 (55.4%)	
Age	Young (25-40)	8 (21.1%)	61(36.7%)	
	Middle age (41-54)	12(31.6)%	60(36.1%)	*0.038
	Elderly (≥55)	18(47.4%)	45(27.1%)	
TC (mg/dL) [Ref. Value: 120-200]	Mean	209.89± 60.38	191.49 ±45.95	*0.038
	>200	23 (60.5%)	67 (40.4%)	
	≤200	15 (39.5%)	99 (59.6%)	*0.024
TG (mg/dL) [Ref Value: 70-150]	Mean	231.47± 130.01	186.04 ±92.46	
	>150	26 (68.4%)	84 (50.6%)	*0.013
	≤150	12 (31.6%)	82 (49.4%)	*0.047
HDL (mg/dL) [Ref Value:>35]	Mean	38.05 ± 10.94	36.82 ± 8.75	
	≤35	18 (47.4%)	70 (42.2%)	0.457
	>35	20 (52.6%)	96 (57.8%)	0.559
LDL (mg/dL) [Ref Value:80-130]	Mean	121.72± 37.90	118.95 ± 38.25	
	>130	17 (44.7%)	60 (36.1%)	0.687
	≤130	21 (55.3%)	106 (63.9%)	0.324

[Table/Fig-1]: Comparison of various parameters between the hypothyroid and euthyroid groups.
*Data are presented as frequency (percentage) and mean ± SD for parametric value. Pearson Chi-Square-test was performed to analyze data. *p<0.05 is considered significant. n = Number of study population; TC = total cholesterol; TG = triglyceride; HDL = High density lipoprotein; LDL = Low density lipoprotein.*

The mean TC and TG levels in the hypothyroid group were significantly higher (191.49±45.95 vs. 209.89±60.38, p= 0.038 and 186.04±92.46 vs. 231.47±130.01, p= 0.013) as compared to those in the euthyroid group and these values were higher than the reference values. The HDL and LDL levels were higher in the hypothyroid group as compared to those in the euthyroid group (36.82±8.75 vs. 38.05±10.94, p=0.457 and 118.95±38.25 vs. 121.72±37.90, p=0.687), but not significantly and these values were within the reference range.

When these variables were dichotomized into high or low based on the hospital guidelines, it was observed that persons with hypothyroid were more likely to have elevated TC levels (60.5% vs. 40.4%, p = 0.024). It was also observed that persons with hypothyroidism were likely to have a significant elevation in their TG levels (68.4% vs. 50.6%; p = 0.047). No statistically significant differences were found between the euthyroid group and the hypothyroid group with respect to the percentage of respondents with HDL levels, or in LDL levels.

DISCUSSION

Thyroid disorders are known to influence lipid metabolism and are common in dyslipidaemic patients [6]. These hormones appear to serve as a general pacemaker, accelerating the metabolic processes and they may also be associated with metabolic syndromes [7].

The serum cholesterol level generally varies inversely with the thyroid activity [8][9]. This condition is more common in the elderly [10][11][12]. Also, women are more likely than men to develop thyroid disease [13][14]. In this study, the percentage of female subjects in the hypothyroid group was significantly higher than that of the male subjects [Table/Fig 2a].

Moreover, the hypothyroid respondents were more commonly found in the elderly group rather than in the young or the middle aged groups [Table/Fig 2b]. These results corroborated with the findings of other research groups [13][10][14][11][12].

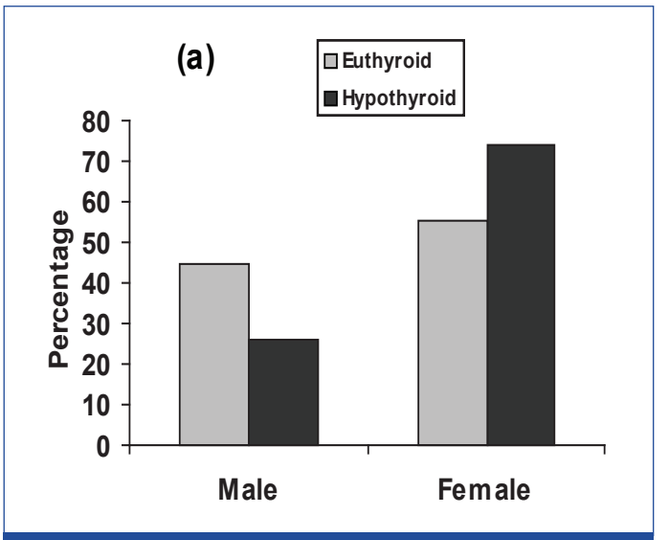
Serum total cholesterol was significantly increased in the hypothyroid subjects as compared to the euthyroid subjects [Table/Fig 2c]. Some other studies have also supported this finding [15][16][17]. Specifically, the thyroid hormone stimulates the hepatic de novo cholesterol synthesis by inducing HMG-CoA reductase that catalyzes the conversion of HMG-Co A to Mevalonate, the first step in the biosynthesis of cholesterol [18].

Despite the reduced activity of HMG-CoA reductase, hypercholesterolaemia in hypothyroidism probably results from the reduced catabolism of lipoproteins, a phenomenon that may be explained by a decreased expression of lipoprotein receptors and LDL cholesterol [19]. The magnitude of elevation in the serum cholesterol concentrations is correlated with the degree of hypothyroidism [20]. Hypothyroid patients usually exhibit elevated levels of HDL, mainly due to the decreased activity of the cholesterol ester transfer protein (CETP), resulting in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing the HDL cholesterol levels. Furthermore, the decreased activity of hepatic lipase (HL) leads to the decreased catabolism of HDL2 HDL OR HDL2 Particles [7]. In this study, it was found that the levels of LDL and HDL were elevated in the hypothyroid group as compared to those in the euthyroid group [Table/Fig 2c]. But no significant difference was found between these groups and the values remained within the reference range. This result corroborated the findings of a previous study [10]. But other studies found significant elevations in the serum LDL concentrations in hypothyroid subjects [21].

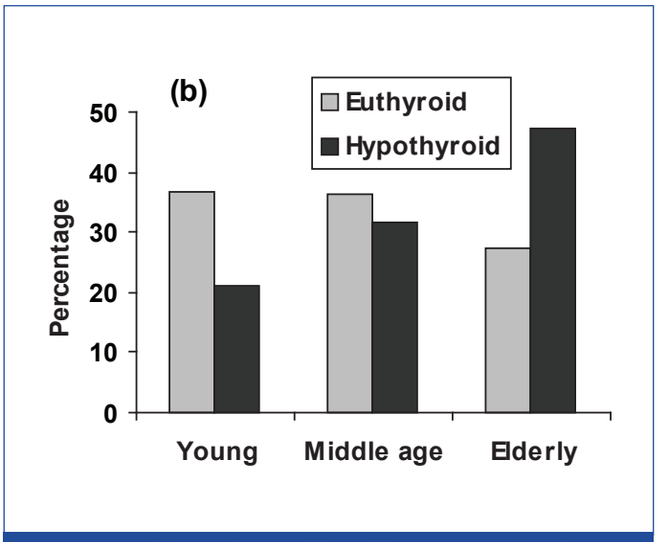
The serum triglyceride levels were also higher in the subjects with hypothyroidism than in the euthyroid subjects [Table/Fig 2c] which concurred with the reports of a previous study [7]. These changes were attributable to the decreased activity of lipoprotein lipase (LPL), which resulted in a decreased clearance of triglyceride-rich lipoproteins [18]. All these abnormalities resolved as the serum T4 concentration became norma [16]. Furthermore, the clearance of the chylomicron remnants was found to be decreased in hypothyroidism [22].

It was also observed that the percentage of the hyperlipidaemia patients was more common in the hypothyroidism group for TC and TG. But no significant relation was found for HDL and LDL [Table/Fig 2d].

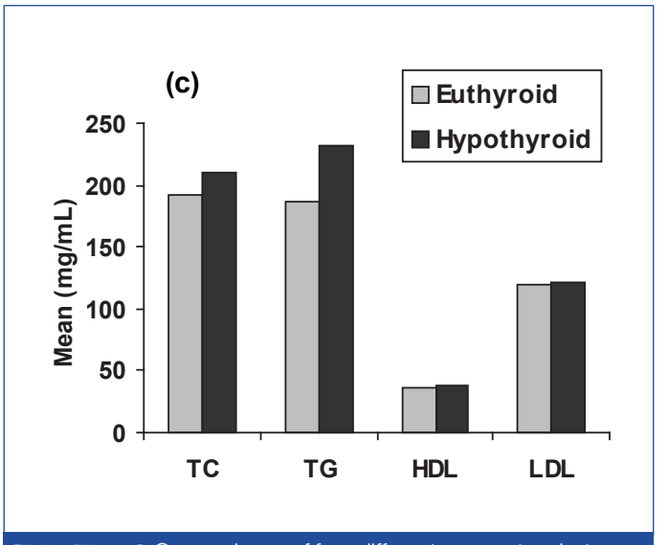
Hypothyroidism has been generally considered as a cardiovascular risk factor in a majority of studies, mainly because of its association with elevated serum total and LDL cholesterol. Important associations



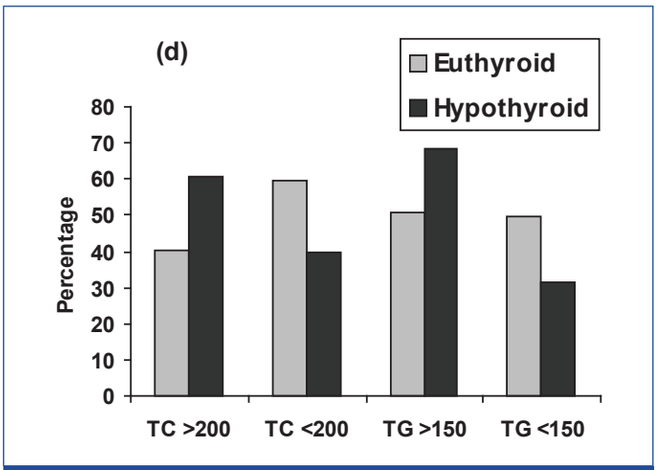
[Table/Fig-2a]: Comparisons of four different parameters between hypothyroid and euthyroid groups: sex(a), age groups(b), mean values of lipid profile(c) and clinical range of TC and TG(d).



[Table/Fig-2b]: Comparisons of four different parameters between hypothyroid and euthyroid groups: sex(a), age groups(b), mean values of lipid profile(c) and clinical range of TC and TG(d).



[Table/Fig-2c]: Comparisons of four different parameters between hypothyroid and euthyroid groups: sex(a), age groups(b), mean values of lipid profile(c) and clinical range of TC and TG(d).



[Table/Fig-2d]: Comparisons of four different parameters between hypothyroid and euthyroid groups: sex(a), age groups(b), mean values of lipid profile(c) and clinical range of TC and TG(d).

have been identified for other risk factors for atherosclerosis, including hyperhomocysteinaemia, elevated C-reactive protein (CRP) levels, coagulation abnormalities, endothelial dysfunction, and insulin resistance in individuals with overt hypothyroidism and, in some cases, subclinical hypothyroidism [23].

The present study indicated that hypothyroidism was associated with an abnormal lipid profile, especially with respect to the levels of TC and TG. Hence, persons suffering from hypothyroidism should make lifestyle and dietary adjustments to avoid future cardiovascular complications. A large-scale study is warranted to further validate the findings of the present study.

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