Original Article

Lipid Profile in Hypothyroid Patients: A Cross Sectional Study

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Abstact

Hypothyroidism is an important metabolic disorder and is associated with many biochemical abnormalities. Many studies were done regarding the biochemical status of hypothyroid patients including lipid profile. But controversies still prevail. So, a cross sectional study was done in our population to evaluate lipid profile status of hypothyroid patients compared to age and sex matched healthy euthyroid persons. In our study mean serum total cholesterol, LDL cholesterol and triacylglycerol levels in cases and controls were 241.56 ± 60.05 vs 146.94 ± 23.21 mg/dL, 151.96 ± 59.60 vs 71.43 ± 26.83 mg/dL and 212 ± 100.73 vs 98.87 ± 39.69 mg/dL respectively with p values < 0.001 whereas HDL cholesterol was found significantly decreased in cases compared to controls (49.59 ± 11.69 vs 55.89 ± 11.70 mg/dL with p value < 0.05). Results of our study suggest that dyslipidemias are associated with hypothyroidism. Therefore, patients presenting with dyslipidemia are recommended for investigation to explore hypothyroidism

Key words: Hypothyroidism, total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol

Introduction

Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones, which in turn results in a generalized slowing down of metabolic processes[1]. It is a common metabolic disorder in general population[2]. The thyroid dysfunction increases with age, especially in women[3].

Hypothyroidism is associated with many biochemical abnormalities. Levels of total cholesterol and low density lipoprotein cholesterol tend to increase as thyroid function declines[2]. Thus hypothyroidism constitutes a significant cause of secondary dyslipidemia[4]. In hypothyroid patients, despite the reduced activity of HMG CoA reductase, there is often an increase in the serum total cholesterol concentration, mainly due to raised levels of serum LDL cholesterol and intermediate density lipoprotein (IDL) cholesterol[5]. Decreased thyroid secretion greatly increases the plasma concentration of cholesterol because of decreased rate of cholesterol secretion in the bile and consequent diminished loss in the feces due to decreased number of low density lipoprotein receptors on liver cells[6]. Decreased activity of LDL receptors resulting in decreased receptor-mediated catabolism of LDL and IDL is the main cause of the hypercholesterolemia observed in hypothyroidism[7].

Serum concentration of high density lipoprotein cholesterol was reported to be higher among newly diagnosed hypothyroid patients with the value more than 40 mg/dL in subclinical or clinical hypothyroidism whereas serum concentrations of HDL cholesterol were significantly lower among euthyroid and previously reported hypothyroid cases who were on thyroid replacement therapy[8]. Hypothyroid patients usually exhibit elevated levels of high density lipoprotein cholesterol (HDL-C) mainly due to increased concentration of HDL_2 particles[9]. In some studies we find confronting results regarding high density lipoprotein cholesterol levels in hypothyroidism. In thyroidectomized rats there was 25.9% decrease in HDL-C level, suggesting a defect in HDL metabolism[10]. HDL cholesterol level was found reduced in some other studies on hypothyroid patients[9].

Decreased thyroid secretion greatly increases the plasma concentration of triglycerides[6]. Nikkilia & Kekki[11] have stated that hypertriglyceridemia in hypothyroidism is due to decreased activity of lipoprotein lipase (LPL), which results in decreased clearance of triglyceride-rich lipoproteins.

Dyslipidemia is a well-known risk factor for cardiovascular diseases. The risk of coronary heart disease and other forms of atherosclerotic vascular disease rises with rising plasma cholesterol concentration and in particular with rising ratio of total cholesterol to high density lipoprotein (HDL) cholesterol. A weak positive correlation of coronary heart disease also exists with plasma triglyceride concentration[12]. Early diagnosis and proper management can significantly reduce the mortality and morbidity of dyslipidemic cardiovascular diseases. Extensive large-scale randomized trials have shown that lowering total cholesterol and LDL cholesterol reduces the risk of cardiovascular events like angina, myocardial infarction and stroke, and also reduces the need for revascularization[12].

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Many studies were done to assess the lipid profile status of hypothyroid patients. But controversies still prevail and that needs to attain consensus. So, we have designed this study in our population for evaluation of lipid profile in hypothyroid patients that might be helpful for clinical management of hypothyroid patients with dyslipidemia.

Materials and Methods

This cross sectional study was conducted in the department of Biochemistry of Bangabandhu Sheikh Mujib Medical University, Dhaka to evaluate the lipid profile of hypothyroid patients and to find out relationship of dyslipidemia with severity of hypothyroidism. Clinically and biochemically newly diagnosed hypothyroid patients of both sexes, age 20 to 60 years, with no history of thyroxine and hypolipidemic drugs in the last 3 (three) months were included in the study. Patients with chronic renal failure, diabetes mellitus, liver diseases, chronic diseases, pregnancy and age less than 20 and more than 60 years were excluded. Hypothyroidism was diagnosed by clinical history, physical examinations and relevant laboratory investigations. Total 111 subjects were included in the study and out of them 80 overt hypothyroid patients were grouped as cases (Group I) and 31 euthyroid subjects were grouped as normal controls (Group II). Cases were further grouped on the basis of their serum TSH concentration into Group A (TSH level 5.01-50.00 mIU/L), Group B (TSH 50.00-100.00 mIU/L) and Group C (TSH level>100.00 mIU/L). Specimen was collected in fasting condition, allowed to clot; serum was separated and analyzed for serum total cholesterol, triacylglycerol and HDL cholesterol levels. LDL cholesterol level was calculated by Friedewald's equation.

Statistical analysis

Statistical analyses were performed by using SPSS for Windows version 12.0. Mean values of the findings were compared among and between groups. Analysis of variance (ANOVA) test and Unpaired 't' test were done to assess the significance among the groups and between groups respectively. Pearson correlation coefficient test was done to evaluate the correlation of biochemical parameters with the severity of hypothyroidism. 'p' values <0.05 were considered significant.

Results

Table I shows the comparison of the lipid profile parameters between the cases and the controls. Mean total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides level in cases were higher than controls. HDL cholesterol was found significantly decreased in cases compared to controls.

Table II shows lipid profile parameters in different groups of cases. There was no significant difference among the groups for serum total cholesterol, but a rising trend was found from Group A to Group C. For HDL cholesterol levels, significant differences were observed among the groups with maximum in Group B and minimum in Group C. Mean LDL cholesterol levels showed significant difference among the groups with maximum in Group C and minimum in Group A. Mean serum triglyceride levels showed no significant difference among groups.

Table I: Lipid profile of study subjects

Parameters	Cases (n= 80)	Controls (n=31)	'p' values
Total cholesterol (mg/dL)	241.56 ± 60.05	146.94 ± 23.21	< 0.001
HDL cholesterol (mg/dL)	49.59 ± 11.69	55.89 ± 11.70	< 0.05
LDL cholesterol (mg/dL)	151.96 ± 59.60	71.43 ± 26.83	< 0.001
Triglycerides (mg/dL)	212.28 ± 100.73	98.87 ± 39.69	< 0.001

Table II: Lipid profile in different groups of cases

Parameters	Group A (n=14)	Group B (n= 29)	Group C (n= 37)	'p' values
Total cholesterol (mg/dL)	215.93 ± 43.25	237.10 ± 64.49	254.76 ± 59.61	> 0.05
HDL cholesterol (mg/dL)	51.36 ± 9.84	53.34 ± 13.01	45.97 ± 10.35	< 0.05
LDL cholesterol (mg/dL)	119.64 ± 45.00	150.41 ± 61.28	165.41 ± 59.57	< 0.05
Triglycerides (mg/dL)	224.36 ± 88.83	221.16 ± 112.39	221.16 ± 112.39	> 0.05

Table III shows correlation between serum free thyroxine level and lipid profile parameters of cases. FT4 has shown significant negative correlation with serum total cholesterol, LDL cholesterol and triglyceride levels. No correlation was found between serum FT4 level and serum HDL cholesterol level.

Table IV shows correlation between serum TSH level and lipid profile parameters of cases. Total cholesterol and LDL cholesterol were found to maintain significant positive correlation with serum TSH. But TSH was found to show no correlation with serum HDL cholesterol and serum triglycerides level.

Table III: Correlation between free thyroxine level and lipid profile of cases

	Lipid profile in mg/dL	r values	'p' values
FT4 (in pmol/L)	Total cholesterol	- .278	< 0.05
	HDL cholesterol	.020	> 0.05
	LDL cholesterol	- .238	< 0.05
	Triglycerides	-.278	< 0.05

Table IV: Correlation between TSH level and lipid profile of cases

	Lipid profile in mg/dL	r values	'p' values
TSH (in mIU/L)	Total cholesterol	.221	< 0.05
	HDL cholesterol	- .026	> 0.05
	LDL cholesterol	.261	< 0.05
	Triglycerides	-.138	> 0.05

Discussion

Hypothyroidism is a common metabolic disorder. The prevalence of primary hypothyroidism is 1:100, but it may

be 5:100 if patients with subclinical hypothyroidism (normal T4, raised TSH) are included[13]. According to a study done by Sawin[14], hypothyroidism is a common disorder with a prevalence rate up to 20%. In another cross-sectional study on twelve hundred and twelve subjects of both sexes and age 20-60 years, the incidence of subclinical hypothyroidism was 19.7%[15].

In our study, mean total cholesterol, LDL cholesterol and triglycerides were found significantly increased whereas HDL cholesterol was found significantly decreased in cases compared to controls. Jung[16] found mean plasma total cholesterol and LDL cholesterol levels elevated in hypothyroid cases than in normal controls. In another study, average serum total cholesterol level was found elevated in primary and secondary hypothyroidism[17]. Keyes & Heimberg[18], Laker & Mayes[19] found triglyceride level elevated in hypothyroid patients. So, our study findings were consistent with the previous studies done by other investigators.

Thompson[7] and Abrams & Grundy[20] have stated decreased activity of LDL receptors as the main cause of hypercholesterolemia in hypothyroidism.

Serum concentrations of high density lipoprotein cholesterol was reported to be higher among newly diagnosed hypothyroid patients (subclinical or clinical) whereas serum concentrations of HDL cholesterol were significantly lower among euthyroid and previously reported hypothyroid cases who were on thyroxine replacement therapy[8]. Studies done by Michalopoulou[21], Diekman[22], Tsmihodimos[23] and Olukoga[24] showed average serum concentration of HDL higher in subclinical or clinical hypothyroidism. But, on the other hand, in a study on thyroidectomized rats, HDL-C showed a 25.9% decrease compared to controls[10]. In another study on thyroidectomized rats, there was 25% decrease in HDL cholesterol level compared to control rats[25]. Abrams & Grundy 20 have shown in their studies reduction of HDL cholesterol in hypothyroidism. So, our study is consistent with some of the studies and inconsistent with the others. A large scale study on overt hypothyroid patients is recommended to come to a final conclusion.

Increase in HDL cholesterol concentration is mainly due to increased concentration of HDL_2 particles[9]. Dullaart[26] have stated that decreased activity of CETP (cholesteryl ester transport protein) results in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL cholesterol levels. Lam[27] have stated that in hypothyroid patients decreased activity of hepatic lipase leads to the decreased catabolism of HDL_2 particles leading to increased HDL. So, decrease in HDL cholesterol level in our study might be due to increased activity of CETP and lipoprotein lipase in hypothyroid patients.

There was no significant difference in serum total cholesterol concentrations among the groups, but a rising trend was found from Group A to Group C ($p = 0.0395$), making our results apparently consistent with the severity of hypothyroidism. This theme seems to be further consolidated by increasing LDL concentrations in line with the increasing severity of hypothyroidism from Group A to Group C as revealed in our study. This is further strengthened by our findings of negative correlation of FT4 and positive correlation of TSH with total cholesterol and LDL cholesterol levels.

Significant difference in serum HDL cholesterol levels was observed among the groups with maximum in Group B and minimum in Group C. This finding partially indicates the lowest HDL with maximum degree of hypothyroidism. But the characteristic pattern of decreasing HDL with increasing severity of hypothyroidism could not be revealed in this study. This is further supported by our finding of no correlation of HDL with FT4 or TSH. This might be due to our small sample size.

Regarding triglycerides levels, no significant difference was found among the groups, indicating no changing impact on triglycerides metabolism with severity of hypothyroidism. It is claimed that thyroid hormones facilitate the LPL activity[11], but deficiency of thyroid hormones to inhibit LPL probably follows a ceiling point beyond which further reduction of thyroid hormones does not cause further inhibition of LPL.

In our study FT4 has shown significant negative correlation with serum total cholesterol, LDL cholesterol and triglycerides level. No correlation was found between serum FT4 level and serum HDL cholesterol level. Total cholesterol and LDL cholesterol were found to maintain significant positive correlation with serum TSH. But TSH was found to show no correlation with serum HDL cholesterol and serum triglycerides level. Significant negative correlation of FT4 with triglycerides level and no correlation of TSH with triglycerides appear to make a sense of functional disharmony between FT4 and TSH and, therefore, a large scale study is recommended to make it clear.

Results of our study suggest the findings of dyslipidemia in hypothyroid patients. Therefore, patients presenting with dyslipidemia are recommended to be investigated for hypothyroidism. As our sample size was small and duration of study was limited, another study with large sample size and longer duration is also recommended.

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