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Clinical Investigation

Serum Lipoprotein (a) and lipid profile in Hypothyroidism.

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Abstract

Background: Hypothyroidism has been found to be a predictor of cardiovascular disease. Among various reasons, dyslipidemia and elevated lipoprotein (a) is a significant cause. This study was conducted to determine the serum lipid disturbances and the significance of lipoprotein (a) in hypothyroid patients. ***Methods:*** The study subjects were 40 hypothyroid patients along with 30 normal persons matched for age and gender as controls. All were tested for serum lipoprotein (a), thyroid and lipid profile. The data was analysed using Mann-Whitney U test. ***Results:*** Majority were females (89%) in the age group of 41-50 years. Cases had significantly higher TC, LDL, VLDL, Triglycerides, LDL: HDL ratio, TC: HDL and Reduded HDL ratio compared to controls. The number of cases with Lp (a) of≥ 30 mg/dl is found to be significantly higher than that of controls.***Conclusion:*** The study suggests that hypothyroidism contributes to the development of atherosclerosis by making the lipid profile more atherogenic.

Key words: Hypothyroidism, Lipoprotein (a), atherosclerosis.

Introduction

Hypothyroidism is one of the most common disorders seen in present days especially among women. It causes a derangement of most of the parameters of our body which collectively contributes to the risk of development of atherosclerotic cardiovascular disease. These include alterations in lipid profile, hemodynamic changes, endothelial dysfunction, coagulation disturbances, hormonal and metabolic changes, and changes in homocysteine and C-reactive protein levels.

There is a known pathogenic relationship of patients with hypothyroidism developing atherosclerotic cardiovascular disease. This risk of atherosclerotic cardiovascular disease is attributable to dyslipidemia noticed in hypothyroid states (i.e., increased circulating levels of LDL- Cholesterol and lipoprotein (a). The suggested mechanism for elevated levels of LDL- Cholesterol is due to decrease in its catabolism caused by hypothyroidism[(1)].

Increased levels of Lp (a) has been reported in hypothyroidism and also Lp (a) is a predominantly genetically determined independent risk factor for development of atherosclerosis. Lp (a) is metabolized by an LDL- Cholesterol receptor independent pathway. It is suggested that thyroid hormone has a direct effect on Lp (a) synthesis (i.e., excess thyroid hormone as in hyperthyroidism inhibits Lp (a) synthesis)[(2)]

Several studies have shown decreased Lp (a) concentration following thyroid hormone replacement, while other studies have not confirmed this approach[(3-5)]. Hence, we conducted a study at our hospital to assess the significance of lipoprotein (a) and serum lipid parameters in hypothyroid patients.

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Materials and Methods

This study was conducted after obtaining institutional ethics committee approval at KIMS Hospital Bangalore, during the year 2010-11. Forty hypothyroid patients and thirty euthyroid controls attending the outpatient and inpatient departments were recruited in the study.

Criteria for subject selection:

Patients with hypothyroidism between the age group of 18 to 65 years were included and patients with history of Diabetes mellitus, hyperlipidemia, renal and liver failure, on systemic drugs especially lipid lowering agents, smoking, alcohol and other conditions that probably alter lipid profile were excluded from the study.

About 5 ml of plain venous fasting blood sample after overnight fasting of 12 hours was obtained by venepuncture from patients and controls after obtaining informed consent form. A pre-structured and pre-tested Proforma was used to collect the data. Baseline data including age, gender, Body Mass Index (BMI), detailed medical history, clinical examinations and relevant investigations were included as part of the methodology. Estimations of fasting blood glucose, blood urea, serum creatinine, serum total cholesterol, serum triglycerides, LDL, HDL cholesterol, serum Lipoprotein (a), serum T3, T4 and TSH were performed as per recommended procedure. Fasting urine sample was collected in a clean dry container and was tested for urine sugar and albumin immediately.

Results

The results of this case controlled study evinced predominantly female population which comprised 90% in the case group and 87% in the controlled group respectively. Nearly 40% of patients among cases were in the age group of 41-50 years; majority (30%) of controls were in 31-40 years age group. Higher mean TSH (37.2) was recorded in cases compared to controls (2.2); and the difference in mean TSH between the two groups is found to be statistically significant with p value <0.05 as shown in table 1.

Serum Lipid metabolites

The means of following parameters had significant difference between cases and controls – total cholesterol, serum triglycerides, LDL, VLDL, HDL, TC/HDL ratio and LDL/HDL ratio (table 2).Higher mean Lp (a) was recorded in cases compared to controls but the difference in mean Lp (a) between the two groups were not found to be statistically significant, while Lp (a) when grouped below and above 30mg/dl; the group ≥ 30 mg/dl had significant association (table 3).

Parameter	Cases	Controls	P-Value
	Mean ± SD	Mean ± SD	
T3 (ng/dl)	89.53±36.22	124.73±23.72	<0.001*
T4 (µg/dl	6.17±3.25	8.62±2.04	<0.001*
TSH (mc IU/dl)	37.19±47.35	2.39±1.07	<0.001*

*p<0.05 –*is considered as Statistical significant.*

Table :1- Comparison of T3, T4, TSH between Hypothyroid cases and Euthyroid controls

Parameter	Patient Group	Control Group	
	Mean ± SD	Mean ± SD	p- Value
Cholesterol	202.57±61.11	166.70±31.50	0.006*
TG	186.10±101.9	122.53±40.01	0.002*
HDL	39.05±10.55	45.30±14.27	0.028*
VLDL	38.77±21.82	27.31±12.22	0.010*
LDL	125.4±48.11	95.03±28.27	0.005*
TC/HDL	5.40±2.03	3.95±0.91	<0.001*
LDL /HDL	3.47±1.45	2.25±0.67	<0.001*
TG/HDL	5.05±2.86	3.06±1.60	0.001*
Lp (a)	28.41±21.19	18.45±7.41	0.141

*p<0.05 –*is considered as Statistical significant.*

Table :2- Comparison of Lipid parameters between Hypothyroid cases and Euthyroid controls

Lp (a)	Patients (%)	Controls (%)	Total	Chi-square	P-value
<30	26 (65)	27 (90)	53	5.827	0.016*
>30	14 (35)	3 (10)	17		

Table :3- Distribution of Lp (a) among Hypothyroid cases and Euthyroid controls

Discussion

The present study findings revealed that hypothyroidism is associated with significant alterations in the lipid profile. A study conducted in eight cities of India to assess the prevalence of hypothyroidism in adults has reported that 1 in 10 adults have hypothyroidism and majority of population were females

belonging to the older age group [7]. The National Health and Nutrition Examination Survey (NHANES III) in the United States population reported that a significant number of women aged 50-59 and 60-69 met criteria for subclinical and clinical hypothyroidism compared to men in the same age groups[7].In our study also, we had similar findings with incidence of hypothyroidism high among females of older age group.

Hypothyroidism is one of the main causes of secondary dyslipidemia [2]. A study conducted in Minnesota, had assessed the lipid profile of 268 hypothyroid patients and dyslipidemia was detected in 91.4%[8]. Various studies support a biologically plausible role for hypothyroidism increasing the risk of atherosclerotic cardiovascular diseases, via altering the lipid profile and making it more atherogenic[9]. In addition, hypothyroidism also increases the oxidation of plasma cholesterol mainly because of (i) an altered pattern of binding and (ii) due to the increased levels of cholesterol, which presents substrate for oxidative stress [10], which further increases the risk of atherosclerosis. The variables of lipid metabolism that were assessed in our study among both the cases and controls were total cholesterol, serum triglyceride, LDL, VLDL and HDL. The differences between the values of these parameters were statistically significant when compared to controls.

The hypothyroid subjects in our study had higher levels of TC and LDL, similar findings was observed by Staub JJ et al., which reportedhigher total cholesterol, LDL cholesterol and apolipoprotein B in overt hypothyroidism[11]. A study conducted by Archana et al., has shown that hypothyroidism results in a small increase in low density lipoprotein (LDL)-C, total serum cholesterol and decrease in high density lipoprotein (HDL)-C that enhance the risk for development of atherosclerosis and coronary artery disease [10]. Our study results were consistent with the findings of Mayer et al., who had found that females with untreated hypothyroidism (both overt and subclinical) had significantly higher total and LDL cholesterol. Females with total cholesterol greater than 7 mmol/L(270mg/dl) had about a 7 times higher risk of Hypothyroidism. However, the same study found no such association in males [12].

Decreased levels of HDL cholesterol were found in hypothyroid cases than in controls in our study and the difference was found to be statistically significant. This finding is in agreement with some studies that have shown that hypothyroidism is associated with a lower HDL cholesterol level. In a report comparing 52 patients with subclinical hypothyroidism and 18 with overt hypothyroidism with 46 euthyroid controls matched for age, sex, and body mass index, Althaus et al. [13] found a significantly lower HDL cholesterol fraction in even the sub clinically hypothyroid patients. Caron et al.[14] also reported that the HDL cholesterol level was significantly decreased among 29 women who had subclinical hypothyroidism, compared with 41 euthyroid women matched for age and metabolic parameters. Furthermore, Caron et al.[14] observed a significant increase in the HDL cholesterol level with T4 therapy, which normalized the serum TSH concentration.

In contrast to our study some studies had exhibited elevated levels of HDL-C [5] in hypothyroidism, mainly due to increased concentration of HDL2 particles. Our study, we found a significantly higher mean TG and mean VLDL in cases than in controls which correlate well with some earlier studies. A few studies have shown a moderate elevation of plasma triglyceride concentration in hypothyroidism [15-16] and occasional cases have also reported gross hyperlipemia in myxedema [15,17]. In hypothyroidism, the slight or moderate hypertriglyceridemia that develops is as a result of impaired removal of endogenous triglycerides, and also due to a decreased elimination of exogenous fat particles [18]. In recent studies as well, overt hypothyroid patients may also present with elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia [19-20]. Relatively, few studies have been carried out on the alterations of triglyceride and very low density lipoprotein (VLDL) metabolism in clinical thyroid disease. This is in sharp contrast to the situation in cholesterol metabolism, which is well explored in both hyper- and hypothyroidism and is generally believed to undergo typical and consistent changes in both conditions [18]. The TC/HDL ratio and LDL/HDL ratio were also significant when compared to other studies [21-22].

Lp (a) was higher in cases compared to controls, the difference is not statistically significant. Several studies have shown an increase in the lipoprotein (a) [Lp (a)] levels in hypothyroid patients , which is associated with increased CVD risk [23-24]. Erem C. et al., showed that plasma Lp(a) concentrations increase in hypothyroid patients and they attributed the observed relationships between thyroid status and Lp(a) levels to impaired catabolism of apo B and Lp(a) in hypothyroidism [25]. A. Becerra et al., which evaluated thirty-six patients with hypothyroidism who had a basal Lp(a) >30mg/dl and 165 age-matched control euthyroid subjects, showed a decrease in Lp(a) concentrations by Thyroxine therapy, and these normalized in eight cases [26] which supports the present study.

Conclusion

The derangements among lipoprotein (a) and serum lipid metabolites in hypothyroid patients are significant. The study findings confirm that hypothyroidism contributes to the development of atherosclerosis by making the lipid profile more atherogenic.Further studies are required with higher number of cases to confirm the contribution of hypothyroidism to the alterations in the Lp (a) levels.

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