

Lipid Profile in Thyroid Dysfunction Patients

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Abstract:

Objective: To assess the levels of lipid parameter in patients with thyroid dysfunction and to study the association between thyroid dysfunction and lipid profile.

Study design and setting: Cross-sectional study conducted in the Department of Biochemistry, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur.

Materials and Methods: Fasting blood samples were collected from 112 thyroid dysfunction patients and 100 healthy individuals. Serum triiodothyroxine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) were quantitatively estimated by Enzyme linked immunosorbent assay (ELISA) while total cholesterol (TC), low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and triglycerides (TG) were estimated by colorimetric method. The results were analyzed using SPSS version 16.0.

Results: Out of 112 sera tested, 60(53.5%), 40(35.7%), 6(5.4%) and 6(5.4%) had subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and overt hyperthyroidism respectively. Total cholesterol, LDL-cholesterol and triglycerides were significantly raised, while HDL cholesterol was decreased in patients with hypothyroidism as compared to control group. In hyperthyroidism patients levels of total cholesterol and triglycerides were significantly lower while HDL cholesterol was higher than controls.

Keywords: Hyperlipidemia, hyperthyroidism, hypothyroidism.

I. Introduction

Thyroid hormones have profound metabolic effects, the most striking action being an increase in energy expenditure [1,2]. Thyroid hormones play an important role in regulating lipid metabolism; and thyroid dysfunctions can result in lipid abnormalities which increase the risk of endothelial dysfunction, hypertension and cardiovascular disease [3]. It is well known that alterations in thyroid functions result in changes in the composition and transport of lipoproteins [4-6].

In hyperthyroidism, the metabolic effects include the increased utilization and oxidation of all major fuel substrates that is, protein, glucose and lipids [1,2]. The metabolic effects of hypothyroidism are not well characterized. The condition is characterized by increased fasting plasma cholesterol and triglycerides [7,8]. The effects of hypothyroidism on HDL cholesterol level has been contradictory. HDL cholesterol levels have been reported to be increased [8], decreased [9] and normal [10] in hypothyroidism. It is well-known that hypothyroidism is associated with hypercholesterolemia and increases the risk of atherosclerosis [11,12].

Hyperlipidemia observed in hypothyroidism is a metabolic result currently treatable with thyroid hormone. Before the availability of sensitive thyroid hormone analysis, increased serum or plasma cholesterol level was accepted as important evidence supporting the diagnosis of hypothyroidism [13]. Classical signs and symptoms of clinical hypothyroidism may not be observed when it is mild or moderate. The present study was planned to assess the levels of total cholesterol (TC), LDL-cholesterol, VLDL-cholesterol, HDL-cholesterol and triglyceride (TG) in patients with thyroid dysfunction (hypo and hyperthyroidism) and to study the association between thyroid dysfunction and lipid profile.

II. Materials and methods

A cross-sectional study was conducted in the Department of Biochemistry, Regional Institute of Medical Sciences, Imphal, Manipur, from January 2013 to December 2015. A total of 112 patients with suspicion of thyroid disorders were taken as cases. One hundred patients with normal thyroid profile and no history of other chronic diseases were taken as control group. Detailed informations of the

patients were collected after taking informed consent with the help of pre-test proforma that included age, sex and family or personal history of chronic diseases. Ethical clearance was obtained from the Institutional Ethics Committee, Regional Institute of Medical Sciences and confidentiality was maintained.

After 12 hours overnight fasting, 6ml blood was collected by standard venipuncture method, and the serum was separated. T3, T4 and TSH were quantitatively estimated by Enzyme linked immunosorbent assay (ELISA) method. Estimation of total cholesterol (TC) was carried out by the enzymatic method of Allain CC et al [14]. Quantitative estimation of serum triglycerides (TG) was done by method adopted by Bucolo G [15]. Enzymatic determination of serum high density lipoprotein (HDL) cholesterol was done by precipitation technique as described by Steele BW et al [16]. LDL cholesterol and VLDL cholesterol values in mg/dl were indirectly calculated by using the formulae of Friedewald WT et al [17]. All the investigations were recorded in the proforma designed for the study. SPSS version 16.0 was used for statistical analyses of different parameters.

III. Results

Figure 1: Prevalence of thyroid dysfunction

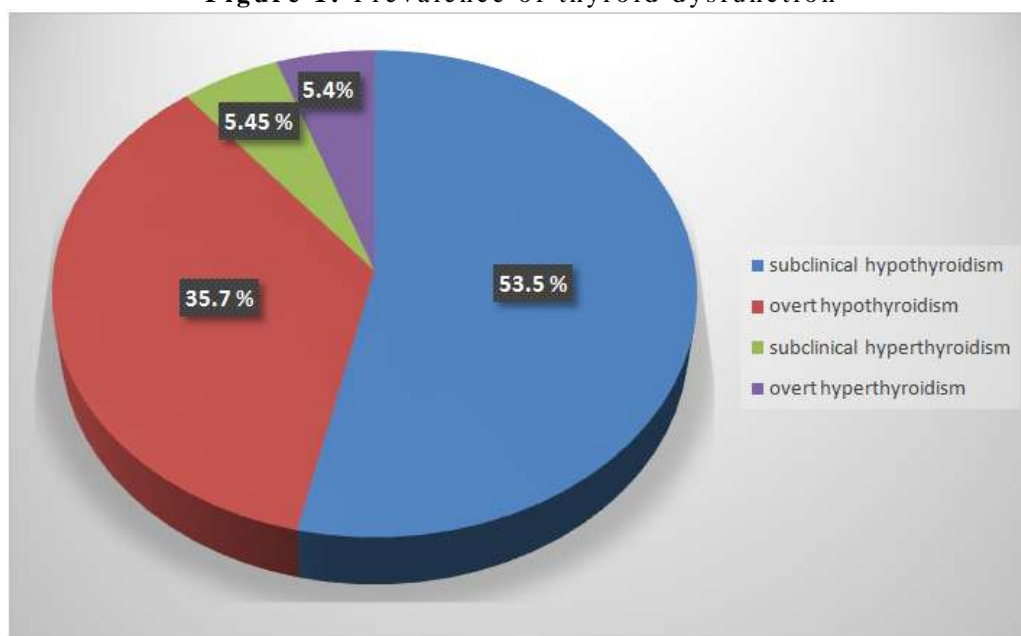


Fig. 1 shows that the prevalence of thyroid dysfunction viz. subclinical hypothyroidism, overt hypothyroidism, subclinical hyperthyroidism and overt hyperthyroidism were 53.5%, 35.7%, 5.45% and 5.4% respectively.

Table1: Distribution of subclinical and overt

Age in years	Hypothyroidism		Hyperthyroidism		Total N(%)
	Subclinical n(%)	Overt n(%)	Subclinical n(%)	Overt n(%)	
18-29	10(16.6)	11 (27.5)	2 (33.3)	2 (33.3)	25 (22.4)
30-44	17(28.3)	19 (47.5)	1 (16.6)	2 (33.3)	39 (34.8)
45-59	28 (46.6)	8 (20.0)	1 (16.6)	1 (16.6)	38 (33.9)
≥60	5 (8.3)	2 (5.0)	2 (33.3)	1 (16.6)	10 (8.9)
TOTAL	60 (100.0)	40 (100.0)	6 (100.0)	6 (100.0)	112 (100.0)

Thyroid dysfunctions in different age groups.

It is evident from table 1, that there was a trend towards a higher prevalence of overt thyroid dysfunction in the age group <45 and that of subclinical thyroid dysfunction in the age group 45-60.

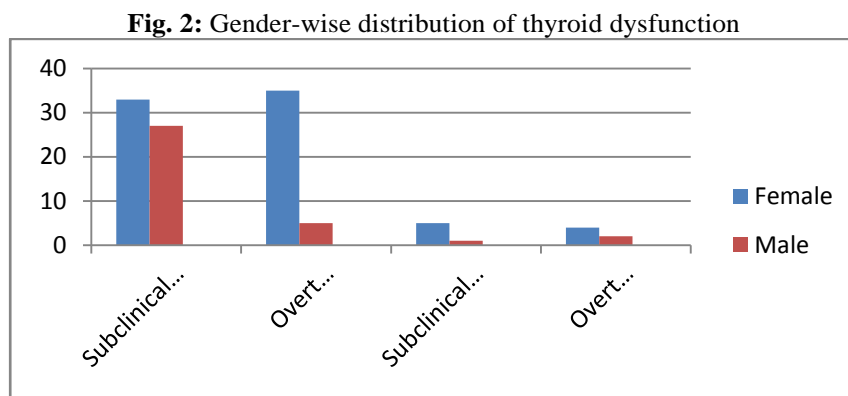


Fig. 2 shows that female had higher prevalence in all forms of thyroid dysfunction.

Table 2: Comparison of mean lipid profiles between normal controls and thyroid dysfunction patients.

	Overt hypothyroidism	Subclinical hypothyroidism	normal	Overt hyperthyroidism	Subclinical hyperthyroidism
TC (mg/dl)	297.00 ± 75.18 (p < 0.001)	264.65 ± 14.75 (p < 0.001)	155.46 ± 30.19	143.82 ± 5.53 (p = 0.002)	182.00 ± 20.08 (p = 0.170)
HDL (mg/dl)	31.48 ± 6.38 (p < 0.001)	43.41 ± 15.02 (p = 0.780)	54.79 ± 13.93	37.31 ± 2.98 (p = 0.005)	37.48 ± 3.84 (p = 0.007)
LDL (mg/dl)	120.87 ± 36.64 (p < 0.001)	98.85 ± 17.62 (p = 0.036)	80.00 ± 13.38	81.70 ± 8.39 (p = 0.405)	91.16 ± 23.19 (p = 0.088)
TG (mg/dl)	236.97 ± 45.99 (p < 0.001)	206.93 ± 48.56 (p < 0.001)	121.87 ± 18.31	60.77 ± 42.67 (p < 0.001)	117.73 ± 24.61 (p = 0.226)

Table 2 shows that the total cholesterol, LDL-cholesterol and triglycerides were found to be significantly raised, while HDL cholesterol was decreased in patients with hypothyroidism as compared to control group. In overt hyperthyroidism patients levels of total cholesterol, triglycerides and HDL-cholesterol were significantly lower while LDL-cholesterol was found to be higher than controls (P>0.05). In subclinical hyperthyroidism, HDL-cholesterol (P<0.05) and triglycerides were decreased while total cholesterol and LDL-cholesterol were increased.

Table 3: Pearson correlation coefficient between T3, T4, TSH and lipid profile.

		TC	HDL	TG	LDL
Overt hypothyroidism	T3	0.147	-0.301	-0.176	-0.194
	T4	0.087	-0.274	-0.203	-0.204
	TSH	0.452**	0.041	0.965**	0.973**
Subclinical hypothyroidism	T3	-0.041	-0.074	-0.062	-0.061
	T4	-0.174	-0.447**	-0.065	-0.204
	TSH	0.959**	0.309	0.940**	0.725**
Subclinical hyperthyroidism	T3	0.355	-0.225	-0.551	0.063
	T4	0.390	-0.290	-0.496	0.024
	TSH	0.495	0.049	-0.051	0.213
Overt hyperthyroidism	T3	0.206	-0.187	0.391	-0.556
	T4	-0.351	0.561	-0.437	-0.368
	TSH	0.287	-0.487	0.331	0.452

**Correlation is significant at the 0.01 level (1-tailed).

*Correlation is significant at the 0.05 level (1-tailed).

In overt hypothyroidism, thyroid stimulating hormone (TSH) has a positive correlation with TC, TG and LDL-C. Similarly, a positive correlation was also observed between TSH and TC, TG and LDL-C in case of subclinical hypothyroidism. HDL-C was negatively correlated with T4 in subclinical hypothyroidism.

Table 4: Lipid profile in categoral TSH value.

TSH (µU/ml)	TC (mg/dl) (mean ± SD)	HDL (mg/dl) (mean ± SD)	LDL (mg/dl) (mean ± SD)	TG (mg/dl) (mean ± SD)
0.00 – 0.30	153.00 ± 21.45	37.46 ± 3.19	81.90 ± 8.26	99.27 ± 58.66
0.30 – 6.20	204.33 ± 49.72	36.33 ± 8.53	83.74 ± 17.08	130.01 ± 44.54
6.2 – 10.00	268.58 ± 12.84	45.30 ± 15.14	102.94 ± 15.54	220.32 ± 41.42
>10	297.00 ± 75.18	31.48 ± 6.38	120.87 ± 36.64	236.97 ± 45.99

Table 4 shows that with increasing level of TSH, levels of total cholesterol, LDL-cholesterol and triglycerides also increased.

IV. Discussion

In this study, the prevalence of thyroid dysfunction, viz., subclinical hypothyroidism, overt hypothyroidism, overt hyperthyroidism and subclinical hyperthyroidism was 53.6%, 35.7%, 5.4% and 5.4% respectively. There was a trend towards a higher prevalence of overt thyroid dysfunction in the age group < 45 and that of subclinical thyroid dysfunction in the age group 45-60 which is in accordance with the findings from previous studies [6,16-18]. Higher prevalence of thyroid dysfunction in the middle age and younger age group may be attributed to stress and environmental pollutants [19]. This could be due to the slight changes with aging either as a result of its participation in the senescence process or as an effect of other system changes. In accordance with the results published by other studies, this study also found higher prevalence of thyroid dysfunctions in female [16,20,21]. Sisk reported that women are 5-8 times more likely to develop hypothyroidism and 8-10 times more likely to develop hyperthyroidism [22]. Women face a greater risk of developing thyroid diseases than men due to sex difference in the prevalence of autoimmune diseases [23]. Although overt hypothyroidism has always been associated with hypercholesterolemia, there is much controversy regarding the association of subclinical hypothyroidism and hypercholesterolemia. In this study, the parameters of lipid profile i.e, TC, LDL and TG were found to be increased in subclinical hypothyroidism and overt hypothyroidism whereas levels of HDL-cholesterol were found to be decreased. Positive correlation was observed between TSH and TC, TSH and LDL, TSH and TG which were all statistically significant in subclinical hypothyroidism patients. Increase in TC and LDL can be attributed to the effect of thyroid hormone on expression of LDL receptors and CYP7A, a rate limiting enzyme in bile acid synthesis [24].

Decrease thyroid function not only increases the number of LDL particles but also promote LDL oxidability, thereby increasing the risk of atherosclerosis [25]. TG level was also seen to be increased in both overt and subclinical hypothyroidism. The difference was statistically significant in both cases ($p=0.000$). The increase in TG level in hypothyroidism is attributable to the decrease activity of lipoprotein lipase, which is responsible for the clearance of TG rich lipoprotein [26]. The mean TC, LDL, and TG levels rose with a significant trend across grades of thyroid function (Table 4) as observed by Canaris et al [6]. In our study, we also found increased levels of TC, LDL-C and TG with increase in the level of TSH. It was not able to show in this study that the mean TC, LDL and TG of subjects with modest elevations of serum TSH (i.e. between 6.2-10 mIU/ml) observed in table 3 & 4 were higher than that of euthyroid group while several studies have linked hyperlipidemia with cardiovascular morbidity, it is arguable whether this reflects a clinically significant difference [27-29]. HDL-C was however decreased in both overt and subclinical hypothyroidism. Decrease in HDL level was found to be statistically significant in overt hypothyroidism. A decrease in HDL-C levels is due to increased CETP-mediated transfer of cholesteryl esters from HDL to VLDL and increased HDL mediated catabolism of HDL₂ [30,31]. Normalising subclinical hypothyroidism may have a role in the treatment of hyperlipidemia and perhaps the prevention of cardiovascular morbidity but to what degree is unclear [8].

The TC, HDL, and TG levels were found to be decreased in overt hyperthyroidism while LDL level was increased. The decreased levels of TC and TG in overt hyperthyroidism were statistically significant only whereas the increase in LDL level was not statistically significant. In subclinical hyperthyroidism, however, TC level was slightly increased but was statistically not significant. Despite the increase activity of HMG-CoA reductase, total cholesterol and LDL-C levels tend to increase in subclinical hyperthyroidism. This might be due to augmented excretion of cholesterol by bile together with enhanced receptor mediated catabolism of LDL particles [32,33]. Variations observed in TG levels could be due to the action of thyroid hormone on VLDL. Catabolism of VLDL is accelerated in hyperthyroidism which is probably related to changes in activity of lipoprotein lipase and or hepatic TG lipase.

V. Conclusion

Biochemical screening for thyroid dysfunction is of paramount importance in all dyslipidemic patients, as well as in all patients with unexpected improvement or worsening of their lipid profile. Underlying thyroid disorders should be recognized and treated in this setting. On the other hand, there is an absolute need for large studies designed to answer the question as to whether thyroid abnormalities (and especially TSH) are associated with increased risk for CAD and whether therapy of these disorders might influence cardiovascular mortality.

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