

Lipid Profile in Subclinical Hypothyroidism: A Case-control Study

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Abstract—Subclinical Hypothyroidism is a much more common disorder with a world-wide occurrence as compared to overt Hypothyroidism. Overt Hypothyroidism is associated with abnormalities of lipid metabolism, but the significance of dyslipidemia in subclinical hypothyroidism (SCH) remains controversial.

Aims: To compare the lipid profile between subclinical hypothyroid patients & healthy controls (age & sex matched) so as to determine any association between lipid profile & subclinical hypothyroidism.

Materials and Methods: In a case-control study, Thyroid stimulating hormone (TSH), free T3, free T4, anti thyroperoxidase (TPO) antibodies, total cholesterol, high density lipoprotein(HDL) cholesterol, low density lipoprotein (LDL) cholesterol, Very low density lipoprotein (VLDL) cholesterol, serum triglycerides were measured in 50 patients with subclinical hypothyroidism and 50 age- and sex-matched Euthyroid controls after an overnight fasting.

Results: Mean serum triglycerides (TG) and very low-density cholesterol (VLDL) were significantly higher in patients with SCH than controls ($P < 0.05$). No association was found between serum total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and SCH.

Conclusions: Dyslipidemia is more common in SCH compared to controls. High serum triglycerides and VLDL were observed in patients with SCH.

Keywords: Subclinical hypothyroidism (SCH), TSH, Lipid Profile.

I. INTRODUCTION

Subclinical hypothyroidism (SCH) can be best defined as a high serum thyroid stimulating hormone (TSH) and normal serum total/free thyroxine (T4), triiodothyronine (T3) concentrations associated with few or no symptoms/signs of hypothyroidism. It is referred to as a state of mild thyroid failure and is essentially a laboratory diagnosis.^{1,2} Subclinical hypothyroidism is much more common than overt hypothyroidism^{3,4} with a world-wide prevalence of about 7.5% to 8.5% in women and 2.8% to 4.4% in men.⁵

Thyroid hormones have significant effects on the synthesis, mobilization and metabolism of lipids. They affect serum cholesterol mainly by altering lipoprotein metabolism. A relationship between dyslipidemia and atherosclerosis is well established in overt hypothyroidism.

Similarly, subclinical hypothyroidism may be associated with increased risk of coronary artery disease (CAD), peripheral vascular disease and various biochemical abnormalities including increased LDL-C

levels, increased total cholesterol and serum triglyceride values.⁶ Therefore, early diagnosis and treatment may prevent the onset of overt hypothyroidism and its associated effects.

It is uncertain whether subclinical hypothyroidism is also associated with hyperlipidemia. The results of lipid profile alterations in subclinical hypothyroidism are controversial in different studies; some of those showing positive correlation^{7,8} and while other refusing any correlation.⁹

Hence the present study was planned to determine any association between serum lipid abnormalities and subclinical hypothyroidism.

II. METHODOLOGY

A hospital based case control analytical type of study was conducted from July 2012 to June 2013 at SMS Hospital, Jaipur. Study was conducted on 50 eligible cases of subclinical hypothyroidism cases and 40 age and sex matched healthy controls.

Case of subclinical hypothyroidism was defined as the patients with elevated TSH (5.0 to 10 microIU/ml) and normal total free T3 /T4 levels. The patients suffering from overt hypothyroidism (TSH>10mIU/ml and/or clinical signs of hypothyroidism), end stage renal disease, underlying known cardiac disease, type 1&2 diabetes mellitus, severe systemic disease, hypertension undergoing treatment with thyroxine/anti thyroid drugs or anti lipidemic drugs pregnant women and women on oral contraceptive drugs and those who did not give consent were excluded from study. And finally 50 eligible cases of subclinical hypothyroidism cases were enrolled for the study.

50 normal healthy controls (age & sex match) were selected randomly from subjects attending outpatient department of hospital for minor ailments or routine medical check-up. The other exclusion criteria were same for controls as that for cases. Ethical clearance was obtained from Institution's Research Review Board and informed consent was obtained from the study participants prior to Data collection.

All the subjects were assessed by clinical examination. After overnight fasting Serum lipid profile, thyroid function test including free T3, free T4, TSH and anti thyroperoxidase (TPO) antibodies, along with complete blood counts, (ESR), Peripheral blood film, renal function, liver function etc were done and results were recorded.

Estimation of lipids was done by using enzymatic method (CHOD-PAP) for Total cholesterol and enzymatic GPO-PAP method for Triglycerides. HDL-C was determined by the method given by Burstein *et al.*, 1970. Serum LDL was estimated from the Freidwald and Fredrickson's (1972) formula, which is $LDL = Total\ Cholesterol - [HDL + VLDL]$. VLDL was estimated by TG/5 based on the average ratio to cholesterol in VLDL. Free T3, freeT4 and TSH estimated by fully automated immunofluorescence immunoassay analyzer. CBC measurement was done by the Symex (^R) SF-3000, a technically advance automated analyzer.

Statistical analysis: Microsoft Excel and SPSS 17.0 trial version for Windows were used for data storage and analysis. Continuous variables were expressed as mean $\pm$ standard deviation, and Unpaired Student's t test was used to determine statistical difference between variables. Statistical significance was set at P value < 0.05.

III. RESULTS

Age range of cases was found 18-65 years with female preponderance. Age and sex matched subject for control group was from healthy subjects. Case group i.e. subject having subclinical hypothyroidism, and control group i.e. healthy subjects were well comparable in age and sex. Mean age of controls and cases was found 38.46 ± 12.34 and 40.64 ± 13.73 years respectively with female predominance (M:F=7.3:1) in both the groups. (Table1)

Table 1

Baseline Characteristics of Patients with Subclinical Hypothyroidism (SCH) and Healthy Control

S. No.	Parameters	Subclinical Hypothyroidism (N=50)	Healthy Control (N=50)	P Value
1	Age (in years) Mean $\pm$ SD	38.46 ± 12.34	40.64 ± 13.73	>0.05
2	Sex			
A	Male	6	6	>0.05
B	Female	44	44	

The mean value of serum TSH in controls and cases were found to be 2.52 ± 0.82 and 7.38 ± 1.33 ($P < 0.001$); difference was highly significant. Mean serum TSH of anti TPO positive cases was significantly lower (7.19 ± 1.39 mg/dl) as compared to anti TPO negative cases (7.44 ± 1.30 mg/dl), $P > 0.05$. Mean serum T3 and T4 of subclinical hypothyroid cases was not significantly different ($P > 0.05$). (Table 2)

Table 2

Comparison of Status of Thyroid Hormones in Patients with SCH and Healthy Control

S. No.	Parameters	Subclinical Hypothyroidism (N=50)	Healthy Control (N=50)	P Value
1	TSH	7.38 ± 1.33	2.52 ± 0.82	< 0.001
2	FT4	1.20 ± 0.25	1.25 ± 0.23	>0.05
3	FT3	2.30 ± 0.60	2.37 ± 0.47	>0.05

The mean value of serum triglycerides in controls and cases were found to be 143.40 ± 19.05 and 163.54 ± 31.76 ($P < 0.001$) respectively; this difference was found highly significant. Abnormal serum TGL level were more in patients with subclinical hypothyroidism (40%) than control subjects (10%). (Table 3 & Figure 1)

Figure 1

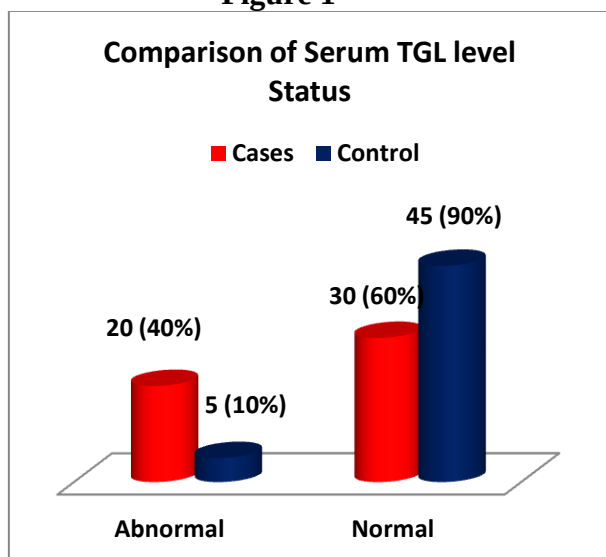
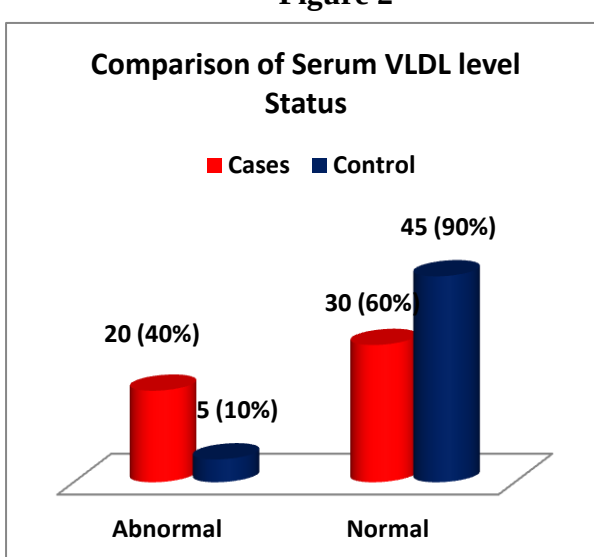


Figure 2



The mean value of serum VLDL in controls was significantly lower (28.70 ± 3.80) as compared to subclinical hypothyroid cases (32.74 ± 6.29), $P < 0.001$. Abnormal serum VLDL level were more in patients with subclinical hypothyroidism (40%) than control subjects (10%). Mean serum TC, LDL and HDL of Subclinical Hypothyroid cases was not found to be significant different from healthy controls ($P > .05$). (Table 3 & Figure 2).

Table 3
Comparison of Serum Lipid Profile in Patients with SCH and Healthy Control

S. No.	Parameters	Subclinical Hypothyroidism (N=50)	Healthy Control (N=50)	P Value
1	Total Cholesterol, mg/dL	181.88 ± 35.50	170.34 ± 34.31	>0.05
2	Triglyceride, mg/dL	163.54 ± 31.76	143.40 ± 19.05	< 0.001
3	LDL-Cholesterol, mg/dL	103.48 ± 36.10	93.12 ± 35.59	> 0.05
4	HDL-Cholesterol, mg/dL	47.68 ± 10.73	48.52 ± 8.17	>0.05
5	VLDL, mg/Dl	32.74 ± 6.29	28.70 ± 3.80	< 0.001

IV. DISCUSSION

Overt hypothyroidism is associated with increased risk of cardiovascular disease, which is attributed to increased TC and LDL-C. Elevation of plasma LDL-C is due to impaired clearance of LDL, probably reflecting decreased LDL receptor expression. Hypercholesterolemia is favored due to the hormone deficit and to the decreased activity of the lipoprotein lipase.¹⁰

Multiple studies over the past 20 years have focused on associations between SCH and serum lipids, which has remained incompletely understood. Inconsistent results have been reported in literature regarding the association between SCH, serum lipids and cardiovascular disease.^{11,12}

Among 8586 adults from the National Health and Nutrition Examination Survey III database, SCH was not associated with alterations in TC, LDL-C, TG, or HDL-C after adjustment for age, race, sex, and use of lipid-lowering drugs.¹³

The present study showed significantly higher levels of triglycerides and VLDL levels in patients with sub clinical hypothyroidism. Another study done by William J. Hueston et al¹⁴ also supports our results. No statistically significant relation was found between total cholesterol, low density lipoprotein, high density lipoprotein and subclinical hypothyroidism in present study. These findings are similar to a study done by William J. Hueston et al¹. Another study done by Sing K, Sing S.¹⁵ also found no significant Changes in levels of serum HDL and LDL level.

V. CONCLUSION

It can be concluded from present study that subjects with laboratory finding of hypertriglyceridemia should be further examined and tested for serum thyroid profile and particularly thyroid stimulating hormone (TSH) should be assessed carefully. Early diagnosis and treatment of such patients may prevent the onset of overt hypothyroidism and its associated complications. Further studies are required to support the significance of early thyroid evaluation and its treatment.

CONFLICT OF INTEREST

None declared till now.

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