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Update on Dyslipidemia in Subclinical Hypothyroidism : A Case-Control Study

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ABSTRACT

Hypothyroidism is a common metabolic disorder, results from inadequate production of thyroid hormones. Subclinical hypothyroidism is a condition usually asymptomatic, in which TSH level is above the reference range and free T3 and T4 levels are within reference range. Thyroid hormone plays a vital role in the regulation of energy homeostasis, in the metabolism of glucose and lipids and regulation of enzymes of lipoprotein transport. Lipid abnormalities are more common in overt hypothyroidism patients and also contribute to the inconsistent increase in cardiovascular risk in those patients. In the recent years, subclinical hypothyroidism is known to be associated with normal or high total cholesterol, raised LDL, serum TG and small dense LDL-C levels and lower levels of HDL. SH is also related with endothelium dysfunction, aortic atherosclerosis and myocardial infarction. It was observed that serum total cholesterol and triglycerides levels were raised in patients with SH as compared to euthyroid patients. Hence while estimating the lipid profile levels, the thyroid function of the individual should be taken into consideration.

Keywords: Thyroid dysfunction, overt hypothyroidism, subclinical hypothyroidism, lipid profile.

INTRODUCTION

Hypothyroidism is a common metabolic disorder with a prevalence range of 4% to 20% in adults **[1]** , and there is progressive increase in the prevalence with age. Thyroid failure is more common in women. Hypothyroidism results from inadequate production of thyroid hormones. It is classified as overt or subclinical depending on the extent of abnormalities in thyroid hormone levels and degree of clinical severity. Subclinical hypothyroidism (SH) is a hypothyroid condition usually asymptomatic, in which TSH level is above the reference range and free T3 and T4 levels are within reference range **[2]** or if a thyrotropin releasing hormone (TRH) test is done, there's a greater than normal rise in TSH response **[3]** .The rate of progression of the disease is higher with the simultaneous presence of

thyroperoxidase antibodies (TPO-Ab) or elevated levels of TSH. Thyroid hormone plays a vital role in the regulation of energy homeostasis, in the metabolism of glucose and lipids and regulation of enzymes of lipoprotein transport. Lipid abnormalities are more common in overt hypothyroidism patients and also contribute to the inconsistent increase in cardiovascular risk in those patients. SH is known to be associated with disorders in lipids, characterized by normal or high total cholesterol, raised LDL, serum TG and small dense LDL-C (sdLDL-C) levelsand lower levels of HDL **[4,5]** . SH is also related with endothelium dysfunction, aortic atherosclerosis and myocardial infarction **[4]** .

MATERIAL AND METHOD

The present study was conducted in Department of General Medicine, VIMSAR,Sambalpur, Odisha in which thyroid profile and lipid profile in 150 patients aged between 18 and 85 years of age of either sex, were estimated. They were further divided into subclinical hypothyroidism (SCH) group (n = 53) and euthyroid (EU) group (N=97) based on on the thyroid function test. SCH was defined as TSH between 5 and 10 mU/L and normal FT4. The EU group was classified as those with normal TSH values between 0.3 and 4.9 mU/L. Patients with a history of hypothyroidism, hyperthyroidism, diabetes mellitus, coronary artery disease, pregnancy, psychiatric disorder, or on drug therapy such as oral contraceptives, hormone replacement therapy and cholesterol-lowering agents were excluded from the study. 5 ml of venous blood was drawn from antecubital vein under all aseptic precautions for the estimation of biochemical parameters. Serum TSH levels was estimated by sandwich immunoassay using direct chemiluminiscent technology **[6]** , Serum FT4 were estimated by competitive immunoassay using direct chemiluminiscent technology **[7]** ,Serum total cholesterol estimation was done by fully enzymatic cholesterol oxidase-peroxidase method (CHODPOD) **[8]** . Serum triglycerides estimation was done by fully enzymatic glycerol phosphate oxidaseperoxidase method (GPO-POD) **[9]** .Serum high density lipoprotein (HDL) cholesterol estimation was done by autozyme precipitation reagent method in conjunction with autozyme cholesterol reagent **[10]** .Serum low density lipoprotein (LDL) cholesterol was calculated by the method of Friedwald's formula **[11]** .

LDL Cholesterol mg% = Total Cholesterol – (HDL Cholesterol + (Triglyceride ÷ 5)

The data was analyzed using computer software Microsoft Excel and IBM SPSS version 22.0 for Windows. Mean and standard deviation (SD) was calculated and reported for quantitative variables. The statistical difference in mean value was tested using unpaired't' test. For comparison of frequencies, F ischer's exact test was used. A p-value of <0.05 was considered as statistically significance.

RESULTS

Table 1: Comparison of mean lipid values in SCH and EU groups

Lipid (mg/dl)	SCH group (n=53)	EU group (n=97)	Statistical Inference
	Mean ±SD	Mean±SD	
Total Cholesterol	202.98±73.10	164.25±45.6	P=0.0001 (highly significant)

Triglycerides	116.21±29.24	101.43±28.16	P=0.003 (highly significant)
LDL	108.43±21.24	104.57±27.18	P=0.33 (not significant)
HDL	43.72±6.32	44.19±8.18	P=0.69 (not significant)

A total of 150 patients of either sex were included in this study. The patients were divided into two groups – SCH (subclinical hypothyroidism) group comprising of 53 patients including 35 females and 18 males and EU (euthyroid) group comprising of 97 patients including 57 females and 40 males. On analyzing the mean lipid values in either group, serum cholesterol and triglycerides levels were found to be elevated in the SCH group. Statistically significant difference was seen when serum TC (p=0.0001) and triglycerides (p=0.003) were compared between the two groups using unpaired t- test. However, no such difference was seen in other lipid parameters as shown in Table 1.

Table 2: Comparison of abnormal lipid values between SCH and EU groups

Lipid (mg/dl)		SCH group (n=53)		EU group (n=97)		Statistical Inference
		No	%	No	%	
Total Cholesterol	>200	23	43.39	12	12.37	P<0.0001 Highly significant
	≤200	30	56.61	85	87.63	
Triglycerides	>250	2	3.77	1	1.03	P=0.28 Not significant
	≤250	51	96.23	96	98.97	
LDL	>130	14	26.42	19	19.58	P=0.41 Not significant
	≤130	39	73.58	78	80.41	
HDL	<35	12	22.64	24	24.74	P=0.84 Not significant
	≥35	41	77.36	73	75.26	

On comparing abnormal lipid values, patients with SCH showed significantly elevated TC levels but no significant variations were observed in serum triglyceride, LDL and HDL levels as shown in Table 2.

Table 3: Comparison of lipid profiles between SCH and EU groups according to sex

Sex	Lipid (mg/dl)	SCH group (n=53)		EU group (n=97)		Statistical Inference
		No. of Cases	Mean±SD	No. of Cases	Mean±SD	
Male	TC	18	204.98±75.01	40	168.45±45.84	P=0.02 (significant)
	TG		111.18±18.31		98.58±17.25	P=0.01(highly significant
	LDL		108.87±20.78		104.17±19.34	P=0.41(not

						significant
	HDL		44.22±6.88		46.30±9.21	P=0.34 (not significant
Female	TC	35	160.05±45.76	57	200.98±72.01	P=0.001 (highly significant
	TG		113.31±18.87		104.71±17.77	P=0.03(significant
	LDL		108.01±17.12		105.10±18.78	P=0.44 (not significant
	HDL		42.22±6.84		42.08±8.87	P=0.93(not significant

On comparing the lipid profile between the two groups according to sex, the mean serum cholesterol and triglyceride values were found to be elevated in both male and female patients of the SCH group. By comparing the lipid profiles in male patients between SCH and EU groups, statistically significant changes were seen in serum TC (p=0.02) and triglycerides (p=0.01). Similarly in female patients statistically significant changes were also seen in serum TC (p=0.001) and triglycerides (p=0.03) as shown in Table 3.

DISCUSSION

It has been observed that serum cholesterol and triglycerides level were raised in patients with subclinical hypothyroidism as compared to euthyroid patients. Similar results were observed by Walsh et al in a community based study conducted in 2108 Australian participants and found that serum TSH was positively correlated with total cholesterol, triglycerides and LDL-C whereas no association was observed between serum TSH and HDL-C **[12]** . Other researchers also observed similar findings **[13,14]** . In contrast, Vierhapper et al, in a cross-sectional study done in 7000 thyroid clinic outpatients, observed that total cholesterol and LDL-C were elevated in overt hypothyroid patients, but no significant differences in serum total cholesterol, LDL-C, HDL-C, or triglyceride levels in SH patients and the euthyroid control group **[15]** . In another study done by Hueston et al, it was found that SH (defined as a serum TSH of 6.7 to 14.99 mIU/liter) was not associated with alterations in total cholesterol, LDL-C, triglycerides, or HDL-C **[16]** . Thyroid hormones stimulate enzyme, 3- hydroxy-3-methylglutarylcoenzyme A (HMG-CoA) reductase, which is required for the first step in cholesterol biosynthesis. Triiodothyronine (T3) causes upregulation of LDL receptors by controlling the LDL receptor gene activation. T3 also regulates LDL receptor's gene expression by controlling the sterol regulatory element-binding protein-2 (SREBP2). T3 also protects LDL from oxidation. Thyroid hormones increases cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL2 to the very low density lipoproteins (VLDL) and TGs to the opposite direction thereby influencing HDL metabolism. Thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the TG-rich

lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL and in turn LDL to sdLDL **[17]** . T3 also leads to upregulation of ApoAV which have been associated with decreased levels of TGs. Besides their effect on lipid profile, thyroid hormones can equally affect a number of other metabolic parameters related to CVD risk. Thyroid function can also influence the production of adipokines and adipocyte metabolism **[18]** .

CONCLUSION

Abnormalities in the thyroid function can have an impact on lipid profile. So, while diagnosing or treating dyslipidemic patients, biochemical screening for thyroid dysfunction should be taken into consideration. Further research should be done to evaluate the role of TPO-antibodies on dyslipidemia and whether the thyroid dysfunction influences the morbidity and mortality of CVD patients.

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Conflict of Interest – None declared

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