ORIGINAL ARTICLE

EFFECT OF SUB-CLINICAL HYPOTHYROIDISM ON CHOLESTEROL AND TRIGLYCERIDES

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Background: Sub-clinical Hypothyroidism (SCH) is associated with dyslipidemias which may increase the cardiovascular risk. The objective of this study was to compare the serum levels of cholesterol and triglycerides in subclinical hypothyroidism and normal euthyroid subjects. **Methods:** This cross-sectional comparative study had control group of 50 euthyroid subjects selected from Mayo Hospital, Lahore who were advised to get thyroid profile checked. Fifty sub-clinical hypothyroid patients were included on the basis of their thyroid profile reports. Fasting blood samples were taken from both the groups for analysis of serum levels of T4, total cholesterol and Triglycerides. Student's *t*-test was used to compare the mean values, and $p \leq 0.05$ was considered statistically significant. **Results:** Mean Triglyceride level in SCH was 168.28 mg/dl, and in euthyroid controls it was 133.62 mg/dL ($p<0.001$). There were no differences of total cholesterol in both groups with value of 190 mg/dL in SCH group and 189.12 in control group ($p=0.912$). Triglycerides level was raised in SCH and there was no pronounced effect on total cholesterol. **Conclusion:** The effects of SCH are more pronounced on triglycerides and less on total cholesterol.

Keywords: Sub clinical Hypothyroidism, SCH, Thyroid Stimulating Hormone, TSH, Lipid profile, Thyroxin, T4, Triiodothyronine, T3

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INTRODUCTION

Sub clinical hypothyroidism and hyperlipidemia are quite common in general population. Sub clinical hypothyroidism is a condition in which the levels of TSH are above normal whereas the T3 and T4 levels are normal or towards lower edge of normal with no symptomatology of disease. Its prevalence is 7.5–8.5% in women and 2.8–4.4% in men the world over.[1] If this condition is not corrected at beginning of the disease process it could end up in disastrous consequences.[2] This disorder is found more in aging population and is twice common in woman as compared to men.[3] The frequency of this disease is more as compared to full blown hypothyroidism and timely intervention can prevent hypothyroid to manifest and lay down its drastic effects.[4]

If timely care is not taken, with passing time the TSH levels continue to rise and T3 and T4 levels fall and full-blown hypothyroidism results. The serum levels of T3 and T4 continue in the normal range due to excessive production of TSH, but when the disease is advanced the levels start to fall, this is the time when signs and symptoms also appear. When full blown hypothyroidism is noticeable, the patient feels tiredness without physical activity; other symptoms are obesity, cold intolerance, constipation, dry thick skin, voice changes, slow mental activity, mood variations, poor appetite, pains and body aches. Apart from these, biochemical changes also start to occur, affecting lipid metabolism which increase the tendency of lipid deposition inside vessel walls, would cause atherosclerosis, and increase the chances of coronary disease. This is the result of high levels of triglyceride and cholesterol in patients of sub clinical hypothyroidism.[5]

TSH level >4.5 mlU/L in the absence of symptoms and presence of normal levels of thyroid hormones has become an important biochemical tool not only in identifying sub clinical hypothyroidism, but its evolution to clinical hypothyroidism, since approximately 4% of these patients develop it over time.[6]

Thyroxin has a key role in lipid metabolism, lipid formation, absorption and breakdown into fragments. Various studies have proved that in overt hypothyroidism the triglyceride and total cholesterol levels rose beyond normal limits, which regress if the subject takes Levothyroxine over a period of time. This occurs due to reduced activity of the enzymes Hepatic Lipase (HL) and Cholesteryl Esters Transfer Protein (CETP) which are controlled by Thyroid Hormone. The low activity of CETP and HL results in reduced transport of cholesteryl esters from High density Lipid 2 (HDL2) to High Density Lipid 3 (HDL3). The configuration and carriage of cholesterol and triglyceride are significantly upset in thyroid malfunction. The two enzymes which effect lipid metabolism, CETP and HL, are again dependent on thyroid hormone, when the level of the TH is less in the body the enzymes are unable to mobilize lipids and as a consequence the cholesterol and triglyceride levels rise.

The link of SCH with lipid profile and cardiovascular disease is not yet clear. Apolipoprotein B

levels may be raised in patients with SCH. Though some studies have confirmed that total cholesterol and LDL-C levels are higher in patients with sub clinical hypothyroidism, others have not revealed any effect of sub clinical hypothyroidism on these lipid measurements. LDL-Cholesterol, serum triglycerides, lipid sub particle size may be changed in sub clinical hypothyroidism.

The objective of this study was to determine and compare the serum levels of cholesterol and triglycerides in sub clinical hypothyroidism and normal euthyroid subjects.

MATERIAL AND METHODS

This cross-sectional comparative study was carried out at Department of Physiology, King Edward Medical University, Lahore with a sample size of 100 subjects. Sample size was calculated by using sample size determination in health studies. They were divided in two batches, 50 Subclinical Hypothyroid subjects (A) and 50 Euthyroid controls (B) with ages ranging 18–65 years. After the approval of the study from Institutional Review Board and Ethical Committee, informed written consent was taken from the subjects enrolled for the study selected from the OPD of ENT and General Medicine, Mayo Hospital, Lahore and were advised to get Thyroid profile checked.

50 Subjects were selected on the basis of their Thyroid profile reports as Sub Clinical Hypothyroid patients. Subjects having Diabetes Mellitus, Hypertension, any vascular disease, diagnosed case of Hypothyroidism were excluded from the study. Fasting blood samples were drawn from both the groups; samples were taken in a plain gel vacutainer tube with a disinfected blood collection method. They were centrifuged within one hour of sample collection at 3,000 rpm. These samples were centrifuged to obtain serum for the estimation of serum lipid and thyroid profile. Free thyroid hormones T3, T4 were estimated through radioimmunoassay (RIA) and TSH was estimated by the enzyme-linked immunosorbent assay (ELISA) method. Serum levels of TC, TG and HDL-C were measured using a spectrophotometric assay with commercial kits.

Data was analysed using SPSS-21. Quantitative variables were expressed as Mean±SD and qualitative variables as frequencies and percentages. Confounding variables like age and gender were stratified. Comparison of mean values of triglycerides and cholesterol between groups was done using student's *t*-test, and $p \leq 0.05$ was considered significant.

RESULTS

There were 78 (78%) females, 22 (22%) males the study. Mean age of patients in SCH was 37.50±8.13 years and in control group it was 35.84±8.67 years.

Mean values of TSH were significantly higher in SCH as compare to controls ($p<0.001$). Mean of FT4 and FT3 in SCH were on the lower margins of normal and were statistically significant when compared with controls ($p<0.001$) (Table-1).

Mean serum Triglyceride level in SCH patients was significantly higher (168.28±34.37 mg/dl) when compared to healthy controls (133.62±24.17 mg/dl, $p<0.001$). Mean total Cholesterol level in SCH patients was 190±42.66 mg/dl and in Euthyroid (controls) was 189.12±36.51 mg/dl, which was statistically not significant (Table-2).

Sub-clinical Hypothyroidism caused a rise in the Triglyceride levels, with a visible difference in the controls and SCH cases. The decreased level of free T4 have started to affect the Triglyceride levels in the blood, whereas there was very little effect on total Cholesterol.

Table-1: Hormonal status of the sub clinical hypothyroidism patients and healthy controls

Parameter	Sub clinical hypothyroids (n=50)	Control group (n=50)	*p*
TSH mIU/L	8.69±3.83	1.39±0.82	<0.001*
T4 pmol/L	12.45±6.08	17.42±2.72	<0.001*
T3 pmol/L	2.57±1.03	4.82±0.46	<0.001*

*significant

Table-2: Comparison of triglyceride and cholesterol between SCH patients and healthy controls

Parameter	Sub clinical hypothyroids (n=50)	Control group (n=50)	*p*
Triglyceride (mg/dL)	168.28±34.37	133.62±24.17	<0.001*
Cholesterol (mg/dL)	190.00±42.66	189.12±36.51	0.912

*significant

DISCUSSION

It is an established fact that hyperlipidemias are linked with overt hypothyroidism. Though there was great emphasis of multiple studies to find out the relationship between sub-clinical hypothyroidism and serum lipids over the last two decades, yet the association between lipid profile, sub-clinical hypothyroidism and CVD outcomes remain only partially understood. We tried to determine and compare the serum levels of cholesterol and triglycerides in sub-clinical hypothyroidism and normal euthyroid subjects.

The men age of our patients was 37.50±8.13 years and that of controls was 35.84±8.67 years. This is the age at which the thyroid disease manifests itself the most. Study by Luboshitzky *et al*[6] also showed the average age of 40.85 years in patients of SCH. The frequency of females and males in this study were 78% and 22% respectively, this was also shown in a study by Bhandopadhyay *et al*[7] who quantified that females constituted 78% of study population of hypothyroidism. These facts led many study groups to check out correlation of different parameters in hypothyroidism in

female populations. This was due to the fact that thyroid dysfunction was more pronounced (5 to 8 times) in females compared to males.

In this study, mean triglyceride levels were significantly higher in sub-clinical hypothyroid patients compare to healthy controls. Stored calories in triglycerides are those which we do not use immediately after eating. Later, different hormones help our body in using triglyceride as a source of energy. Some studies have also indicated that in SCH, dyslipidemia may also be accompanied by increased TG levels.[8] Lipoprotein lipase activity in the adipose tissue has been shown normal or decreased, in addition to decreased hepatic lipase activity resulting in normal or increased levels of TG in patients of hypothyroidism.[9] Toruner *et al*[10] have reported that the TG concentrations of SCH patients are higher than control subjects. Results of our study showed that sub-clinical hypothyroidism has caused a rise in the triglyceride levels as there was visible difference in the mean value of triglyceride in SCH and controls. The levels of fasting cholesterol in SCH and controls were nearly the same. There was no significant difference between the mean values of both groups. The level of cholesterol in the blood within the range of <200 mg/dl was taken as a safe normal range. According to our results, mean value of cholesterol in both groups were within normal range but towards upper limits. It is more of a surprise that in normal healthy individuals, the cholesterol level is towards the higher side. It may indicate that the eating habits and lack of physical activity in our general population particularly in females are the factors that cause increase in cholesterol levels. Moreover, age group of females we encountered was mainly menopausal. So female sex hormones changes which start at this age could also contribute to raised cholesterol levels. Small size of samples, gender difference and age of patients and short duration of illness may also be the possible causes for insignificancy of our results.

Velkosa Nakova *et al*[11], expressed mean value of free T4 as 0.006 pmol/L and serum cholesterol as 241.96 mg/dL in subjects of hypothyroidism. Efstathiadou *et al*[12], in a similar study reported total cholesterol as 221.5 mg% in patients with overt hypothyroidism. Hueston and Pearson[4] reported total cholesterol as 216.5 mg%. Almost all these studies have shown cholesterol to be on the higher side, more than that we found. As we were checking the sub-clinical hypothyroids in which the disease process had just initiated so in our study the cholesterol was not extremely high, but showed an upward trend. We noted mean triglyceride level as 155.18 mg/dL in SCH patients, whereas in controls it was 138 mg/dL. In a study by Kong *et al*[13] the triglyceride was shown to be 159 mg/dL and mean of cholesterol was 216 mg/dL in sub clinical hypothyroid patients. Hueston and Pearson[4] exhibited that triglyceride was 178.1% in the cases of hypo thyroids. This study further showed that all lipids were raised except HDL which was significantly reduced. Rajan *et al*[14] enlisted subjects diagnosed as sub clinical hypothyroids and with full bloom explicit hypothyroids. Total serums cholesterol, triglycerides, and low density lipoproteins (LDL) were found to be raised in both groups compared to controls whereas HDL levels were variable. In a study conducted by Lai *et al*[15] on Chinese population, patients with SCH had lower HDL-C and higher triglycerides than healthy controls.

Canaris *et al*[16] tried to establish an association between mal-functioning thyroid (both hypo- and hyper) and lipid levels in a state of Colorado, they informed that in most of the hypothyroid subjects the lipids were elevated as compared to controls. They further brought up that serum triglyceride and HDL did not show significant differences in both groups. The results of this study are somewhat supportive of our finding. Madani *et al*[17] in a project study on Sudanese women evaluated the serum levels of total cholesterol, triglycerides, and LDL in subjects reported with SCH and euthyroid control groups, the levels of TC, TG and LDL-C were on the higher side in SCH group whereas HDL showed no noteworthy change. The results of this study are in agreement with our study.

Due to higher occurrence of sub-clinical hypothyroidism in general population and its link with hyperlipidemia, it is suggested to do screening of patients with dyslipidemia for thyroid abnormality. It is recommended by the American Thyroid Association to screen all adults for thyroid dysfunction starting at age 35 years.[18] All patients with hyperlipidemia should be evaluated for hypothyroidism.[19] However, large scale randomized studies are required for evidence based recommendations with respect to screening for mild thyroid failure and substitution therapy for this condition.

CONCLUSION

Hypothyroidism is more prevalent in the elderly females. In patients with subclinical hypothyroidism, triglycerides were raised whereas serum total cholesterol was not significantly different from euthyroids. It is advisable that the patients keep a check on their lipid profile and thyroid profile, as dyslipidemias are a contributing factor in causation of atherosclerosis and ultimately heart disease.

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