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# Thyroid dysfunction and total cholesterol - experience in a tertiary care hospital

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## ABSTRACT

Thyroid hormones have their effect on lipid metabolism. Thyroid disorders are likely to increase risk of CVD by affecting levels of cholesterol. To evaluate the levels of fT3, fT4 and cholesterol in patients with elevated TSH levels and to correlate total cholesterol level with TSH, fT3 and fT4. 60 subjects with elevated TSH levels were selected for the study group. TSH, fT3 and fT4 levels were estimated by Access 2 chemiluminiscent immunoassay System. Total cholesterol was measured by timed enzymatic end point method on Synchron CX9 Autoanalyzer. Data analysis was done by SPSS 17.0. Patients were divided into three groups on the basis of TSH levels (>6 µIU/ml, 6-20 µIU/ml and >20 µIU/ml). ANOVA showed TSH, Total Cholesterol ($p<0.001$ for both) and fT3 ($p<0.05$) were significantly different in the three groups. Pearson correlation coefficient (r) for Total Cholesterol Vs TSH showed a significant positive correlation ($r = 0.916$, $p<0.01$) while fT3 and fT4 had negative correlation (r values -0.265, -0.250 respectively). All patients of hypothyroidism should be screened for hypercholesterolemia and patients of hypercholesterolemia should be screened for thyroid dysfunction if any symptoms are suggestive.

**Keywords**: TSH, Total Cholesterol, CVD, Thyroid Dysfunction

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## INTRODUCTION

Hypothyroidism is defined as a deficiency of thyroid hormones resulting from reduced secretion of both T4 and T3 [1]. Biochemically decrease in T4 and T3 concentrations lead to hyper secretion of pituitary TSH and an amplified increase in serum TSH levels. This is a key laboratory finding, particularly in the early detection of thyroid dysfunction [2]. Lipid abnormalities are reported to be more common in patients with overt hypothyroidism and are thought to contribute to the disproportionate increase in cardiovascular risk laboratory finding, particularly in the early detection of thyroid dysfunction [3]. Hence, hypothyroid patients are at high risk of cardiovascular diseases laboratory finding, particularly in the early detection of thyroid dysfunction [4].Levothyroxine replacement therapy significantly improved the lipid profile in hypothyroid patients laboratory finding, particularly in the early detection of thyroid dysfunction [5] indicating the possible relation between thyroid hormones and lipid levels in the blood of hypothyroid patients. Relation between thyroid dysfunction and cardiovascular diseases has been a subject of interest for many clinical investigators for a long time. Overt hyperthyroidism and hypothyroidism is the established risk factor for Cardiovascular Disease (CVD) but the relation between Subclinical Hypothyroidism (SHT) defined as an elevated Thyroid Stimulating Hormone (TSH) with normal thyroid hormones (fT3, & fT4) and hypercholesterolemia related to cardiovascular risk is still controversial laboratory finding, particularly in the early detection of thyroid dysfunction [6,7,8,9]. Thyroid has also important effects and influences in the Basal Metabolic Rate (BMR) and the metabolism of carbohydrate, lipid and proteins laboratory finding, particularly in the early detection of thyroid dysfunction [10]. Hypothyroidism has been generally considered as cardiovascular risk factor in majority of studies, mainly because of its association with elevated Total Cholesterol (TC) and LDL cholesterol. Hypercholesterolemia in hypothyroidism probably results from reduced catabolism of lipoproteins, a phenomenon that may be explained by a decreased expression of lipoprotein receptors laboratory finding, particularly in the early detection of thyroid dysfunction [11]. Hence, it is important to see the relation of total cholesterol and thyroid dysfunction. The result can also be useful for screening thyroid dysfunction in the patient having high total cholesterol level in the serum.

## MATERIALS AND METHODS

This study was carried out in the department of clinical biochemistry, Lady Hardinge Medical College and Smt SSK Hospital, New Delhi, from May 2010 to July 2010. Subjects in our study were selected from the patients referred to the hormone lab unit (Clinical Biochemistry Department), for TFT with signs and symptoms suggestive of thyroid disorder. Prior verbal consent was taken before interviewing the subject. None of the subject in the study group was on any hypolipidemic drugs or on levothyroxine treatment. After noting the name, age and sex, venous samples were drawn after 12 hours of overnight fasting. Serum was separated and TSH assay was performed within 24 hrs. After screening by TSH levels, a total of sixty subjects with elevated levels of TSH i.e. >6 µIU/ml (since the upper limit of reference range for our lab is 6µIU/ml) were included in the study group. As per serum TSH level the cases were further

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subdivided into three groups: Group I with levels of 6-20 µIU/ml, group II with levels of 21-40 µIU/ml and group III with level above 40 µ IU/ml .This resulted in a sampling distribution different from the general population. Patients were selected in such a way that the groups were comparable in age and sex distribution. Apart from these criteria, the selection was random. Total of sixty samples were included which were with raised TSH, collected during the period and samples were further analyzed for fT3, fT4, and total cholesterol. TFT was done on Access 2 Chemiluminiscent Immunoassay system (Beckman) using Kits from Beckman. Cholesterol was measured by a timed-end point method after enzymatic hydrolysis and oxidation (using Synchron CX9 auto analyzer). The indicator quinoneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase. Change in absorbance was measured at 500nm. Statistical analysis was done by using SPSS version 17. Data collected was subjected to standard statistical analysis, such as Mean and Standard Error of Mean for each of the parameters in individual groups. Analysis of Variance was done to compare the significance of difference between the three groups for all the parameters. Coefficient of correlation and its significance (p value) was calculated for Total Cholesterol with TSH,fT3, fT4.

## RESULTS

**Table 1 Comparison of TSH, fT3, fT4 and Total Cholesterol in the three groups.**

| Parameters | Group I (n=30) Mean±SE | Group II (n=20) Mean±SE | Group III (n=20) Mean±SE | P Value (by ANOVA) |
|---|---|---|---|---|
| **TSH (µIU/ml)** | 13.10±0.58 | 25.86±1.16 | 113.9±7.34 | **<0.001**** |
| **FT3 (pg/ml)** | 2.57±0.08 | 2.69±0.69 | 2.20±0.15 | **<0.05*** |
| **FT4 (ng/dl)** | 1.10±0.33 | 0.58±0.13 | 0.28±0.03 | >0.05 |
| **Total cholesterol (mg/dl)** | 172.7±3.52 | 257.2±4.65 | 357.9±11.70 | **<0.001**** |

n = number of subject *p= <0.05;significant **p= <0.001,highly significant;

Results are given in the table 1. In group-I subjects the mean value of fT3, fT4 and TSH were found to be 2.57±0.08 pg/ml, 1.10±0.33ng/dl and 13.10±0.58 µIU/ml (mean ± S.E.M) respectively. The mean levels of total serum cholesterol found to be 172.7±3.52 mg/dl. In group-II patients the mean fT3, fT4 and TSH levels were 2.69±0.69 pg/ml, 0.58±0.13 ng/dl and 25.86±1.16 µIU/ml respectively and the mean value of total cholesterol was 257.2±4.65 mg/dl. The mean values of fT3, fT4 and TSH (in group III) were found to be2.20±0.15 pg/ml, 0.28±0.03 ng/dl and 113.9±7.34 µIU/ml respectively. The mean levels of total serum cholesterol were 357.9±11.70 mg/dl. On doing analysis of variance (ANOVA) it was found that TSH, Total Cholesterol ($p<0.001$ for both) and fT3 ($p<0.05$) were significantly different in the three groups.

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**Table 2 Correlation between Total Cholesterol and TSH,fT3 and fT4 for all Subjects**

| Parameter | Pearson Correlation (r) All Subjects(N=60) | P value |
|---|---|---|
| Total Cholesterol Vs TSH | **0.916** | **<0.001** |
| Total Cholesterol Vs fT3 | **-0.265** | **<0.05** |
| Total Cholesterol Vs fT3 | -0.250 | >0.05 |

Table 2 shows the results of correlation between total cholesterol and TSH,fT3 and fT4. Pearson correlation coefficient (r) for total cholesterol Vs TSH showed a significant positive correlation ($r = 0.916$, $p<0.01$). fT3 and fT4 both showed negative correlation with Total Cholesterol with r values -0.265 and -0.250 respectively. Out of these only correlation of total cholesterol with fT3 was significant with $p<0.05$.

## DISCUSSION

Thyroid has important effect in the metabolism of carbohydrate, lipid and proteins. Level of serum total cholesterol is maintained by the level of thyroid hormone through its catabolism, by up regulating or down regulating LDL receptors. Our study has also revealed significant negative correlation between TC & fT3 ($r = - 0.265$, $p <0.05$), and significant positive correlation between TSH and TC ($r = 0.916$, $p<0.001$) which is comparable to the study done by Teixeira et al [5]. This positive correlation between thyroid hormone and total cholesterol suggests the role of hormone in enhancing lipid metabolism. Thyroid dysfunction is one of the important causes of CVD. However it still remains to be established how strongly the relationship exists in our population. Therefore, screening of total cholesterol is quite reasonable in patient with hypothyroidism and subclinical hypothyroidism in our setting to prevent cardiovascular diseases.

Hypothyroidism result 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. Different mechanisms of hypothyroidism increasing cholesterol levels and thereby atherosclerosis risk have been elucidated.

Hypothyroidism 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. Hypothyroidism is often accompanied by diastolic hypertension that, in conjunction with the dyslipidemia, may promote atherosclerosis. However, thyroxine therapy, in a thyrotropin (TSH) suppressive dose, usually leads to a considerable improvement of the lipid profile [12].

Another reported mechanisms for the development of hypercholesterolemia in hypothyroidism include decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver in addition to decreased receptor activity [13,14,15].

The catabolism of cholesterol into bile is mediated by the enzyme cholesterol 7α hydroxylase. This liver-specific enzyme is negatively regulated by T3 and may contribute to the decreased catabolism and increased levels of serum cholesterol associated with hypothyroidism [16].

The current studies reveal a molecular mechanism for the association between hypercholesterolemia and hypothyroidism. It has been established previously that expression of the LDL receptor gene and protein was repressed when thyroid hormone levels were artificially decreased, but the mechanism for this drop in expression was not defined previously. It has been demonstrated recently that gene encoding SREBP-2, a major transcriptional regulator of genes involved in cholesterol uptake and synthesis, is directly regulated by thyroid hormone. This experimental model predicts that as thyroid hormone levels fall, SREBP-2 levels decline followed closely by a drop in LDL receptor mRNA. This results in a decline in high affinity LDL cholesterol uptake in the liver resulting in hypercholesterolemia, which is fundamentally linked to thyroid hormone status. Thyroid hormone depletion in animals not only lowers liver LDL receptor mRNA and protein (26), but hypothyroid humans have increased serum LDL cholesterol and reduced LDL uptake that can be reversed by adding T3. Therefore, this model accounts for the association between low serum thyroid hormone levels and hypercholesterolemia in humans as well [17].

## CONCLUSION

We conclude that elevated cholesterol level in hypothyroidism and subclinical hypothyroidism can be important risk factor causing CVD. We, therefore, recommend screening of total cholesterol level in these patients which would help to take preventive action for occurrence of CVD. Also, we recommend that patients with deranged lipid profile with any symptomatolgy of thyroid disorder should be screened by TSH estimation.

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