 DOI: 10.18231/2394-6377.2017.0099

Cardiovascular disease risk factors and its association with subclinical hypothyroidism

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Abstract

Aim: Hypothyroidism is proved to be associated with atherosclerosis and cardio-vascular disease. But correlation between subclinical hypothyroidism (SCH) and increased cardiovascular risk is yet to be established. This study was done to investigate subclinical hypothyroidism and its associations with cardiovascular diseases.

Objectives: To quantitatively detect the levels of lipid profile parameters and range of blood pressure, in subclinical hypothyroid and euthyroid subjects. To correlate cardio vascular disease risk factors and their association with subclinical hypothyroidism.

Materials and Method: total sixty SCH cases and sixty euthyroid controls were compared. Serums levels of T3, T4, TSH were estimated by standard ELISA kit method, Serum LDL-Cholesterol using Friedewald equation, Triglycerides by GPO-POD with espas method, and Total-Cholesterol, HDL-Cholesterol by enzymatic CHOD-PAP by enzyme colorimetric method.

Result: Study showed increased mean serum levels of LDL Cholesterol, Total cholesterol, TSH, Triglycerides, systolic & diastolic BP. Serum levels of T4, HDL-Cholesterol remained normal. Number of people with increased Total Cholesterol, Triglycerides, LDL-C, systolic BP & diastolic BP and decreased HDL-C were more in subclinical hypothyroidism compared to euthyroid cases suggesting the dyslipidemic and hypertensive changes in SCH cases.

Conclusion: Study showed that cardio-vascular risk factors are highly associated with hypertension and dyslipidemic state seen in subclinical hypothyroidism cases, suggesting the higher association with subclinical hypothyroidism and risk factors of cardio-vascular disease.

Keywords: Euthyroid, Cardio-vascular risk, Sub-clinical hypothyroidism.

Received: 5th August, 2017 **Accepted:** 7th September, 2017

Introduction

Subclinical hypothyroidism is high serum TSH levels above upper limit of normal TSH range and normal serum FT4 levels.(1) A two times decrease in FT4 will produce a hundred times increase in TSH. So little decrease of FT4 in normal limits will show marked increase in serum TSH above the normal limits.(2)

Subclinical hypothyroidism is found to be related with higher levels of some cardiovascular risk factors. Although studies have shown different results, many studies have shown that subjects with hypothyroidism have increased total cholesterol and LDL cholesterol levels as compared to euthyroids. But results of the studies on coronary heart disease in subjects with subclinical hypothyroidism are highly controversial.(4)

Cardiovascular diseases (CVDs) are the most common cause of mortality, primarily affecting older adults. Previous studies have suggested the abnormal (TSH) levels are major cardio vascular risk factor(5) in SCH.

Materials and Method

All cases are selected from laboratory of clinical Biochemistry, Shri B M P Medical College, Bijapur. Sixty sub-clinical hypothyroid cases and sixty euthyroids are studied. Ethics Committee clearance was taken informed consent was taken from all cases. Study was done from November 2011 to May 2013.

Inclusion criteria: euthyroid controls having normal TSH [0.3-4.5 mlU/L.] levels, Subclinical hypothyroidism patients with TSH levels of above 15.00 mlU/L, and normal levels of T3 and T4 were considered in the study.

Exclusion criteria: known cases of dyslipidemia, hypothyroidism, thyroidectomy, radioactive iodine therapy, drugs induced SCH, diabetes mellitus, other systemic illness, hepatic & renal failure cases, patients on oral hypolipidemic drugs were not included in the study.

Collection of blood samples: Venous blood samples were drawn at 8 a.m. following a 12 hours of fasting, in a plain bulb from the subjects, with all the aseptic precautions. Blood samples were centrifuged for 5 min at 3000 rpm within 30 minutes of collection and serum was separated. Serum samples were stored at -20°C. Serum T3, T4, TSH were detected by Enzyme linked immunosorbant assay kit method.(6-8) Serum total cholesterol estimation and HDL-C was detected by enzymatic CHOD-PAP enzyme colorimetric method,(9) LDL-C was a calculated by Friedewald formula.(10) Triglycerides by GPO-POD method.

Results

Table 1: Comparison of parameters between subclinical hypothyoidism subjects and healthy controls

Variable	SCH Patients (Mean±SD)	Euthyroid controls (Mean±SD)
TSH (µIU/dl)	9.56 ± 1.98	3.46 ± 1.28**
T3 (nmol/dl)	1.68 ± 0.31	2.10 ± 0.88**
T4 (nmol/dl)	88.22 ± 14.22	92.71 ± 24.66
TC (mg/dL)	250.22 ± 40.36	190.46 ± 37.22**
TG (mg/dL)	170.52 ± 20.74	108.73 ± 23.48**
LDL-C (mg/dL)	194.74 ± 49.89	129.04 ± 37.05**
HDL-C (mg/dL)	29.13 ± 5.18	39.13 ± 7.58**
SBP (mm Hg)	130.63 ± 5.86	112.73 ± 5.15**
DBP (mm Hg)	99.43 ± 2.18	88.76 ± 3.68**

** Indicates p<0.001- Highly Significant

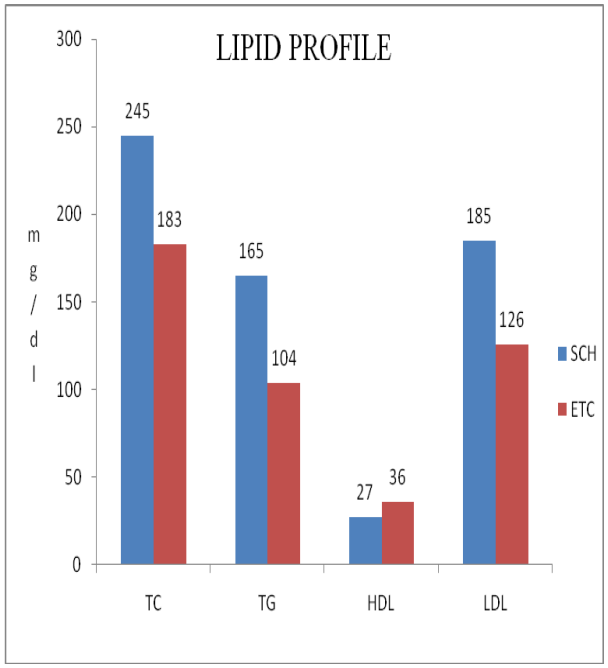

Fig. 1

Fig. 1 showing mean lipid profile of study group. Subclinical Hypothyroid cases showing significantly higher levels of Triglycerides, Low density lipoprotein cholesterol levels, Total Cholesterol and High density lipoprotein cholesterol levels.

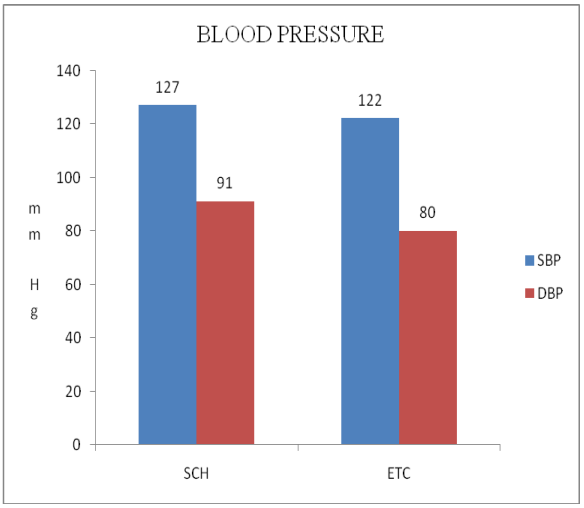

Fig. 2

Fig. 2 showing mean BP in study group. Subclinical Hypothyroid cases showed significantly higher Mean systolic BP and diastolic BP as compared to euthyroid.

Table 2: Percentage of parameters for cardiovascular disease in SCH patients

Variable	SCH Patients (%)	Euthyroid controls (%)
TC (> 200 mg/dL)	83.3	30
TG (> 150 mg/dL)	73.3	10
LDL (> 130 mg/dL)	95	33.3
HDL (< 30 mg/dL)	62.02	14.03
SBP (≥ 140 mm Hg)	6.07	0.5
DBP (≥ 90 mm Hg)	76.08	0.3

Table 2 shows the percentage of cases with higher blood pressure and lipid profile parameters in the study group. The percentage of subjects having hypertension (>140/90 mm Hg), elevated TC (>200.00 mg/dL), LDL (130> mg/dL), TG (150> mg/dL), and decreased HDL (<30 mg/dL) was higher in SCH patients than in euthyroid.

Discussion

The frequency of occurrence of Subclinical Hypothyroidism is high as compared to frank hypothyroidism. Although the view that frank hypothyroidism causes secondary hyperlipidemia and promotes atherosclerosis has been generally accepted,[11] studies examining the relationships between hyperlipidemia, atherosclerosis, and SCH have yielded less convincing results. In recent times subclinical hypothyroidism is being diagnosed more frequently than overt hypothyroidism.[12]

Despite that subclinical hypothyroidism being more common, its clinical significance is still debatable. Still there is controversy pertaining to

routine screening of SCH so as to prevent it from progressing to overt hypothyroidism.[3] Subclinical hypothyroidism is found to be related with increased risk for atherosclerosis. Coronary heart disease (CHD) in subclinical hypothyroidism reports are controversial.[4]

The present study revealed that subclinical hypothyroid cases showed significant increased levels for serum TG, High and Low density lipoprotein cholesterol, Thyroid stimulating hormone, Total Cholesterol levels, Systolic & Diastolic BP where as no significance for T4 levels compared to the euthyroids.

Zoe Efstathiadou et al[13] showed significantly increased serum total cholesterol and Low density lipoprotein cholesterol in subclinical hypothyroidism compared to euthyroids. Our study also showed the similar results. Our study is in accordance with study done by Rafael Luboshitzky et al,[14] who demonstrated that the percentage of subjects with increased total cholesterol, triglycerides, LDL-C were more in SCH as compared euthyroid controls. Study done by Nadia Caraccio[15] showed the same conclusion about the Total cholesterol and Low density lipoprotein cholesterol in subclinical hypothyroidism as concluded in our study. Total cholesterol and High density lipoprotein cholesterol were elevated in several reports, but were not different from those in the controls in most studies.[16]

Recent evidences show increased triglyceride levels are important risk factor for atherosclerosis. Stephen Rahula et al[17] showed that triglyceride levels were significantly increased in subclinical hypothyroid cases.our study is in accordance with study done by stephen Rahula indicating that Triglyceride levels are increased in subclinical hypothyroidsm. Several studies, have reported variable and inconsistent increase in total cholesterol, Low density lipoprotein cholesterol, higher and inconsistent changes in serum HDL-C. Two large population based studies were done in this aspect, Whickhm survey and NHANES III. SCH was not associated with hyperlipidemia, in Whickham survey,[12] where as NHANES III reported, higher levels of mean cholesterol in SCH subjects as compared to euthyroids but no difference was reported in LDL-C or HDL-C.[18] Bindels et al.[19] estimated that an increase of in serum TSH was linked with a rise in serum cholesterol in women.

Present study showed SCH cases had significantly higher systolic and diastolic blood pressure than the euthyiods. In our study we found that 6.07% of SCH patients had increased systolic blood pressure and 76.08% had increased diastolic blood pressure compared with 0.5% and 0.3% respectively in the euthyroids. Rafael Luboshitzky[14] showed similar increased percentage of elevated systolic and diastolic blood pressure were seen in sub clinical hypothyroidism as compared to euthyriods.

Hence it shows correlating evidence of SCH with dyslipidemia and hypertension as an important indicators of disease risk for cardiovascular diseases in future.

It is importance to evaluate subclinical hypothyroidism, and coexisting dyslipidemia and hypertension which can lead to cardiovascular disease. The increasing rate of chances of subclinical hypothyroidism to convert into frank hypothyroidism justifies it to be treated.

Conclusion

Our study reveals that significantly higher levels of serum Triglycerides, TSH, Total Cholesterol, Low Density Lipoprotein-C, systolic and diastolic BP and lower levels of High Density Lipoprotein-C are seen in subclinical hypothyroidism as compared to euthyroids. Indicating hypertensive and dyslipidemic state associated with SCH which can lead to cardiovascular disease. Suggesting subclinical hypothyroidism association with risk factors of cardiovascular disease.

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