Original Article

Hypothyroidism

Evaluation of Serum Triglyceride and Cholesterol in Subclinical Hypothyroidism

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ABSTRACT

Objective: This study was aimed to evaluate the effects of subclinical hypothyroidism on lipid profile with special reference to total cholesterol and triglyceride levels.

Study Design: Analytic study

Place and Duration Study: This study was carried out at the Punjab Institute of Nuclear Medicine (PINUM), Faisalabad and IMBB, university of Lahore from January 2011 to September 2011. (Eight months)

Materials and Methods: 100 female patients of age ranges from 20-50 years having subclinical hypothyroidism (SCH) and 20 euthyroidsubject of same age and sex (control) were included in this study. Serum FT_4, FT_3, TSH, total cholesterol and triglyceride of subclinical hypothyroid patients and control group were determined.

Result: In subclinical hypothyroid patients total cholesterol were significantly increased as compared to euthyroid group. Serum TSH and total cholesterol showed positive correlation. Serum triglyceride did not significantly increased in SCH.

Conclusion: The total cholesterol level elevated in SCH. This increases the risk of atherosclerotic coronary artery disease (CAD) in subclinical hypothyroid patients.

Key Words: Subclinical hypothyroidism (SCH), Free thyroxine (FT_4), Free triiodothyronine (FT_3), Thyroid stimulating hormone (TSH), Cholesterol, Triglyceride

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INTRODUCTION

Subclinical hypothyroidism is defined as increased Thyroid Stimulating hormone (TSH) levels from normal reference range but free thyroxine (FT_4) levels and triiodothyronine (T_3) levels are within normal range[1].

Subclinical hypothyroidism is also defined with serum TSH concentration above the clinically defined limits of the reference range when serum free T_4 (FT_4) concentration is within its reference range. The Third National Health and Nutrition Examination Survey[2], who examined the serum TSH value in a "disease free" subset (n = 13344) of an ethnically diverse reference population, aged 12 years and older. This selected population showed, the normal serum TSH in between 0.45mIU to 4.12mIU. The reference range varied with age, sex and ethnic groups but as the differences were small, there was no need to adjust the reference value.

The reference range of normal serum TSH concentration was 0.45mIU to 4.5m IU/L and FT_4 concentration is 0.8mg/dL to 2.0 mg/dL[1].

Patients showed few or no definite clinical signs or symptoms of hypothyroidism with subclinical form. The subclinical hypothyroidism is based on laboratory diagnosis[3].

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Subclinical hypothyroid patients having an elevated TSH level showed value of TSH lower than 10 m IU/L in 75%. About 20% patient were taking thyroid medications having subclinical hypothyroidism[4].

The progression from subclinical hypothyroidism to overt hypothyroidism was 2% to 5%. The overt hypothyroidism may be defined as a low serum FT_4 concentration with elevated serum TSH concentration[5,6].

In individuals who were not taking thyroid hormone treatment, serum TSH returned to normal after 1 year of follow-up in approximately 5% but remained elevated in the remainders[5].

It was observed that an elevated thyrotropin level was associated with higher serum cholesterol level and LDL-cholesterol[7,8].

Patient with subclinical hypothyroidism have a high rate of progression to overt, symptomatic hypothyroidism[9].

Subclinical hypothyroid patients show elevated total cholesterol, total triglyceride, LDL-cholesterol but decreased HDL- cholesterol. This increases the risk of developing atherosclerosis.[10]

There was significant reduction in total cholesterol and LDL-cholesterol levels with L-thyroxine treatment in patient with subclinical hypothyroidism.[11]

There was linear and significant increase in total cholesterol, triglyceride and LDL-cholesterol with

increasing TSH. HDL-cholesterol also showed linear decrease with TSH increase.[12]

The prevalence of subclinical hypothyroidism and its association with coronary heart disease was studied. This showed no association between cardiovascular mortality and subclinical hypothyroidism.[13]

The CAD and mortality due to CAD is more in subjects with higher TSH level (> 10ml U/L). This risk increases by increasing TSH. Subclinical hypothyroid patients showed increased risk of CAD in comparison to euthyroid subjects.[14]

It was observed that thyroid dysfunction were more common in women. The serum cholesterol and triglycerides levels were found elevated in hypothyroid patients.[15]

Thyroid hormones affect lipid metabolism. In Subclinical hypothyroidism & overt hypothyroidism, the increased cholesterol levels are important risk factor in developing coronary heart diseases.[16]

Total cholesterol and HDL-C were significantly higher in females in a gender specific comparison in Subclinical hypothyroid patients. SCH were more common in female.[17]

MATERIALS AND METHODS

This study was conducted at Punjab Institute of Nuclear Medicine, Faisalabad. Two groups A and B were included in study. Group "A" included the 100 female patients of SCH with age range from 20-50 years diagnosed on the basis of history, clinical examination and relevant laboratory findings from PINUM OPD.

The second group "B" comprised of 20 normal euthyroid subjects of same age and sex as in group A having normal FT_3, FT_4 and TSH for comparison.

Measurement of TSH: The serum thyroid stimulating hormone (TSH) was determined quantitatively by enzyme immunoradiometric assay method, using commercially available kit (TSH IRMA kit) by Beckman Coulter[18].

We added the 100 ml of calibrator, control or sample and 100 ml of tracer to coated tubes and mixed.

Then added the 100 ml of tracer to two additional tubes. We incubated the content for one hour at $18\text{-}25^0$ after shaking (280 rpm). After that we aspirated the contents of tubes except 2 tubes containing tracer only and washed twice with 2 ml of wash solution.

Finally counted bound cpm (B) and total cpm (T) for 1 min. Results were obtained from standard curve by interpolation. The curve serves for the determination of TSH concentration in samples measured at the same time as the calibrators.

Measurement of Serum FT4: Serum thyroxine (FT4) was determined quantitatively by radio immunoassay technique, using commercially available kit (FT4 RIA Kit) by Beckman coulter[19].

We added 25 ml of calibrator or sample, 400 ml of tracer and 100 ml of ligand to coated tubes successively and then mixed. Also added 400 ml of tracer to two additional tubes to obtain total CPM.

Then incubated for 60 min at $18\text{-}25^oC$ with shaking (350 rpm). We aspirated the contents of tube except two tubes containing 400 ml of tracer only. At last we counted the bound cpm (B) and total com (T) for 60 minutes.

Results were obtained from the standard curve by interpolation. The curve serve for the determination of FT4 concentration in samples measured at the same time as the calibrator.

Measurement of Serum FT3: Serum triiodothyronin (FT3) was determined quantitatively by radioimmunoassay technique using commercially available kit (FT3 RIA Kit) by Beckman coulter[19].

We added 100 ml of calibrator or sample and 400 ml of tracer to coated tubes successively and then mixed. Also added 400 ml of tracer to two additional tubes to obtain total CPM.

Then incubated for 120 min at $18\text{-}25^oC$ with shaking (350 rpm). We aspirated the contents of tube except two tubes containing 400 ml of tracer only. At last we counted the bound CPM (B) and total com (T) for 60 minutes.

Results were obtained from the standard curve by interpolation. The curve serve for the determination of FT3 concentration in samples measured at the same time as the calibrator.

Serum Cholesterol: Total cholesterol will be estimated by CHOD PAP Method[20,21] by using spectrophotometer. The commercially available kit for determination of cholesterol by DiaSys was used. The standard laboratory procedure and instruction of the manufacturer were observed.

Serum Triglycerides: Triglyceride will be determined by GPO-PAP Method[22,23] by using spectrophotometer. The commercially available kit for determination of triglyceride by DiaSys was used. The standard laboratory procedure and instruction of the manufacturer were observed.

Statistical Analysis: Results are expressed as mean±SD. T-test was applied for comparison of cholesterol and triglyceride, TSH, FT3, FT4 between subclinical hypothyroid patients and euthyroid subjects. Pearson's correlation was used to establish correlation between TSH and cholesterol & triglyceride. The statistical program used was SPSS[24]. $P < 0.05$ was considered statistically significant.

RESULTS

Subclinical hypothyroid patients showed significantly elevated TSH levels as compared to euthyroid subjects ($P<0.05$). The value of TSH in subclincial

hypothyroid patients were higher than the reference value.

The cholesterol level of subclinical hypothyroid patients was significantly higher (P<0.05) compared to that of euthyroid group and was greater than the reference value. The subclinical hypothyroid patients showed insignificant increase in triglyceride (P<0.05).

Table No.1: Statistical analysis and t-test of Cholesterol, Triglycerides, FT_4, FT_3 and TSH insubclinical hypothyroid and euthyroid subject (control)

Parameters	Group	Mean±SD	P. Value
Cholesterol	Sub clinical Hypothyroidism	222.11±28.968	0.000*
	Control	140.30±15.698	
Triglyceride	Sub clinical Hypothyroidism	118.26±17.060	0.77^{NS}
	Control	111.05±13.012	
FT_4	Sub clinical Hypothyroidism	14.545±2.582	0.000*
	Control	17.214±2.235	
FT_3	Sub clinical Hypothyroidism	3.267±0.5935	0.001*
	Control	3.900±0.733	
TSH	Sub clinical Hypothyroidism	10.595±6.270	0.000*
	Control	1.453±0.698	

***Significant as P<0.05 NS = Non significant**

The results of Cholesterol, Triglycerides, FT_4, FT_3 and TSH are given in table 1 as mean±SD and P value in subclinical hypothyroid and euthyroid subjects.

The average of cholesterol in patients of subclinical hypothyroidism was 222.11±28.968 mg/dl and average of cholesterol in control group was 140.30±15.698 mg/dl. There is significant difference of cholesterollevel in both groups.($p < 0.05$)

The average of triglycerides in patients of subclinical hypothyroidism was 118.26±17.060mg/dl and average of triglycerides in control group was 111.05±13.012 mg/dl. There is insignificant difference of triglycerides level in both groups.($p < 0.05$)

The average of FT_4 in patients of subclinical hypothyroidism was 14.545±2.582pmol/L and average of FT_4 in control group was 17.214±2.235pmol/L. There is significant difference of FT_4 level in both groups within normal limits.($p < 0.05$)

The average of FT_3 in patients of subclinical hypothyroidism was 3.267±0.5935 pmol/L and average of FT_3 in control group was 3.900±0.733 pmol/L. There is significant difference of FT_3 level in both groups within normal limits.($p < 0.05$)

The average of TSH in patients of hypothyroidism was 39.198±14.732mIU/L and average of TSH in control group was 1.508±0.643 mIU/L. There is significant difference of TSH level in both groups. ($p < 0.05$).

There is a significant positive correlation between TSH and cholesterol in subclinical hypothyroid patients i.e. with increase of TSH level, the level of cholesterol also increases.

The FT_4 showed insignificant negative correlation with cholesterol. The decreased level of FT_4 showed insignificant elevated cholesterol.

There is insignificant positive correlation between TSH and triglycerides in subclinical hypothyroid patients.

The FT_3showedinsignificant negative correlation with cholesterol and insignificant positive correlation with triglyceride.

Table No.2: Correlation between TSH, FT_4, FT_3 and LDL & HDL in subclinical Hypothyroidism

	Cholesterol	Triglyceride
TSH Pearson Correlation	0.544**	0.055
Sig (2 tailed)	0.000	0.587
FT4 Pearson Correlation	--0.066	-0.264
Sig (2 tailed)	0.512	0.108
FT3 Pearson Correlation	-0.055	0.022
Sig (2 tailed)	0.589	0.828

***=Correlation is significant at the 0.05 level P<0.05**
**** = Correlation is significant at the 0.01 level P<0.05**

DISCUSSION

The present research work was aimed to check the significance of cholesterol and Triglyceride, FT_4, FT_3 and TSH levels in diagnosed patients of subclinical hypothyroidism. One hundred subclinical hypothyroid patients (Group A) enrolled in this study along with twenty euthyroid subjects (Group B) for comparison.

In the present research significant difference (P<0.05) was found in cholesterol of euthyroid subjects (control) and subclinical hypothyroid patients. The cholesterol is higher (222.11±28.968) in subclinical hypothyroid patients as compared to euthyroid (140.30±15.598)

The Triglyceride level in subclinical hypothyroid patients also insignificantly higher (118.26±17.060) as compared to control (111.05±13.012).

The finding of present research had correlation with the past work of Asvoldwho observed the linear and significant increase in serum cholesterol, LDL-cholesterol and Triglyceride with increasing TSH.[12]

It was observed that LDL cholesterol and total cholesterol level were higher in subclinical hypothyroid patient[25]. The elevation in serum cholesterol and LDL- cholesterol was associated with the increase in TSH.[4] This support the findings of present study.

The results contradict with the conclusion by Diekman,that there was no significant decrease in total

cholesterol and LDL-C after replacement therapy with L-thyroxine in SCH patients[26].

The results obtainedby Hueston and Pearson favour the results of present research i.e. SCH have higher total cholesterol and triglyceride[27].

In present study higher TSH level in subclinical hypothyroidism showed positive significant correlation with Cholesterol. The higher Cholesterol level may be responsible for atherosclerotic coronary artery disease.

CONCLUSION

It was concluded through the present study that cholesterol increased in subclinical hypothyroidism. This may lead to atherosclerotic cardiac disease.

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