Thyroid Function Test, C- Reactive Protein And Blood Lipids In Subclinical Hypothyroidism Patients Reporting At Surgical Wards

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ABSTRACT:

Objective: To investigate the thyroid function, C-reactive protein (CRP) and blood lipid profile in the subclinical hypothyroidism (SH) patients in surgical wards and outpatient department.

Study design: Cross sectional study

Place and Duration: Department of surgery, Isra University Hospital from August 2014 to May 2017.

Materials and Methods: 100 subclinical hypothyroid cases and 100 controls were included according to inclusion and exclusion criteria. Serum TSH level > 6.2 (µIU /ml) with normal free T_4 and T_3 was considered as subclinical hypothyroidism. Venous blood was taken from ante cubital vein, centrifuged and processed. Sera were used for the assay of thyroid hormones, TSH, blood lipids and C-reactive protein. Data variables were analyzed by Statistix 8.0 (95% confidence interval) (P-value =0.05).

Results: Age in controls and cases was noted as 51.3±12.5 and 50.8±11.95 years respectively. SH cases show serum T_3, T_4 and TSH as 0.89±0.18 µg/dl, 4.96±0.85 µg/dl and 11.95±2.85 µU/ml respectively. Serum total cholesterol, triglycerides and LDLc were raised with concomitant low HDLc in SH cases. C- reactive protein in SH cases was 6.91±3.38 ng/ml compared to controls 2.56±1.51 ng/ml (P=0.0001). Serum TSH showed negative correlation with HDLc, serum T_3 and T_4.

Conclusion: The present study reports dyslipidemia with elevated inflammatory marker of C-reactive protein in subclinical hypothyroid patients.

Key words: Subclinical hypothyroidism, Dyslipidemia, C-reactive protein

INTRODUCTION:

Low normal thyroid function with minimal or no clinical symptoms is termed as subclinical hypothyroidism (SH).[1] It is biochemical rather than clinical diagnosis, characterized by raised thyroid stimulating hormone (TSH) levels, normal free T4 and asymptomatic patients. Raised TSH is a response to the decreased secretory capacity of thyroid gland this clinical entity is defined as SH[2] with few or no symptomatic characteristics of hypothyroidism. Absence of clinical symptoms is a hallmark of SH.[3] There are many cases of hypothyroidism which fall into the category of SH being very common among female subjects.[4,5] Thyroid function tests show normal free thyroxin (FT4) and triiodothyronine (T3) in the presence of raised serum TSH.[6] Dyslipidemia is a most common metabolic abnormality in hypothyroidism, similar may be the problem in the SH. Dyslipidemia is characterized by raised serum low density lipoprotein cholesterol (LDL-c), total cholesterol and triglycerides in the presence of low high density lipoprotein cholesterol (HDL-c), a condition which is considered as pro-atherogenic. It is speculated that the hypothyroid state causes low expression of LDLc receptors on liver cells. This casues defective removal of LDLc from blood, the result is a hyper-LDLc in blood.[7] This is still debatable and just a speculation. In SH, such metabolic abnormality does occur or not is debatable, as previous studies[8,9] reported no changed in blood lipids. However, other studies[10,11] reported dyslipidemia is evident in patients suffering from SH. Dyslipidemia is pro-atherogenic condition in itself with a tendency of ischemic coronary atherosclerotic disease. This needs further studies to gather the information. Dyslipidemia plays role in the pathogenesis of atherosclerosis and related vascular disorders, this may particularly be more dangerous in the SH patients.[11] C-reactive protein (CRP) is one of reliable inflammatory markers. CRP is known future predictors of atherosclerosis related vascular disease.[12] CRP has been used as risk factor for the coronary artery disease (CAD).[13] CRP with dyslipidemia may be more creative in predicting the vascular disorders in SH patients. However, some of previous studies[13,14] have produced conflicting results on the dyslipidemia and CRP in SH. Many cases of thyroid swellings present in the surgical wards and outpatient departments with abnormal thyroid function test.

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The present case control study was conducted to determine the lipid profile and C-reactive protein of subclinical hypothyroid cases at our tertiary care hospital.

SUBJECTS AND METHODS:

The present case control study was conducted at the Department of surgery, Isra University Hospital after ethical approval was taken. The study covered duration from August 2014 to May 2017. Over the study duration, many cases of thyroid lesions were evaluated for the inclusion and exclusion criteria. Finally, a sample of 100 cases of subclinical hypothyroidism (SH) was isolated for the study. Subjects were selected by non- probability purposive sampling. Subclinical hypothyroidism was defined as serum TSH > 6.2 µIU /ml (normal serum T_4 and T_3).[15] Age >20 and <50 years and both male and female were included. Diagnosed cases of overt hypothyroidism were strictly excluded. Patients taking thyroxine therapy, pregnant women, diabetics, systemic hypertension and those smoking were also excluded. Age and gender matched controls were also inducted. Cases and control subjects were interviewed. Confidence was taken by informing them about the purpose of study. They were informed that the study will cause no harm or financial burden on them. The participants were informed that the study needs biodata, physical examination and blood samples for biochemical analysis. Willing participants were further asked that they can ask any issue if they are thinking of it about any financial loss or physical harm. Volunteers were asked to sign the research consent form. Complete biodata and findings of physical examination were noted. Thyroid gland was examined. Systemic blood pressure was checked by mercury sphygmomanometer and body weight on weighing scale. Information was noted in a pre- structured designed proforma. This was followed by blood sampling. Ante-cubital fossa was sterilized with alcohol swab. Tourniquet was applied above cubital fossa to engorge the veins. 10 ml venous blood was taken from ante- cubital vein. Sera were separated by blood centrifugation (3000 rpm for 10 minutes). Thyroid function test (TSH, T_3 & T_4) and C-reactive protein (CRP) were assayed by ELISA assay kit. Lipids were analysed on chemistry analyzer using standard methods while LDLc was estimated by Friedewald's formula.[16] Signing consent form was mandatory. A structured proforma was used for data collection. Data variables were analyzed on Statistix 8.0. Continuous and categorical data variables were analysed by Student`s t-test and Chi square test respectively at 95% confidence interval (P-value =0.05).

RESULTS:

Mean ± SD age of controls and cases was 51.3±12.5 and 50.8±11.95 years respectively. Body weight, BMI, Systolic BP and Diastolic BP showed statistically non- significant differences between controls and cases. Cases showed serum T_3, T_4 and TSH as 0.89±0.18 µg/dl, 4.96±0.85 µg/dl and 11.95±2.85 µU/ml respectively. These were found statistically significant compared to controls (P=0.0001). Serum total cholesterol and triglycerides were raised in cases while HDLc was found low. C- reactive protein in cases was 6.91±3.38 ng/ml compared to controls 2.56±1.51 ng/ml (P=0.0001) (table 1). Serum TSH showed negative correlation with HDLc, serum T_3 and T_4 as shown in table 2.

	Controls	Cases	P-value
Age (years)	51.3±12.5	50.8±11.95	0.76
Body weight (kg)	76.3±10.89	71.4±14.53	0.108
BMI (kgm^{-2})	29.87±3.65	29.21±2.78	0.71
Systolic BP (mmHg)	120.9±10.5	120.5±9.80	0.83
Diastolic BP(mmHg)	76.6±11.5	77.5±10.55	0.96
Serum T_3 (µg/dl)	0.91±0.17	0.89±0.18	0.001
Serum T_4 (µg/dl)	5.45±2.35	4.96±0.85	0.0001
Serum TSH (µU/ml)	3.81±1.12	11.95±2.85	0.0001
Total Cholesterol (mg/dl)	193.5±16.5	237.5±11.5	0.0001
Triglycerides (mg/dl)	198.5±9.5	409.5±27.5	0.0001
LDL-cholesterol (mg/dl)	99.0±21.5	173.5±11.5	0.0001
HDL-cholesterol (mg/dl)	41.7±5.5	33.9±10.5	0.0001
C- reactive protein (ng/ml)	2.56±1.51	6.91±3.38	0.0001

Table 1. Demographic and laboratory findings of study subjects

	r-value	P- value
CRP (ng/dl)	0.616**	0.0001
Cholesterol	0.813**	0.0001
HDLc	-0.316**	0.0001
LDLc	0.671**	0.0001
Serum T_3	-0.275**	0.0001
Serum T_4	-0.339**	0.0001

**. Correlation is significant at the 0.01 level (2-tailed)

Table 2. Pearson`s correlation of serum thyroid stimulating hormone (TSH)

DISCUSSION:

The present study observed statistically significant differences of T3, T4, TSH, blood lipids and CRP between controls and SH cases ($P < 0.05$). This is the first study being reported form Surgical wards of a tertiary care hospital. The null hypothesis was rejected as significant difference was noted between the controls and SH cases. Mean ± SD age of controls and cases was 51.3±12.5 and 50.8±11.95 years respectively. Body weight, BMI, Systolic BP and Diastolic BP showed statistically non- significant differences between controls and cases. These findings are in agreement with previous studies.[17-19] SH cases showed very high serum TSH (11.95±2.85 µU/ml) with normal T_3 and T_4, the finding is in keeping with a recent study.[20] Serum TSH showed negative correlation with total cholesterol, LDLc, HDLc, serum T_3 and T_4 and CRP (table 2) in SH cases. Serum TSH showed significant rise in SH cases with dyslipidemia. The CRP is a risk factor for the coronary artery disease (CAD) [17] myocardial infarction (MI)[18] and rheumatoid arthritis (RA)[19] which is found high in SH cases in the present study. High CRP has been reported in overt hypothyroidism[21] the finding is consistent with the present study. In present study, serum total cholesterol, triglycerides and LDLc were raised with low HDLc, this is in contrast to previous studies.[21,22] However, other studies[23,24] had reported dyslipidemia similar to the present study. A previous study[25] reported low HDLc in hypothyroidism that is in agreement to present study. In present study, the C- reactive protein in cases was raised i.e. 6.91±3.38 ng/ml compared to controls 2.56±1.51 ng/ml (P=0.0001) (table 1). CRP is raised in inflammatory conditions.[26,27] Raised CRP of present study is in agreement with a previous study.[28] The findings indicates the subclinical hypothyroidism (SH) is associated with dyslipidemia and raised CRP which is a marker of inflammatory process. Serum TSH reveals positive correlation with CRP (r=0.616, p=0.0001) which is agreement with a recent study.[20] The HDLc, serum T_3 and T_4 showed inverse correlation with TSH in subclinical hypothyroid cases (Table 2). These findings are in agreement with previous studies.[29-31] The finding of dyslipidemia with raised CRP in subclinical hypothyroid cases is consistent with another previous study[32] which had reported similar observations. A previous study[33] the dyslipidemia with raised levels of high sensitivity CRP (hs-CRP) is a consistent risk factor for coronary artery disease in subclinical hypothyroid cases. Raised CRP levels in subclinical hypothyroid patients of present study is in concordance with another previous study.[34] The present study shows the subclinical hypothyroid patients are at increased risk of developing coronary artery disease and related vascular complications. Hence it is suggested the subclinical hypothyroid patients presenting at surgical wards and outpatient departments should be screened for the dyslipidemia and C-reactive protein for timely intervention in order to halt atherosclerotic pathologies. This will help prevent atherosclerosis and related morbidities in subclinical hypothyroid patients.

CONCLUSION:

It is concluded that the subclinical hypothyroidism is associated with dyslipidemia and inflammatory process. These patients should be screened for timely intervention for preventing the atherosclerosis related coronary artery disease. Further large scale studies are warranted to make guideline on dyslipidemia in subclinical hypothyroid patients for future prevention.

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