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Association of lipid abnormalities with thyroid dysunction in patients of subclinical hypothyroidism

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***Abstract*---**Background: Dyslipidemia is thought to associated with the risk of cardiovascular disease development. Overt hypothyroidism is associated with lipid abnormalities. However, the relationship between subclinical hypothyroidism (SCH) and pattern of lipid abnormalities is not well eastablished. The aim of this study was to find the lipid abnormalities in patients of subclinical hypothyroidism (SCH) and determine relationship between lipid level and TSH. Methods: Serum lipid levels of 92 patients with subclinical hypothyroidism (SCH) and 110 age and sex matched healthy controls were evaluated in this cross sectional case control study. Results: In this study total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) were significantly higher (p value<0.05) in patients with subclinical hypothyroidism (SCH) as compared to control group. Triglycerides (TG) and very low density lipoprotein cholesterol (VLDL-C) were also increased in these patients as compared to control but the difference was not statistically significant. High density lipoprotein cholesterol (HDL-C) was found to be marginally lower in these patients than control. Conclusions: Total cholesterol (TC) and low density lipoprotein (LDL-C) are higher in patients with subclinical hypothyroidism (SCH) as compared to healthy controls. Other lipid

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like Triglycerides (TG) and very low density lipoprotein cholesterol (VLDL-C) may be marginally raised whereas high density lipoprotein cholesterol (HDL-C) may be slightly reduced in these patients as compared to healthy control. There is also a positive correlation of LDL-cholesterol and TC with TSH level. As abnormal lipids are associated with development of cardiovascular diseases, lipid profile in these patients needs careful monitoring.

***Keywords*---**Antithyroid peroxidase antibodies, Thyroid stimulating hormone, Free thyroxine, Atherosclerosis, Euthyroid.

Introduction

Subclinical hypothyroidism (SCH) is the condition where serum thyroid-stimulating hormone (TSH) level is above the upper limit of normal despite normal levels of serum free thyroxine (FT4). Subclinical hypothyroidism or mild thyroid failure is a common problem, with a prevalence of 3% to 8% in the population without known thyroid disease.[2,3] Hypothyroidism is one of the important causes of abnormal lipid metabolism.[4,5] Patients with overt hypothyroidism are more likely to develop hypertension, cardiovascular disease, and atherosclerosis.[6] Lipid abnormalities in overt hypothyroidism includes raised total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG).[5] However the association between subclinical hypothyroidism (SCH) and dyslipidemia is still controversial. Changes in lipid profile in these patients have been highlighted in several studies.[7-10] Many researcher have reported significant increase in TC, and LDL-C and TG in patients with SCH.[11-13] Present study aimed to asses lipid abnormalities in patients of subclinical hypothyroidism (SCH) and determine the relationship between lipid level and TSH.

Methods

The study was a cross sectional case control study carried out at Uttar Pradesh University of Medical Sciences. 92 patients of subclinical hypothyroidism (case) and 110 healthy controls were recruited from OPD of the hospital. Study was conducted during December 2020 to February 2022. Study was startrd after taking permission from institute ethical committee. Informed consent was taken from all participants before including in study.

Inclusion criteria

For cases

Individuals with elevated d serum TSH level (greater than 5.5 μIU/mL), normal Free thyroxine (T4) (0.9-1.75 ng/dL) and normal free triiodothyronine (T3) (2.30-4.20 pg/mL) levels.

For control

Age and sex matched individual who have normal serum TSH level (0.35-5.5 μIU/mL), normal Free T4 (0.89-1.76 ng/dL) and normal free T3 (2.30-4.20 pg/mL) levels.

Exclusion criteria

Subjects having conditions/disorders known to influence on lipid profile like nephrotic syndrome, renal failure, obesity (BMI>30 kg/m^2), malnutrition (BMI<18.5 kg/m^2), smoking, alcoholism, and diabetes were excluded from study.[14,15] Patients on any prior medicine were also excluded from study. After detailed history and physical examination all participants were subjected to following investigations: complete blood count (CBC), fasting serum thyroid stimulating hormone (TSH), free thyroxin (T4), free triiodothyronine (T3), antithyroid peroxidase antibody (anti TPO), serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (VLDL-C), liver function test (LFT) (serum bilirubin, albumin, SGOT, SGPT and alkaline phosphatase), fasting plasma sugar, post prandial plasma sugar (2 hour after 75gm of oral glucose), kidney function test (KFT) (serum urea and creatinine), 24 hour urinary protein.

Free T4, free T3, TSH and Anti TPO were measured by chemiluminescent immunoassay. CBC was estimated using analyser sysmex xp-100 (transasia). LFT, KFT, and plasma Sugar were estimated using randox rximola clinical chemistry analyser. Direct estimation of TC, HDL-C levels and TG were done using randox rximola clinical chemistry analyser. Low and very low density lipoprotein cholesterols (LDL-C and VLDL-C) were calculated employing the Friedewald's formula.[16] Value of anti TPO >60U/mL were taken as positive.

Statistical analysis

Statistical analyses were done using IBM SPSS statistics version 23. Continuous variables were expressed as mean and standard deviation and categorical variables were shown as percentage or ratio. Unpaired t test and chi- squared test were applied for comparison of continuous and categorical variables respectively. Pearson correlation test was used to determine relationship between TSH and lipid level. Correlation was expressed as Pearson correlation coefficient(r). A 'p' value <0.05 were taken as significant.

Results

Baseline characteristics of case (SCH patients) and control is shown in Table 1. Comparison of lipid profile of case (SCH patients) and control is shown in Table 2 Correlation analysis of total cholesterol (TC) and low density lipoprotein (LDL-C) with TSH is shown in Figure 1and 2 respectively.

Table 1: Baseline characteristics of case (SCH patients) and controls.

	CASE	CONTROL	P VALUE
AGE	26.30±6.55	25.87±6.79	0.772
SEX(M:F)	10:82	12:98	0.654
BMI (KG/M^2)	24.76±1.20	25.25±2.12	0.32
TSH (μIU/ML)	7.23±1.87	2.29±0.74	<0.001
FREE T4 (NG/DL)	0.95±0.04	1.45±0.06	<0.001
ANTI TPO+(%)	52.24	28.62	<0.001

Table 2: Comparison of lipid profile of case (SCH patients) and controls.

LIPIDS(MG/DL)	CASE	CONTROL	P VALUE
TC	182.11±25.79	178.67±21.29	0.001
LDL-C	106.38±14.49	95.63±19.25	0.001
TG	145.32±50.91	141.68±21.32	0.214
VLDL-C	29.063±9.03	26.936±8.24	0.339
HDL-C	46.70 ±11.68	56.02 ±9.48	0.318

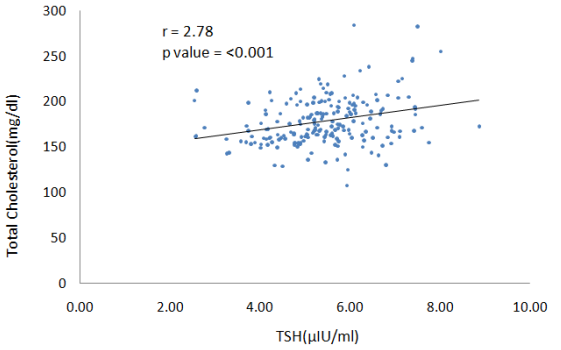

Fig. 1. Scatter plot depicting correlation of Total cholesterol with thyroid stimulating hormone(TSH),(r = correlation coefficient)

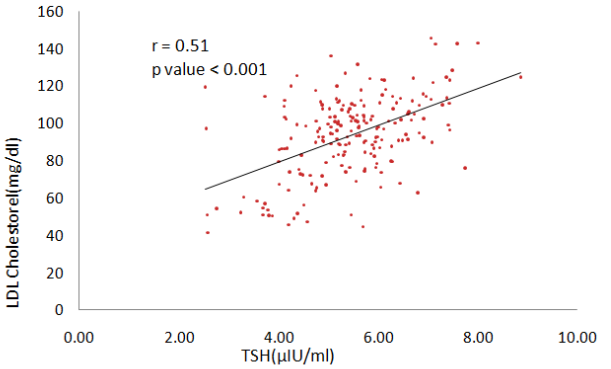

Fig. 1. Scatter plot depicting correlation of LDL cholesterol with thyroid stimulating hormone (TSH),(r = correlation coefficient)

Discussion

Dyslipidemia is thought to increase the risk of cardiovascular disease development.[17,18] Overt hypothyroidism is associated with lipid abnormalities.[19,20] However, the relationship between subclinical hypothyroidism (SCH) and lipid abnormalities is still unclear. Among 8586 adults from the National Health and Nutrition Examination Survey III database, SCH was not associated with abnormalitiesin TC, LDL-C, TG, or HDL-C after adjustment for age, race, sex, and using lipid- lowering drugs.[21] Vierhapper et al reported that there were not much differences in serum TC, LDL-C,HDL-C, or TG between patients with SCH and the euthyroid control group.[22]

However, in our study TC and LDL-C were significantly higher (p value <0.05) in SCH patients as compared to control group. TG and VLDL-C were found to be increased in SCH patients as compared to control group but the difference was not statistically significant. HDL-C was marginally lower in SCH patients than healthy control (Table 2). Laway et al also found significantly high Mean serum total cholesterol (TC), triglycerides (TG) and very low-density cholesterol (VLDL-C)

in patients with SCH as compared to controls (P<0.05).[23] Similarly Asranna et al also reported significantly higher Mean total cholesterol and mean LDL-C levels in SCH as compared to controls; however they observed that there was no significant difference in the mean HDL-C, VLDL-C, and TG between SCH and controls.[24] Similarly Bandyopadhyay et al reported significantly elevated TC and LDL-C in SCH patients of age group 40-50 year. They also found high TG in SCH patients in same age group.[25] Guntaka et al also found significantly increased TC and LDL-C in SCH subjects compared to control.[26] Marwaha et al also reported significantly higher Serum total cholesterol (TC), and LDL-C in adult patients of SCH with TSH >10mIU/L compared to controls.[27] Among 25862 participants in a health fair in Colorado, fasting TC, TG, and LDL-C levels were significantly greater in patients with SCH than those euthyroid subjects.[28] Unlike our study Lai et al reported significantly higher TG and lower HDL-C in patients with SCH than euthyroid individuals in their study on 1534 Chinese adults.[29] In our study LDL-C and TC were positively correlated with TSH level (p value<0.05) (Figure 1 and 2) in patients of subclinical hypothyroidism.. Santi et al also reported a positive correlation of LDL-C and TC with TSH such patients.[30]

Conclusion

Patients of SCH may have higher TC and LDL-C than euthyroid individuals. Other lipid like TG, VLDL-C may be marginally increased whereas HDL-C may be slightly reduced in these patients as compared to euthyroid individuals. There is also a positive correlation of LDL-C and TC with TSH level. As abnormal lipids are associated with development of cardiovascular diseases, lipid profile in these patients require careful monitoring.

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