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Original Article

Serum Lipid Status in Subclinical Hypothyroidism

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Abstract

Introduction: Hypothyroidism, a thyroid deficient state, influences various metabolic pathways of our body. Subclinical hypothyroidism (SCH) is a condition of decreased thyroid stimulating hormone (TSH) secretion and presents with no significant clinical symptoms. The burden of SCH is increasing in the country with increasing iodine deficiency. Various studies have shown conflicting results regarding dyslipidemia in SCH, but many others have supported the finding of increased total cholesterol (TC), Low-density lipoprotein (LDL), Triglycerides (TGs), and very LDL (VLDL) in subclinical hypothyroid subjects when compared with euthyroid patients.

Materials and Methods: This study was conducted on 100 patients of SCH and 100 euthyroid. After 12 h of fasting venous, blood sample was collected from each participant and analyzed for thyroid profile (TSH, fT3, and fT4) and lipid parameters (TC, LDL, TG, VLDL, and HDL).

Results: TC, TG, and VLDL were significantly higher in SCH patients when compared to that of the control subjects ($P < 0.0001$). The mean value of TC/HDL and LDL/HDL ratio shows a significant difference, while mean value of HDL does not show significant difference between SCH patients and control subjects. All the lipid parameters were correlated with TSH values in SCH patients, using Pearson correlation coefficient, showing highest positive correlation low-density lipoprotein cholesterol (r=0.252) with TSH values.

Conclusions: Dyslipidemia is a more common in SCH compared to controls. Furthermore, there is TSH dependent increase in TC, LDL, VLDL, and TG levels. Regular screening of the society for the presence of thyroid disorder and dyslipidemia forms an important aspects in management of thyroid diseases.

Key words: Dyslipidemia, Euthyroid, Hypothyroidism, Metabolic, Subclinical hypothyroidism

INTRODUCTION

Thyroid disease is one of the chronic non-communicable diseases which is being increasingly diagnosed with greater awareness. This disease may result from either hyper or hyposecretion of tri-iodothyronine (T3) and thyroxin (T4) from thyroid gland. Hypothyroidism is found to be a common health issue in India, as well as in the worldwide, affecting women population predominantly though male one is not spared of it. It has been estimated that approx. 200 million people are at the risk of development of iodine deficiency disease in our country.[1] OH is defined as a combination of high thyroid stimulating hormone (TSH) with low free thyroxine (fT4), while subclinical hypothyroidism (SCH) is defined as a combination of high TSH with normal fT4 levels.[2]

Among the elderly people, the incidence of SCH is more common in women than men, almost, twice.[3] Worldwide prevalence of SCH is found to be 7.5-8.5% in women and 2.8-4.4% in men.[4] According to an Indian epidemiological study prevalence of SCH is 8.73% in females and 7.17% in males.[5] Patients of SCH are mostly asymptomatic or have minimal symptoms. Thus, SCH is solely a laboratory diagnosis.[6] Although clinical diagnosis of thyroid dysfunction is suspected by the presence of a small swelling of the thyroid gland.

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Due to the effects of thyroid hormones on nearly all major metabolic pathways, the disease is associated with various metabolic abnormalities. It is well known that thyroid hormones and TSH affects synthesis, fate, and mobilization of lipids.[7] Overt hypothyroidism (OH) leads to an increase in plasma cholesterol levels is well known.[8] But in various previous studies, total cholesterol (TC), triglycerides (TGs) and low-density lipoprotein (LDL) have been shown to be elevated in SCH patients.[9,10] On the contrary, do not support this finding.[11-13] Dyslipidemia is considered to be an important global health problem, particularly in the elderly population. Traditionally, it is considered a "natural phenomenon" with its high prevalence among elderly people. SCH is one of the most important risk factors for dyslipidemia.[14] Thyroid hormones are involved in the expression of enzymes of lipid metabolism, thus, showing the development of qualitative and quantitative changes in thyroid diseases. Other metabolic abnormalities including hypertension, insulin resistance, and oxidative stress, which are themselves risk factors for other diseases, also coexists with dyslipidemia. Hence, Caparevic *et al.*, in his studies, observed that initial treatment of SCH patients with thyroxine may prevent the disease progression to OH, and slow down the progression of coronary heart disease, because of its beneficial effects on lipids.[15] Thus, it may be a good practice to screen patients with hypothyroidism for evidence of metabolic syndrome and in preventing various other complications. The screening and treatment for SCH should be done as early as possible to prevent its adverse effects on lipid metabolism.

Hence, this study was aimed to estimate the levels of lipid parameters in patients with SCH and to see their relationship with TSH values.

MATERIALS AND METHODS

A case-control study was conducted in the Department of Clinical Biochemistry, IGIMS, Patna. Patients of 35 years and above belonging to both sexes, attending the Outpatient Department of Endocrinology, IGIMS, Patna, having one or more clinical manifestations of hypothyroidism, e.g., fatigue, weakness, loss of strength, loss of stamina, weight gain, coarse dry hair, dry, rough and pale skin, hair loss, cold intolerance, muscle cramps, frequent muscle aches, constipation, depression, irritability, memory loss, and in women abnormal menstrual cycle were recruited for the study.

These patients were screened for fT3, fT4, and TSH. 100 cases with raised TSH but normal fT3, fT4 were included in the study and evaluated further for lipid profile pertaining to TC, TGs, High density lipoprotein cholesterol (HDL), and Low density lipoprotein-cholesterol (LDL-C). These were then compared with that of the 100 healthy controls of the same age and sex.

Under all aseptic and antiseptic precautions 5 ml blood sample after 12 h of fasting was drawn from the median cubital vein. Thyroid profile was estimated by Beckman Coulter assess 2 chemiluminiscense and serum TC, TG, LDL, and HDL by fully automated auto-analyzer AU 400 in both groups. Quality controls were done before analyzing all the parameters. Methods of estimating parameters: TC: Cholesterol oxidase - Peroxidase (POD) enzymatic method, TG: GPO-POD enzymatic method, HDL: Homogeneous enzymatic method.

Inclusion Criteria

About 100 newly diagnosed and untreated cases for SCH.

Exclusion Criteria

Known hypothyroidism cases, thyroidectomy cases, patient with external radiation, previous radioactive iodine therapy, consumption of drugs known to cause SCH, primary or secondary dyslipidemia, patients with diabetes mellitus, patients with other systemic illness, renal and hepatic failure cases, patients on statins, oral contraceptive pills and other medications that alter thyroid functions and lipid levels led to exclusion from the study. Pregnancy also accounted for exclusion from the study.

Statistical Analysis

Statistical analysis was performed using Graph pad Prism 5.0. Data obtained were presented as mean ± SD. One-way analysis of variance (ANOVA) was applied to the result data of different groups of patients. Correlation of TSH with lipid parameters was done by Pearson correlation coefficient.

Results of the study were discussed at 95% confidence interval; interpretation of the test results was done according to p value ($P < 0.05$ - significant and $P \geq 0.05$ - not significant).

RESULTS

This study consists of 100 patients of SCH and 100 euthyroid patients. SCH group includes 55% of females as the majority while euthyroid group includes 77% males as majority (Figure 1). The mean age of the SCH subjects was 44.18 ± 7.12 years while that of the euthyroids was 45.93 ± 9.66 years ($P = 0.0167$). Serum TSH was given as 8.06 ± 2.01 μg/ml and 2.79 ± 1.07 μg/ml in SCH and euthyroid patients respiratory with $P < 0.0001$. Levels of serum fT3 and fT4 were within the normal reference range and does not show a significant difference (Table 1).

Mean values of serum TC, TG and very LDL (VLDL) were significantly higher in SCH patients when compared to that of the control subjects ($P < 0.0001$) (Figure 2). Furthermore, mean value of LDL-C was higher in SCH patients ($P = 0.0205$).

Mean value of TC/HDL and LDL/HDL ratio show significant difference, while mean value of HDL does not show significant difference between SCH patients and control subjects (Table 2).

SCH patients were randomly divided into three age groups: Group-I (Age 36-44 years), Group-II (Age 45-54 years), and Group-III (Age 55-65 years). Values of lipid parameters among these groups were compared by one-way ANOVA (Table 3). The value of all the lipid parameters were correlated with TSH values in SCH patients, using Pearson correlation coefficient. Among all lipid parameters, LDL-C (r=0.252) shows highest positive correlation with TSH values (Table 4).

DISCUSSION

Thyroid disorders are among the most common endocrine disorders and usually alter lipid metabolism. In that SCH is more common than OH. It is being diagnosed more frequently with great awareness than OH these days.[3] Pirich *et al.* reported an incidence of 1.1% for newly diagnosed SCH and no case of OH.[10] Jung *et al.*, in his studies, reported a high incidence of SCH (0.64%) than that of OH (0.16%).[16] Similarly, Ravishekhar *et al.*[17] reported the prevalence of SCH as 8.29%, and Tehrani *et al.*[18] noted 21.2% of SCH cases in reproductive age group women. In our study, mean age of the SCH patients was 44.48 years. This finding was more or less similar with that of Raza Azad *et al.*[19] and Sadariya *et al.*[20] Hallowell *et al.* showed max. Incidence of SCH in 40-60 years of age.[21] In this study, SCH patients comprises 55% women and 36.7% men, which shows that SCH is more common in women than in men. This finding was consistent with that of many other studies.[20,22,23] Sadariya *et al.*,[20] Sharma *et al.*,[22] and Arem *et al.*[25] reported mean TSH value more or less similar with our findings. This study shows increase in the values of all lipid parameters except HDL as compared to that of the euthyroids. This finding was similar with that of a study conducted by Laway *et al.*[9] According to Colorado study, patients with SCH had significantly higher TC and LDL-C concentrations when compared with euthyroid subjects.[4] Sadariya *et al.* found that levels of all lipid parameters were significantly increased in SCH patients except increase in HDL which was not statistically significant.[20] In our study, TC/LDL ratio was significantly increased. A similar finding was observed by various studies: Sadariya *et al.*[20] and Adriana Santi *et al.*[26] Contrary to our observations, National Health and Nutrition Examination Survey III reported no significant differences in lipid parameters in SCH subjects

Table 1: Baseline characteristics among the SCH and euthyroid patients

Parameters	SCH (*n*=100)	Control (*n*=100)	*P* value
Age (years)	44.48±7.12	45.93±9.66	0.0167
TSH (µgm/ml)	8.06±2.01	2.79±1.07	<0.0001
FT4 (ng/dl)	0.87±0.30	0.87±0.30	<0.0001
FT3 (pg/ml)	3.02±0.43	3.02±0.43	0.0007

TSH: Thyroid stimulating hormone, FT_4: Free thyroxine, FT_3: Free triiodothyronine, SCH: Subclinical hypothyroidism

Table 2: Comparison of lipid parameters between subclinical hypothyroid patients and euthyroid patients

Parameter	SCH (*n*=100)	Control (*n*=100)	*P* value
TC	214.60±62.15	135.30±33.71	<0.0001
LDL	161.15±47.11	94.27±28.63	0.0205
HDL	40.63±7.18	44.11±7.72	0.0006
TG	184.54±71.09	125.57±28.70	<0.0001
VLDL	38.53±19.30	25.73±6.90	<0.0001
TC/HDL	5.42±1.76	3.19±1.14	<0.0001
LDL/HDL	4.07±1.36	2.24±0.96	>0.10

TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, SCH: Subclinical hypothyroidism

Table 3: Comparison of study parameters in different groups

Parameter	Group A (36-44 years)	Group B (45-54 years)	Group C (55-64 years)	*P* value
Age	39.88±2.74	49.13±4.03	58.5±3.16	0.033
TSH	8.04±2.21	8.02±1.76	7.89±1.95	0.320
TC	208.71±57.88	220.22±67.94	213.83±46.40	0.344
LDL	152.85±46.61	174.44±48.04	157.31±25.98	0.190
HDL	39.89±7.94	41.45±6.23	42.77±3.93	0.043
TG	175.41±41.83	193.35±96.68	183.25±40.27	<0.0001
VLDL	38.65±7.94	38.77±19.24	32.21±9.61	0.112
TC/HDL	5.39±1.65	1.29±0.29	5.004±1.02	0.117
LDL/HDL	3.92±1.29	4.31±1.45	3.70±0.69	0.947

TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, TSH: Thyroid stimulating hormone

Table 4: Correlation of TSH with lipid parameters in subclinical hypothyroidism

Parameters	TSH (µgm/dl)	
	Correlation "r"	*P* value
TC	0.245	0.014
LDL	0.252	0.011
HDL	0.041	0.680
TG	0.098	0.331
VLDL	−0.037	0.714
TC/HDL	0.185	0.064
LDL/HDL	0.185	0.034

TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, TSH: Thyroid stimulating hormone

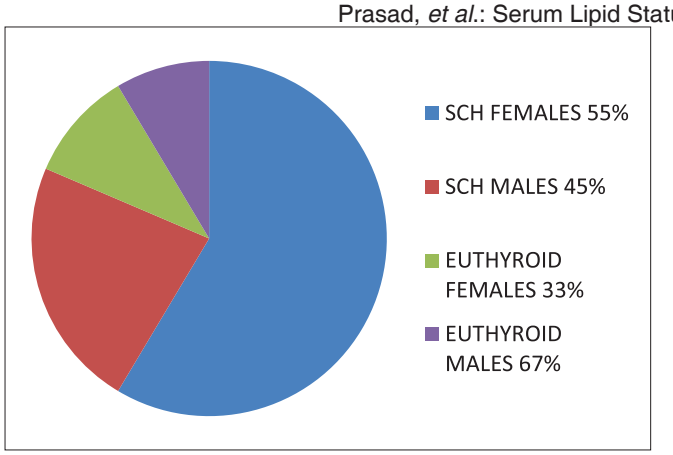

Figure 1: Sex wise distribution of patients

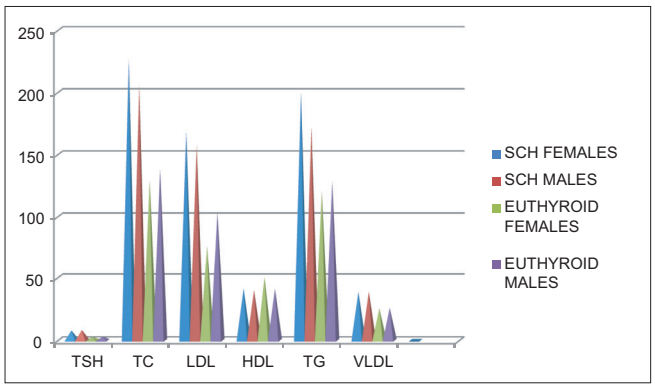

Figure 2: Lipid parameters in male and female of SCH and euthyroid patients

as compared to euthyroid individuals when adjusted for confounding variables.[11] In spite of high prevalence of SCH in elderly women Akbar *et al.* observed no increased risk of hypertension, hyperlipidemia or ischaemic heart disease in their sample.[27] The possible explanation for dyslipidemia here could be decreased LDL and IDL catabolism. This might either be due to reduction in cell surface receptor for LDL[28] or due to their decreased activity. This would increase TC and LDL concentration in blood. Moreover, decreased activity of hepatic lipase results in increase in the level of TG-rich lipoproteins; resulting in high concentration of VLDL and TG in blood.Thus, our study shows, TSH is positively correlated with values of all the lipid parameters estimated in SCH patients except VLDL, though it is not good correlation. Shashi *et al.*[29] found a similar correlation of TSH with values of TC, TG and LDL in SCH. In a study conducted by Ali Nouh *et al.*, it was shown that TSH was positively correlated with lipid profile values in cases with thyroid dysfunction.[30]

CONCLUSION

From this study, it is concluded that there is dyslipidemia which is secondary in patients of SCH and is particularly associated with increase in levels of TC, TG, LDL, VLDL, TC/HDL and LDL/HDL ratio. Due to apparently asymptomatic nature of illness, there is inconsistent reports about the prevalence of dyslipidemia in SCH among Indian Population. According to the American Thyroid Association, there is recommendation of routine screening of both sexes at 35 years of age, thereafter, every 5 years for the early diagnosis of SCH. This would, thus, aid in the early management of the disease. The findings of this study impress the fact that there is secondary dyslipidemia in SCH which may unfortunately contribute to risk of many disorders including cardio metabolic disorders. SCH is a matter of significant concern to the society as well as for the health-care professionals.

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