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LIPID PROFILE STATUS ASSESSMENT IN SUBJECTS WITH OVERT & SUBCLINICAL HYPOTHYROIDISMS AND WITHOUT HYPOTHYROIDISMS

Biochemistry

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ABSTRACT

Thyroid disorders are known to influence lipid metabolism. Overt and subclinical hypothyroidisms have an adverse effect on the serum lipid profile that may predispose to the development of atherosclerotic disease. In this comparative study, serums of 150 Subjects (50-OH, 50-SCH and 50-Controls) were analysed for Thyroid Profile and Lipid Profile. A significant increase in TC, TG, HDL-C, VLDL-C and LDL-C concentrations were found in OH and SCH than Controls ('p'= 0.000) except HDL-C level which was not significantly increased in SCH ('p'=0.110). In OH highly significant Positive correlations were seen between TSH levels and serum lipids concentrations ('p'= 0.000). In SCH, TSH levels were also in Positive correlation with TC, TG, VLDL-C and LDL-C ('p'= <0.05) but the correlation was not significant with HDL-C ('p'= <0.477). This shows that higher the TSH levels, higher will be serum lipids levels.

KEYWORDS

Hypothyroidism, Lipid Profile, Dyslipidemia.

INTRODUCTION

Hypothyroidism is the most prevalent non-curable endocrine disorder that leads to mental and physical slowing. Actually it is the subnormal activity of thyroid gland in which gland is unable to produce enough thyroid hormones.[1] Since thyroid hormones are involved in physiological growth and maturation of the body, controlling lipid, carbohydrate, protein and mineral metabolisms,[1,2] it can lead to a variety of clinical situations including, dyslipidemia, electrolytes and minerals disturbances, congestive heart failure and coma. Incidence and prevalence are considered to increase with age. Among the 42 million people suffering from thyroid diseases in India, hypothyroidism is the commonest.[3]The mean annual incidence rate of hypothyroidism is up to 4 per 1000 women, 1 per 1000 men, 1 in 4000 inborn.[4]

Because thyroid hormones have significant effects on synthesis, mobilization and metabolism of lipids,[1] lipid abnormalities are reported to be more common in patients with overt hypothyroidism[5] and hence, hypothyroid patients are thought to be at a high risk of cardiovascular diseases.[6] Levothyroxine replacement therapy significantly improved the lipid profile in hypothyroid patients[7] indicating the possible relation between thyroid hormones and lipid levels in the blood of hypothyroid patients.

Review of the articles related to serum lipid profile levels in hypothyroidism showed conflicting results. Some studies had reported decreased levels, while others had reported increased levels of these parameters in hypothyroidism. As the effects of hypothyroidism on the lipid profile concentrations has not been well established and also the underlying mechanisms are quite complex and not well understood. So, the present study was undertaken to evaluate the frequencies of serum lipids levels in subjects with and without hypothyroidisms and also to investigate their correlations with TSH levels to illuminate the patho-physiological consequences of hypothyroidism on the body.

MATERIAL AND METHODS

Upon ethical clearance, this hospital based Retrospective study was conducted in biochemistry department on **150 subjects (**50 newly diagnosed and untreated cases of Overt hypothyroidism **(OH),** 50 newly diagnosed and untreated cases of Subclinical hypothyroidism **(SCH)** and 50 healthy **controls** in the similar age group, attending OPD of general medicine of Rama Medical College, Hospital & Research Centre, Kanpur, Uttar Pradesh, India. Detailed information of the patients was collected with the help of pre-test proforma that included age, sex and family or personal history of chronic diseases.

Inclusion criteria

- Subjects between 21–60 years age group were considered.
- Both males and females were included.

Exclusion criteria

- Patients having history of coronary heart disease and acute illness,
- Pregnant women,
- Patients having Disorders that affect lipid metabolism (e.g. diabetes mellitus, nephritic syndrome, pancreatitis, hepatic diseases, alcoholism etc.).
- Patients on thyroid hormone therapy,
- Patients taking any lipid-lowering drug.

Method of Analysis:

5ml of fasting venous blood sample was collected from each participant in a plain vacutainer under all aseptic conditions. Serums were separated and used for various biochemical assays.

Thyroid function assays:

TSH, T4 and T3 were measured by Fluorescence Enzyme Immunoassay method on TOSOH AIA-360 auto analyzer[8].

Lipid profile:

The lipids were analyzed on Erba Chem 5-*plus* semi-auto analyzer according to the protocol mentioned in the test kits from Erba Mannheim.

a) Serum Total cholesterol (TC) was estimated by CHOD-PAP end point method[9].
b) Serum Triglycerides (TG) was estimated by Trinder's method[10].
c) High Density Lipoprotein- cholesterol (HDL-C) was estimated by direct method[11].
d) Very Low Density Lipoprotein- cholesterol (VLDL-C) and Low Density Lipoprotein- cholesterol (LDL-C) were calculated by Friedewald's formulae[12]

- VLDL = TG/5 mg/dl
- LDL-C = TC – (HDL+TG/5) mg/dl

Statistical analysis:

All the Parameters of OH, SCH and Controls were analyzed using statistical software **SPSS VERSION 21.0** and the results were expressed as Mean ± SD. The comparisons of serum levels of these parameters between hypothyroidisms (OH and SCH) and controls have been done using *Student's 't' test*. Pearson's correlation coefficient was also used to find the correlation between TSH and serum concentration of lipids.

RESULTS

Table 1- Comparison Of Thyroid Profile Levels Between Patients (oh & Sch) And Controls.

Para meters	OH (Mean ± SD)	Controls (Mean ± SD)	SCH (Mean ± SD)
TSH (µU/ml)	38.11 ± 32.01	2.27 ± 1.12	7.69 ± 2.97
	'p' value .000		'p' value .013

T4 (µg/dl)	1.05 ± 1.69	9.41 ± 1.08	8.48 ± 0.97
	'p' value .000		'p' value .113
T3 (ηg/ml)	0.65 ± 0.21	1.16 ± 0.18	1.03 ± 0.18
	'p' value .000		'p' value .083

A 'p' value < 0.05 was considered significant.
A 'p' value < 0.01 was considered highly significant.

A Highly significant higher mean TSH and lower mean T4 and T3 were recorded in OH (*'p'*= 0.000) compared to Control. The increase in mean TSH was also significant in SCH (*'p'*= 0.013) than Control but the changes in mean T4 and T3 were not significant (*'p'*= >0.05).

Table 2- Comparison Of Lipid Profile Levels Between Patients (oh & Sch) And Controls.

Para meters	OH (Mean ± SD)	Controls (Mean ± SD)	SCH (Mean ± SD)
TC (mg/dl)	236.70 ± 30.97	167.38 ± 12.41	190.31 ± 18.52
	'p' value **.000**		'p' value **.007**
TG (mg/dl)	189.48 ± 29.51	114.01 ± 10.21	138.37 ± 19.8
	'p' value **.000**		'p' value **.000**
HDL-C (mg/dl)	47.7 ± 11.32	39.21 ± 5.35	42.3 ± 4.16
	'p' value **.009**		'p' value **.110**
VLDL-C (mg/dl)	37.89 ± 5.90	22.80 ± 2.04	28.07 ± 2.25
	'p' value **.001**		'p' value **.012**
LDL-C (mg/dl)	151.11 ± 18.96	105.37 ± 13.61	120.34 ± 19.35
	'p' value **.000**		'p' value **.000**

A 'p' value < 0.05 was considered significant.
A 'p' value < 0.01 was considered highly significant.

A significant increase in TC, TG, VLDL-C and LDL-C concentrations were found in OH (*'p'*= 0.000) and SCH (*'p'*= <0.01) than Controls. HDL-C was also found significantly higher in OH than Controls (*'p'*= 0.000) but the increase in HDL-C level in SCH than controls was not significant (*'p'*= 0.110).

Table 3- Pearson Correlation Between Serum Tsh And Lipid Profile Levels In Oh And Sch.

Lab variables	TSH Group	N	Pearson Correlation	'p' value
TC (mg/dl)	OH	50	.915	**.000**
	SCH	50	.471	**.001**
TG (mg/dl)	OH	50	.893	**.000**
	SCH	50	.103	**.006**
HDL-C (mg/dl)	OH	50	.852	**.000**
	SCH	50	.387	**.477**
VLDL-C (mg/dl)	OH	50	.893	**.000**
	SCH	50	.240	**.024**
LDL-C (mg/dl)	OH	50	.708	**.000**
	SCH	50	.346	**.014**

N = Number of observations
A 'p' value < 0.05 was considered significant.
A 'p' value < 0.01 was considered highly significant.

In OH highly significant Positive correlation was seen between TSH level and serum lipids concentrations (*'p'*= 0.000). In SCH, TSH was in Positive correlation with TC, TG, VLDL-C and LDL-C (*'p'*= <0.05) but the correlation was not significant with HDL-C (*'p'*= <0.477).

DISCUSSION

The present study was conducted in the Department of Biochemistry, Rama Medical College, Hospital & Research Centre, Kanpur, Uttar Pradesh, India. The results of the present Retrospective study evinced female preponderance both in patients and controls**.** Although all age groups were presented with a high prevalence of OH and SCH, our study indicated that there was a trend toward a higher prevalence of OH and SCH in the age group 31-40 and 21-30 years respectively. This is in accordance with earlier studies in which statistics have suggested that hypothyroid status is more prevalent in females as compared to males.[13,14]

Although OH has always been associated with hypercholesterolemia, there is much controversy in association of SCH and hypercholesterolemia.[14] In this study all the parameters of lipid profile were significantly elevated in OH as compared to controls. TC, TG, VLDL-C and LDL-C were also elevated significantly in SCH as compare to control. However, the increase was not found significant for HDL-C in SCH. Our figures were in consistent with the figures mentioned in local as well as in the international literatures of authors, *Xiao-Li Liu et al.,*[13] *A. Regmi et al.*[14] *and Roopa Murgod et al.*[15] who reported higher TC, TG, HDL-C, VLDL-C and LDL-C values in hypothyroidism. However in the study done by *Sushma M et al*.,[16] *Abdelgayoum A. Abdel-Gayoum*[17] and *Hussein Kadhem Al–Hakeim*[18], though the serum TC, TG, VLDL-C and LDL-C levels were higher but the levels of serum HDL-C were significantly lower in cases as opposed to our study.

Thyroid hormones regulate cholesterol and lipoprotein metabolism, whereas thyroid disorders, including OH and SCH, considerably alter lipid profile and promote cardiovascular disease (CVD)[19]. Although decreased thyroid function is accompanied by reduced activity of HMG-CoA reductase, TC and LDL-C levels are increased in patients with OH and SCH.[13] The elevation in TC and LDL-C in hypothyroidism is accounted for by the effect of thyroid hormone on the expression of the LDL receptor[14] through control over sterol regulatory element-binding protein 2 (SREBP-2)[19] and expression of CYP7A, a rate limiting enzyme in bile acid synthesis.[14] This decreases LDL-receptors' activity, resulting in decreased catabolism of LDL and IDL. Moreover, a decrease in lipoprotein-lipase (LPL) activity is found in overt hypothyroidism, decreasing the clearance of TG-rich lipoproteins. Therefore, overt hypothyroid patients may also present with elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia.[20] Decreased thyroid function not only increases the number of LDL particles but also promote LDL oxidation, thereby increasing the risk of atherosclerosis.[14]

HDL-C metabolism is complex and changes in plasma levels are due in part to remodeling of HDL-C particles by hepatic lipase (HL) and cholesterol ester transfer protein (CETP).[21] Activity of both enzymes is low in hypothyroidism, correlating with plasma HDL-C. The increase in serum HDL-C is mainly due to increased concentration of HDL_2 particles.[22] It could also be due to decreased activity of the CETP[15]results in reduced transfer of cholesteryl esters from HDL-C to VLDL-C, thus increasing HDL-C levels.[19] Furthermore, decreased activity of the HL also leads to decreased catabolism of HDL_2 particles.[22]

Patients with hypothyroidism usually have higher LDL-C, leading to increased oxidized (oxi)-LDL. Oxi-LDLs are taken up by macrophages in the arterial walls to produce foam cells, and as such may be a risk factor for atherosclerosis. The high levels of oxi-LDL are reversible with L-T4 treatment in both OH and SCH.[7,23]

There was a highly significant positive association between serum TSH levels and TC, TG, HDL-C, VLDL-C and LDL-C levels in both OH and SCH (except HDL-C in SCH). It was noticed that the effect of hypothyroidism on lipid metabolism is more marked in patients with higher serum TSH levels. Even mild elevation in TSH in SCH was associated with raised serum TC, TG, and LDL-C levels. Our figures are in consistent with the figures mentioned in local as well as in the international literature.[24-27]

However, to some extent, we have succeeded in correlating hypothyroidism with the altered lipid profile but the results inferred may not be considered as the reflection of larger population because our study involved a small sample size due to limited period. So, there is an absolute need for large study designs to answer the questions to whether hypothyroidism is associated with increased risk for CAD and whether restoration of euthyroidism might influence cardiovascular morbidity and mortality.

CONCLUSIONS

It can be concluded that hypothyroidism is most common in women and middle aged subjects. So, clinicians should remain highly suspicious in middle aged women with hypothyroidism for increase in lipid parameters. Our data statistically suggests that the effect of hypothyroidism is associated with lipid disorders. So, biochemical screening for hypothyroidism is of paramount importance in all dyslipidemic patients, as well as in all patients with unexpected worsening of their lipid profile.

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