



RESEARCH ARTICLE

BIOCHEMISTRY

STUDY OF VARIATIONS IN SERUM LIPID PROFILE AND TRANSAMINASE LEVELS IN OVERT HYPOTHYROIDISM

DR. D.V.KRISHNAVENI

Department of Biochemistry, Bhaskar Medical College, Yenkapally, Moinabad, RangaReddy district, Andhra Pradesh, India.



DR. D.V.KRISHNAVENI

Department of Biochemistry, Bhaskar Medical College, Yenkapally, Moinabad, Ranga Reddy District, Andhra Pradesh, India.

*Corresponding author

ABSTRACT

This study was undertaken to evaluate the variations in thyroid profile, lipid profile and transaminase levels in overt hypothyroid patients, compared to healthy controls. Thirty hypothyroid patients, both male & female, in the age group of 20 to 50 years (study group) and 30 age & sex matched healthy subjects (control group) were enrolled in the study. We found significant increase in mean levels of total cholesterol, serum triglycerides, LDL-c, AST & TSH and significant decrease in T3 & T4 in study group compared to controls. There was no significant difference in HDL -c values between two groups. The ALT and VLDL-c values were near the upper limits of normal range in study group, while they were near the lower limit in control group, the difference being significant.



KEY WORDS

Hypothyroidism, Thyroid Profile, lipid profile, Transaminases.

INTRODUCTION

Hypothyroidism is a graded disorder, it may be severe with obvious myxoedema, or moderate to mild or can be sub-clinical hypothyroidism. Deficiency of thyroid hormones affects entire metabolism of the body. The amount of Triiodothyronin (T3) converted from Tetraiodothyronin (T4) was a major determinant of serum T3 concentration in normal subjects as well as in patients with hypothyroidism before and after treatment.¹ T3 is considered to be the metabolically active form of all thyroid hormones.

Alterations of thyroid functions result in change in the composition & transport of lipoproteins^{2,3}. Overt & sub-clinical hypothyroidism are associated with hypercholesterolemia mainly due to elevation of Low-Density Lipoprotein (LDL-c) levels, whereas High Density Lipoprotein (HDL-c) can be normal or elevated. On the other hand, hyperthyroidism is accompanied by a decrease in serum levels of total LDL-c & HDL-c.² Thyroid hormones increase lipolysis in adipose tissue both by direct effect through adenylate cyclase -C AMP system and by sensitizing the tissue to other lipolytic agents. Hepatic synthesis of triglycerides is increased, as a result of the increased availability of free fatty acids & glycerol mobilized from adipose tissue. Thyroid hormones enhance the synthesis of cholesterol at the stage of conversion of β -hydroxy β methyl glutaryl Co A to mevalonate, probably by increasing the activity of the enzyme concerned.^{2,4} However, the maintenance of normal plasma cholesterol level in health is presumed to occur by enhancing the cholesterol excretion or degradation more than cholesterol synthesis. Profound elevation of LDL in hypothyroidism is due to the decreased LDL clearance, as a result of decreased LDL-receptor expression.

Although serum enzymes are integral part of cardiac and hepatic profile, they are not organ specific. Hypothyroidism is associated with unexplained increase of serum enzyme levels. In the present study the lipid profile and transaminase levels in 30 hypothyroid patients and 30 normal controls were estimated and compared, to know the effect of decreased thyroid hormone levels on these parameters.

MATERIALS & METHODS

The study was conducted on 60 subjects selected from the outpatient unit of Department of Endocrinology, Osmania General Hospital, Hyderabad, over a period of one year between 2000-2001. This proposal was approved by hospital ethics committee of Osmania General Hospital. Thirty hypothyroid patients, 6 Males and 24 females in age group of 20-50 years, with no other co-morbidities were selected as study group. Hypothyroid patients were defined as those patients with clinical features of hypothyroidism with raised TSH levels above 6.5 μ IU/ml. 30 healthy subjects, 5 male & 25 female of the same age group without any medical or clinical evidence suggestive of thyroid disease; diabetes & hypertension were selected as the control group. Both the study and the control group were asked to fast over night for 12 hours. 10 ml of fasting venous blood without any anticoagulant was collected in to sterile, clean dry bottles and the serum was separated. The sample was made into 2 aliquots one for Lipid profile and transaminase levels and another for thyroid profile. Sample for lipid profile and transaminase was analyzed immediately and the sample for thyroid profile is stored at -20°C for batch analysis. Total cholesterol is estimated by Zak & Boyle method,



triglycerides by enzymatic colorimetric method (autopak, Bayer Diagnostics), HDL-C by colorimetric (phosphotungstate /magnesium) method, LDL, VLDL calculated by Friedwald's formula $[LDL-c=TC-\{HDL-c+(TG/5)\}]$, transaminases by Reitman & Frankel method, T3 (normal range 0.7 to 2 ng/ml), T4 (normal range 5.5 to 13.5 µg/dl), TSH (normal range 0.3 to 6.5 µIU/ml), were estimated by commercially available RIA & IRMA kits (RIA k-4/4A, RIA k-5/5A & IRMAK-9) respectively on I-125 Gamma counter (Electronics corporation of India).

Statistical analysis: In statistical analysis, descriptive statistics like mean, standard deviation were calculated for all variables by groups. Using student t' test, mean value of all variables was compared. Level of significance was considered as 0.05.

RESULTS

A total of 60 subjects (30 cases & 30 controls) were investigated for lipid profile, thyroid profile and transaminase levels (6 Male and 24 female in study groups and 5 male & 25 female in controls). The results of the biochemical parameters of patients, controls & their percentages are given in table 1 and their mean, standard deviation and p values are given in the table 2.

Results of Thyroid profile:

In the control group, T3 and TSH were within normal limits in all 30 samples (100%) and T4 was within normal limits in 28/30 samples (94%). In study group (hypothyroid patients), TSH levels were raised in all 30 (100%) of samples. The T3 & T4 levels are low in 26/30 samples (87%) and 27/30 samples (90) % of samples respectively. The difference between the control and study groups for TSH, T3 and T4 values was statistically significant ($p=0.000$).

Results of lipid profile:

Total cholesterol was within normal limits in all the controls (100 %). On the other hand in 24/30 (80%) cases of the study group, serum total cholesterol (TC) was high and in 6/30 cases (20 %) it was within normal limits, the difference between control and study groups being statically significant ($p = 0.000$).

In the control group, Serum triglyceride (TG) levels were normal in 28/30 samples (93%), low in 2/30 samples (7%). In the study group, their levels were high in 12/30 cases (40%) and normal in 18/30 cases (60%), the difference being statically significant. ($p = 0.002$).

The LDL-c levels were low in all the controls (100%) but they were high in 22/30 cases (73%) and low in 8/30 cases (27%) of the study group, with increase in the mean levels of LDL-c being statistically significant in study group compared to controls ($p = 0.000$). HDL-c levels were within normal limits both in controls and in all the patients (100%). There was no significant difference in HDL cholesterol levels in both the controls and study group ($p = 0.758$). VLDL-c levels were normal in all the controls (100%) but in the study group their levels were normal in 25/30 cases (83%) and high in 5/30 cases (17%). However, the difference in VLDL-c values between controls and study group is statistically significant ($p = 0.001$).

Results of Transaminases:

Aspartate transaminase (AST) levels were normal in all the controls (100%) while in the study group, AST levels were raised in 25/30 cases (83 %). The difference between controls and study group was significantly significant ($p = 0.000$). Alanine transaminase (ALT) levels were within normal limits both in controls & in the study group (100%). Nonetheless, the difference between ALT values of the controls and study group was statistically significant. ($p = 0.000$).

**Table 1*****The results of the biochemical parameters of patients, controls & their percentages.***

Parameter		Control (n=30)	Hypothyroid cases (n=30)
T3	Low	-	26 (87%)
	Normal	30 (100%)	4 (13%)
	high	-	-
T4	Low	2 (7%)	27 (90%)
	Normal	28 (93%)	3 (10%)
	high	-	-
TSH	Low	-	-
	Normal	30 (100%)	-
	high	-	30 (100%)
Cholesterol	Low	-	-
	Normal	30 (100%)	6 (20%)
	high	-	24 (80%)
Triglycerides	Low	-	-
	Normal	28 (93%)	18 (60%)
	high	2 (7%)	12 (40%)
LDL	Low	30(100%)	8 (27%)
	Normal	-	-
	high	-	22 (73%)
HDL	Low	-	-
	Normal	30 (100%)	30 (100%)
	high	-	-
VLDL	Low	-	-
	Normal	30(100%)	25 (83%)
	high	-	5 (17%)
AST	Low	-	-
	Normal	30(100%)	5 (17%)
	high	-	25 (83%)
ALT	Low	-	-
	Normal	30(100%)	30 (100%)
	high	-	-



Table 2

The mean, standard deviation & P values of Lipid Profile and Transaminase levels between controls & hypothyroid patients.

Subjects	Controls(n=30)	Hypothyroid cases (n=30)	P value
T3(ng/ml)	0.832±0.25	0.44 ± 0.25* * *	0.000
T4 (µg/dl)	7.75 ±1.72	2.73 ± 1.88* * *	0.000
TSH(µIU/ml)	2.93±1.65	35.56 ±24.8* * *	0.000
Cholesterol (mg %)	175±17.62	266.50±47.60* * *	0.000
Triglycerides (mg%)	120±20.84	150.26±45.97* *	0.002
LDL (mg %)	118.23±15.46	203.76± 50.11* * *	0.000
HDL (mg %)	33.13 ±3.19.	32.60 ± 8.84	0.758
VLDL (mg %)	23.96 ± 4.10	30.13 ± 8.95*	0.001
AST (units %)	71.63 ± 11.39	160.70 ±48.41* * *	0.000
ALT (units %)	41.30 ± 9.81	55.13 ± 15.69* * *	0.000

* * * $P < 0.001$: * * $P < 0.05$: * $P < 0.01$

DISCUSSION

In the present study observations were made on changes in lipid profile and serum transaminase levels in age and sex matched healthy controls and hypothyroid patients. The mean levels of serum cholesterol were significantly higher in hypothyroid patients than that of healthy controls in our study. This finding is consistent with other studies.^{2,5,6,7} In hypothyroid patients, despite the reduced activity of β -hydroxy β methyl glutaryl Co A (HMG-CoA) reductase, there is often an increase in the serum total cholesterol concentration, mainly due

to raised levels of serum LDL cholesterol and intermediate density lipoprotein (IDL) cholesterol.² In addition incompletely degraded VLDL particles enriched in cholesterol and apo- E accumulate in thyroid subjects. A defective receptor mediated LDL catabolism and changes in intravascular metabolism as defined by decreased activities of lipoprotein lipase & hepatic lipase, seem to contribute to these alterations.⁸ In a study in support of this hypothesis,⁹ it was observed that serum cholesterol levels were significantly elevated only in severely hypothyroid patients when compared with controls.



In the present study we observed a significant increase in mean levels of TG and LDL-c in study group compared with controls. Similar observations were made in previous studies of hypothyroid patients showing significant increase in TC and LDL-C^{11,12} with decrease in HDL-c levels¹² as in hypothyroidism both synthesis and the degradation of lipids are decreased, the net effect being one of the lipid accumulation, especially of LDL & triglycerides. The decrease in lipid degradation rate may reflect the decrease in post-heparin lipolytic activity¹³ as well as reduced LDL receptors. Hypothyroid patients usually exhibit elevated levels of HDL-C mainly due to increased concentration of HDL₂ particles.¹⁴ Decreased activity of cholesterol ester transfer protein (CETP) results in reduced transfer of cholesterol esters from HDL to VLDL, thus increasing HDL-C levels¹⁵. In addition, decreased activity of the hepatic lipase (HL) also leads to decreased catabolism of HDL₂ particles¹⁶.

Conversely, there was no significant change in HDL-c levels between cases and controls in our study and similar observations were made in a study of 35 hypothyroid patients¹⁰ where the serum TC, TG, LDL were increased and HDL-c was normal. However, in another study there was a significant decrease in HDL-c and a significant increase in TC & LDL-C¹¹. Interestingly, in the present study, the VLDL-c values between controls and patients (study group) were within the normal range with values of study group being significantly higher compared to controls.

Comparing results of our study with above mentioned studies we can conclude that hypothyroidism is associated with major alterations in lipid profile i.e. significant increase in total cholesterol, triglycerides &, LDL-c levels and no significant difference in HDL-c levels.

Abnormal serum enzyme activities have been recorded in previous studies in patients with hypothyroidism in ALT, AST, CPK etc^{17,18}. In the present study we observed that the AST levels were significantly raised and ALT levels were within higher the normal range in hypothyroid

patients. This is in agreement with some of the studies done previously^{17, 18, 19, 20, 21}. In a study of Burnett the serum AST level was 2-6 times higher than reference limits in 3 cases of hypothyroidism¹⁸. This elevation in transaminase level was considered to be due to myopathy in hypothyroid patients.²² Elevated serum enzyme levels can facilitate the diagnosis of hypothyroidism, especially when muscle weakness is a symptom.^{22,23}

CONCLUSION

The present study demonstrated a multiple biochemical abnormalities in serum lipids and enzymes in hypothyroid subjects. In agreement with the other studies, significant elevation in total cholesterol, triglycerides, LDL & AST levels was observed in hypothyroid patients compared with healthy controls. Interestingly, there was a statistically significant difference in ALT & VLDL-c levels between study and control groups, while the actual values were within normal limits. However, the present study did not show significant difference in HDL-c levels between study and control groups.

In conclusion, in a patient clinically suspected to have hypothyroidism, the lipid and transaminase abnormalities not only support the diagnosis of hypothyroidism but also provide information about the metabolic changes occurring due to decreased thyroid function.

ABBREVIATIONS

T3- tri iodothyronin , T4- tetra iodo thyronin , TSH- thyroid stimulating hormone , TC-total cholesterol, TG- triglycerides , HDL- high density lipoproteins, LDL- low density lipoproteins, VLDL- very low density lipoproteins, AST- aspartate transaminase, ALT - alanine transaminase.

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