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ORIGINAL RESEARCH

LIPID PROFILE IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT:

BACKGROUND:Subclinical hypothyroidism (SCH) is defined as an elevated serum thyroid-stimulating hormone (TSH) level with a normal serum free tri-iodothyronine (FT3) & free thyroxine(FT4) concentration. Hypothyroidism is associated with dyslipidemia and increased risk of atherosclerosis. SCH can progress to overt hypothyroidism. Lipid profile changes in SCH, however, are controversial.

AIMS AND OBJECTIVES: To study the lipid profile in patients with SCH.

MATERIAL & METHODS:The present study was a case-control study involving 35 individuals with newly diagnosed / untreated SCH were studied. 35 age and sex matched adults with normal thyroid profile were taken as controls. Serum TSH, FT3, FT4, Total cholesterol, Triglyceride, Low density lipoprotein cholesterol (LDL-C), High density lipoprotein cholesterol (HDL-C)and Very low density lipoprotein cholesterol(VLDL-C) levels were measured in all study subjects.

RESULTS: The average total cholesterol and LDL-C in the patients with SCH in our research were statistically significantly higher than the control group. The mean serum triglyceride, HDL-C and VLDL-C levels were not statistically different in patients as compared to controls.

CONCLUSION: SCH is associated with dyslipidemia which is a risk factor for atherosclerosis, with a resultant risk of cardiovascular disease and stroke. Thus, it is important to detect this condition early so that appropriate steps may be taken to prevent its deadly complications.

KEYWORDS: Subclinical hypothyroidism; Lipids; Atherosclerosis.

INTRODUCTION

The normal range of the serum Thyroid stimulating hormone(TSH) concentration is most commonly 0.4 to 4.2 µIU/mL. Subclinical hypothyroidism (SCH) is defined as an elevated serum TSH level with a normal serum free T4 (FT4) concentration.[1,2] It is thought to be associated with few or no apparent clinical features of hypothyroidism. Other terms previously used for subclinical hypothyroidism are mild hypothyroidism, early thyroid failure, preclinical hypothyroidism, and decreased thyroid reserve. The prevalence has been reported to range from 6-8% in women and 3% in men (up to 10% in women more than 60 years).[3] Around 54% of patients with subclinical hypothyroidism have Hashimoto's disease with increased serum concentrations of anti-thyroid microsomal or anti-thyroid peroxidase antibodies.[4]

Subclinical hypothyroidism can progress to overt hypothyroidism, as well as be associated with

clinical manifestations in some patients and may benefit from treatment.[5]
The other causes of elevated serum TSH are non-thyroidal illness, assay variability, pulsatile TSH secretion, nocturnal surge in TSH secretion, Heterophilic antibodies, TSH secreting pituitary adenomas,metoclopramide, domperidone&thyroid hormone resistance syndromes.

THYROID HORMONES AND LIPID METABOLISM

Thyroid hormones have a vital role in glucose and lipid metabolism .They regulate a wide range of metabolic functions, involving lipid metabolism.[6]Hypothyroidism is linked to a considerable rise in low-density lipoprotein (LDL) levels in the blood, which can contribute to coronary artery disease.[7] Even within the normal range of TSH levels, rising TSH was found to cause a linear rise in total cholesterol, LDL and triglyceride (TG), as well as a linear drop in high-density lipoprotein cholesterol(HDL) levels in some studies.[8] An increase in total cholesterol and LDL may be related to numerous alterations in synthesis, metabolism, and fat mobilization.[9] Thyroid hormones boost the activity of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-COA) reductase in the liver, lowering cholesterol levels. Thyroid hormones also increase LDL receptors on fibroblasts, liver, and other tissues, as well as cholesterol absorption from the intestine. These hormones also regulate the excretion of cholesterol from the gut via bile acids, as well as the levels of HDL cholesterol and hepatic lipase activity.[9] While some researchers have found a link between subclinical hypothyroidism and an increased risk of cardiovascular disease caused by atherosclerosis, other studies have not.[9,10] Although the consequences of subclinical hypothyroidism on serum lipids are unknown, the alterations that occur in clinical hypothyroidism are expected to occur in subclinical hypothyroidism as well, albeit to a lesser extent.Different studies have looked at the link between lipid problems, SCH, and thyroid hormone levels in patients, with varying results.[11,12]
The current study aims to investigate the incidence of dyslipidemia in patients with subclinical hypothyroidism as dyslipidemia is as an essential risk factor for atherosclerosis and needs tobe identified at an early stage.

AIMS &OBJECTIVES: -of this study were

1. To investigate lipid profile in patients with subclinical hypothyroidism and
2. Correlate lipid parameters with TSH.

MATERIAL AND METHODS

The current study was a case-control clinical trial conducted in the Department of General Medicine at M.M. Medical College and Hospital, Kumarhatti, Solanfrom January 2020 to September 2021. The first group consisted of 35 subjects with subclinical hypothyroidism who were newly diagnosed and untreated and were between the ages of 18 and 60. A group of 35 healthy persons of similar age and sex with a normal thyroid profile served as the controls. The collected data was compiled into excel sheets and further analysed in Stata software version 14.1 and Statistical package for social sciences (SPSS) software. The proposed study was undertaken after the approval by the Institutional Ethical Committee.

INCLUSION CRITERIA: -

All patients were included,

1. Who were >18 years old.
2. With serum TSH >4.2 µIU/mL and normal serum Free T3 and Free T4 levels detected on screening.

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EXCLUSION CRITERIA: -

1. Patients with overt hypothyroidism and on treatment with thyroxine or anti-thyroid drugs
2. Patients with end stage renal disease
3. Post myocardial infarction
4. Congestive heart failure
5. Diabetes mellitus
6. Patients on treatment of lipid lowering drugs or 3 months prior history of taking lipid lowering drugs
7. Pregnant women or female on oral contraceptives
8. Patient with acute medical illness admitted in Intensive care unit (ICU)
9. Primary dyslipidemia
10. Patient with concomitant inflammatory disease
11. Patients with history of smoking
12. History of alcoholic intake
13. Patient with hypothalamic-pituitary disorder
14. Malignancy
15. Phenytoin, Carbamazepine, Sertraline, Furosemide, Metformin and non-steroidal anti-inflammatory drugs.

All of the subjects were subjected to a comprehensive clinical evaluation, which included a detailed history and clinical examination. The ADVIA Centaur XP immunoassay system was used to assess FT3, FT4, and TSH utilising the Chemiluminescence immunoassay (CLIA) technique.

RESULTS

This research included 35 individuals with subclinical hypothyroidism as cases and 35 patients with euthyroidism as controls. Confounding variables had been eliminated.

Table no. 1

MEAN AGE IN CASES AND CONTROLS

	Cases	Controls	P Value
Age	46.25±10.7	41.11±11.19	0.06

Patients with subclinical hypothyroidism had a mean age distribution of 46.25 ± 10.7 years, while euthyroid controls had a mean age distribution of 41.11± 11.19.(Table 1) Thus, the patients in both groups were of similar ages.

Table no. 2

SEX DISTRIBUTION IN CASES AND CONTROLS

	Cases	Controls	Cases	Controls
Male	6	8	17.14%	22.85%
Female	29	27	82.85%	77.14%

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Males accounted for 17.14 percent of cases and 22.85 percent of controls, respectively.
Females made up 82.85% of cases, while controls made up 77.14 percent.(Table 2)
Females dominated the subclinical hypothyroidism patients, while the control group was similarly balanced.

Table no. 3
BODY MASS INDEX IN CASES AND CONTROLS GROUPS

	Cases	Controls	P Value
BMI	23.76±1.77	23.12±1.73	0.1321

The mean BMI of the cases was 23.76 ± 1.77 percent, whereas the BMI of the controls was 23.12 ± 1.73%. Thus, both groups were nearly identical in terms of BMI. (Table 3)

The Changes in lipid profile in our study are enlisted in Table 4 and Figure 1.

Table no. 4
LIPID PROFILE IN CASES AND CONTROLS

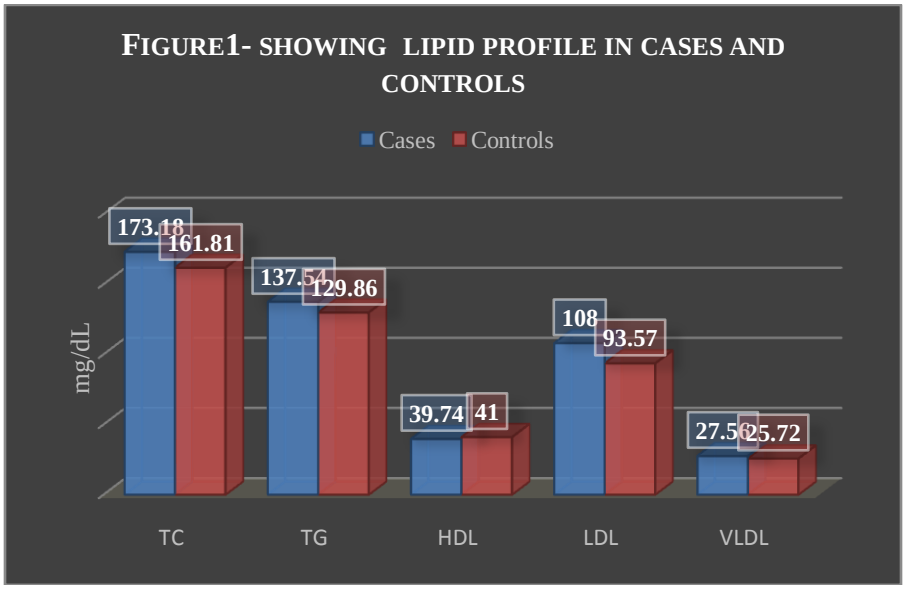
	CASES (mg/dL)	CONTROLS (mg/dL)	P Value	Correlation with TSH
TC	173.18±21.5	161.81±25.71	0.0487	0.05
TG	137.54±39.93	129.86±26.35	0.3455	-0.28
HDL-C	39.74±7.75	41±5.29	0.4319	0.25
LDL-C	108±25	93.57±26.37	0.0212	0.08
VLDL-C	27.56±8	25.72±5.58	0.2698	-0.28

(TC= Total Cholesterol, TG= Triglyceride, HDL-C= High density lipoprotein cholesterol, LDL-C= Low density lipoprotein cholesterol, and VLDL-C= Very low-density lipoprotein cholesterol)

The average total cholesterol level in those with subclinical hypothyroidism was 173.18 ± 21.5 mg/dL. In the controls, the average total cholesterol level was 161.81 ± 25.71 mg/dL. The statistical significance of the p value of 0.0487 was established. As a result, total cholesterol levels in the study group of individuals with subclinical hypothyroidism were considerably higher. Serum total cholesterol had a modest correlation with serum TSH in our investigation, with a value of 0.054.
The mean serum triglyceride value in instances with subclinical hypothyroidism was 137.54 ± 39.93 mg/dL, compared to 129.86 ± 26.35 mg/dL in euthyroid controls, with a p value of 0.3455, which was not statistically significant. As a result, the study group's triglycerides were not substantially elevated. Serum triglycerides were only slightly linked with serum TSH in our study, with a value of -0.28.
Patients with subclinical hypothyroidism had an average HDL level of 39.74 ± 7.75 mg/dL, compared to 41 ± 5.29 mg/dL in euthyroid controls. With a p value of 0.4319, however, this was not considered statistically significant. Serum HDL-C had a modest correlation with serum TSH in our research, with a value of 0.2469.
The mean LDL cholesterol level in patients with subclinical hypothyroidism was 108 ± 25 mg/dL, compared to 93.57 ± 26.37 mg/dL in euthyroid controls, with a statistically significant p

value of 0.0212. As a result, LDL-cholesterol levels in the study group, which included individuals with subclinical hypothyroidism, were considerably higher. Serum LDL-C had a modest correlation with serum TSH in our study, with a value of 0.0822.

The average VLDL cholesterol level in patients with subclinical hypothyroidism was 27.5 ± 5.68 mg/dL. Euthyroid controls had an average result of 25.7 ± 25.58 mg/dL. This was shown to be statistically significant with a p value of 0.2698. In terms of VLDL cholesterol, both groups were nearly identical. Serum VLDL-C had a poor correlation with serum TSH in our investigation, with a value of -0.284.



DISCUSSION

Thyroid hormones have a crucial role in regulating lipid production, absorption, and metabolism.[7]Female predominance was seen in our study, with females accounting for 82.85% of those with subclinical hypothyroidism.

The average total cholesterol in the participants in our study was 173.18 ± 21.5 mg/dL, with a statistically significant p-value of 0.0487. The other studies that found statistically significant higher serum total cholesterol levels in SCH are by Nadia et al.,[13]Serpil et al.,[14]Asranna et al.,[12]Karthick et al.,[15]Laway et al.,[16] James et al.,[17]Jaysingh et al.,[18]Hussain et al.[19] Serum total cholesterol had a weak correlation with serum TSH in our investigation, with a value of 0.0547. But another study conducted by Nadia et al.,[13] showed a positive correlation between serum TSH and serum total cholesterol. A study conducted by Alamdari et al.,[20] did not observe any significant difference between patients with subclinical hypothyroidism and controls. They did not observe any correlation between TSH and lipid profile in patients with subclinical hypothyroidism. They concluded that dyslipidemia is not a risk factor for cardiovascular disease in patients with subclinical hypothyroidism.

In our investigation, the mean serum triglyceride value in instances with subclinical hypothyroidism was 137.54 ± 39.9 mg/dL, compared to 129.86 ± 26.3 mg/dL in euthyroid controls, with a p-value of 0.3455 that was not statistically significant. But many studies showed that there were statistically significant higher levels of serum triglycerides in patients with subclinical hypothyroidism. These were by Serpil et al.,[14]Karthick et al.,[15]Laway et al.,[16] James

et al.,[17]Hussain et al.,[19]and Madhura et al.[21] Serum triglycerides had a poor correlation with serum TSH in our research, with a value of -0.28. But a study conducted by Madhura et al.,[21] showed a strong positive correlation between serum TSH and serum triglyceride levels.

In our study, the mean LDL-cholesterol level in instances with subclinical hypothyroidism was 108 ± 25 mg/dL, compared to 93.57 ± 26.37 mg/dL in euthyroid controls, with a statistically significant p-value of 0.0212. The other studies that found statistically significant higher serum LDL-C levels are Nadia et al.,[13]Zeynep et. al.,[22]Serpil et al.,[14]Asranna et al.,[12] James et al.,[17]Hussain et al.,[19]Maleki et al.,[23] and Haghi et al.[24] Serum LDL-C had a weak correlation with serum TSH in our study, with a value of 0.0822.

The average HDL level in individuals with subclinical hypothyroidism was 39.74 ± 7.75 mg/dL in our research, compared to 41 ± 5.29 mg/dL in healthy controls which was not statistically significant. But many studies showed statistically lower serum HDL-C levels & these studies were conducted by Li et al.,[25]Karthick et al.,[15]Hussain et al.,[19]and Haghi et al.[24] Serum HDL-C had a weak correlation with serum TSH in our research, with a value of 0.2469.

The average VLDL cholesterol level in persons with subclinical hypothyroidism was 27.5 ± 5.68 mg/dL in our research. The average euthyroid control result was 25.72 ± 5.58 mg/dL, with a p-value of 0.2698, which was not significant. But a study that found statistically significant higher serum VLDL-C levels was conducted by Laway et al.[16] Serum VLDL-C had a weak correlation with serum TSH in our investigation, with a value of -0.284.

Thus,Serum total cholesterol and LDL-C were elevated and weakly correlated with serum TSH. However, the mean serum triglyceride, HDL-C and VLDL-C values were not significantly different from controls.

CONCLUSION

Subclinical hypothyroidism is an important condition which has been neglected and needs more attention as it may be associated with dyslipidemia and the resultant risk of cardiovascular disease. In the present study it was associated with significant increase in serum Total Cholesterol levels & LDL-C levels which are highly atherogenic. Thus, it is important to detect this condition early so that appropriate steps may be taken to prevent its deadly complications.

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