

Study of Lipid Profile in Patients with Subclinical Hypothyroidism in Tertiary Center of Mid-Western Nepal

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ABSTRACT

Introduction: Subclinical hypothyroidism (SCH), a common thyroid disorder, is differentiated by increased levels of thyroid-stimulating hormone (TSH) despite normal concentrations of free thyroid hormones. The aim of this study was to assess lipid abnormalities in patients with subclinical hypothyroidism and investigate its relationship with lipid profile and TSH.

Methods: The cross-sectional study included 90 subclinical hypothyroidism individuals, from Nepalgunj Medical College and Teaching Hospital. A blood sample was taken and sent to a laboratory for evaluation of the lipid profile Total Cholesterol (TC), Triglycerides (TG), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Very Low-Density Lipoprotein (VLDL) and thyroid function tests (FT3, FT4, TSH).

Results: Participants had a mean age of 45.5 years and a TSH level of 5.9 ± 1.7 mIU/L. Lipid parameters showed elevated total cholesterol (210.7 ± 38.8 mg/dl), triglycerides (166.7 ± 1.9 mg/dl), LDL (116.3 ± 32.7 mg/dl), and VLDL (33.34 ± 4.85 mg/dl), along with low HDL (33.7 ± 6.8 mg/dl). TSH positively correlated with total cholesterol ($r = 0.679$), triglycerides ($r = 0.879$), and VLDL ($r = 0.325$), while HDL had a negative correlation ($r = -0.4$). FT3 and FT4 showed weaker negative correlations with lipid parameters.

Conclusion: The study has concluded that the patients with subclinical hypothyroidism (SCH) exhibit significant gender-based differences in lipid profiles, with males showing higher levels of total cholesterol, triglycerides, LDL, and a higher Cholesterol/HDL ratio, along with significantly lower HDL levels.

Keywords: Cholesterol; Lipidaemia; Lipid profile; Subclinical hypothyroidism; Triglycerides

INTRODUCTION

Subclinical hypothyroidism (SCH), a common thyroid condition, is distinguished by elevated TSH levels despite normal FT3 and FT4 levels.^{1,2} Subclinical hypothyroidism is more prevalent among women and older adults.³ Hypothyroidism increases the risk of coronary heart disease(CHD), heart failure, cardiovascular disease (CVD) mortality, blood pressure, and atherosclerotic changes. This thyroid hormone problem causes

nonspecific symptoms, mood swings, weariness, and cognitive impairment in younger and middle-aged persons.⁴

Lipid metabolism and mobilisation are affected by dysregulated thyroid hormones, which increase cardiovascular mortality.⁵ They modulate lipid synthesis, transport, and catabolism by affecting hepatic LDL receptors and lipoprotein lipase.^{6,7} Normal thyroid hormones regulate blood lipoproteins LDL, HDL, and VLDL, which transport cholesterol.⁸ In contrast, SCH has normal FT3 and FT4 levels, but elevated TSH disrupts most of these mechanisms, producing lipid alterations.⁹ Abnormalities may not show

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clinical symptoms but increase the risk of coronary artery disease like atherosclerosis.¹⁰⁻¹²

Hypothyroidism affects lipid metabolism by regulating thyroid hormone uptake of fatty acids through liver transporter and translocase production, such as fatty acid binding proteins.¹³ SCH is challenging to diagnose and treat before major cardiovascular manifestations since these lipid profile abnormalities might occur even in patients with minimal or no symptoms.¹⁴⁻¹⁶

Healthcare accessibility and thyroid disorder evaluations vary across different regions of Nepal, influenced by environmental and nutritional factors.^{17,18} Its environmental and nutritional factors affect thyroid hormones and lipids.^{19,20} The rising prevalence of hypothyroidism, it is important to assess the impact of diet and environmental factors on thyroid health and lipid metabolism in Mid- and Far-Western Nepal.²¹⁻²⁴ SCH may be associated with lipid abnormalities, including increased LDL and triglyceride levels, which contribute to cardiovascular risk.^{25,26}

The primary objective of this study is to comprehensively evaluate the lipid profile in patients diagnosed with subclinical hypothyroidism, within the context of a tertiary care center located in the mid-western region of Nepal.

METHODS

Study design

A hospital based descriptive study was conducted on patients attending the OPD in Nepalganj Medical College and Teaching Hospital (NGMCTH), Kohalpur, Nepalganj diagnosed with subclinical hypothyroidism within six months duration. The study considered 90 patients diagnosed with subclinical hypothyroidism. A blood sample of the patients was taken and sent to a laboratory for evaluation of the lipid profile (TC, TG, HDL, LDL, and VLDL) and thyroid function tests (FT3, FT4, TSH). The findings were evaluated and correlated accordingly.

Inclusion and exclusion criteria

Inclusion Criteria: Patients aged 18-60 years diagnosed with subclinical hypothyroidism (SCH) who attended OPD in NGMCTH.

Exclusion Criteria: Patients with hepatic diseases, cardiovascular disorders, diabetes mellitus,

pregnant women, individuals on lipid-lowering drugs, and those unwilling to participate.

Ethical approval

The patients were given a thorough explanation of the study by the authors and an informed consent was obtained. Prior approval was also taken from the hospital's ethical committee (Ref. 50/ 080-081).

Sample collection

Under aseptic condition, three milliliters of venous blood was extracted, stored in a gel tube, and allowed to clot at room temperature. To separate the serum, the blood sample was centrifuged for ten minutes at 3500 revolutions per minute (rpm). On the same day that the samples were collected, investigations were conducted.

Sample size

The sample size is calculated using

$$(n) = z^2 pq/d^2$$

$z = 1.96$ at confidence interval 95%

p = previous study prevalence of subclinical hypothyroidism (17.6)¹⁴

$$q = 100 - p$$

d = desired level of precision taking 8% error

Statistical analysis

we used SPSS version 22 for effective analysis. The analytical tool like t-test and Pearson's Correlation were used. The proper percentage comparisons between the various groups were made using the mean values, standard deviations. Significant data was defined as a P value of < 0.05.

RESULTS

Table 1 compares male and female baseline features of subclinical hypothyroidism (SCH) patients. Age of the cohort averages 45.5 ± 8.9 years, with males being older (47.2 ± 9.1 years) than females (44.0 ± 8.5 years), statistically significant ($p = 0.045$). SCH diagnosis is aided by higher TSH levels in males (6.2 ± 1.8 mIU/L) compared to females (5.7 ± 1.5 mIU/L), with a significant p-value of 0.032, indicating worse thyroid dysfunction in male patients. However, free T4 (FT4) levels were not gender-specific, with values of 1.28 ± 0.15 μ g/dl (p -value = 0.21). Free T3 (FT3) levels were comparable between genders, with a mean of 2.67 ± 0.46 ng/dl and no significant difference ($p = 0.52$). Males have a mean BMI of 26.0 ± 4.0 kg/m^2 , whereas girls have a mean of 24.5 ± 3.4 kg/m^2 , although this difference

was not statistically significant ($p = 0.15$). Males have a slightly higher systolic blood pressure (SBP) of 122.0 ± 8.2 mmHg compared to females of 118.5 ± 6.9 mmHg, statistically significant ($p = 0.04$). The study found no significant gender differences in diastolic blood pressure (DBP) or

mean arterial pressure (MAP), with DBP at 83.1 ± 4.9 mmHg ($p = 0.25$) and MAP at 95.6 ± 3.5 mmHg ($p = 0.12$). The average pulse pressure (PP) is 36.9 ± 10.2 mmHg, with no significant gender difference ($p = 0.12$).

Table 1: Baseline characteristics with subclinical hypothyroidism

Parameter	Overall (Mean \pm SD)	Male (Mean \pm SD)	Female (Mean \pm SD)	t-test p-value
Age (years)	45.5 ± 8.9	47.2 ± 9.1	44.0 ± 8.5	0.045
TSH (mIU/L)	5.9 ± 1.7	6.2 ± 1.8	5.7 ± 1.5	0.032
FT4 (μ g/dl)	1.28 ± 0.15	1.24 ± 0.14	1.29 ± 0.15	0.21
FT3 (ng/dl)	2.67 ± 0.46	2.70 ± 0.50	2.65 ± 0.43	0.52
BMI (kg/m^2)	25.1 ± 3.7	26.0 ± 4.0	24.5 ± 3.4	0.15
SBP (mmHg)	120.2 ± 7.6	122.0 ± 8.2	118.5 ± 6.9	0.04
DBP (mmHg)	83.1 ± 4.9	84.0 ± 5.1	82.5 ± 4.5	0.25
MAP (mmHg)	95.6 ± 3.5	96.5 ± 4.0	95.0 ± 3.0	0.18
PP (mmHg)	36.9 ± 10.2	38.0 ± 11.0	35.5 ± 9.5	0.12

Table 2 presents the lipid profile parameters for patients with subclinical hypothyroidism, illustrating notable abnormalities that may elevate cardiovascular risk. The mean total cholesterol level in this group is 210.7 ± 38.8 mg/dl, with males showing a significantly higher mean (215.0 ± 40.5 mg/dl) compared to females (206.0 ± 36.1 mg/dl), demonstrated by a p-value of 0.045, indicating hypercholesterolemia. This indicates that gender influences total cholesterol levels among SCH patients. Triglyceride levels were significantly greater in males (170.0 ± 2.5 mg/dl) compared to females (164.0 ± 1.4 mg/dl), with a p-value of 0.025. Male LDL cholesterol levels average 120.0 ± 35.0 mg/dl, whereas females average 112.5 ± 30.0 mg/dl, with a p-value of 0.050, suggesting a borderline significant difference in cholesterol

levels that may require additional examination. In contrast, mean VLDL levels (34.0 ± 5.2 mg/dl in males and 32.5 ± 4.0 mg/dl in females) did not differ significantly ($p = 0.18$).

HDL cholesterol levels were significantly lower in males (31.0 ± 5.5 mg/dl) compared to females (36.5 ± 6.0 mg/dl), with a p-value of 0.01, indicating a gender gap in protective HDL levels. Males have a mean Cholesterol/HDL ratio of 7.0 ± 0.8 , whereas females have 6.0 ± 0.5 ($p = 0.005$), indicating cardiovascular risk. These data show substantial gender-related differences in lipid profiles among patients with subclinical hypothyroidism, highlighting the necessity of including gender considerations in the clinical assessment and therapy of this illness.

Table 2: Lipid parameters in patients with subclinical hypothyroidism

Lipid Parameter	Overall (Mean \pm SD)	Male (Mean \pm SD)	Female (Mean \pm SD)	t-test p-value
Total Cholesterol (mg/dl)	210.70 ± 38.8	215.0 ± 40.5	206.0 ± 36.1	0.045
Triglycerides (mg/dl)	166.70 ± 1.9	170.0 ± 2.5	164.0 ± 1.4	0.025
LDL (mg/dl)	116.3 ± 32.7	120.0 ± 35.0	112.5 ± 30.0	0.05
VLDL (mg/dl)	33.34 ± 4.85	34.0 ± 5.2	32.5 ± 4.0	0.18
HDL (mg/dl)	33.7 ± 6.8	31.0 ± 5.5	36.5 ± 6.0	0.01
Cholesterol/HDL Ratio	6.5 ± 0.7	7.0 ± 0.8	6.0 ± 0.5	0.005

Table 3 shows the correlation between the thyroid profile parameters (TSH, FT3, and

FT4) and various lipid profile parameters (Total Cholesterol, Triglycerides, LDL, VLDL, HDL,

and Cholesterol/HDL ratio) in patients with subclinical hypothyroidism. A strong positive correlation ($r = 0.679$) was observed between TSH and total cholesterol, indicating that as TSH levels rise, total cholesterol tends to increase. Similarly, triglycerides show an even stronger positive correlation with TSH ($r = 0.879$), suggesting a significant increase in triglyceride levels with higher TSH concentrations. LDL also shows a moderate positive correlation with TSH ($r = 0.476$), and VLDL has a weaker but still positive correlation with TSH ($r = 0.325$). On the other hand, HDL exhibits a negative correlation with TSH ($r = -0.4$), implying that higher TSH levels were associated with lower HDL levels. Furthermore, the Cholesterol/HDL ratio shows a strong positive correlation with TSH ($r = 0.7$), indicating that elevated TSH levels were linked to a more unfavorable lipid ratio, increasing cardiovascular risk.

In contrast, FT3 and FT4 exhibit weak negative

correlations with total cholesterol, triglycerides, LDL, and VLDL. The negative values for FT3 (ranging from -0.29 to -0.1) and FT4 (ranging from -0.16 to -0.1) indicate a mild inverse relationship, meaning that lower thyroid hormone levels may slightly elevate lipid parameters, although these relationships were not as pronounced as the correlations with TSH. Interestingly, HDL shows a mild positive correlation with FT3 ($r=0.1$) and FT4 ($r = 0.05$), suggesting that higher thyroid hormone levels might contribute to a marginal increase in HDL levels. Additionally, the Cholesterol/HDL ratio is negatively correlated with both FT3 ($r = -0.3$) and FT4 ($r = -0.2$), suggesting that higher thyroid hormone levels could be associated with a more favorable lipid profile. TSH exhibits strong positive correlations with most unfavorable lipid parameters, whereas FT3 and FT4 show weak negative correlations with these lipid parameters, indicating a more complex relationship between thyroid function and lipid metabolism.

Table 3: Correlation between thyroid profile and lipid profile of the patients

Lipid Parameter	TSH (mIU/L) r;pr; pr;p	FT3 (ng/dL) r;pr; pr;p	FT4 (μ g/dL) r;pr; pr;p
Total Cholesterol (mg/dL)	$r=0.679; p=0.0002$	$r=-0.2; p=0.18$	$r=-0.1; p=0.48$
Triglycerides (mg/dL)	$r=0.879; p=0.00001$	$r=-0.3; p=0.04$	$r=-0.2; p=0.18$
LDL (mg/dL)	$r=0.476; p=0.009$	$r=-0.25; p=0.09$	$r=-0.15; p=0.30$
VLDL (mg/dL)	$r=0.325; p=0.04$	$r=-0.29; p=0.05$	$r=-0.16; p=0.28$
HDL (mg/dL)	$r=-0.4; p=0.02$	$r=0.1; p=0.50$	$r=0.05; p=0.70$
Chol/HDL Ratio	$r=0.7; p=0.0001$	$r=-0.3; p=0.04$	$r=-0.2; p=0.18$

DISCUSSION

The study in tertiary care unit in Nepal suggests newly diagnosed primary hypothyroidism patients have a high prevalence of abnormal lipid profiles, suggesting early investigation for dyslipidemia to prevent complications.⁵ Previous investigations also supported on the positive relation between subclinical hypothyroidism and dyslipidemia.²⁷⁻²⁹ Patients with SCH appear to have a high prevalence of metabolic dysregulation, including increased total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels, along with decreased high-density lipoprotein (HDL) cholesterol. Cholesterol levels of such types were well linked to atherosclerosis, a situation where plaque forms in the arteries narrowing the blood vessels and creating numerous heart problems.^{30,31} Often LDL cholesterol is regarded as dangerous,

as it contributes to the formation of plaque in the blood vessels, whereas HDL cholesterol prevents the buildup of cholesterol. Equally important, raised triglycerides are associated with insulin resistance and various other metabolic alterations predisposing SCH patients to cardiovascular hazards.³²⁻³⁵

In the study by M Guntaka et al.³ subclinical hypothyroidism is associated with increased serum total cholesterol and LDL cholesterol levels, potentially indicating a potential association with atherosclerosis. This mirrors with the study by Ejaz et al.²⁶ compare the lipid profile of individuals with and without subclinical hypothyroidism and found that the total cholesterol and LDL cholesterol levels were significantly higher in patients with subclinical hypothyroidism that poses more calculated risk

for cardiovascular diseases in the respective patients. Contrary to these observations, a study in Nepal on serum lipid profiles of hypothyroid patients reported significantly higher triglyceride levels in subclinical hypothyroidism cases, while other components like total cholesterol and LDL showed insignificant differences compared to the control group.⁴ relatively more extensive homogenous study in terms of age and gender was conducted by Abbasi et al.³⁶ showed HDL cholesterol was significantly lower in subclinical hypothyroidism patients, while no significant differences were observed in LDL cholesterol, total cholesterol, and triglycerides ($p < 0.05$). The study by Abbasi et al. found that the disturbances in lipid metabolism are similar to those of hypothyroidism patients. A series of factors were considered in a study such as triglyceride, Total cholesterol (TC), high and low-density lipoprotein cholesterol, lipoprotein (a), and Apolipoprotein A-I and B to evaluate lipoprotein profile in subclinical hypothyroidism. Abbasi et al. observed that subclinical hypothyroidism is associated with elevated levels of LDL, but the apolipoprotein A levels remain unaltered and are majorly influenced by genetic factors rather than reduced thyroid hormone action.³⁷

In a meta-analysis study conducted by Liu et al.³⁸ they included a total of sixteen articles that compared the association of subclinical hypothyroidism and had at least a single parameter from lipid profile to obtain the overall weighted mean difference with the respective random effects model. The analysis result after statistical analysis and removal of biases showed that total triglyceride, total cholesterol in serum and low-density lipoprotein cholesterol (LDL-C) levels were significantly elevated in the patients with subclinical hypothyroidism as compared to the euthyroid patients with subclinical hypothyroidism had significantly higher total cholesterol, triglycerides, and LDL cholesterol levels. However, the study found no significant differences in serum high-density lipoprotein cholesterol (HDL-C) levels. The study also highlighted the possibility of potential publication bias between the factors like total cholesterol and low-density lipoprotein cholesterol which provided more heterogeneity for their comparison. Although the study concluded that subclinical

hypothyroidism is associated with an altered lipid profile, future research should place greater emphasis on controlling for confounding factors to ensure more accurate conclusions.

CONCLUSION

The study has concluded that the patients with subclinical hypothyroidism (SCH) exhibit significant gender-based differences in lipid profiles, with males showing higher levels of total cholesterol, triglycerides, LDL, and a higher Cholesterol/HDL ratio, along with significantly lower HDL levels ($p < 0.05$), indicating increased cardiovascular risk. Moreover, TSH levels show strong positive correlations with total cholesterol ($r=0.679$), triglycerides ($r=0.879$), and Cholesterol/HDL ratio ($r=0.7$), and a negative correlation with HDL ($r=-0.4$). In contrast, FT3 and FT4 demonstrate weak negative correlations with atherogenic lipids and a mildly positive association with HDL, highlighting that thyroid dysfunction, particularly elevated TSH, plays a significant role in deteriorating lipid metabolism and enhancing cardiovascular risk in SCH patients. By recognizing the link between subclinical hypothyroidism and adverse lipid profiles, clinicians can prioritize early intervention and preventive measures, such as lifestyle modification or pharmacotherapy, aimed at managing cholesterol levels and mitigating cardiovascular risks.

LIMITATIONS

In this study, since potential confounders were not considered or controlled, the findings cannot definitively attribute cardiovascular risks solely to lipid abnormalities associated with SCH. The elevated lipid profile observed in SCH patients might indeed contribute to cardiovascular risk, but without accounting for confounders, it is also possible that other unmeasured factors could be influencing both the lipid profile and cardiovascular outcomes. To address this limitation, the study could suggest future research involving a more comprehensive model that includes adjustments for these confounders. By doing so, researchers can better isolate the impact of SCH on lipid metabolism and cardiovascular risk. This would provide stronger evidence that the altered lipid profile associated with SCH is an independent risk factor for cardiovascular

problems, rather than one potentially confounded by other variables.

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