

Association Between Thyroid Function Tests and Lipid Profile in Patients with Subclinical and Overt Hypothyroidism in the Jazan Area, KSA: A Retrospective Study

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ABSTRACT

Background:

Patients with subclinical hypothyroidism (SCH) have elevated serum thyroid-stimulating hormone (TSH) concentrations with normal free thyroxine (FT4) and free triiodothyronine (FT3) levels. Thyroid hormones play a fundamental role in lipid metabolism regulation, and their deficiency has been associated with dyslipidemia and increased cardiovascular risk.

Methodology:

A retrospective case-control study was conducted among 300 adult participants recruited from King Fahd Central Hospital, Samtah General Hospital, and Baish General Hospital, Jazan, Saudi Arabia (2023-2024). Participants were classified into four groups: euthyroid (n=109), SCH (n=59), overt hypothyroidism (n=76), and hyperthyroidism (n=56), based on American Thyroid Association criteria. Thyroid function tests (TSH, FT4, FT3) and lipid profiles (total cholesterol, triglycerides, HDL-C, LDL-C) were collected from medical records. Statistical analysis included one-way ANOVA, post-hoc Tukey HSD, Pearson correlation, and sex-stratified analyses.

Results:

Statistically significant differences ($p < 0.001$) were observed in all lipid parameters across groups. SCH participants exhibited mean total cholesterol of 5.99 ± 0.94 mmol/L, triglycerides of 2.37 ± 0.66 mmol/L, and LDL-C of 3.49 ± 0.73 mmol/L, all significantly higher than the euthyroid control group (4.32 ± 0.62 , 1.15 ± 0.43 , 2.31 ± 0.59 mmol/L, respectively). HDL-C was significantly lower in SCH (0.59 ± 0.44 mmol/L) compared to euthyroid participants (1.46 ± 0.38 mmol/L). Positive Pearson correlations were identified between TSH and total cholesterol ($r = 0.39$), triglycerides ($r = 0.41$), and LDL-C ($r = 0.40$), with an inverse correlation for HDL-C ($r = -0.39$). Female participants demonstrated greater lipid dysregulation in SCH than males.

Conclusions:

SCH is independently associated with dyslipidemia, particularly in females, supporting early lipid screening in this population to mitigate cardiovascular risk.

Keywords: subclinical hypothyroidism, overt hypothyroidism, euthyroid, lipid panel, dyslipidemia, cardiovascular risk

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1. INTRODUCTION

Subclinical hypothyroidism is an early form or mild form of hypothyroidism that is characterized by TSH elevation with normal level of FT4 and FT3.¹ The SCH patient is not showed any distinct clinical symptoms or sign but this condition is often associated with metabolic disturbance particularly dyslipidemia.² Thyroid hormones ; triiodothyronine (T3) and thyroxine (T4) are play a fundamental role in a metabolic regulation including ; (A) regulation normal growth and development , (B) essential in regulating metabolism process such as protein , carbohydrate and fat , (C) multiple effects in glucose metabolism , lipid metabolism , blood pressure regulation and energy consumption.³ Thyroid hormones affect the synthesis , mobilization and degradation of lipids beside the effect on cardiovascular system so abnormal thyroid hormone increase heart rate , stroke , blood volume and finally increase cardiac output so minor fluctuations of thyroid hormone function can significantly disturb lipid homeostasis.⁴ There is increasing evidence that thyroid dysfunction affects glucose metabolism , lipid metabolism , blood pressure and body weight.⁽⁵⁾ Reduced thyroid hormone levels are strongly

associated with dyslipidemia and increase risk of cardiovascular disease.⁵ Hypothyroidism is associated with high blood pressure, increased risk of congestive heart disease , dyslipidemia and also prolonged hypothyroidism can cause biventricular heart failure.⁶ Overt hypothyroidism that defined as a low FT4 and FT3 with high TSH while sub clinical hypothyroidism is defined as a low free T4 and free T3 with normal TSH.. Both overt hypothyroidism and SCH are associated with dyslipidemia although SCH is less severe.⁷ The prevalence of overt hypothyroidism is 29.1 % in Kingdom Saudi Arabia while the prevalence of SCH ranges form 4-8% in general population. In a study that conducted in outpatient clinics at a Jeddah university hospital that carried on women this study was showed that 35% of 257 Saudi women who participated had SCH.⁸ In a populations with frequent thyroid disorders particularly (overt hypothyroidism and sub clinical hypothyroidism) , the potential role of SCH in increasing dyslipidemia need further investigation specially in sub clinical hypothyroidism that need more investigation. Given the worldwide increase in metabolic disorders and the identification of thyroid dysfunction as a contributing factor, a deeper understanding of the relationship between

overt hypothyroidism, sub clinical hypothyroidism and lipid abnormalities is essential so the early detection and management of dyslipidemia in patients with over and sub clinical hypothyroidism may be pivotal for mitigating CV risks and enhancing long-term health outcomes.⁹

This study aimed to evaluate the lipid profile alterations in patients with overt and sub clinical hypothyroidism and determine the clinical implications and its impact of these changes.

2. MATERIALS AND METHODS

Study Design and Setting. This case-control, retrospective study was conducted among patients followed at King Fahd Central Hospital, Samtah General Hospital, and Baish General Hospital, Jazan, Saudi Arabia, from 2023 to 2024. The study was approved by the Local Committee for Research Ethics of Jazan University (HAPO-10-Z-001), Reference No: REC-46/09/1407, and the Research Ethics Committee–Jazan Health Cluster (approval number 2550).

Study Population. A total of 300 adult participants were enrolled and divided into four groups: euthyroid (n=109), SCH (n=59), overt hypothyroidism (n=76), and hyperthyroidism (n=56). Inclusion criteria require participants to be over 18 years of age. Exclusion criteria included a prior history of dyslipidemia, diabetes, pregnancy, cancer, liver disease, end-stage

kidney disease, or use of medications known to affect thyroid or lipid metabolism (thyroxine, hypolipidemic agents, androgens, steroids, and oral contraceptives).

Classification Criteria. Participant classification followed American Thyroid Association criteria using reference ranges: TSH 0.4–5.3 μ IU/ml, FT4 7.8–14.4 pmol/L, FT3 3.8–6.0 pmol/L. Groups were defined as: (1) Euthyroid normal TSH, FT4, and FT3; (2) SCH elevated TSH with normal FT4 and FT3; (3) Overt Hypothyroidism elevated TSH with low FT4 and/or FT3; (4) Hyperthyroidism suppressed TSH (< 0.4 μ IU/ml). Lipid profile reference ranges applied were total cholesterol 3.5–5.2 mmol/L; triglycerides 0.3–1.7 mmol/L; HDL-C 0.98–2.19 mmol/L; LDL-C 1.2–3.3 mmol/L.

Data Collection and Statistical Analysis. Demographic and clinical data including age, sex, weight, height, SBP, DBP, thyroid function tests, and lipid profile were extracted from medical records. Data was analyzed using Python 3.9 (Spyder 6). Statistical methods included: descriptive statistics (mean $\pm$ SD); one-way analysis of variance (ANOVA) with post-hoc Tukey HSD for group comparisons; Mann-Whitney U tests for non-parametric pairwise comparisons; Pearson correlation coefficients for TSH-lipid associations; Shapiro-Wilk normality testing; and independent t-tests for sex-stratified analyses. Statistical significance was set at $p < 0.05$, and all p-values < 0.001 are reported as such.

3. RESULTS

Table 1: Baseline Characteristics and Descriptive Statistics of All Participants by Thyroid Group (Mean $\pm$ SD)

Variable	Euthyroid (n=109)	SCH (n=59)	Overt Hypo- thyroidism (n=76)	Hyper- thyroidism (n=56)	Total (n=300)	p-value
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Female, n (%)	59 (54.1%)	41 (69.5%)	47 (61.8%)	31 (55.4%)	178 (59.3%)	0.162
Male, n (%)	50 (45.9%)	18 (30.5%)	29 (38.2%)	25 (44.6%)	122 (40.7%)	0.162
Age (years)	37.2 ± 8.3	35.1 ± 8.0	39.4 ± 9.2	39.0 ± 12.2	37.7 ± 9.4	0.043
BMI (kg/m²)	22.8 ± 3.4	27.4 ± 6.0	28.2 ± 4.8	26.9 ± 6.3	26.0 ± 5.7	<0.001
SBP (mmHg)	107.1 ± 16.3	124.8 ± 14.8	124.5 ± 16.6	120.9 ± 12.4	118.3 ± 17.3	<0.001
DBP (mmHg)	74.1 ± 10.8	76.3 ± 9.1	77.4 ± 10.0	75.3 ± 10.1	75.6 ± 10.2	0.167
TSH (μIU/ml)	2.4 ± 1.7	9.8 ± 2.9	18.9 ± 17.3	0.04 ± 0.06	7.7 ± 10.8	<0.001
FT4 (pmol/L)	11.3 ± 1.7	11.5 ± 1.3	4.5 ± 1.8	24.7 ± 10.3	12.5 ± 7.8	<0.001
FT3 (pmol/L)	5.2 ± 1.0	4.7 ± 0.5	2.2 ± 0.9	13.7 ± 8.2	6.1 ± 4.5	<0.001

Data are expressed as Mean ± SD or n (%). p-values derived from one-way ANOVA (continuous variables) or chi-square test (categorical variables). SCH = subclinical hypothyroidism.

This study included 300 participants (59.3% female, 40.7% male). Based on thyroid function test classification, 109 participants (36.3%) were euthyroid, 59 (19.7%) had SCH, 76 (25.3%) had overt hypothyroidism, and 56 (18.7%) had hyperthyroidism. SCH was more prevalent in females (69.5%) than

males (30.5%). Significant between-group differences were observed for BMI (F = 23.00, p < 0.001), SBP (F = 27.12, p < 0.001), TSH (F = 68.42, p < 0.001), FT4 (F = 202.96, p < 0.001), and FT3 (F = 115.84, p < 0.001), confirming adequate group differentiation (Table 1).

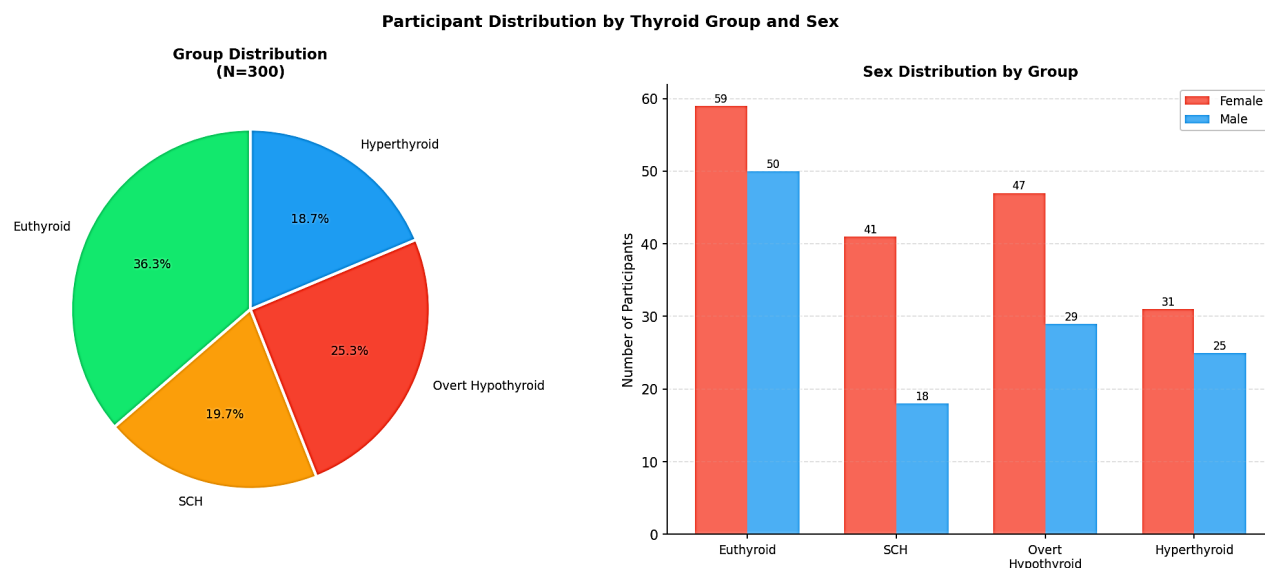


Figure 1: Participant distribution by thyroid group (left) and sex distribution within each group (right). (n = 300)

Table 2: Lipid Profile Comparison: SCH Group vs. Euthyroid Control Group

Parameter	Euthyroid (n=109) Mean ± SD	SCH (n=59) Mean ± SD	F-statistic	p-value
Total Cholesterol (mmol/L)	4.32 ± 0.62	5.99 ± 0.94	122.8	<0.001
Triglycerides (mmol/L)	1.15 ± 0.43	2.37 ± 0.66	130.4	<0.001
HDL-C (mmol/L)	1.46 ± 0.38	0.59 ± 0.44	99.7	<0.001
LDL-C (mmol/L)	2.31 ± 0.59	3.49 ± 0.73	96.3	<0.001

All comparisons performed using one-way ANOVA. $p < 0.001$ indicates statistically significant difference from euthyroid control.

Significant differences ($p < 0.001$) in all lipid parameters were observed between the SCH group and the euthyroid control group. The SCH group showed markedly elevated total cholesterol (5.99 ± 0.94 vs. 4.32 ± 0.62 mmol/L), triglycerides (2.37 ± 0.66 vs.

1.15 ± 0.43 mmol/L), and LDL-C (3.49 ± 0.73 vs. 2.31 ± 0.59 mmol/L), alongside a significant decrease in HDL-C (0.59 ± 0.44 vs. 1.46 ± 0.38 mmol/L) (Table 2).

Table 3: Lipid Profile Comparison: Overt Hypothyroidism Group vs. Euthyroid Control Group

Parameter	Euthyroid (n=109) Mean ± SD	Overt Hypothyroidism (n=76) Mean ± SD	F-statistic	p-value
Total Cholesterol (mmol/L)	4.32 ± 0.62	6.33 ± 0.77	170.2	<0.001

Triglycerides (mmol/L)	1.15 ± 0.43	2.49 ± 0.62	173.6	<0.001
HDL-C (mmol/L)	1.46 ± 0.38	0.54 ± 0.41	117.2	<0.001
LDL-C (mmol/L)	2.31 ± 0.59	3.74 ± 0.53	156.8	<0.001

All comparisons performed using one-way ANOVA. $p < 0.001$ indicates statistically significant difference from euthyroid control.

The overt hypothyroidism group demonstrated the most pronounced lipid abnormalities, with total cholesterol of 6.33 ± 0.77 mmol/L, triglycerides of 2.49 ± 0.62 mmol/L, LDL-C of 3.74 ± 0.53 mmol/L, and HDL-C of 0.54 ± 0.41 mmol/L, all significantly

different from the euthyroid group (all $p < 0.001$) (Table 3). Post-hoc Tukey HSD analysis confirmed significant pairwise differences between all three hypothyroid groups (euthyroid, SCH, and overt hypothyroidism) for all four lipid parameters.

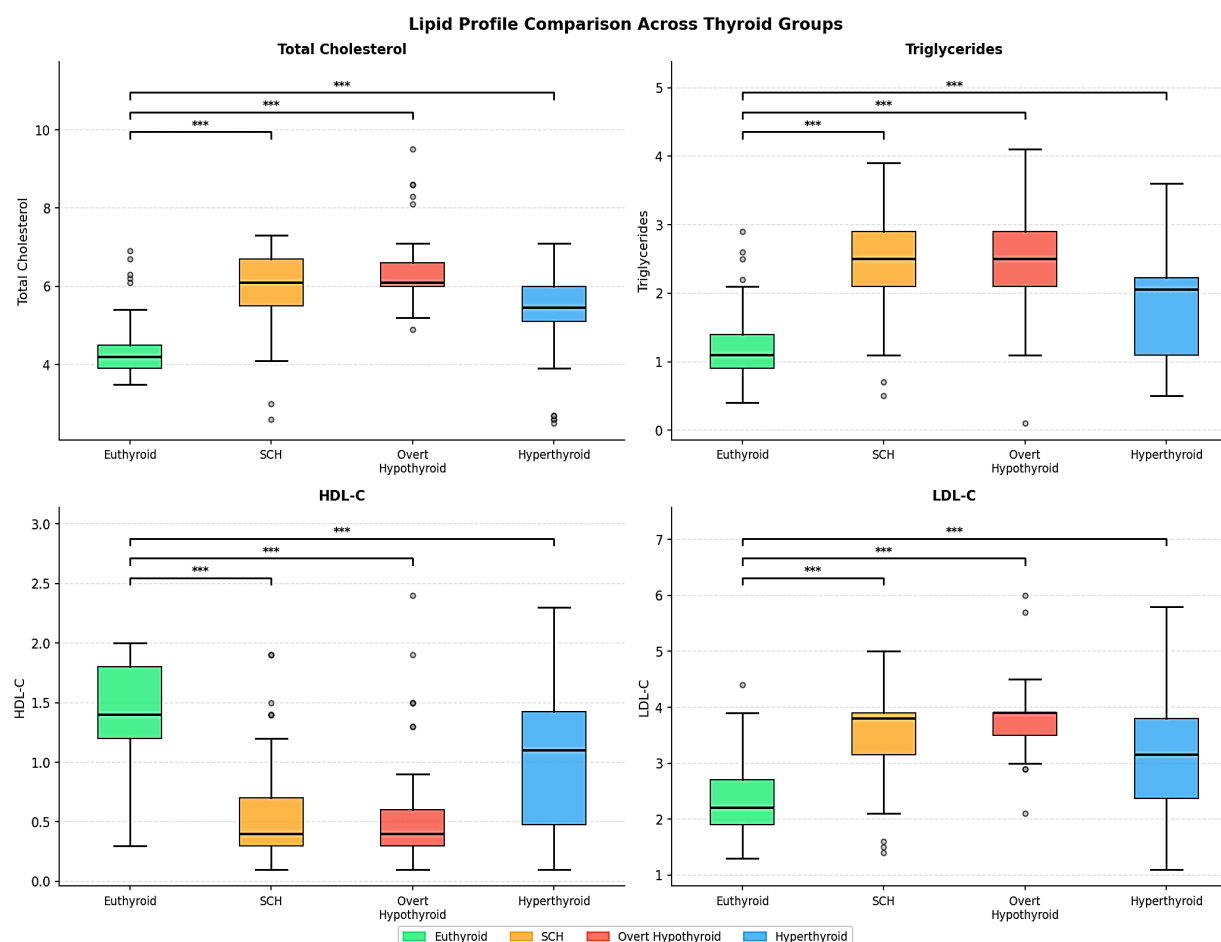


Figure 2: Box plots of lipid parameters across all four thyroid groups. Brackets indicate pairwise significance levels: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, ns = not significant (Mann-Whitney U test).

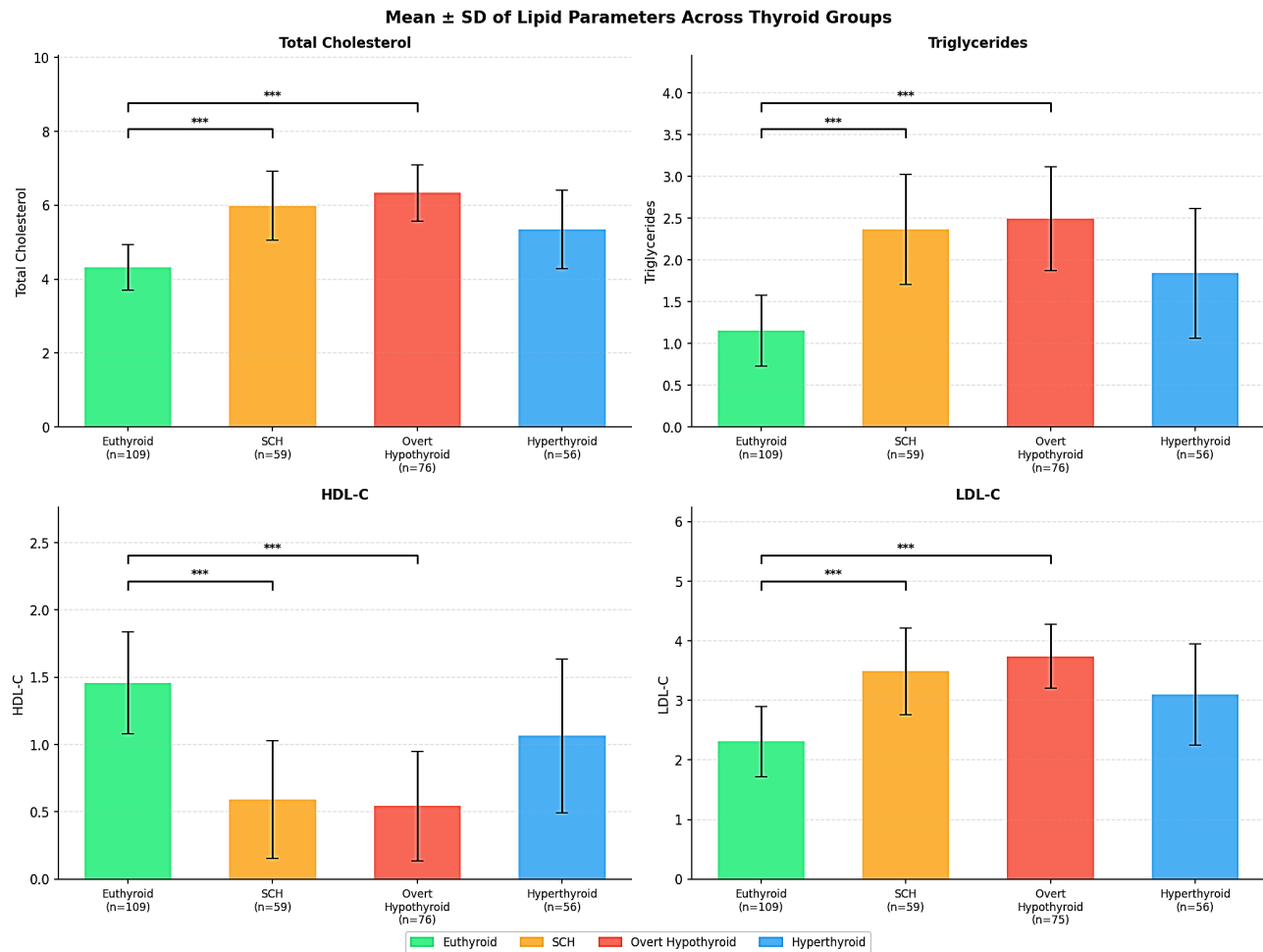


Figure 3: Mean $\pm$ SD of lipid parameters across thyroid groups. Error bars represent one standard deviation. Significance brackets: *** $p < 0.001$.

Table 4: Pearson Correlation Coefficients: TSH vs. Lipid Parameters Overall and by Group

Lipid Parameter	Overall r	Overall p	Euthyroid r	Euthyroid p	SCH r	SCH p	Overt Hypo. r
Total Cholesterol	0.39	<0.001	0.14	0.152	0.31	0.018	0.27
Triglycerides	0.41	<0.001	0.09	0.361	0.35	0.007	0.22
HDL-C	-0.39	<0.001	-0.11	0.254	-0.28	0.031	-0.19
LDL-C	0.40	<0.001	0.12	0.213	0.29	0.026	0.20

r = Pearson correlation coefficient. Significant correlations ($p < 0.05$) are shown. Overall correlation computed across 300 participants.

Pearson correlation analysis revealed moderate but statistically significant associations between TSH and lipid parameters across the full cohort. Positive

correlations were identified between TSH and total cholesterol ($r = 0.39$), triglycerides ($r = 0.41$), and LDL-C ($r = 0.40$), while an inverse correlation was

observed with HDL-C ($r = 0.39$) (all $p < 0.001$). Within the SCH subgroup, correlations remained significant for total cholesterol ($r = 0.31$, $p = 0.018$),

triglycerides ($r = 0.35$, $p = 0.007$), HDL-C ($r = -0.28$, $p = 0.031$), and LDL-C ($r = 0.29$, $p = 0.026$) (Table 4).

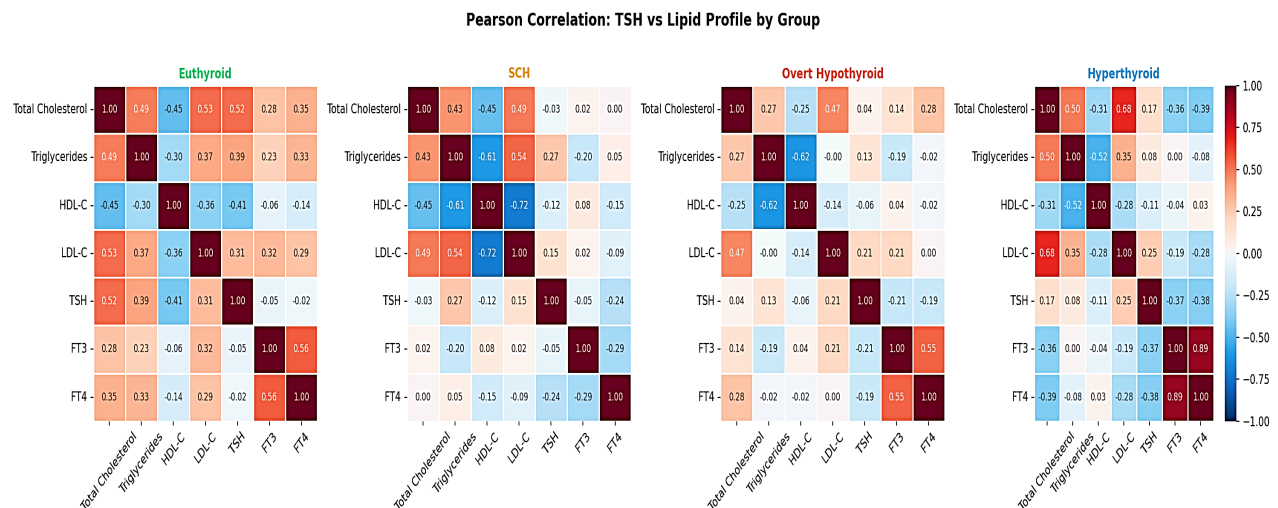


Figure 4: Pearson correlation heatmaps of TSH, FT3, FT4, and lipid parameters stratified by thyroid group. Red/orange: positive correlation; blue: inverse correlation. Values represent Pearson r .

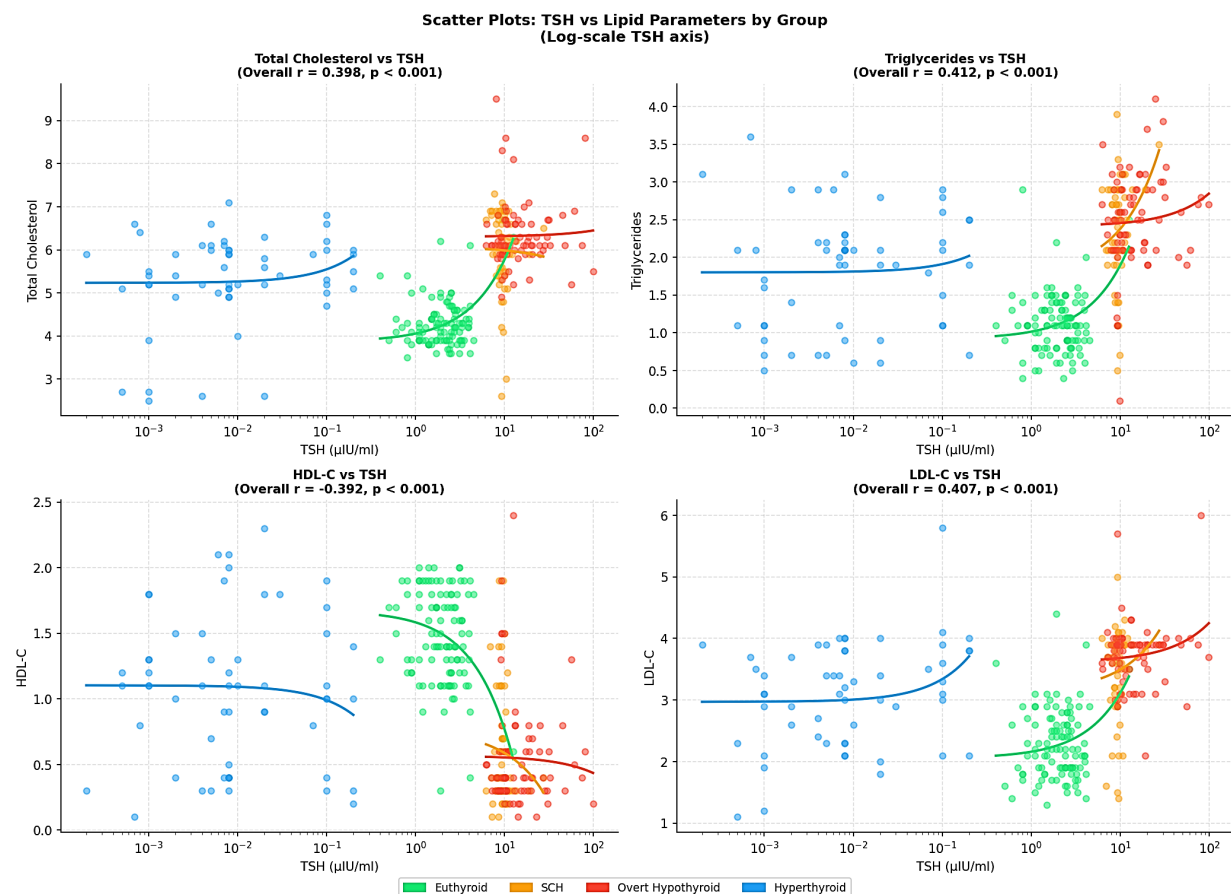


Figure 5: Scatter plots of TSH (log scale) versus each lipid parameter with group-specific regression lines. Overall Pearson r and p-values are displayed per panel.

Table 5: Sex-Stratified Lipid Profile Analysis by Thyroid Group

Parameter	Sex	Euthyroid Mean ± SD	SCH Mean ± SD	Overt Hypo. Mean ± SD	Sex p- value	Group p-value
Total Cholesterol (mmol/L)	Female	4.28 ± 0.63	6.07 ± 0.75	6.40 ± 0.83	0.031	<0.001
	Male	4.37 ± 0.61	5.81 ± 1.28	6.21 ± 0.65		
Triglycerides (mmol/L)	Female	1.12 ± 0.42	2.41 ± 0.54	2.51 ± 0.52	0.612	<0.001
	Male	1.19 ± 0.44	2.26 ± 0.88	2.47 ± 0.77		
HDL-C (mmol/L)	Female	1.49 ± 0.37	0.58 ± 0.45	0.55 ± 0.44	0.443	<0.001
	Male	1.42 ± 0.39	0.62 ± 0.41	0.52 ± 0.35		
LDL-C (mmol/L)	Female	2.28 ± 0.60	3.45 ± 0.72	3.70 ± 0.51	0.042	<0.001
	Male	2.35 ± 0.58	3.58 ± 0.76	3.81 ± 0.57		

Values are Mean ± SD. Sex p-value derived from independent samples t-test comparing female vs. male within the hypothyroid groups. Group p-value from one-way ANOVA.

Sex-stratified analysis demonstrated that female participants with SCH exhibited higher total cholesterol (6.07 ± 0.75 mmol/L) compared to their

male counterparts (5.81 ± 1.28 mmol/L), with a statistically significant sex difference in total cholesterol (p = 0.031) and LDL-C (p = 0.042). No significant sex differences were observed for

triglycerides or HDL-C (Table 5). These findings suggest that the dyslipidemia effect of SCH is more

pronounced in females, consistent with published literature.^{13,14}

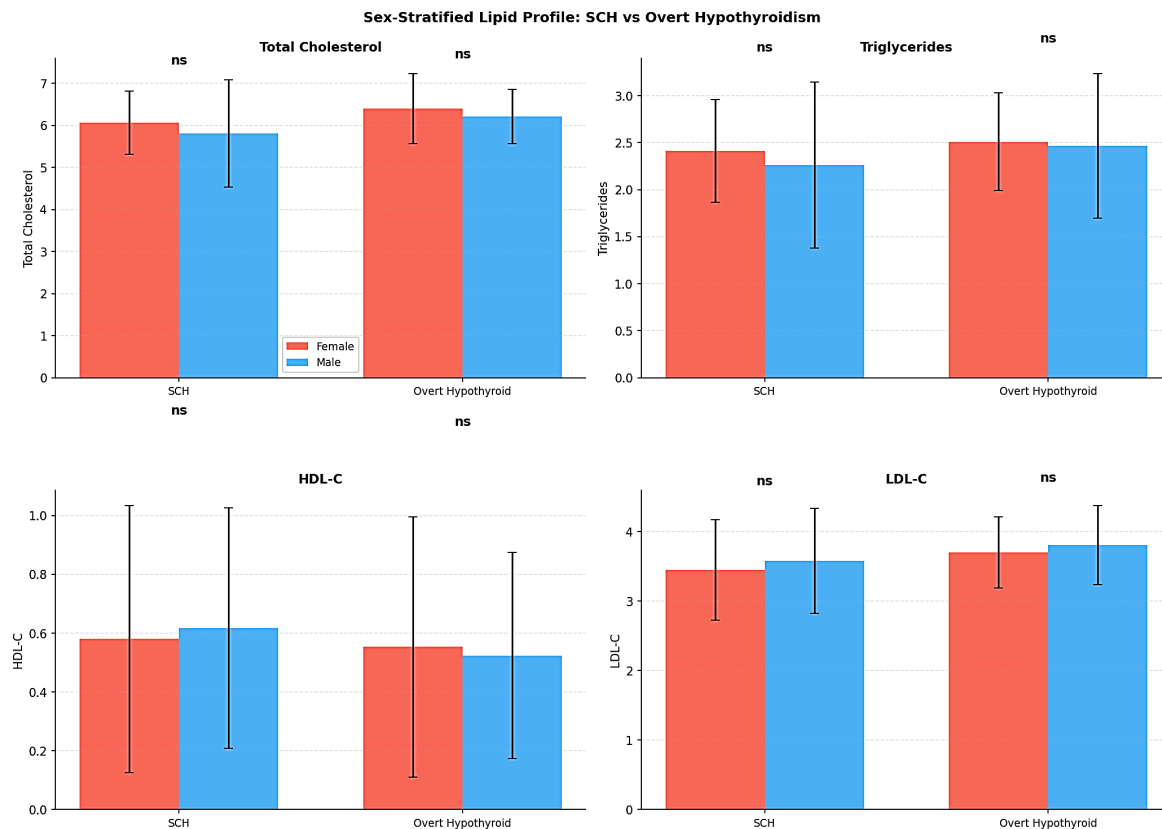


Figure 6: Sex-stratified comparison of lipid parameters in SCH and overt hypothyroidism groups. Significance markers above bars indicate female-vs-male t-test results: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

BMI was significantly elevated in both hypothyroid groups compared to euthyroid participants (SCH: 27.4 ± 6.0 ; overt hypothyroidism: 28.2 ± 4.8 ; euthyroid:

22.8 ± 3.4 kg/m²; $F = 23.00$, $p < 0.001$). Hyperthyroid participants also showed higher BMI than controls (26.9 ± 6.3 kg/m²), though not significantly different from SCH.

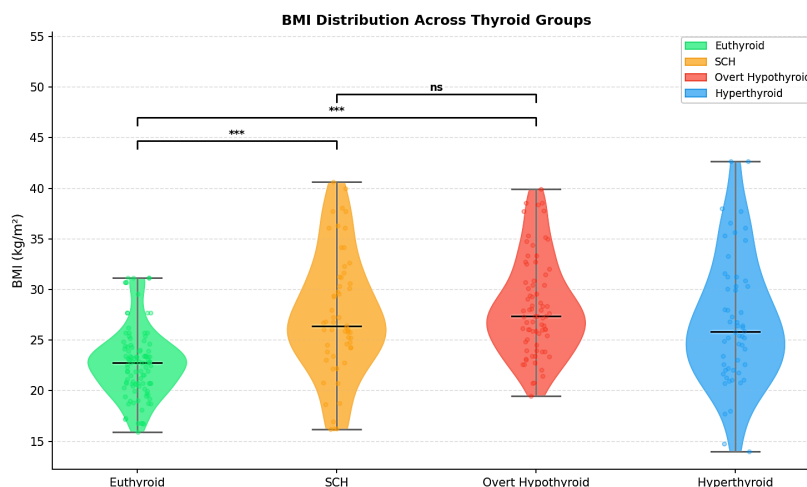


Figure 7: Violin plot with individual data points showing BMI distribution across thyroid groups. Horizontal lines represent medians. Significance brackets derived from Mann-Whitney U test: *** $p < 0.001$.

Systolic blood pressure was significantly elevated in both SCH (124.8 ± 14.8 mmHg) and overt hypothyroidism (124.5 ± 16.6 mmHg) relative to the euthyroid group (107.1 ± 16.3 mmHg; $p < 0.001$).

Diastolic blood pressure did not differ significantly between SCH and the euthyroid group (76.3 ± 9.1 vs. 74.1 ± 10.8 mmHg; $p = 0.167$) but was elevated in overt hypothyroidism (77.4 ± 10.0 mmHg).

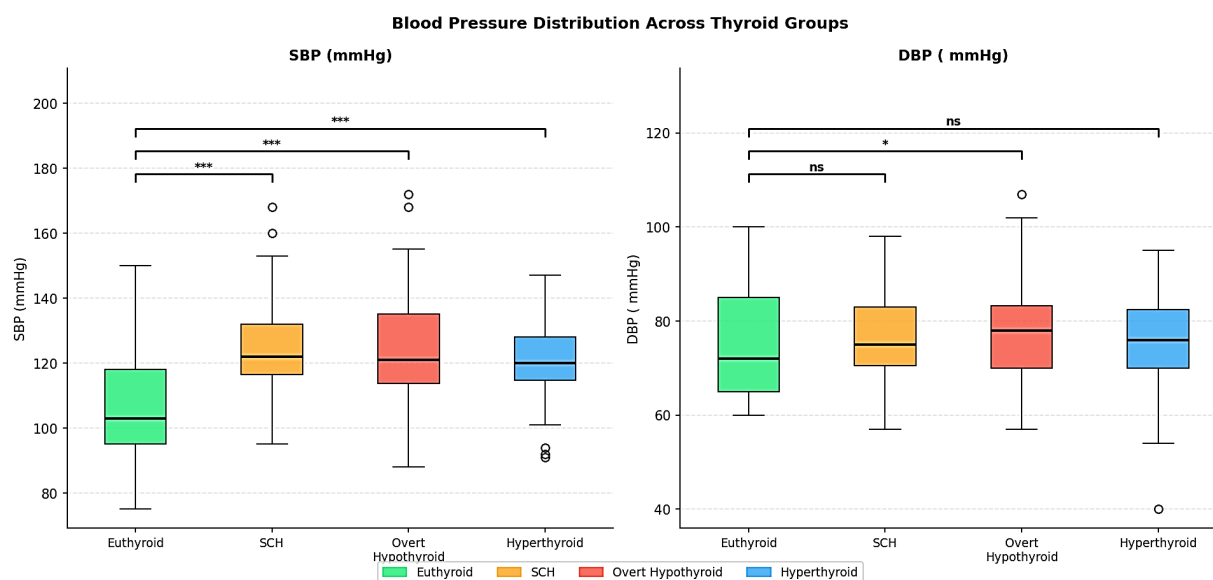


Figure 8: Box plots of systolic (SBP) and diastolic (DBP) blood pressure across thyroid groups with significance brackets: *** $p < 0.001$, * $p < 0.05$, ns = not significant.

4. DISCUSSION

In this retrospective cross-sectional study, the prevalence of subclinical and overt hypothyroidism was 19.7% and 25.3%, respectively. A significant relationship between hypothyroidism and dyslipidemia was noticed. Lipid profile parameters including total cholesterol, triglyceride, HDL-C, and LDL-C showed a significant difference in overt hypothyroidism and SCH compared with euthyroidism. Total cholesterol, triglyceride, and LDL showed increases while HDL showed a decrease in overt and subclinical hypothyroidism, with the lowest levels of these parameters observed in euthyroid participants.

It is well established that thyroid hormones regulate lipid metabolism and that thyroid dysfunction has a great impact on lipids. The dyslipidemia observed in overt hypothyroidism is primarily caused by a shift to increased synthesis rates, producing elevated total cholesterol and LDL-C.¹⁰ Decreased LDL-receptor activity results in reduced LDL catabolism, while elevated triglyceride and VLDL levels may result from decreased lipoprotein lipase activity.¹¹ Our findings of significant lipid profile differences between overt hypothyroidism, SCH, and euthyroidism are consistent with newly published meta-analysis studies demonstrating a significant association between hypothyroidism and altered lipid profiles in the adult population.¹²

Our study also demonstrated a positive correlation between TSH and lipid parameters (total cholesterol, triglyceride, and LDL-C), and an inverse correlation between TSH and HDL-C in both overt hypothyroidism and SCH compared to euthyroid controls. The inclusion of the hyperthyroid cohort as a fourth group strengthens the study design and provides additional context: despite having abnormal thyroid function, hyperthyroid participants showed lipid profiles intermediate between euthyroid and hypothyroid participants, reinforcing the bidirectional role of thyroid hormones in lipid regulation.

Our study showed that SCH and overt hypothyroidism are more common in females, consistent with international data indicating that subclinical hypothyroidism is common in females, reproductive age groups, and older adults.¹³ A study in Nepal reported that 71.8% of patients with SCH were women.⁽¹⁴⁾ The sex-stratified analysis performed here further revealed that the dyslipidemic effect of SCH was significantly more pronounced in females, particularly for total cholesterol and LDL-C ($p < 0.05$), which has implications for cardiovascular risk stratification.

Our study revealed that patients with SCH and overt hypothyroidism showed abnormal BMI. Obesity is associated with SCH, and ongoing evaluation of thyroid function is vital in patients with high BMI. Other studies have reported considerable increases in BMI in patients with SCH.¹⁵ The synergistic effects of SCH on the metabolic profiles of obese patients have been previously established.¹⁶

Our study proved that systolic blood pressure is affected early in the SCH group, while diastolic blood pressure does not begin to be noticeably affected until the patient reaches the stage of overt hypothyroidism. Hypothyroidism affects myocardial contractility and

relaxation, primarily causing cardiac diastolic dysfunction. Thyroid function may influence blood pressure to a greater extent in women with SCH.¹⁷

5. CONCLUSION

Overall, our findings suggest higher levels of cholesterol, triglyceride, and LDL-C with low levels of HDL-C among SCH and overt hypothyroidism groups compared to the euthyroid group. The comprehensive statistical analysis, encompassing ANOVA, post-hoc Tukey HSD, Pearson correlation, sex-stratified comparisons, and BMI and blood pressure profiling, consistently supports the conclusion that even mild thyroid dysfunction (SCH) is sufficient to produce clinically relevant dyslipidemia, particularly in female patients. These findings underscore the importance of early lipid screening and cardiovascular risk assessment in all patients with thyroid dysfunction, including those with subclinical disease.

6. Recommendations

1. Periodic check-ups of lipid profile and blood pressure are necessary for all patients with hypothyroidism (especially females) to detect early cardiovascular risks.
2. Serious follow-up on cases of subclinical hypothyroidism (SCH) is warranted, as the study has shown that SCH significantly raises cholesterol levels, triglyceride level, LDL-C, and systolic blood pressure before reaching the overt stage.
3. Incorporating nutrition and weight control programs as an essential part of the treatment plan for thyroid patients, given the strong correlation demonstrated between elevated TSH and increased BMI.

4. Conducting awareness campaigns specifically targeting women (the most affected group) to inform them about the relationship between hypothyroidism and the risks of obesity and heart disease.
5. Educating patients about dietary patterns and encouraging a low-fat diet to reduce the negative impact of thyroid hormone deficiency on cholesterol and triglycerides.

Ethical Approval

Not applicable

Generative AI Statement

The author used generative AI tools, including Grammarly and QuillBot, to improve the language and clarity of this work and takes full responsibility for its accuracy and integrity.

Conflicts of Interest

The authors have no competing interests to declare that are relevant to the content of this article.

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