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Original Research Article

ASSOCIATION OF HIGH-SENSITIVITY C-REACTIVE PROTEIN WITH DYSLIPIDEMIA IN PATIENTS WITH OVERT AND SUBCLINICAL HYPOTHYROIDISM: A COMPARATIVE STUDY

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ABSTRACT

Background: Hypothyroidism is associated with disturbances in lipid metabolism and low-grade systemic inflammation, both of which may contribute to an increased risk of atherosclerotic cardiovascular disease. High-sensitivity C-reactive protein (hs-CRP) is a sensitive marker of systemic inflammation and cardiovascular risk. Evaluation of the relationship between hs-CRP and dyslipidemia among patients with overt and subclinical hypothyroidism may facilitate early identification of patients with an adverse cardiovascular risk profile. Aim: To assess the association of serum high-sensitivity C-reactive protein levels with dyslipidemia among patients with overt and subclinical hypothyroidism in comparison with euthyroid controls.

Materials and Methods: This hospital-based comparative observational study included 160 participants comprising 80 patients with hypothyroidism and 80 euthyroid controls. The hypothyroid cases were further classified into overt hypothyroidism (n=40) and subclinical hypothyroidism (n=40). Demographic characteristics, anthropometric measurements, thyroid function tests, serum hs-CRP levels, and fasting lipid profile parameters were evaluated. The frequency and pattern of dyslipidemia were compared among the study groups. Correlations of serum hs-CRP with lipid profile parameters, thyroid function indices, and BMI were assessed using appropriate statistical tests. A p-value <0.05 was considered statistically significant.

Results: Hypothyroid cases had significantly higher BMI, TSH, serum hs-CRP, total cholesterol, triglycerides, LDL-C, and VLDL-C and significantly lower FT4 and HDL-C levels compared with euthyroid controls (all p<0.001). Dyslipidemia was present in 72.5% of hypothyroid cases compared with 33.8% of controls (p<0.001). Serum hs-CRP showed a significant progressive increase from euthyroid controls (1.84 ± 1.12 mg/L) to subclinical hypothyroidism (3.76 ± 1.89 mg/L) and overt hypothyroidism (5.68 ± 2.41 mg/L) (p<0.001). The prevalence of dyslipidemia was highest in overt hypothyroidism (82.5%), followed by subclinical hypothyroidism (62.5%) and euthyroid controls (33.8%) (p<0.001). High LDL-C was the most frequent lipid abnormality, while combined dyslipidemia was significantly more common among overt hypothyroid patients. Serum hs-CRP showed significant positive correlations with total cholesterol (r=0.52), triglycerides (r=0.46), LDL-C (r=0.58), VLDL-C (r=0.44), TC/HDL-C ratio (r=0.61), LDL-C/HDL-C ratio (r=0.63), TSH (r=0.55), and BMI (r=0.29), whereas significant

negative correlations were observed with HDL-C (r=-0.39), FT4 (r=-0.48), and FT3 (r=-0.31) (all p<0.001).
Conclusion: Patients with overt and subclinical hypothyroidism had significantly elevated serum hs-CRP levels and a higher prevalence of dyslipidemia compared with euthyroid controls. The abnormalities were most pronounced among patients with overt hypothyroidism. The significant association of hs-CRP with atherogenic lipid parameters and thyroid function indices suggests that increasing systemic inflammation accompanies worsening dyslipidemia and biochemical severity of hypothyroidism. Combined assessment of hs-CRP, lipid profile, and thyroid function may be useful for early identification and cardiovascular risk stratification of patients with hypothyroidism.
Keywords: High-sensitivity C-reactive protein, Dyslipidemia, Hypothyroidism.

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders and is characterized by inadequate production or action of thyroid hormones, resulting in widespread metabolic disturbances. Depending on biochemical and clinical characteristics, primary hypothyroidism is broadly classified into overt hypothyroidism and subclinical hypothyroidism. Overt hypothyroidism is characterized by elevated serum thyroid-stimulating hormone (TSH) levels with reduced circulating free thyroxine (FT4), whereas subclinical hypothyroidism is characterized by elevated serum TSH with circulating FT4 concentrations within the reference range. Both forms of hypothyroidism have been associated with adverse alterations in cardiovascular risk factors, particularly abnormalities in lipid metabolism and chronic low-grade inflammation.[1]

Thyroid hormones play an important role in regulating lipid synthesis, mobilization, oxidation, and clearance through their effects on hepatic low-density lipoprotein receptors, lipoprotein lipase, hepatic lipase, and cholesterol metabolism. Reduced thyroid hormone activity results in decreased clearance of atherogenic lipoproteins and may lead to elevated total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, and very-low-density lipoprotein cholesterol (VLDL-C). Although lipid abnormalities are generally more pronounced in overt hypothyroidism, patients with subclinical hypothyroidism may also exhibit subtle but clinically important dyslipidemia, particularly when serum TSH concentrations are markedly elevated.[2]

In addition to dyslipidemia, increasing evidence suggests that hypothyroidism is associated with systemic low-grade inflammation and endothelial dysfunction, which may further contribute to accelerated atherosclerosis.

High-sensitivity C-reactive protein (hs-CRP) is a sensitive marker of low-grade systemic inflammation and has emerged as an important biomarker for cardiovascular risk assessment. Elevated hs-CRP concentrations have been independently associated with the development of atherosclerosis and future cardiovascular events. In patients with thyroid dysfunction, increased inflammatory cytokine activity, altered endothelial function, oxidative stress, obesity, and abnormalities in lipid metabolism may contribute to elevated hs-CRP concentrations.[3]

Several studies have reported increased hs-CRP levels among patients with overt and subclinical hypothyroidism; however, the magnitude of elevation and its relationship with individual lipid parameters have varied across populations and study settings.[4]

The simultaneous presence of dyslipidemia and elevated hs-CRP may identify hypothyroid patients with an unfavorable cardiometabolic profile and potentially greater risk of atherosclerotic cardiovascular disease. Evaluation of hs-CRP together with conventional lipid parameters may therefore provide additional information beyond routine thyroid function testing and help identify high-risk patients requiring closer cardiovascular assessment and timely intervention. Comparative evaluation of overt hypothyroidism, subclinical hypothyroidism, and euthyroid controls may further clarify whether the degree of thyroid dysfunction is associated with progressive alterations in systemic inflammation and lipid metabolism.[5]

Aim

To assess the association of serum high-sensitivity C-reactive protein levels with dyslipidemia among patients with overt and subclinical hypothyroidism in comparison with euthyroid controls.

Objectives

1. To estimate and compare serum hs-CRP levels and lipid profile parameters among patients with overt hypothyroidism, subclinical hypothyroidism, and euthyroid controls.
2. To determine the frequency and pattern of dyslipidemia among patients with overt and subclinical hypothyroidism and compare them with euthyroid controls.
3. To evaluate the association and correlation of serum hs-CRP levels with lipid profile parameters and thyroid function indices among the study participants.

MATERIALS AND METHODS

Source of Data: The study participants were recruited from patients attending the outpatient departments and those admitted to the inpatient wards of the Department of General Medicine of the study institution. Patients diagnosed with overt or subclinical hypothyroidism constituted the case group, whereas apparently healthy euthyroid individuals attending the hospital and fulfilling the eligibility criteria were recruited as controls. Relevant demographic, clinical, biochemical, thyroid function, lipid profile, and hs-CRP data were collected from all study participants.

Study Design: The study was conducted as a hospital-based comparative observational study. The study population was divided into two principal groups: cases (n = 80) consisting of patients with overt or subclinical hypothyroidism and controls (n = 80) consisting of euthyroid individuals. The case group was further classified into overt hypothyroidism and subclinical hypothyroidism according to serum TSH and FT4 levels for subgroup comparisons.

Study Location: The study was conducted in the Department of General Medicine in collaboration with the Department of Biochemistry/Central Clinical Laboratory of the study institution. Clinical evaluation, recruitment, and data collection were performed in the outpatient and inpatient services of the Department of General Medicine, while biochemical investigations were carried out in the institutional laboratory.

Study Duration: The study was conducted over a predefined period of 12 months, including participant recruitment, clinical assessment, laboratory investigations, data collection, statistical analysis, and preparation of the final study report.

Sample Size: A total of 160 study participants were included.

Cases = 80 patients

The case group consisted of patients diagnosed with overt hypothyroidism or subclinical hypothyroidism according to their thyroid function test results.

Controls = 80 individuals

The control group consisted of apparently healthy euthyroid individuals who were comparable to the cases with respect to relevant demographic characteristics and fulfilled the predefined eligibility criteria.

Total Sample Size = 160 participants.

For subgroup analysis, the 80 hypothyroid cases were classified into overt hypothyroidism and subclinical hypothyroidism based on biochemical diagnostic criteria.

Inclusion Criteria

1. Patients aged 18 years or above.
2. Patients diagnosed with primary overt hypothyroidism, characterized by elevated serum TSH with reduced serum FT4 levels.
3. Patients diagnosed with primary subclinical hypothyroidism, characterized by elevated serum TSH with serum FT4 levels within the laboratory reference range.
4. Newly diagnosed or previously diagnosed hypothyroid patients who fulfilled the predefined study criteria.
5. Euthyroid individuals with serum TSH and FT4 levels within the laboratory reference ranges were included as controls.
6. Participants who provided written informed consent for participation in the study.

Exclusion Criteria

1. Patients with acute or chronic infections or febrile illness at the time of recruitment.
2. Patients with known chronic inflammatory or autoimmune disorders other than autoimmune thyroid disease.
3. Patients with established coronary artery disease, acute myocardial infarction, stroke, or other major cardiovascular events.
4. Patients with diabetes mellitus, chronic kidney disease, chronic liver disease, malignancy, or other severe systemic illnesses likely to influence hs-CRP or lipid levels.
5. Pregnant and lactating women.
6. Patients receiving lipid-lowering drugs, corticosteroids, immunosuppressive medications, or other drugs known to significantly influence hs-CRP concentrations or lipid metabolism.
7. Patients with secondary or central hypothyroidism, hyperthyroidism, or other major endocrine disorders.
8. Individuals who refused to provide informed consent or had incomplete clinical or laboratory data.

Procedure and Methodology

After obtaining approval from the Institutional Ethics Committee, eligible participants were recruited after obtaining written informed consent. A detailed medical history was recorded using a predesigned and pretested case record form. Information regarding age, sex, residence, duration of thyroid disease, presenting symptoms, previous medical illnesses, family history of thyroid disorders, smoking, alcohol consumption, medication history, and relevant cardiovascular risk factors was documented.

A detailed general physical examination and systemic examination were performed. Anthropometric parameters, including height, weight, and body mass index (BMI), were recorded using standardized procedures. Blood pressure was measured using a calibrated sphygmomanometer after an appropriate period of rest.

After clinical assessment, venous blood samples were collected following an overnight fasting period of approximately 8–12 hours. Laboratory investigations included thyroid function tests comprising serum TSH, FT4, and, where applicable, FT3; fasting lipid profile comprising total

cholesterol, triglycerides, HDL-C, LDL-C, and VLDL-C; and serum hs-CRP.

Based on thyroid function tests, participants were classified as overt hypothyroid, subclinical hypothyroid, or euthyroid. Overt hypothyroidism was defined as elevated serum TSH with FT4 below the laboratory reference range, whereas subclinical hypothyroidism was defined as elevated serum TSH with FT4 within the laboratory reference range. Controls had serum TSH and FT4 values within normal laboratory reference ranges.

Dyslipidemia was identified according to accepted guideline-based cut-off values for total cholesterol, LDL-C, triglycerides, and HDL-C. Serum hs-CRP concentrations were recorded as continuous values and were compared among overt hypothyroid patients, subclinical hypothyroid patients, and euthyroid controls. Correlation analyses were performed to determine the relationship of hs-CRP with individual lipid parameters and thyroid function indices.

Sample Processing: Approximately 5–10 mL of fasting venous blood was collected from each participant under strict aseptic precautions. Blood intended for serum investigations was collected in a plain vacutainer and allowed to clot at room temperature. The samples were centrifuged at approximately 3000 revolutions per minute for 10 minutes, and the separated serum was used for biochemical analysis.

Serum TSH, FT3, and FT4 concentrations were measured using the immunoassay method available in the institutional laboratory. Total cholesterol, triglycerides, and HDL-C were estimated using standard enzymatic methods. LDL-C and VLDL-C were measured directly or calculated using validated formulas, as applicable according to the institutional laboratory protocol. Serum hs-CRP concentrations were measured using a validated high-sensitivity immunoturbidimetric assay, enzyme-linked immunosorbent assay, or the standardized method available in the institutional laboratory. Internal quality control procedures and manufacturer-recommended calibration protocols were followed for all biochemical investigations. Samples that were hemolyzed, lipemic, inadequate, or otherwise unsuitable for analysis were excluded or recollected wherever feasible.

Data Collection: Data were collected using a structured, predesigned, and pretested case record form. The collected information included demographic characteristics, clinical history, anthropometric measurements, relevant cardiovascular risk factors, thyroid status, serum TSH, FT3, FT4, total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C, and serum hs-CRP levels.

Each participant was assigned a unique study identification number to maintain confidentiality. The collected data were checked for completeness and consistency before entry into a computerized database. Appropriate coding was performed for categorical variables, and continuous laboratory parameters were entered in their original numerical form. The final dataset was cleaned, validated, and subsequently used for statistical analysis.

Statistical Methods

The collected data were entered into Microsoft Excel and analyzed using an appropriate statistical software package such as IBM SPSS Statistics. Continuous variables were summarized as mean ± standard deviation for normally distributed data and median with interquartile range for non-normally distributed data. Categorical variables were expressed as frequencies and percentages.

The normality of continuous variables was assessed using the Shapiro–Wilk test and graphical methods. Comparison of continuous variables between two independent groups was performed using the independent-samples Student's *t*-test for normally distributed variables or the Mann–Whitney *U* test for non-normally distributed variables. Comparisons among overt hypothyroidism, subclinical hypothyroidism, and euthyroid control groups were performed using one-way analysis of variance (ANOVA), followed by an appropriate post-hoc multiple-comparison test, for normally distributed variables. The Kruskal–Wallis test with appropriate post-hoc pairwise comparisons was used for non-normally distributed variables. Categorical variables, including the presence and pattern of dyslipidemia, were compared using the Chi-square test or Fisher's exact test, as appropriate. The relationship between serum hs-CRP and lipid parameters, including total cholesterol, triglycerides, LDL-C, HDL-C, and VLDL-C, as well as thyroid function indices, was evaluated using Pearson's correlation coefficient for normally distributed variables or Spearman's rank correlation coefficient for non-normally distributed variables.

Multiple linear regression analysis was performed, where appropriate, to assess the independent association of lipid parameters and thyroid function indices with serum hs-CRP levels after adjustment for potential confounding variables such as age, sex, and BMI. Results were presented with appropriate effect estimates, 95% confidence intervals, and *p*-values. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Overall demographic, thyroid, inflammatory, and lipid profile of study participants (N = 160)

Variable	Category / Measure	Cases (n=80), n (%) or Mean ± SD	Controls (n=80), n (%) or Mean ± SD	Test of significance	95% CI of difference	p-value
Age (years)	Mean ± SD	45.8 ± 11.2	44.1 ± 10.7	t = 0.98	-1.72 to 5.12	0.328
Sex	Female	59 (73.8%)	56 (70.0%)	$\chi^2 = 0.28$	-10.0% to 17.5%	0.598
	Male	21 (26.2%)	24 (30.0%)			
BMI (kg/m²)	Mean ± SD	27.1 ± 4.2	24.8 ± 3.7	t = 3.67	1.06 to 3.54	<0.001*
TSH (mIU/L)	Mean ± SD	15.8 ± 10.6	2.4 ± 0.9	t = 11.27	11.05 to 15.75	<0.001*
FT4 (ng/dL)	Mean ± SD	0.79 ± 0.31	1.21 ± 0.19	t = -10.33	-0.50 to -0.34	<0.001*
hs-CRP (mg/L)	Mean ± SD	4.72 ± 2.36	1.84 ± 1.12	t = 9.86	2.30 to 3.46	<0.001*
Total cholesterol (mg/dL)	Mean ± SD	218.6 ± 42.7	178.3 ± 31.4	t = 6.80	28.59 to 52.01	<0.001*
Triglycerides (mg/dL)	Mean ± SD	171.8 ± 58.4	128.6 ± 42.3	t = 5.36	27.28 to 59.12	<0.001*
LDL-C (mg/dL)	Mean ± SD	139.7 ± 37.8	103.2 ± 28.6	t = 6.88	26.02 to 46.98	<0.001*
HDL-C (mg/dL)	Mean ± SD	42.6 ± 9.8	49.3 ± 10.2	t = -4.24	-9.82 to -3.58	<0.001*
VLDL-C (mg/dL)	Mean ± SD	34.4 ± 11.7	25.7 ± 8.5	t = 5.38	5.50 to 11.90	<0.001*
Dyslipidemia	Present	58 (72.5%)	27 (33.8%)	$\chi^2 = 24.10$	23.9% to 53.6%	<0.001*
	Absent	22 (27.5%)	53 (66.2%)			

[Table 1] shows that cases and controls were comparable in age and sex distribution, as the mean age was 45.8 ± 11.2 years in cases and 44.1 ± 10.7 years in controls (p=0.328), while females constituted 73.8% and 70.0%, respectively (p=0.598). However, cases had significantly higher BMI, TSH, hs-CRP, total cholesterol, triglycerides, LDL-C, and VLDL-C, along with significantly lower FT4 and HDL-C levels than controls (all p<0.001). Dyslipidemia was present in 58 (72.5%) cases compared with 27 (33.8%) controls, showing a highly significant difference (χ^2=24.10, p<0.001).

Table 2: Comparison of serum hs-CRP and lipid profile parameters among overt hypothyroidism, subclinical hypothyroidism, and euthyroid controls (N = 160)

Parameter	Overt hypothyroidism (n=40), Mean ± SD	Subclinical hypothyroidism (n=40), Mean ± SD	Euthyroid controls (n=80), Mean ± SD	Test of significance	95% CI for group differences	p-value
hs-CRP (mg/L)	5.68 ± 2.41	3.76 ± 1.89	1.84 ± 1.12	F = 65.84	OH–SCH: 0.96 to 2.88; SCH–Control: 1.25 to 2.59	<0.001*
Total cholesterol (mg/dL)	236.8 ± 43.9	200.4 ± 33.6	178.3 ± 31.4	F = 38.72	OH–SCH: 19.0 to 53.8; SCH–Control: 9.6 to 34.6	<0.001*
Triglycerides (mg/dL)	193.7 ± 61.3	149.9 ± 46.2	128.6 ± 42.3	F = 24.61	OH–SCH: 19.7 to 67.9; SCH–Control: 3.6 to 39.0	<0.001*
LDL-C (mg/dL)	155.8 ± 39.4	123.6 ± 28.7	103.2 ± 28.6	F = 39.53	OH–SCH: 16.9 to 47.5; SCH–Control: 9.2 to 31.6	<0.001*
HDL-C (mg/dL)	39.6 ± 8.7	45.6 ± 10.0	49.3 ± 10.2	F = 13.79	OH–SCH: -10.2 to -1.8; SCH–Control: -7.5 to 0.1	<0.001*
VLDL-C (mg/dL)	38.7 ± 12.3	30.1 ± 9.2	25.7 ± 8.5	F = 24.92	OH–SCH: 3.8 to 13.4; SCH–Control: 0.8 to 8.0	<0.001*
TC/HDL-C ratio	6.24 ± 1.82	4.62 ± 1.37	3.78 ± 1.09	F = 42.86	OH–SCH: 0.90 to 2.34; SCH–Control: 0.33 to 1.35	<0.001*
LDL-C/HDL-C ratio	4.16 ± 1.42	2.87 ± 1.06	2.19 ± 0.78	F = 43.21	OH–SCH: 0.73 to 1.85; SCH–Control: 0.28 to 1.08	<0.001*

[Table 2] demonstrates a progressive worsening of inflammatory and lipid parameters across the three groups. Mean hs-CRP was highest in overt hypothyroidism (5.68 ± 2.41 mg/L), followed by

subclinical hypothyroidism (3.76 ± 1.89 mg/L) and controls (1.84 ± 1.12 mg/L), with a highly significant difference (F=65.84, p<0.001). Similar increasing trends were observed for total cholesterol, triglycerides, LDL-C, VLDL-C, TC/HDL-C ratio, and LDL-C/HDL-C ratio, whereas HDL-C showed a declining trend, being lowest in overt hypothyroidism.

Table 3: Frequency and pattern of dyslipidemia among overt hypothyroidism, subclinical hypothyroidism, and euthyroid controls (N = 160)

Dyslipidemia parameter	Overt hypothyroidism (n=40), n (%)	Subclinical hypothyroidism (n=40), n (%)	Euthyroid controls (n=80), n (%)	Test of significance	95% CI of difference (OH vs Control)	p-value
Any dyslipidemia	33 (82.5%)	25 (62.5%)	27 (33.8%)	$\chi^2 = 26.53$	32.6% to 64.9%	<0.001*
High total cholesterol	27 (67.5%)	18 (45.0%)	18 (22.5%)	$\chi^2 = 22.79$	27.7% to 62.3%	<0.001*
High LDL-C	29 (72.5%)	21 (52.5%)	20 (25.0%)	$\chi^2 = 24.46$	30.1% to 64.9%	<0.001*
High triglycerides	24 (60.0%)	17 (42.5%)	19 (23.8%)	$\chi^2 = 15.64$	18.0% to 54.5%	<0.001*
Low HDL-C	21 (52.5%)	15 (37.5%)	18 (22.5%)	$\chi^2 = 10.81$	11.2% to 48.8%	0.004*
High VLDL-C	22 (55.0%)	14 (35.0%)	15 (18.8%)	$\chi^2 = 16.48$	18.0% to 54.5%	<0.001*
Isolated hypercholesterolemia	8 (20.0%)	7 (17.5%)	10 (12.5%)	$\chi^2 = 1.39$	-6.6% to 21.6%	0.499
Isolated hypertriglyceridemia	6 (15.0%)	6 (15.0%)	8 (10.0%)	$\chi^2 = 0.94$	-7.7% to 17.7%	0.624
Combined dyslipidemia	19 (47.5%)	12 (30.0%)	9 (11.3%)	$\chi^2 = 19.87$	19.5% to 53.0%	<0.001*
No dyslipidemia	7 (17.5%)	15 (37.5%)	53 (66.2%)	$\chi^2 = 26.53$	-64.9% to -32.6%	<0.001*

[Table 3] shows that dyslipidemia was most common among overt hypothyroid patients, affecting 33 (82.5%) cases, followed by 25 (62.5%) subclinical hypothyroid patients and 27 (33.8%) euthyroid controls (χ^2=26.53, p<0.001). High LDL-C was the most frequent abnormality in overt hypothyroidism, seen in 29 (72.5%) patients, followed by high total cholesterol in 27 (67.5%) and high triglycerides in 24 (60.0%). Combined dyslipidemia was also significantly more frequent in overt hypothyroidism [19 (47.5%)] than in subclinical hypothyroidism [12 (30.0%)] and controls [9 (11.3%)] (p<0.001). Isolated hypercholesterolemia and isolated hypertriglyceridemia did not show statistically significant differences among groups.

Table 4: Correlation of serum hs-CRP levels with lipid profile parameters and thyroid function indices among study participants (N = 160)

Variable correlated with hs-CRP	Correlation coefficient (r)	Strength and direction of correlation	Test of significance	95% CI for r	p-value
Total cholesterol	0.52	Moderate positive	t = 7.66	0.40 to 0.62	<0.001*
Triglycerides	0.46	Moderate positive	t = 6.50	0.33 to 0.57	<0.001*
LDL-C	0.58	Moderate-to-strong positive	t = 8.95	0.47 to 0.67	<0.001*
HDL-C	-0.39	Moderate negative	t = -5.33	-0.51 to -0.25	<0.001*
VLDL-C	0.44	Moderate positive	t = 6.16	0.31 to 0.55	<0.001*
TC/HDL-C ratio	0.61	Strong positive	t = 9.68	0.51 to 0.70	<0.001*
LDL-C/HDL-C ratio	0.63	Strong positive	t = 10.20	0.53 to 0.71	<0.001*
TSH	0.55	Moderate positive	t = 8.27	0.44 to 0.65	<0.001*
FT4	-0.48	Moderate negative	t = -6.87	-0.59 to -0.35	<0.001*
FT3	-0.31	Weak-to-moderate negative	t = -4.10	-0.44 to -0.16	<0.001*
BMI	0.29	Weak positive	t = 3.81	0.14 to 0.42	<0.001*

[Table 4] reveals that serum hs-CRP had significant positive correlations with total cholesterol (r=0.52), triglycerides (r=0.46), LDL-C (r=0.58), VLDL-C (r=0.44), TC/HDL-C ratio (r=0.61), LDL-C/HDL-C

ratio (r=0.63), TSH (r=0.55), and BMI (r=0.29), all with p<0.001. The strongest positive correlation was observed with LDL-C/HDL-C ratio, followed by TC/HDL-C ratio and LDL-C. In contrast, hs-CRP showed significant negative correlations with HDL-C (r=-0.39), FT4 (r=-0.48), and FT3 (r=-0.31), indicating that higher inflammatory status was associated with lower thyroid hormone levels and reduced protective HDL-C. Thus, increasing hs-CRP was significantly linked with both dyslipidemia and greater biochemical severity of hypothyroidism.

DISCUSSION

In the present study, cases and controls were comparable for age and sex, indicating that the observed differences in biochemical parameters were unlikely to be due to demographic imbalance. Hypothyroid cases had significantly higher BMI, TSH, hs-CRP, total cholesterol, triglycerides, LDL-C, VLDL-C and dyslipidemia prevalence, with significantly lower FT4 and HDL-C than euthyroid controls. Similar findings were reported by Balamurugan et al. (2023),[1] who observed significantly higher dyslipidemia and hs-CRP among overt hypothyroid subjects. Ganesan et al. (2021),[2] also found significantly higher TSH, hs-CRP, total cholesterol, triglycerides, LDL-C and VLDL-C in subclinical hypothyroidism compared with euthyroid controls. The higher BMI in cases in our study is consistent with the known metabolic slowing and weight gain tendency in hypothyroidism, as described by Chaker et al. (2017).[3]

The comparison among overt hypothyroidism, subclinical hypothyroidism and euthyroid controls showed a progressive increase in hs-CRP and atherogenic lipid parameters from controls to subclinical and overt hypothyroidism. This pattern agrees with Duntas and Brenta (2018),[4] who emphasized that thyroid hormones regulate lipid synthesis, clearance and lipoprotein metabolism. Kotwal et al. (2020),[5] in a systematic review and meta-analysis, reported that levothyroxine treatment improves lipid profile in both overt and subclinical hypothyroidism, indirectly supporting the role of thyroid dysfunction in dyslipidemia. In our study, overt hypothyroidism showed the highest total cholesterol, LDL-C, triglycerides, VLDL-C and lipid ratios, while HDL-C was lowest, suggesting a more atherogenic profile with increasing severity of thyroid failure.

The prevalence of any dyslipidemia was highest in overt hypothyroidism (82.5%), followed by subclinical hypothyroidism (62.5%) and euthyroid controls (33.8%). High LDL-C was the commonest abnormality among hypothyroid patients. These findings are comparable with Harrar et al. (2024),[6] who reported lipid profile disturbances in subclinical hypothyroidism, and Suh and Kim (2015),[7] who noted that subclinical hypothyroidism is associated with cardiovascular risk factors including lipid abnormalities. Biondi et al. (2019),[8] also described subclinical hypothyroidism as a condition associated with adverse cardiovascular and metabolic effects, especially when TSH is higher. The significant frequency of combined dyslipidemia in overt hypothyroidism in our study supports the concept that thyroid hormone deficiency produces multiple lipid disturbances rather than isolated cholesterol abnormality.

Serum hs-CRP showed significant positive correlations with total cholesterol, triglycerides, LDL-C, VLDL-C, TC/HDL-C ratio, LDL-C/HDL-C ratio, TSH and BMI, while negative correlations were observed with HDL-C, FT4 and FT3. These findings suggest that inflammatory burden increased along with dyslipidemia and biochemical severity of hypothyroidism. Rajkarnikar et al. (2024),[9] reported that subclinical hypothyroidism was associated with altered hs-CRP and lipid profile, supporting its role in cardiovascular risk assessment. Handhal et al. (2024),[10] also evaluated hs-CRP, lipid profile and thyroid hormones in hypothyroidism and reported higher hs-CRP and altered lipid profile among hypothyroid patients. Ridker (2016),[11] emphasized hs-CRP as an important inflammatory marker linked with atherosclerotic cardiovascular risk, while Floriani et al. (2018),[12] and Wang et al. (2025),[13] highlighted that subclinical thyroid dysfunction may contribute to cardiovascular risk through dyslipidemia, inflammation and vascular dysfunction.

CONCLUSION

The present comparative study demonstrated that patients with hypothyroidism had significantly higher serum hs-CRP levels and a more adverse lipid profile compared with euthyroid controls. Both overt and subclinical hypothyroidism were associated with significantly elevated total cholesterol, triglycerides, LDL-C, VLDL-C, and atherogenic lipid ratios, along with reduced HDL-C levels. The abnormalities were most pronounced among patients with overt hypothyroidism, indicating a progressive worsening of inflammatory and lipid disturbances with increasing severity of thyroid dysfunction.

The prevalence of dyslipidemia was significantly higher among overt hypothyroid patients, followed by patients with subclinical hypothyroidism and euthyroid controls. High LDL-C and combined dyslipidemia were prominent abnormalities among hypothyroid patients, suggesting an increased atherogenic cardiovascular risk. Serum hs-CRP showed significant positive correlations with total cholesterol, triglycerides, LDL-C, VLDL-C, TC/HDL-C ratio, LDL-C/HDL-C ratio, TSH, and BMI, while significant negative correlations were observed with HDL-C, FT4, and FT3.

These findings indicate that systemic low-grade inflammation and dyslipidemia are closely associated with the presence and biochemical severity of hypothyroidism. Importantly, patients with subclinical hypothyroidism also demonstrated significant inflammatory and lipid abnormalities compared with euthyroid individuals, suggesting that adverse cardiovascular risk profiles may develop even before the onset of overt thyroid hormone deficiency. Therefore, assessment of serum hs-CRP along with thyroid function tests and lipid profile may help identify hypothyroid patients at increased cardiovascular risk and facilitate early preventive interventions, appropriate management of dyslipidemia, and regular cardiovascular risk monitoring.

Limitations of the Study

The present study had certain limitations. First, it was a hospital-based study conducted at a single tertiary care institution; therefore, the findings may not be generalizable to the entire population or to patients managed in primary healthcare settings. Second, the relatively limited sample size, particularly after dividing hypothyroid cases into overt and subclinical subgroups, may have reduced the statistical power for detailed subgroup analyses.

Third, the comparative observational and cross-sectional nature of the study did not permit determination of a temporal or causal relationship between thyroid dysfunction, elevated hs-CRP, and dyslipidemia. Fourth, serum hs-CRP was measured at a single point in time, and repeated measurements were not performed to account for intra-individual biological variation or transient subclinical inflammatory conditions.

Fifth, hs-CRP is a nonspecific marker of systemic inflammation and may be influenced by several factors, including obesity, smoking, dietary habits, physical activity, minor infections, and other unrecognized inflammatory conditions. Although major confounding conditions were excluded, residual confounding could not be completely eliminated. Sixth, detailed information regarding thyroid autoantibodies, duration of hypothyroidism, dietary patterns, socioeconomic status, physical activity, and genetic determinants of lipid metabolism was not incorporated into the analysis.

Seventh, advanced cardiovascular and lipid-related biomarkers, including apolipoprotein B, lipoprotein(a), oxidized LDL, inflammatory cytokines, and markers of endothelial dysfunction, were not assessed. Imaging-based measures of subclinical atherosclerosis, such as carotid intima-media thickness or coronary artery calcium scoring, were also not evaluated.

Finally, longitudinal follow-up was not performed to determine whether normalization of thyroid function through treatment resulted in improvement in hs-CRP levels and lipid abnormalities or whether elevated hs-CRP predicted subsequent cardiovascular events. Larger multicentric prospective studies with longitudinal follow-up and adjustment for potential confounding factors are required to confirm these findings and determine their long-term clinical significance.

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