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Original Research Article

HIGH-SENSITIVE C-REACTIVE PROTEIN AND CARDIOMETABOLIC RISK IN SUBCLINICAL HYPOTHYROIDISM: A PROSPECTIVE ANALYSIS

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is associated with metabolic dysfunction and increased cardiovascular risk, potentially mediated by chronic low-grade inflammation. High-sensitivity C-reactive protein (hs-CRP) is an established marker of systemic inflammation, but its predictive significance in SCH remains unclear. This study evaluates the association of hs-CRP with metabolic parameters and its potential role in identifying individuals at heightened cardiometabolic risk.

Materials and Methods: This prospective observational study included patients with SCH, diagnosed based on elevated thyroid-stimulating hormone (TSH) levels and normal free thyroxine (FT4) levels. Serum hs-CRP, lipid profile, fasting glucose, fasting insulin, and insulin resistance (HOMA-IR) were measured at baseline and follow-up. Correlations between hs-CRP and metabolic parameters were analyzed using Pearson's and Spearman's correlation coefficients. Subgroup comparisons were performed, and receiver operating characteristic (ROC) curve analysis was conducted to determine the predictive value of hs-CRP for metabolic abnormalities.

Results: SCH patients had significantly higher hs-CRP levels (3.0 ± 1.2 mg/L) compared to euthyroid controls (1.7 ± 0.8 mg/L, $p < 0.001$). Elevated hs-CRP (≥3 mg/L) was associated with higher TSH (6.8 ± 1.6 vs. 4.9 ± 1.3 mIU/L, $p < 0.001$), BMI (28.3 ± 3.5 vs. 25.1 ± 3.2 kg/m², $p < 0.001$), LDL (130.2 ± 21.5 vs. 115.4 ± 19.7 mg/dL, $p = 0.002$), and HOMA-IR (3.9 ± 1.2 vs. 2.5 ± 0.8, $p < 0.001$). hs-CRP showed positive correlations with BMI ($r = 0.42$), LDL ($r = 0.38$), triglycerides ($r = 0.40$), fasting insulin ($r = 0.44$), and HOMA-IR ($r = 0.48$), all with $p < 0.01$. ROC analysis demonstrated that hs-CRP ≥3.0 mg/L had an AUC of 0.81 (95% CI: 0.74–0.88, $p < 0.001$) for predicting metabolic risk. Following metabolic optimization, significant reductions were observed in hs-CRP (-0.9 ± 0.6 mg/L, $p < 0.001$), LDL (-10.3 ± 8.5 mg/dL, $p = 0.002$), and HOMA-IR (-0.7 ± 0.5, $p < 0.001$).

Conclusion: Elevated hs-CRP levels in SCH are strongly associated with metabolic dysfunction and insulin resistance, underscoring its potential role as a predictive marker for cardiometabolic risk. Monitoring hs-CRP in SCH patients may facilitate early risk stratification and support targeted interventions to reduce cardiovascular complications.

Keywords: Subclinical hypothyroidism, high-sensitive C-reactive protein, inflammation, metabolic dysfunction, insulin resistance, cardiovascular risk.

INTRODUCTION

Subclinical hypothyroidism (SCH) is a common endocrine disorder affecting approximately 4–10% of the general population, with a higher prevalence in women and older adults.[1] It is characterized by elevated serum thyroid-stimulating hormone (TSH) levels with normal free thyroxine (FT4) concentrations, often detected incidentally during routine thyroid function testing.[2] Although SCH is traditionally considered a mild or asymptomatic condition, accumulating evidence suggests its potential role in the development of cardiovascular diseases (CVD), dyslipidemia, and systemic inflammation.[3]

High-sensitive C-reactive protein (hs-CRP) is a well-established biomarker of low-grade systemic inflammation and a predictor of cardiovascular risk, with elevated levels linked to endothelial dysfunction, atherosclerosis, and adverse cardiovascular events.[4] Review literature indicate that individuals with SCH exhibit significantly higher hs-CRP levels compared to euthyroid individuals, suggesting a pro-inflammatory state that may contribute to increased CVD risk.[5] It was reported that SCH is associated with a 20% higher risk of coronary heart disease (CHD) and a 17% increased risk of cardiovascular mortality, particularly in individuals with TSH levels above 10 mIU/L.[6] Additionally, higher hs-CRP levels in SCH patients have been correlated with impaired lipid metabolism, increased carotid intima-media thickness (CIMT), and reduced endothelial function, further supporting its role as a potential early marker of cardiovascular dysfunction.[7]

Despite these associations, the predictive significance of hs-CRP in stratifying cardiovascular risk in SCH remains incompletely understood. While some studies suggest that hs-CRP could serve as an early indicator for targeted intervention, others highlight inconsistencies in its predictive value across different patient populations.[8,9] Given the growing burden of SCH and its potential cardiovascular implications, further research is required to establish the clinical utility of hs-CRP in risk assessment and early management.[10] This prospective observational study aimed to evaluate the association between hs-CRP levels and SCH, providing insights into its role as a predictive marker for cardiovascular risk and guiding future preventive strategies.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted at a tertiary care centre in the Department of General Medicine at Deen Dayal Upadhyaya Medical College, Churu, Rajasthan, over a period of two years from December 2021 to November 2023. The study aimed to evaluate the predictive significance of high-sensitivity C-reactive protein (hs-CRP) in subclinical hypothyroidism (SCH) and its association with metabolic parameters over time. Ethical clearance was obtained from the Institutional Ethics Committee, and all participants provided written informed consent before enrolment.

Study Population: Participants were recruited from the outpatient internal medicine clinics. The study population comprised two groups: patients newly diagnosed with SCH and an age- and sex-matched euthyroid control group. SCH was defined as a thyroid-stimulating hormone (TSH) level exceeding 4.5 mIU/L, with free thyroxine (FT4) within the normal range. The euthyroid group included individuals with TSH and FT4 levels within reference ranges. Patients aged 18–65 years who met the SCH criteria and had no known acute or chronic inflammatory conditions were considered eligible for the study. Controls were selected from healthy individuals without thyroid dysfunction.

Patients with a history of overt thyroid disorders, diabetes mellitus, cardiovascular disease, chronic kidney disease, or any inflammatory condition were excluded. Additionally, individuals receiving hormone replacement therapy, lipid-lowering agents (e.g., statins), or medications affecting thyroid function or inflammatory markers were not included. Pregnant women and individuals with recent infections or hospitalizations within the past three months were also excluded to minimize confounding factors.

Sample Size Calculation: The sample size was calculated using G*Power software, based on previous studies evaluating hs-CRP levels in SCH. To detect an expected mean difference of 0.8 mg/L in hs-CRP levels between SCH patients and euthyroid controls, with an assumed standard deviation of 1.2 mg/L, a statistical power of 80%, and a significance level of 5% ($\alpha = 0.05$), the minimum required sample size was 100 participants (50 in each group). To account for potential dropouts or incomplete data, an additional 10% were recruited, resulting in a final sample size of 110 individuals.

Clinical and Laboratory Assessments: At baseline, all participants underwent a detailed clinical evaluation, including a structured interview to document medical history, demographic characteristics, and lifestyle factors such as smoking status and physical activity. Anthropometric measurements, including height, weight, and body mass index (BMI), were recorded using standardized protocols. Blood pressure was measured using an automated sphygmomanometer after a 10-minute rest in a seated position; the average of two consecutive readings was used for analysis.

Fasting venous blood samples were collected in the morning after an overnight fast of at least 8 hours. Laboratory investigations included thyroid function tests, lipid profile, fasting glucose, fasting insulin, and hs-CRP levels. TSH and FT4 were measured using a chemiluminescent immunoassay, with

sensitivity and intra-assay coefficients of variation (CV) recorded to ensure reliability. hs-CRP was quantified using a high-sensitivity enzyme-linked immunosorbent assay (ELISA), with an analytical sensitivity of 0.03 mg/L and an intra-assay CV of <5%. The lipid profile, including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, was assessed using an enzymatic colorimetric method. Insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA-IR), calculated as:

HOMA-IR = (Fasting insulin [μU/mL] × Fasting glucose [mg/dL]) / 405.

Follow-Up and Outcome Assessment

Participants in the SCH group were followed prospectively for 6 months, with reassessments at predetermined intervals. At follow-up visits, hs-CRP levels, thyroid function parameters, and metabolic markers—including lipid profile, BMI, and insulin resistance indices—were re-evaluated. The primary outcome was the change in hs-CRP levels over time and its correlation with metabolic parameters. Secondary outcomes included the progression of SCH to overt hypothyroidism and changes in cardiovascular risk markers among SCH patients compared to controls.

Statistical Analysis: Data were analyzed using SPSS version 20.0. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Descriptive statistics were reported as mean ± standard deviation (SD) for normally distributed variables. Comparisons between the SCH and euthyroid groups at baseline were performed using independent t-tests. Paired t-tests were used to assess longitudinal changes within the SCH group. Pearson's correlation coefficient was used to determine associations between hs-CRP levels and metabolic parameters, including BMI, HOMA-IR, and lipid profile. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of hs-CRP in identifying SCH patients at higher risk of metabolic disturbances. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported. A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

Age and sex distribution were comparable between SCH and euthyroid individuals ($p > 0.05$), but SCH patients had significantly higher BMI (27.1 ± 3.6 vs. 25.2 ± 3.3 kg/m², $p = 0.009$) and blood pressure (systolic: $p = 0.034$, diastolic: $p = 0.025$). Thyroid function markers showed elevated TSH (6.2 ± 1.5 vs. 2.4 ± 0.9 mIU/L, $p < 0.001$) and lower FT4 (0.88 ± 0.11 vs. 1.19 ± 0.14 ng/dL, $p < 0.001$) in SCH, while the inflammatory burden was higher in SCH, as indicated by elevated hs-CRP levels (3.0 ± 1.2 vs. 1.7 ± 0.8 mg/L, $p < 0.001$). Metabolic parameters were significantly altered in SCH, with higher LDL (127.5 ± 23.1 vs. 113.2 ± 20.4 mg/dL, $p < 0.001$), lower HDL (41.8 ± 7.5 vs. 47.3 ± 7.2 mg/dL, $p < 0.001$), and higher triglycerides (167.2 ± 36.4 vs. 143.5 ± 31.1 mg/dL, $p < 0.001$), while fasting glucose was slightly elevated ($p = 0.047$). Insulin resistance markers were significantly higher in SCH, with fasting insulin (13.6 ± 4.9 vs. 10.0 ± 3.7 μU/mL, $p < 0.001$) and HOMA-IR (3.4 ± 1.3 vs. 2.3 ± 0.9, $p < 0.001$) indicating greater insulin resistance [Table 1].

Table 1: Baseline Characteristics of Study Participants.

Variable	SCH Group (n=55)	Euthyroid Group (n=55)	p-value
	Frequency (%)/Mean ± SD		
Age (years)	42.9 ± 10.2	41.2 ± 9.5	0.283
Sex			
Male	20 (36.4%)	22 (40.0%)	0.711
Female	35 (63.6%)	33 (60.0%)	
BMI (kg/m²)	27.1 ± 3.6	25.2 ± 3.3	0.009
Blood Pressure (mmHg)			
Systolic	129.2 ± 9.4	125.0 ± 8.9	0.034
Diastolic	85.1 ± 7.1	82.7 ± 6.2	0.025
TSH (mIU/L)	6.2 ± 1.5	2.4 ± 0.9	<0.001
FT4 (ng/dL)	0.88 ± 0.11	1.19 ± 0.14	<0.001
hs-CRP (mg/L)	3.0 ± 1.2	1.7 ± 0.8	<0.001
LDL (mg/dL)	127.5 ± 23.1	113.2 ± 20.4	<0.001
HDL (mg/dL)	41.8 ± 7.5	47.3 ± 7.2	<0.001
Triglycerides (mg/dL)	167.2 ± 36.4	143.5 ± 31.1	<0.001
Fasting Glucose (mg/dL)	99.1 ± 12.7	94.6 ± 11.2	0.047
Fasting Insulin (μU/mL)	13.6 ± 4.9	10.0 ± 3.7	<0.001
HOMA-IR	3.4 ± 1.3	2.3 ± 0.9	<0.001

TSH levels significantly declined from 6.2 ± 1.5 to 4.1 ± 1.2 mIU/L (Δ = -2.1 ± 1.0, $p < 0.001$), while FT4 increased (Δ = +0.14 ± 0.08 ng/dL, $p < 0.001$). hs-CRP showed a notable reduction (Δ = -0.9 ± 0.6 mg/L, $p < 0.001$), indicating decreased inflammation. LDL and triglycerides significantly decreased (Δ = -10.3 ± 8.5 mg/dL, $p = 0.002$ and Δ = -15.4 ± 12.6 mg/dL, $p = 0.003$, respectively), while HDL improved (Δ = +2.8 ± 3.2 mg/dL, $p = 0.011$). Fasting glucose showed a modest reduction

(Δ = -3.8 ± 5.4 mg/dL, p = 0.043), whereas fasting insulin and HOMA-IR significantly decreased (Δ = -2.4 ± 1.8 µU/mL and Δ = -0.7 ± 0.5, both p < 0.001), suggesting improved insulin sensitivity [Table 2].

Table 2: Changes in Metabolic and Inflammatory Parameters from Baseline to Follow-up.

Variable	Baseline	Follow-up	Mean Change (Δ ± SD)	p-value
	Mean ± SD			
TSH (mIU/L)	6.2 ± 1.5	4.1 ± 1.2	-2.1 ± 1.0	<0.001
FT4 (ng/dL)	0.88 ± 0.11	1.02 ± 0.12	+0.14 ± 0.08	<0.001
hs-CRP (mg/L)	3.0 ± 1.2	2.1 ± 1.0	-0.9 ± 0.6	<0.001
LDL (mg/dL)	127.5 ± 23.1	117.2 ± 21.6	-10.3 ± 8.5	0.002
HDL (mg/dL)	41.8 ± 7.5	44.6 ± 7.1	+2.8 ± 3.2	0.011
Triglycerides (mg/dL)	167.2 ± 36.4	151.8 ± 34.7	-15.4 ± 12.6	0.003
Fasting Glucose (mg/dL)	99.1 ± 12.7	95.3 ± 11.5	-3.8 ± 5.4	0.043
Fasting Insulin (µU/mL)	13.6 ± 4.9	11.2 ± 4.3	-2.4 ± 1.8	<0.001
HOMA-IR	3.4 ± 1.3	2.7 ± 1.1	-0.7 ± 0.5	<0.001

At a cutoff of ≥1.0 mg/L, hs-CRP demonstrated a sensitivity of 85.3%, specificity of 60.4%, positive predictive value (PPV) of 68.2%, and negative predictive value (NPV) of 80.5%, with an area under the curve (AUC) of 0.75 (95% CI: 0.68–0.82, p < 0.001). At a cutoff of ≥2.0 mg/L, sensitivity decreased to 74.6%, but specificity improved to 73.1%, with an AUC of 0.78 (95% CI: 0.72–0.85, p < 0.001). The highest performance was observed at a cutoff of ≥3.0 mg/L, with a sensitivity of 62.5%, specificity of 85.7%, PPV of 79.4%, NPV of 72.6%, and an AUC of 0.81 (95% CI: 0.74–0.88, p < 0.001) [Table 3].

Table 3: Diagnostic Performance of hs-CRP for Identifying Metabolic Risk in SCH.

hs-CRP Cutoff (mg/L)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)	p-value
≥1.0	85.3	60.4	68.2	80.5	0.75 (0.68–0.82)	<0.001
≥2.0	74.6	73.1	72.5	75.2	0.78 (0.72–0.85)	<0.001
≥3.0	62.5	85.7	79.4	72.6	0.81 (0.74–0.88)	<0.001

The high hs-CRP group had significantly higher TSH levels (6.8 ± 1.6 vs. 4.9 ± 1.3 mIU/L, p < 0.001) and BMI (28.3 ± 3.5 vs. 25.1 ± 3.2 kg/m², p < 0.001) compared to the low hs-CRP group. Additionally, LDL levels were higher in the high hs-CRP group (130.2 ± 21.5 vs. 115.4 ± 19.7 mg/dL, p = 0.002). The high hs-CRP group also showed a significantly greater HOMA-IR (3.9 ± 1.2 vs. 2.5 ± 0.8, p < 0.001), indicating higher insulin resistance [Table 4].

Table 4: Comparison of Metabolic and Thyroid Parameters Based on hs-CRP Levels.

Variable	Low hs-CRP (<3 mg/L) (n=65)	High hs-CRP (≥3 mg/L) (n=45)	p-value
	Mean ± SD		
TSH (mIU/L)	4.9 ± 1.3	6.8 ± 1.6	<0.001
BMI (kg/m²)	25.1 ± 3.2	28.3 ± 3.5	<0.001
LDL (mg/dL)	115.4 ± 19.7	130.2 ± 21.5	0.002
HOMA-IR	2.5 ± 0.8	3.9 ± 1.2	<0.001

Individuals with HOMA-IR ≥ 2.5 had significantly higher hs-CRP levels (3.9 ± 1.4 mg/L) compared to those with HOMA-IR < 2.5 (2.1 ± 1.0 mg/L, p < 0.001). Similarly, those with LDL ≥ 130 mg/dL had higher hs-CRP levels (3.5 ± 1.3 mg/L) compared to those with LDL < 130 mg/dL (2.4 ± 1.1 mg/L, p = 0.002). Higher hs-CRP levels (3.7 ± 1.5 mg/L) were also observed in individuals with triglycerides ≥ 150 mg/dL, in contrast to those with triglycerides < 150 mg/dL (2.3 ± 1.2 mg/L, p = 0.003). Additionally, obese individuals (BMI ≥ 25 kg/m²) had significantly higher hs-CRP levels (4.1 ± 1.6 mg/L) compared to non-obese individuals (2.0 ± 1.1 mg/L, p < 0.001) [Table 5].

Table 5: hs-CRP Levels Across Different Metabolic Subgroups.

Subgroup	hs-CRP (mg/L) S(Mean ± SD)	p-value
HOMA-IR ≥2.5	3.9 ± 1.4	<0.001
HOMA-IR <2.5	2.1 ± 1.0	
LDL ≥130 mg/dL	3.5 ± 1.3	0.002
LDL <130 mg/dL	2.4 ± 1.1	
Triglycerides ≥150 mg/dL	3.7 ± 1.5	0.003
Triglycerides <150 mg/dL	2.3 ± 1.2	
Obese (BMI ≥25 kg/m²)	4.1 ± 1.6	<0.001
Non-Obese	2.0 ± 1.1	

A significant positive correlation was found between hs-CRP and BMI (r = 0.42, p < 0.001), TSH (r = 0.36, p = 0.002), LDL (r = 0.38, p = 0.001), triglycerides (r = 0.40, p = 0.001), fasting

glucose (r = 0.31, p = 0.008), and fasting insulin (r = 0.44, p < 0.001). A negative correlation was observed between hs-CRP and HDL (r = -0.29, p = 0.01). Additionally, hs-CRP showed a strong positive correlation with HOMA-IR (r = 0.48, p < 0.001), indicating a significant relationship with insulin resistance [Table 6].

Table 6: Correlation of hs-CRP with Metabolic and Thyroid Parameters.

Variable	Pearson's r	p-value
BMI (kg/m²)	r = 0.42	<0.001
TSH (mIU/L)	r = 0.36	0.002
LDL (mg/dL)	r = 0.38	0.001
HDL (mg/dL)	r = -0.29	0.01
Triglycerides (mg/dL)	r = 0.40	0.001
Fasting Glucose (mg/dL)	r = 0.31	0.008
Fasting Insulin (µU/mL)	r = 0.44	<0.001
HOMA-IR	r = 0.48	<0.001

DISCUSSION

Our study highlights the predictive significance of high-sensitivity C-reactive protein (hs-CRP) in subclinical hypothyroidism (SCH), demonstrating its strong associations with metabolic dysfunction, insulin resistance, and dyslipidemia. The findings suggest that SCH is accompanied by a pro-inflammatory state, reinforcing the hypothesis that chronic low-grade inflammation could serve as a crucial link between thyroid dysfunction and cardiovascular risk. We observed significantly elevated hs-CRP levels in the SCH group compared to euthyroid controls (3.0 ± 1.2 vs. 1.7 ± 0.8 mg/L, p < 0.001), consistent with previous studies by Vudu et al. and Nafari et al., suggesting an inflammatory component in early thyroid dysfunction.[11,12] Similarly, Sáenz-Ravello et al. found higher hs-CRP levels in SCH patients, supporting the role of inflammation in the pathogenesis of metabolic abnormalities in this population.[13]

The association between hs-CRP and metabolic parameters was evident in our subgroup analysis, where participants with higher hs-CRP levels (≥3 mg/L) exhibited significantly elevated TSH levels (6.8 ± 1.6 vs. 4.9 ± 1.3 mIU/L, p < 0.001), BMI (28.3 ± 3.5 vs. 25.1 ± 3.2 kg/m², p < 0.001), and adverse lipid profiles, including higher LDL (130.2 ± 21.5 vs. 115.4 ± 19.7 mg/dL, p = 0.002) and HOMA-IR (3.9 ± 1.2 vs. 2.5 ± 0.8, p < 0.001). These results align with the findings of Petersen et al. and Pingitore et al., who emphasized the role of low-grade inflammation in SCH-induced dyslipidemia and insulin resistance, further linking SCH to increased cardiovascular risk.[14,15] Similar observations were made by Balamurugan et al. and Gupta et al., who reported that individuals with SCH had significantly higher markers of inflammation, insulin resistance, and endothelial dysfunction compared to euthyroid individuals.[16,17]

Our correlation analysis further strengthened these associations, demonstrating significant positive correlations between hs-CRP and BMI (r = 0.42, p < 0.001), TSH (r = 0.36, p = 0.002), LDL (r = 0.38, p = 0.001), triglycerides (r = 0.40, p = 0.001), and fasting insulin (r = 0.44, p < 0.001). Notably, hs-CRP exhibited a strong correlation with HOMA-IR (r = 0.48, p < 0.001), indicating a close relationship between systemic inflammation and insulin resistance in SCH. The negative correlation between hs-CRP and HDL (r = -0.29, p = 0.01) suggests that inflammation contributes to HDL reduction, a key factor in atherogenesis. These findings are in agreement with studies by Ahmad et al. and Yu et al., both of which reported that chronic low-grade inflammation in SCH exacerbates metabolic dysfunction and accelerates atherosclerosis through increased oxidative stress and endothelial dysfunction.[18,19]

Furthermore, our subgroup analysis demonstrated that hs-CRP levels were significantly elevated in participants with metabolic abnormalities, including HOMA-IR ≥2.5 (3.9 ± 1.4 vs. 2.1 ± 1.0 mg/L, p < 0.001), LDL ≥130 mg/dL (3.5 ± 1.3 vs. 2.4 ± 1.1 mg/L, p = 0.002), triglycerides ≥150 mg/dL (3.7 ± 1.5 vs. 2.3 ± 1.2 mg/L, p = 0.003), and obesity (4.1 ± 1.6 vs. 2.0 ± 1.1 mg/L, p < 0.001). These results highlight hs-CRP as a potential marker for identifying SCH patients at heightened cardiometabolic risk.[20] Studies by Ahmad et al. and Abdulraheem Handhal et al. support our findings, showing that individuals with elevated hs-CRP levels in SCH exhibited greater susceptibility to metabolic syndrome, reinforcing the inflammatory-metabolic interplay in early thyroid dysfunction.[21,22]

The diagnostic utility of hs-CRP in predicting metabolic abnormalities in SCH was evaluated using ROC analysis. We found that an hs-CRP cutoff of ≥3.0 mg/L demonstrated the highest specificity (85.7%) and a significant AUC of 0.81 (95% CI: 0.74–0.88, p < 0.001), indicating its robustness as a predictive marker. An hs-CRP threshold of ≥2.0 mg/L showed balanced sensitivity (74.6%) and specificity (73.1%) with an AUC of 0.78 (95% CI: 0.72–0.85, p < 0.001), suggesting a useful predictive value in clinical practice. These findings are consistent with the work of Peixoto de Miranda et al., Vyakaranam et al., Panchal et al., and Krishnamurthy et al., who emphasized that hs-CRP is an independent predictor of early cardiovascular changes in thyroid dysfunction, highlighting its role in the early identification of at-risk individuals.[23-26]

Importantly, our study also demonstrated that metabolic optimization in SCH led to a significant reduction in hs-CRP levels (from 3.0 ± 1.2 to 2.1 ± 1.0 mg/L, $p < 0.001$), accompanied by improvements in LDL (-10.3 ± 8.5 mg/dL, $p = 0.002$), triglycerides (-15.4 ± 12.6 mg/dL, $p = 0.003$), fasting glucose (-3.8 ± 5.4 mg/dL, $p = 0.043$), and insulin resistance (HOMA-IR: -0.7 ± 0.5, $p < 0.001$). These findings align with previous research by Toloza et al., which reported that thyroid hormone replacement therapy in SCH led to a significant reduction in inflammation and metabolic risk factors.[27] Additionally, Koeder et al. found that lifestyle modifications in SCH patients significantly reduced hs-CRP levels, supporting the role of targeted interventions in mitigating inflammation.[28]

CONCLUSION

Overall, our findings underscore the predictive and diagnostic value of hs-CRP in SCH, particularly in identifying individuals at higher metabolic and cardiovascular risk. The strong correlations between hs-CRP and key metabolic markers suggest that systemic inflammation plays a crucial role in the pathophysiology of SCH-related metabolic disturbances. Given that hs-CRP serves as an early indicator of atherosclerosis and metabolic syndrome, incorporating hs-CRP assessment in the routine evaluation of SCH patients may help in early risk stratification and intervention. Future longitudinal studies are warranted to establish causality and evaluate the long-term cardiovascular implications of persistent inflammation in SCH.

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