Correlation of Myocardial Ischemia Assessed by Myocardial Perfusion Imaging with High Sensitivity C - Reactive Protein in Patients with Stable Ischemic Heart Disease

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ABSTRACT

Atherosclerosis and plaque formation are driven by inflammation, with high sensitivity C – reactive protein (hs-CRP) serving as a key biomarker of this process and a predictor of coronary heart disease risk. Ischemia occurs when atherosclerotic narrowing limits blood flow, and single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) plays a crucial role in detecting perfusion defects. MPI can distinguish viable from scarred tissue and link the functional impact of atherosclerosis to inflammatory activity in patients with stable ischemic heart disease (SIHD). The study was conducted at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS) between February 2024 to July 2025 with the objective to analyze the correlation between hs-CRP levels and MPI in patients with SIHD. A total of 50 patients with SIHD were selected for SPECT MPI through a single-day stress–(pharmacological) rest protocol. Serum hs-CRP level was measured within one week of SPECT MPI by nephelometry method. The mean age of the participants was 55.2 ± 9.9 years, with a male predominance (76.0%). Hypertension (76.0%) and Diabetes Mellitus (62.0%) were the most common associated risk factors. The mean SSS, SRS, and SDS were 12.4 ± 8.1, 6.5 ± 6.0, and 6.4 ± 2.4, respectively, indicating moderate to severe ischemia. Elevated hs-CRP (>3 mg/L) was found in 38.0% of cases. hs-CRP showed strong positive correlations with SSS ($r = 0.657$, $p < 0.001$) and SDS ($r = 0.528$, $p < 0.001$), and a moderate positive correlation with SRS ($r = 0.479$, $p < 0.001$). These findings indicate that higher hs-CRP levels were closely linked to increased ischemic burden and reduced myocardial function. Therefore, combined assessment of hs-CRP and MPI may improve risk stratification in stable ischemic heart disease.

Keywords: hs-CRP, Stable ischemic heart disease (SIHD), Myocardial perfusion imaging (MPI), Single-photon emission computed tomography (SPECT)

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INTRODUCTION

Coronary artery disease (CAD) represents a major global health challenge, characterized by a continuum of clinical presentations ranging from asymptomatic subclinical disease to stable ischemic heart disease (SIHD) and, ultimately, to acute coronary syndromes (1, 2). CAD is the leading cause of mortality and disability worldwide, accounting for a substantial proportion of global disease burden (3, 4). The burden of CAD is particularly concerning in South Asia, where onset occurs at younger ages. Bangladesh has been reported to rank among the highest in cardiovascular risk factors (5).

Well-established CAD risk factors include hypertension, diabetes, dyslipidemia, smoking, obesity, and sedentary lifestyle (6, 7). In addition, inflammation plays a central role in the initiation and progression of atherosclerosis, as it contributes to plaque instability and rupture (8-11). Hence, biomarkers of inflammation, e.g., high-sensitivity C-reactive protein (hs-CRP), have been widely studied for CAD evaluation (12–14). Several studies demonstrate its association with CAD severity (15, 16), while others show mixed findings (17, 18). hs-CRP also predicts adverse cardiovascular outcomes (19, 20). On the other hand, myocardial perfusion imaging (MPI) using SPECT is a well-established non-invasive modality for assessing myocardial ischemia (21–23). As expected, a correlation of hs-CRP with inducible ischemia detected by MPI has been observed (24–26). This study was, therefore, designed to analyze MPI findings in patients with stable ischemic heart disease, with a view to yielding any relationship with hs-CRP levels.

PATIENTS AND METHODS

This cross-sectional observational study was conducted at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), Dhaka, from February 2024 to July 2025. Patients with stable ischemic heart disease referred for myocardial perfusion imaging (MPI) were selected for the study. MPI was performed using a one-day stress–rest SPECT protocol with adenosine infusion (140

μg/kg/min for 6 minutes) following appropriate patient preparation. At peak stress, ^{99m}Tc-sestamibi was administered intravenously (7–10 mCi for stress and 15–25 mCi for rest). Image acquisition was carried out approximately 60 minutes post-injection using a dual-head gamma camera with standard acquisition parameters and ECG gating. Hemodynamic parameters were monitored throughout the procedure. Serum high-sensitivity C-reactive protein (hs-CRP) levels were measured using a nephelometric method, with established thresholds for cardiovascular risk stratification. Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 50 patients were included in the study, with a mean age of 55.2 ± 9.9 years, with an age range from 37 to 75 years. There was a clear predominance of middle-aged males with a high burden of metabolic risk factors, particularly overweight, hypertension, and diabetes (Table 1).

Table 1: Demographic Characteristics and Cardiovascular Risk Factors of Study Participants

Variables	*Categories*	*Frequency (n)*	*Percentage (%)*
Age (years)	37–50	19	38.0
	51–62	19	38.0
	63–75	12	24.0
Mean ± SD (Age)		55.2 ± 9.9	
Sex	Male	38	76.0
	Female	12	24.0
Body Mass Index (kg/m²)	Normal (18.5–24.9)	12	24.0
	Overweight (25.0–29.9)	30	60.0
	Obese (≥30.0)	8	16.0
Mean ± SD (BMI)		25.9 ± 4.2	
Smoking Status	Non-smoker	17	34.0
	Ex-smoker	27	54.0
	Current smoker	6	12.0
Family History of CAD	Yes	35	70.0
	No	15	30.0
Comorbidities	Hypertension	38	76.0
	Diabetes Mellitus	31	62.0
	Dyslipidemia	26	52.0

The most common diagnosis was stable angina, accounting for 42% (n = 21) of patients. This was followed by old myocardial infarction (OMI) in 28% (n = 14), post-percutaneous coronary intervention (PCI) in 24% (n = 12), and post-coronary artery bypass graft (CABG) in 6% (n = 3). Regarding biochemical parameters (HbA1c, serum creatinine, and lipid profile status), there was a predominance of metabolic and renal abnormalities within the study population.

As for myocardial perfusion imaging (MPI) patterns, the majority (48%) had demonstrated reversible perfusion defects, while 25% had mixed perfusion defects. Only 2% showed normal MPI findings, and 25% had fixed defects. Table 2 summarizes SPECT MPI scoring among study participants.

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Table-2: Distribution of SPECT MPI scoring

Variables	*Categories*	*Frequency (n)*	*Percentage (%)*	*Mean ± SD*	*Range*
Summed Stress Score (SSS)	Mild (4–8)	23	46.0	12.4 ± 8.1	4–35
	Moderate (9–13)	7	14.0		
	Severe (>13)	20	40.0		
Summed Rest Score (SRS)	0 (Normal)	8	16.0	6.5 ± 6.0	0–26
	1–9	32	64.0		
	≥10	10	20.0		
Summed Difference Score (SDS)	Mild Ischemia (3–4)	13	26.0	6.38 ± 2.38	3–11
	Moderate Ischemia (5–6)	16	32.0		
	Severe Ischemia (≥7)	21	42.0		

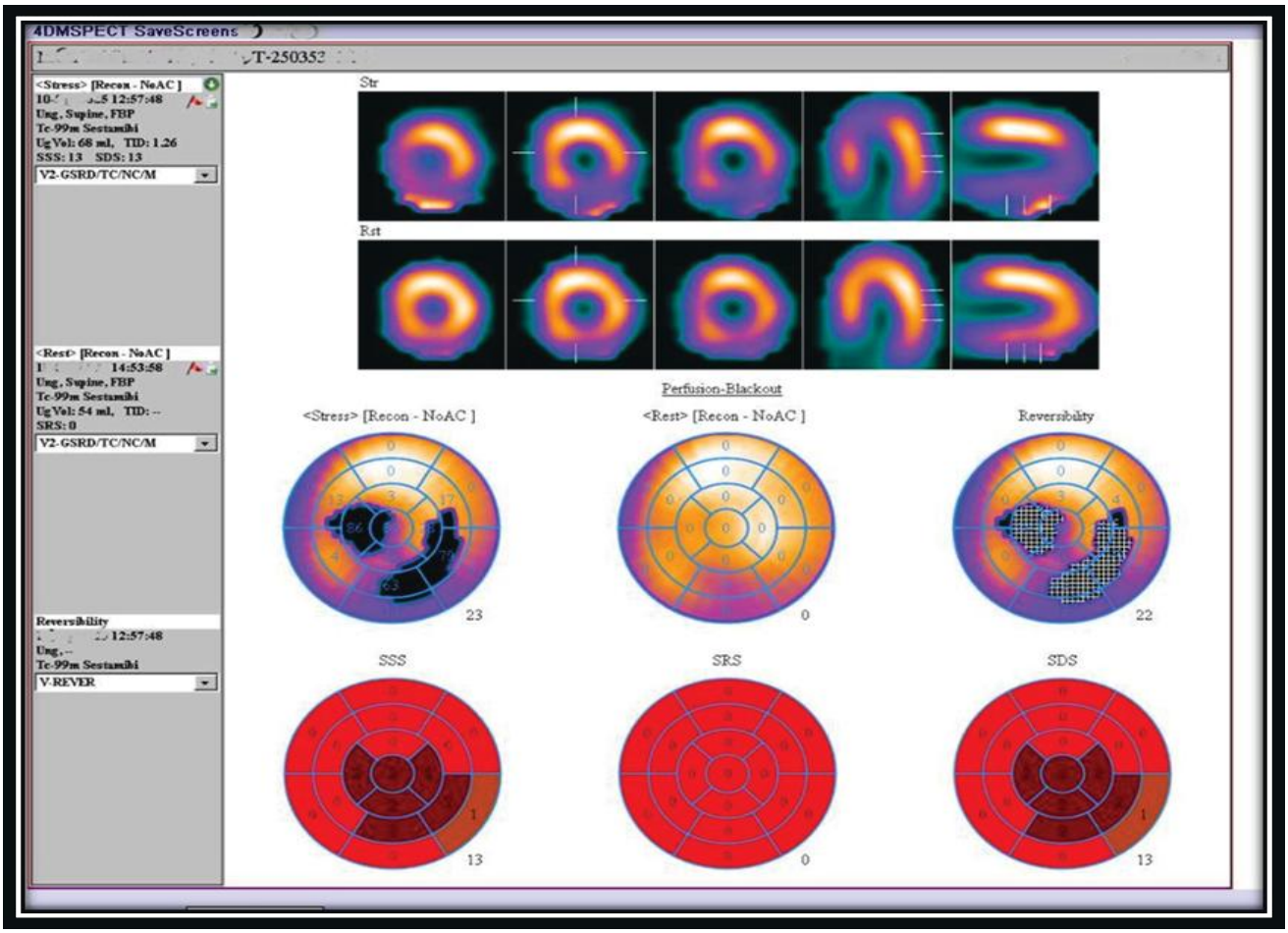


Figure 1: Myocardial Perfusion Imaging (MPI) of a 40-year-old hypertensive and diabetic male with exertional angina demonstrates severe, completely reversible perfusion defects in triple vessel territories (SDS = 13), consistent with significant ischemia. Serum hs-CRP level was 7.72 mg/L.

Significant positive correlation was found between hs-CRP and the Summed Stress Score (SSS) and also between hs-CRP and the Summed Rest Score (SRS). In the case of hs-CRP and the Summed Difference Score (SDS), there was a positive association that did not reach a significant level.

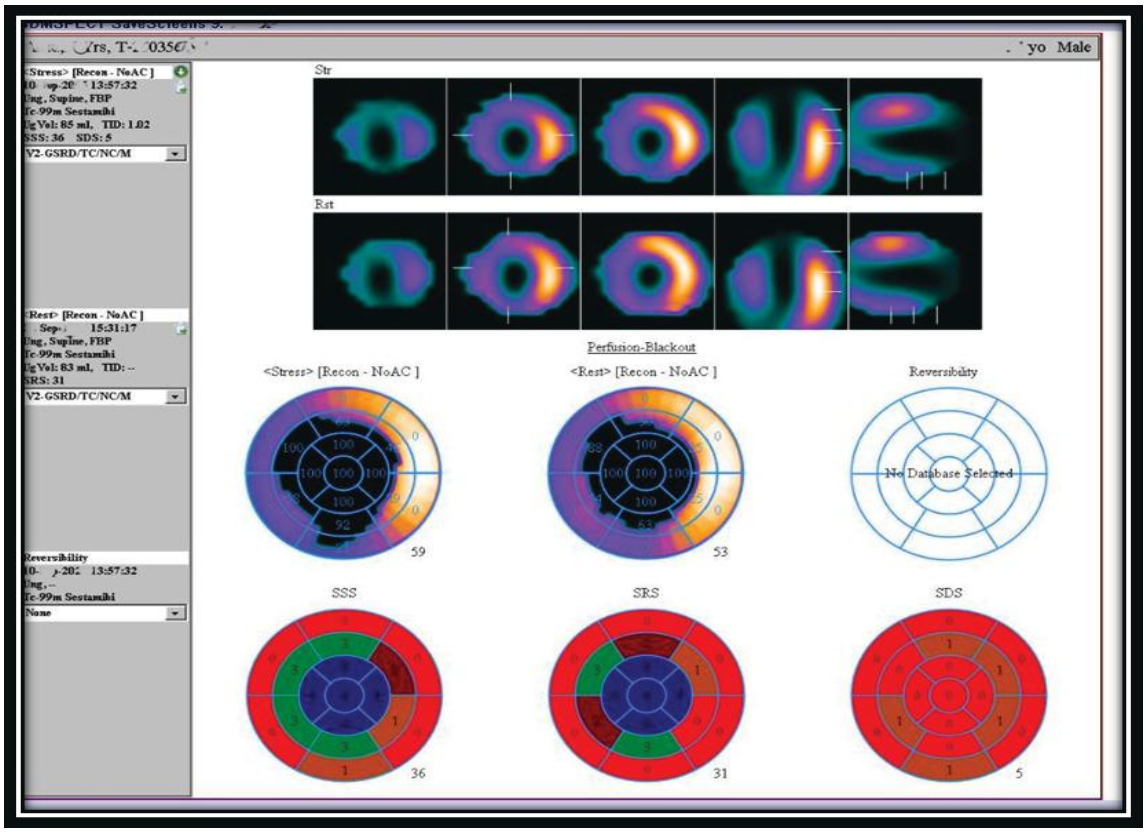
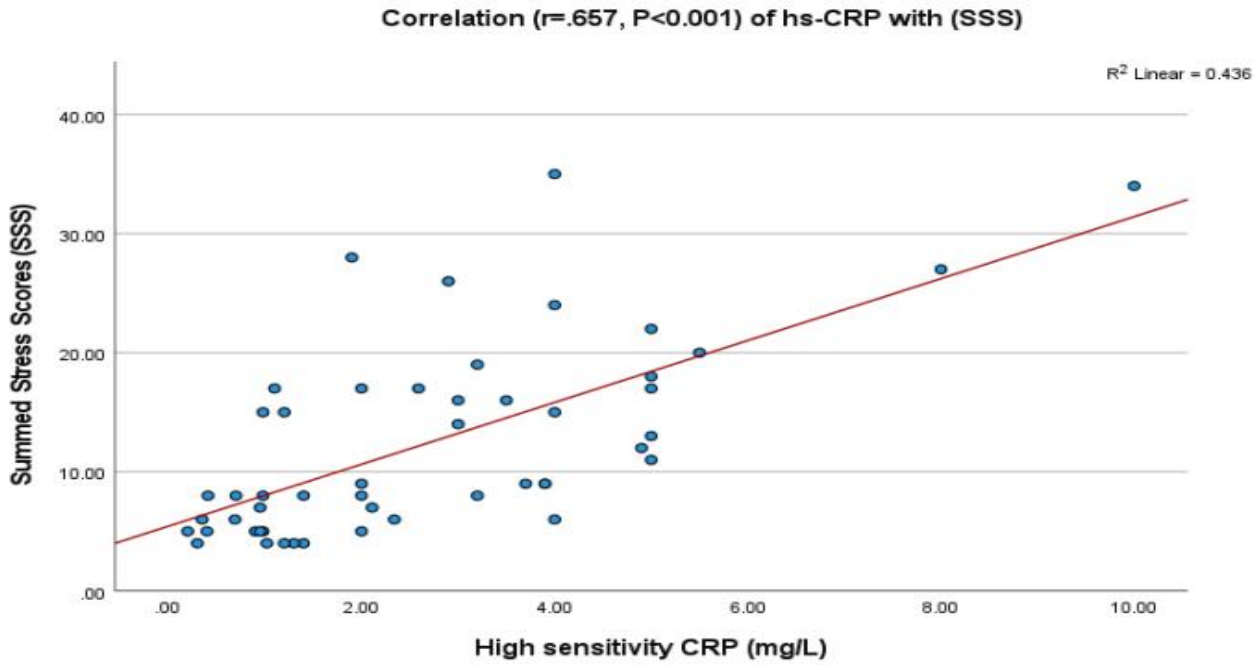


Figure 2 : A 57-year-old male with hypertension, diabetes, dyslipidemia, and prior anterior MI (2022) treated with PCI for double vessel disease, MPI reveals extensive fixed perfusion defects with peripheral reversibility (SSS = 37), representing mixed scar and ischemia. Serum hs-CRP level was 8 mg/L.



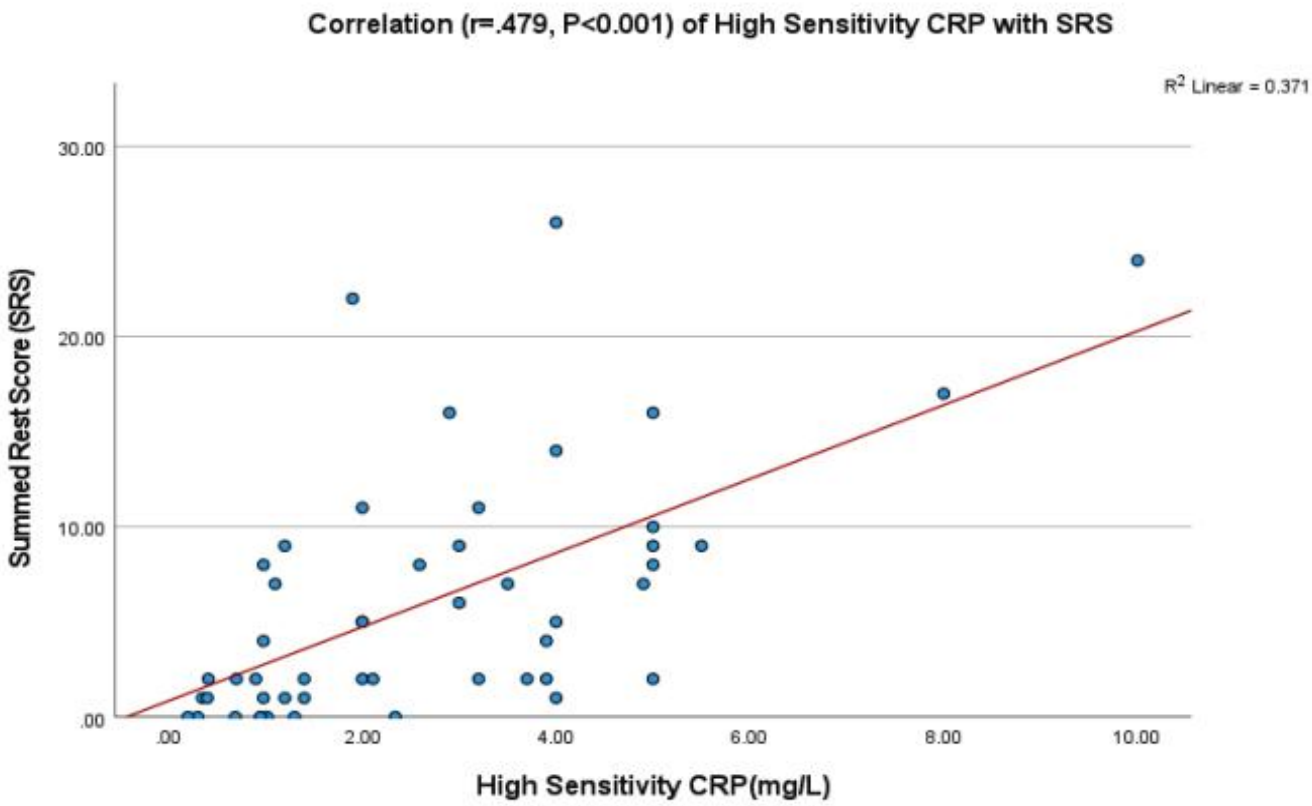


Figure 3: Scatter plots between hs-CRP level and Summed Stress Score (left), between hs-CRP level and Summed Rest Score (right). The Pearson correlation coefficients are 0.657 and 0.479 respectively ($p < 0.001$).

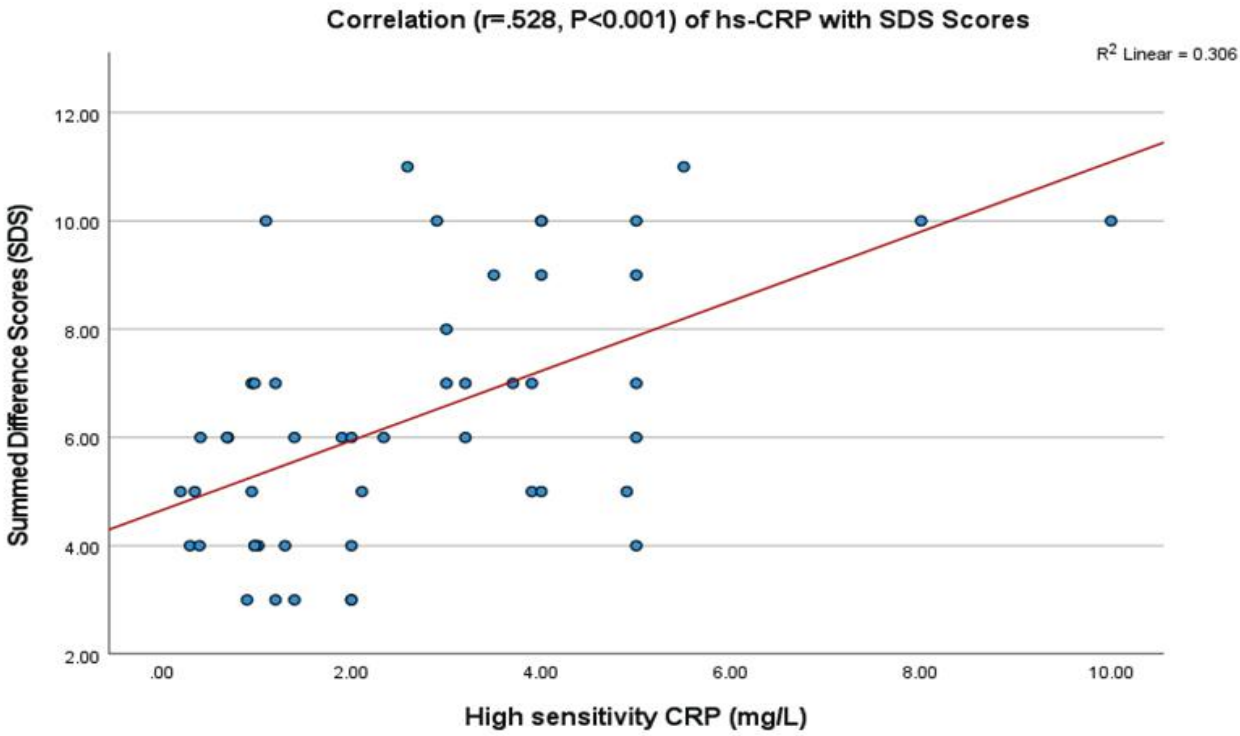


Figure 4: Scatter plot shows the correlation between hs-CRP and Summed Difference Score and A positive upward trend is visible. The Pearson correlation coefficient is $r = 0.528$, and $p < 0.05$, indicating a significant positive correlation. This suggests that patients with higher myocardial ischemia tend to have higher hs-CRP levels

DISCUSSION

The study evaluated the relationship between serum high-sensitivity C-reactive protein (hs-CRP) levels and myocardial perfusion abnormalities assessed by SPECT myocardial perfusion imaging (MPI) in patients with stable ischemic heart disease (SIHD). The findings demonstrate a strong association between systemic inflammation and the severity of myocardial ischemia, highlighting the interplay between metabolic risk factors and functional cardiac impairment.

The study population had a mean age of 55.2 ± 9.9 years, with a predominance of male participants (76.0%), reflecting the well-established epidemiological pattern of coronary artery disease (CAD) being more common in middle-aged and older men (4, 5). The higher prevalence in males may be attributed to earlier onset of atherosclerosis and the protective hormonal effects in premenopausal women (6).

A high burden of cardiovascular risk factors was observed. Overweight (60.0%) and obesity (16.0%) were common, while hypertension (76.0%) and diabetes mellitus (62.0%) were the most prevalent comorbidities. These findings are consistent with previous studies in South Asian populations demonstrating clustering of cardiometabolic risk factors contributing to CAD (1, 2). Such conditions promote endothelial dysfunction, oxidative stress, and chronic inflammation, accelerating atherosclerotic progression (6, 7).

Clinically, 46.0% of patients presented with typical angina, while others exhibited atypical symptoms such as fatigue and dyspnea. This variability aligns with previous observations that ischemic heart disease often presents atypically, particularly in diabetic and older patients (8). The distribution of clinical categories showed that stable angina was most common, followed by old myocardial infarction and post-revascularization states, reflecting real-world referral patterns for nuclear cardiology evaluation (9).

Biochemical analysis revealed a high prevalence of metabolic abnormalities, including elevated HbA1c (64.0%) and dyslipidemia (64.0%), indicating poor glycemic and lipid control. These findings further support the role of metabolic dysfunction in CAD pathogenesis and its association with systemic inflammation (1, 2).

SPECT MPI findings demonstrated a significant ischemic burden in the study population. Severe stress-induced ischemia (SSS >13) was present in 40.0% of patients, while 42.0% had severe reversible ischemia (SDS ≥7). Additionally, the majority of patients showed abnormal perfusion patterns, with 48% exhibiting reversible defects. These findings are consistent with previous studies indicating that higher perfusion defect scores are associated with worse clinical outcomes (9–11).

hs-CRP is well established as an independent predictor of cardiovascular events and reflects underlying vascular inflammation (3, 12, 24). A key finding of this study was the significant positive correlation between hs-CRP levels and MPI-derived indices of ischemia. Strong correlations were observed with the Summed Stress Score (SSS) and the Summed Difference Score (SDS) (Figure 1), while a moderate correlation was noted with the Summed Rest Score (SRS). These findings indicate that higher inflammatory burden is associated with greater myocardial ischemia. Similar results have been reported in previous studies. Habib and Al-Masri and Rashidinejad et al. demonstrated that elevated hs-CRP levels are associated with increased severity of CAD (14, 15). Likewise, Mitevska et al. and Yurtdaş et al. found significant correlations between hs-CRP and inducible ischemia on MPI (16, 17). These consistent findings reinforce the role of inflammation as an active contributor to myocardial ischemia rather than merely a secondary phenomenon. Moreover, the observed association between elevated hs-CRP and higher SDS suggests that inflammation is particularly linked with reversible ischemia, indicating active but potentially salvageable myocardium. This supports the concept of "inflammatory atherothrombosis," where systemic inflammation contributes to plaque instability, endothelial dysfunction, and impaired coronary microcirculation (6, 7).

The integration of hs-CRP measurement with SPECT MPI provides complementary information—biochemical and functional—allowing better risk stratification. Patients with elevated hs-CRP and high ischemic burden may represent a high-risk subgroup requiring more aggressive management. This is supported by large clinical trials such as the JUPITER trial, which

demonstrated that reducing inflammation with statin therapy significantly lowers cardiovascular risk in patients with elevated hs-CRP (22). From a pathophysiological perspective, chronic low-grade inflammation promotes cytokine activation, oxidative stress, and endothelial dysfunction, ultimately impairing myocardial perfusion. These mechanisms explain the strong association observed between hs-CRP levels and MPI abnormalities in this study (24, 26).

Overall, the findings of this study are consistent with current guidelines, which emphasize the importance of inflammation and metabolic dysfunction in chronic coronary syndromes (5, 8). The results support the use of hs-CRP as an adjunct biomarker in conjunction with imaging modalities for improved risk assessment, particularly in high-risk populations such as those in Bangladesh.

This study was limited by its modest sample size and single-center design, which restrict generalizability. The cross-sectional nature prevents conclusions about causality or long-term outcomes. hs-CRP, while sensitive, is nonspecific and may be influenced by other inflammatory states. SPECT MPI also has technical limitations, including availability, radiation exposure, and lower spatial resolution compared with advanced modalities.

CONCLUSION

This study demonstrated that metabolic risk factors, systemic inflammation, and functional ischemia are highly prevalent in patients with stable ischemic heart disease in Bangladesh. Elevated hs-CRP levels showed strong correlations with SPECT MPI parameters, particularly in severe ischemia and mixed perfusion defects, highlighting the link between inflammation and ischemic burden. The combined assessment of hs-CRP and SPECT MPI provides complementary information for risk stratification and underscores the value of hs-CRP as a clinical risk enhancer for identifying high-risk patients early.

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