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C-REACTIVE PROTEIN AND ITS ROLE IN DIAGNOSIS, MYOCARDIAL DAMAGE, AND ANGIOGRAPHIC FINDINGS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Background and Objective

C-reactive protein (CRP), a key acute-phase reactant, is known to reflect systemic and vascular inflammation and has been implicated in the pathogenesis of atherosclerotic plaque instability. This study aimed to evaluate the prognostic utility of CRP levels in diagnosing myocardial injury and predicting angiographic and clinical outcomes in patients presenting with acute coronary syndrome (ACS).

Methods

This prospective, single-center study was conducted in the Department of Cardiology in collaboration with the Department of Pathology at Army Cardia Hospital Lahore, from 1st January 2023 till 31st December 2023. A total of 200 patients presenting with chest pain were enrolled and categorized into four groups: Group 1 (unstable angina), Group 2 (ST-elevation myocardial infarction, STEMI), Group 3 (non-ST-elevation myocardial infarction, NSTEMI), and Group 4 (control group with non-cardiac chest pain). High-sensitivity CRP (hs-CRP) levels were measured at admission. All patients were followed for 90 days for major adverse cardiac events including myocardial infarction, heart failure, and cardiac death.

Results

CRP levels were significantly higher in STEMI and NSTEMI groups compared to those with unstable angina and the control group ($p < 0.00001$). The mean CRP level across all patients was 17.6 ± 7.96 mg/L (95% CI: 1.66–33.6). Elevated CRP (>3.0 mg/L) was associated with a significantly higher incidence of cardiac events during the follow-up period, particularly in Groups 2 and 3. The highest incidence of death, myocardial infarction, and heart failure occurred among patients with elevated CRP in the STEMI and NSTEMI groups.

Conclusion

Measurement of CRP upon admission in patients with suspected ACS provides valuable prognostic information. Elevated CRP identifies individuals at increased risk of adverse cardiovascular events, underscoring the need for aggressive management and close post-discharge surveillance.

Keywords

C-reactive protein, acute coronary syndrome, myocardial infarction, inflammation, prognosis, angiography

INTRODUCTION

Acute coronary syndrome (ACS) is a leading cause of cardiovascular morbidity and mortality worldwide, representing a spectrum of clinical conditions arising from myocardial ischemia due to acute coronary plaque disruption [1]. The spectrum includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), each varying in severity, prognosis, and management approach [2].

The pathophysiology of ACS is largely driven by atherosclerotic plaque rupture or erosion, followed by thrombus formation, resulting in partial or complete occlusion of coronary arteries [3]. Inflammation plays a central role in this process, with evidence indicating that systemic inflammatory activity promotes both plaque vulnerability and subsequent cardiovascular events [4,5].

C-reactive protein (CRP), a hepatic acute-phase protein synthesized in response to interleukin-6, has been identified as a key biomarker of inflammation and a predictor of adverse cardiovascular outcomes [6]. Beyond reflecting inflammation, CRP may actively participate in atherogenesis by inducing endothelial dysfunction, promoting monocyte recruitment, and activating the complement system [7]. Elevated CRP levels have been shown to correlate with the severity of atherosclerosis and predict mortality, recurrent myocardial infarction, and heart failure among patients with ACS [8,9].

In the clinical setting, CRP levels rise rapidly in response to myocardial injury, often within 6 hours of symptom onset, providing early insight into the extent of inflammation and myocardial damage [10]. Prior studies have reported significantly higher CRP levels in patients with STEMI and NSTEMI compared to those with UA or non-cardiac chest pain, with elevated levels serving as independent predictors of mortality [11,12].

Given this context, the present study was conducted to evaluate the diagnostic and prognostic significance of CRP in patients presenting with various forms of ACS. Specifically, it aims to assess whether elevated CRP levels at presentation correlate with angiographic findings and predict short-term cardiovascular outcomes.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at the Department of Cardiology in collaboration with the Department of Pathology at Army Cardia Hospital Lahore , from 1st January 2023 till 31st December 2023 .The study protocol was reviewed and approved by the Institutional Review Board, and informed consent was obtained from all participants in accordance with the Declaration of Helsinki [13].

Sample Size Calculation

The sample size was calculated using the formula for estimating proportions in cross-sectional studies. Assuming a prevalence of elevated CRP in ACS patients of approximately 50%, based on previous studies [14], with a 95% confidence level and a 7% margin of error, the minimum required sample size was 196. To account for potential loss to follow-up, the sample was increased to 200. The calculation was performed using the OpenEpi online tool [15].

Study Population

A total of 200 patients aged 18–65 years who presented to the emergency department with chest pain were enrolled consecutively. They were categorized into four groups:

- **Group 1:** Unstable angina (n = 50)
- **Group 2:** ST-elevation myocardial infarction (STEMI) (n = 50)
- **Group 3:** Non-ST-elevation myocardial infarction (NSTEMI) (n = 70)
- **Group 4:** Control group (non-cardiac chest pain) (n = 30)

The diagnosis of ACS was made based on clinical presentation, ECG changes, and elevated cardiac biomarkers following the WHO and ESC/ACC criteria [16].

Inclusion Criteria
- Age between 18 and 65 years
- Presentation with typical chest pain within the previous 12 hours
- ECG changes suggestive of ischemia (≥0.1 mV ST elevation or depression in contiguous leads)
- Diagnosis of UA, STEMI, or NSTEMI

Exclusion Criteria
- Acute myocardial infarction within the preceding month
- Known chronic inflammatory or neoplastic disorders
- Hepatic or renal failure
- Valvular heart disease
- Pregnant women
- Use of anti-inflammatory or immunosuppressive drugs

Data Collection

Clinical history, physical examination, and 12-lead ECG were recorded at presentation. Baseline data included demographic variables, cardiovascular risk factors, and medication history. Venous blood samples were collected on admission and again at six hours.

Laboratory parameters included:
- **High-sensitivity C-reactive protein (hs-CRP):** Measured by nephelometric assay (Boehringer Diagnostics) with a detection limit of 0.2 mg/L and coefficient of variation <3% at 2 mg/L .
- **Cardiac enzymes:** Troponin I, CK-MB/NAC
- **Other investigations:** Complete blood count, lipid profile, urea, creatinine, and bilirubin

All patients were followed for 90 days post-discharge via telephone for major adverse cardiovascular events (MACE), including myocardial infarction, heart failure, and cardiac death.

Diagnostic Definitions
- **STEMI:** New ST elevation with biomarker elevation
- **NSTEMI:** Elevated troponin or CK-MB without ST elevation
- **UA:** Typical ischemic symptoms with normal or non-diagnostic biomarkers
- **Control group:** Patients with chest pain of non-cardiac origin, normal ECGs, and normal cardiac enzymes

Cardiac deaths included fatalities from myocardial infarction, arrhythmias (ventricular fibrillation, sustained ventricular tachycardia), and cardiogenic shock.

Statistical Analysis

Data were analyzed using **OpenEpi** software. Continuous variables were presented as mean ± standard error (SE), and categorical variables as frequencies and percentages. Intergroup comparisons were conducted using the chi-square test or Student's t-test, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 200 patients were enrolled and categorized into four groups based on clinical diagnosis: Group 1 (Unstable Angina, n = 50), Group 2 (ST-Elevation Myocardial Infarction—STEMI, n = 50), Group 3 (Non-ST-Elevation Myocardial Infarction—NSTEMI, n = 70), and Group 4 (Control group, non-cardiac chest pain, n = 30). The overall mean age was 53.2 ± 5.3 years.

Table 1 summarizes the demographic data, cardiovascular risk profiles, and CRP levels across all four diagnostic groups. Mean CRP levels were notably higher in Groups 2 and 3.

Table 1. Baseline Characteristics of Study Participants by Group

Variable	Group 1 (UA)	Group 2 (STEMI)	Group 3 (NSTEMI)	Group 4 (Control)
Mean Age (years)	53.6	54.4	52.8	50.7
Male Gender (%)	60%	50%	57%	50%
BMI (kg/m²)	28	27	28	28
Diabetes Mellitus (%)	35%	73%	27%	27%
Dyslipidemia (%)	47%	45%	49%	44%
Smoking (%)	42%	38%	37%	45%
Family History of CAD (%)	30%	27%	29%	25%
Mean CRP (mg/L)	5.4 ± 0.48	29.4 ± 1.73	27.1 ± 1.67	2.16 ± 0.11

CRP Distribution and Group Comparisons

CRP levels were significantly higher in the STEMI and NSTEMI groups compared to the UA and control groups ($p < 0.00001$). The overall range of CRP was 0.5 to 95 mg/L, with a mean ± SE of 17.6 ± 7.96 mg/L (95% CI: 1.66–33.6). Elevated CRP (>3.0 mg/L) was observed in 14 patients in Group 1, 35 in Group 2, 55 in Group 3, and only 2 in the control group.

During 90-day follow-up, adverse cardiac events were documented, including myocardial infarction (MI), heart failure (HF), and cardiac death. Events were significantly more common among patients with CRP >3.0 mg/L, particularly in Groups 2 and 3.This is illustrated in table 2 .

Table 2. Cardiac Events According to CRP Levels in Each Diagnostic Group

Group	CRP Status	Number of Patients	Deaths	Myocardial Infarctions	Heart Failure Events
Group 1 (UA)	< 3.0 mg/L	36	0	4	0
	> 3.0 mg/L	14	1	2	4
Group 2 (STEMI)	< 3.0 mg/L	15	1	1	5
	> 3.0 mg/L	35	2	6	17
Group 3 (NSTEMI)	< 3.0 mg/L	15	1	2	1
	> 3.0 mg/L	55	3	8	10
Group 4 (Control)	< 3.0 mg/L	28	0	0	0
	> 3.0 mg/L	2	0	0	0

Among patients with CRP >3.0 mg/L, the cumulative incidence of any cardiovascular event was 87%, compared to 13% among those with CRP <3.0 mg/L ($p < 0.001$).This has been depicted in figure 1 .

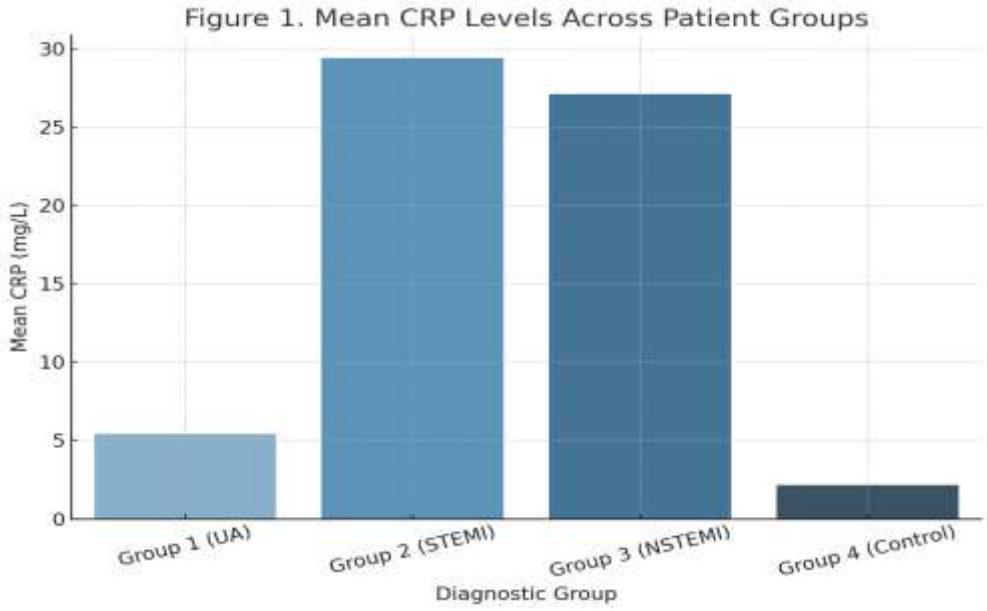

Figure 1. Mean CRP Levels across Patient Groups

Mean CRP levels were highest in patients diagnosed with STEMI and NSTEMI, demonstrating the inflammatory burden and potential myocardial injury in these groups.

DISCUSSION

The findings of this study indicate a clear relationship between elevated CRP levels and the severity of acute coronary syndrome (ACS), as well as subsequent adverse cardiovascular outcomes. Patients diagnosed with STEMI and NSTEMI exhibited significantly higher CRP concentrations compared to those with unstable angina and the control group. These results align with recent evidence supporting inflammation's central role in the pathophysiology of ACS, particularly regarding plaque instability and myocardial injury [17,18].

Elevated CRP levels, reflective of acute inflammatory responses, have been consistently linked to increased plaque vulnerability and subsequent myocardial injury [19]. Zebrack et al. demonstrated that higher baseline CRP concentrations are predictive of long-term mortality and myocardial infarction among patients with unstable angina and NSTEMI [20]. Similarly, Suleiman et al. found CRP measured at admission strongly correlated with the severity of myocardial injury and was predictive of subsequent cardiovascular complications [21].

Our results also highlight a notable finding that CRP levels were comparably elevated in NSTEMI patients and those experiencing STEMI. Although traditionally perceived as less severe, NSTEMI has been increasingly recognized as carrying substantial myocardial damage and inflammatory burden, as confirmed by White and Chew [22]. Aronson et al. further supported this observation, demonstrating a robust association between inflammatory markers like CRP and myocardial necrosis, independent of other cardiovascular risk factors [23].

The prognostic utility of CRP extends beyond initial diagnosis. Serial CRP measurements improve risk stratification in ACS patients by identifying those at heightened risk for recurrent ischemia, heart failure, and cardiovascular death, as demonstrated by Kavsak et al. [24]. Furthermore, CRP significantly enhances prognostic accuracy when combined with conventional cardiac biomarkers such as troponins and natriuretic peptides [25]. In this study, elevated CRP was notably associated with an increased incidence of heart failure events, supporting previous evidence that inflammation actively contributes to adverse cardiac remodeling [26].

These findings emphasize the practical value of CRP as an adjunctive marker for risk stratification in clinical settings. Anand et al. showed that incorporating CRP into routine assessment provides incremental benefit in identifying ACS patients at risk for poor outcomes, who could benefit from intensified therapeutic management [27]. Moreover, the therapeutic modulation of inflammation, such as through statins, has shown promise in reducing cardiovascular events, as illustrated by the JUPITER trial, which specifically targeted individuals with elevated CRP levels [28].

Nevertheless, CRP levels should not be interpreted in isolation. They may be influenced by other inflammatory states or chronic illnesses, necessitating a comprehensive evaluation of each patient's clinical context. Wang et al. suggested using a multimarker approach incorporating inflammatory, cardiac, and metabolic markers to achieve a more precise prediction of cardiovascular risk [29].

Limitations

This study's limitations include its single-center design, which could restrict the generalizability of findings. Although overt inflammatory or malignant conditions were excluded, undetected subclinical inflammation might have persisted. Future studies with larger sample sizes, multicentric designs, and serial CRP measurements over extended periods may provide deeper insights into CRP's predictive value and its role in guiding therapeutic strategies.

CONCLUSION

The findings of this study highlight the prognostic utility of C-reactive protein (CRP) in patients presenting with acute coronary syndromes (ACS). Elevated CRP levels were strongly associated with the severity of myocardial injury and a higher incidence of adverse cardiovascular outcomes, including heart failure, myocardial infarction, and death during short-term follow-up.

Measurement of CRP at the time of admission provides valuable insight into the inflammatory status of the patient and can aid in early risk stratification. Patients with significantly elevated CRP levels represent a high-risk group that may benefit from more aggressive therapeutic strategies, intensive monitoring, and potentially the incorporation of anti-inflammatory approaches in their treatment plan. Given its accessibility, low cost, and strong predictive value, CRP should be considered an important adjunct to conventional cardiac biomarkers and clinical assessment in the management of ACS. Future studies exploring serial CRP measurements, long-term outcomes, and the impact of CRP-lowering interventions will further clarify its role in cardiovascular care.

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