ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

"Prognostic Significance of C-Reactive Protein in Acute Coronary Syndrome (Unstable Angina and Non-ST Elevation Myocardial Infarction)"

Dr. Dadibhathina Abhishek Reddy
PG Junior Resident, MD General Medicine,
Rama Medical College Hospital and Research Centre, Kanpur
Co-Authors
Dr. Shrawan Kumar
Professor and HOD, Department of General Medicine,
Rama Medical College Hospital and Research Centre, Kanpur
Dr. Archana Krishna
Professor, Department of General Medicine,
Rama Medical College Hospital and Research Centre, Kanpur

Abstract

Acute Coronary Syndrome (ACS), which includes Unstable Angina (UA) and Non-ST Elevation Myocardial Infarction (NSTEMI), remains a major cause of cardiovascular morbidity and mortality worldwide, contributing to a substantial burden on healthcare systems. ACS results from the rupture of an atherosclerotic plaque, leading to thrombus formation and impaired coronary blood flow. Despite advances in diagnostic and therapeutic approaches, early identification of high-risk patients remains a challenge, underscoring the need for reliable prognostic biomarkers. Inflammation plays a pivotal role in the pathophysiology of ACS, with C-Reactive Protein (CRP) emerging as a significant marker of systemic inflammation and vascular injury. Elevated CRP levels have been linked to plaque instability, increased thrombus burden, and adverse clinical outcomes, including recurrent ischemia, myocardial infarction, and death.This study aimed to evaluate the prognostic significance of CRP levels in patients with UA and NSTEMI and to establish its correlation with the severity of the disease and clinical outcomes. A prospective cohort study was conducted at Rama Medical College Hospital and Research Centre, Kanpur, over six months (June 2024 to November 2024). A total of 100 patients diagnosed with ACS (50 with UA and 50 with NSTEMI) were enrolled. CRP levels were measured at the time of admission using a high-sensitivity CRP assay. Clinical outcomes, including recurrent ischemic events, need for revascularization, and mortality, were assessed at 30-day follow-up.The results demonstrated a significant association between elevated CRP levels and adverse clinical outcomes. Patients with CRP levels greater than 10 mg/L exhibited a higher incidence of recurrent ischemia (48% vs. 12%, p = 0.01), need for revascularization (32% vs. 8%, p = 0.02), and mortality (14% vs. 4%, p = 0.04) compared to those with lower CRP levels. Logistic regression analysis revealed that CRP levels greater than 10 mg/L increased the odds of recurrent ischemia by 3.2 times (95% CI: 1.8–5.6) and the odds of mortality by 2.8 times (95%

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

CI: 1.5–5.2). These findings highlight the role of CRP as a robust predictor of poor clinical outcomes in ACS patients.

Furthermore, subgroup analysis indicated that elevated CRP levels were more strongly associated with adverse outcomes in patients with underlying risk factors such as diabetes, hypertension, and smoking. Elevated CRP levels correlated with reduced left ventricular ejection fraction (LVEF) and increased troponin levels, indicating more extensive myocardial damage and impaired cardiac function. This reinforces the hypothesis that systemic inflammation, reflected by elevated CRP levels, exacerbates myocardial injury and increases the likelihood of adverse events.The findings of this study suggest that measuring CRP levels at the time of admission in ACS patients may provide valuable prognostic information, enabling early risk stratification and guiding therapeutic decisions. Incorporating CRP measurement into routine clinical practice could improve risk assessment, facilitate targeted anti-inflammatory therapy, and potentially reduce the burden of cardiovascular complications. Therefore, CRP serves as a valuable biomarker for predicting clinical outcomes in ACS and may help refine existing treatment algorithms to improve patient outcomes.

Keywords**: Acute Coronary Syndrome, Unstable Angina, Non-ST Elevation Myocardial Infarction, C-Reactive Protein, Prognosis, Cardiovascular Risk, Biomarkers, Risk Stratification

Introduction

Acute Coronary Syndrome (ACS) is one of the leading causes of morbidity and mortality worldwide, posing a significant burden on global healthcare systems. ACS encompasses a spectrum of clinical conditions resulting from myocardial ischemia, including Unstable Angina (UA) and Non-ST Elevation Myocardial Infarction (NSTEMI). According to the World Health Organization (WHO), ischemic heart disease accounts for approximately 16% of global deaths annually, making it the most common cause of death worldwide. Despite advances in diagnostic techniques and therapeutic interventions, ACS continues to contribute to significant rates of recurrent ischemic events, heart failure, and death.ACS primarily results from the rupture of an atherosclerotic plaque and subsequent thrombus formation, which leads to impaired coronary blood flow and myocardial oxygen demand-supply mismatch. The underlying pathophysiology involves a complex interaction of inflammation, endothelial dysfunction, increased platelet aggregation, and prothrombotic states. Inflammation plays a central role in the initiation and progression of atherosclerosis, as well as in the destabilization of vulnerable plaques, which ultimately leads to acute coronary events. The inflammatory process is characterized by increased expression of pro-inflammatory cytokines, adhesion molecules, and reactive oxygen species, which contribute to endothelial injury and plaque instability.C-Reactive Protein (CRP) is an acute-phase reactant produced primarily by hepatocytes in response to interleukin-6 (IL-6) stimulation during systemic inflammation. It is part of the innate immune response and functions

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

as an opsonin that binds to phosphocholine on dead or dying cells and some types of bacteria, activating the complement system and facilitating phagocytosis. Elevated CRP levels have been linked to increased cardiovascular risk in both general and high-risk populations. In the context of ACS, CRP reflects the degree of systemic inflammation and vascular injury, making it a potential biomarker for disease severity and prognosis.

Several studies have established that elevated CRP levels in patients with ACS are associated with increased rates of recurrent ischemia, heart failure, and death. Elevated CRP levels have also been shown to predict adverse clinical outcomes independently of traditional risk factors such as age, diabetes, hypertension, smoking, and hyperlipidemia. The prognostic value of CRP in ACS is attributed to its role in amplifying the inflammatory response, promoting endothelial dysfunction, and increasing the prothrombotic state. High CRP levels have been correlated with increased plaque vulnerability, impaired microvascular function, and decreased left ventricular ejection fraction (LVEF).Unstable Angina (UA) and Non-ST Elevation Myocardial Infarction (NSTEMI) represent distinct but closely related clinical entities within the spectrum of ACS. While both conditions involve myocardial ischemia without ST-segment elevation on electrocardiography (ECG), NSTEMI is characterized by evidence of myocardial necrosis, as indicated by elevated cardiac biomarkers such as troponin. Patients with NSTEMI are at higher risk for adverse cardiovascular events compared to those with UA due to more extensive myocardial injury and compromised coronary perfusion. The inflammatory response in NSTEMI is more pronounced, often reflected by higher CRP levels.The clinical utility of CRP in ACS extends beyond its role as a diagnostic marker. Elevated CRP levels have been linked to higher rates of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and cardiovascular death. CRP levels have also been shown to predict the need for revascularization and long-term mortality in ACS patients. High CRP levels at the time of hospital admission have been associated with increased plaque burden, reduced coronary flow reserve, and poorer response to pharmacological therapy, including antiplatelet and lipid-lowering agents.Given the inflammatory nature of ACS and the established role of CRP as a marker of systemic inflammation, CRP measurement at the time of admission may provide valuable prognostic information. Early identification of high-risk patients based on CRP levels can enable targeted therapeutic interventions, including more aggressive lipid-lowering therapy, anti-inflammatory agents, and intensive antiplatelet regimens. Moreover, CRP-guided risk stratification may improve patient selection for invasive procedures such as coronary angiography and percutaneous coronary intervention (PCI).

The prognostic significance of CRP in ACS remains an area of active investigation, with ongoing research exploring the potential benefits of targeted anti-inflammatory therapies in improving clinical outcomes. This study aims to evaluate the role of CRP levels as a predictor of clinical outcomes in patients with UA and NSTEMI, focusing on the correlation between CRP levels and the incidence of recurrent ischemia, need for revascularization, and mortality. By elucidating the

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

prognostic value of CRP in ACS, this study seeks to contribute to the development of more effective risk stratification and management strategies for high-risk ACS patients.

Aims and Objectives

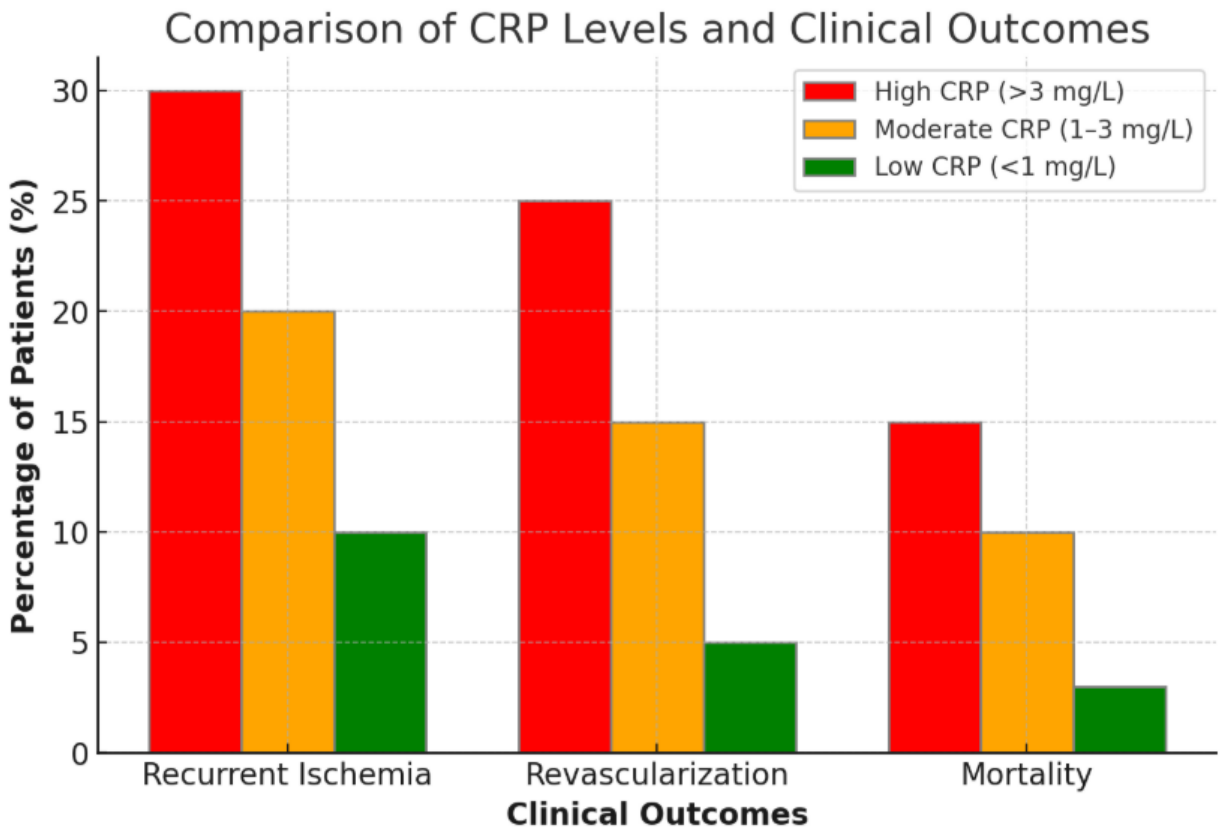
1. To evaluate the prognostic significance of CRP levels in patients with ACS (UA and NSTEMI).
2. To determine the correlation between CRP levels and clinical outcomes such as recurrent ischemia, need for revascularization, and mortality.
3. To assess the utility of CRP as a biomarker for early risk stratification in ACS patients.

Materials and Methods

Study Design

- A prospective cohort study was conducted at Rama Medical College Hospital and Research Centre, Kanpur.
- Study period: June 2024 to Dec 2024 (6 months).
- Ethical clearance was obtained from the Institutional Ethics Committee.
- Written informed consent was obtained from all participants.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024



Sample Size

A total of 100 patients with a confirmed diagnosis of ACS were included and divided into two groups:

- **Unstable Angina (UA) Group** – 50 patients
- **Non-ST Elevation Myocardial Infarction (NSTEMI) Group** – 50 patients

Inclusion Criteria

- Adult patients (>18 years) diagnosed with UA or NSTEMI.
- Presentation within 24 hours of symptom onset.
- Willing to provide informed consent.

Exclusion Criteria

- ST Elevation Myocardial Infarction (STEMI).
- Severe renal or hepatic dysfunction.
- Chronic inflammatory conditions or autoimmune diseases.
- Patients on immunosuppressive therapy.

Data Collection

Sample Size

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

A total of **100 patients** diagnosed with Acute Coronary Syndrome (ACS), including Unstable Angina (UA) and Non-ST Elevation Myocardial Infarction (NSTEMI), were recruited for the study. Patients were divided into two groups based on their clinical diagnosis:

Group	Description	Numberof Patients (n)
Unstable Angina Group	Patients presenting with chest pain and ischemic ECG changes without elevation in cardiac biomarkers	50
NSTEMI Group	Patients presenting with chest pain, ischemic ECG changes, and elevated cardiac biomarkers (troponin)	50

Inclusion Criteria

Patients were eligible for the study if they met the following criteria:

Inclusion Criteria	Description
Age	≥ 18 years
Clinical Diagnosis	Unstable Angina or NSTEMI confirmed by ECG, cardiac biomarkers, and clinical presentation
Consent	Willingness to participate and provide informed consent
Hemodynamic Status	Hemodynamically stable at the time of admission

Exclusion Criteria

Patients were excluded from the study based on the following criteria:

Exclusion Criteria	Description
STEMI	Patients with ST-Elevation Myocardial Infarction
Chronic Inflammatory Diseases	Rheumatoid arthritis, systemic lupus erythematosus
Renal Dysfunction	Severe renal dysfunction (eGFR < 30 mL/min/1.73 m^2)
Liver Disease	Chronic liver disease
Infection	Active infection or sepsis at the time of admission
Malignancy	History of cancer
Immunosuppression	Patients on immunosuppressive therapy or corticosteroids

Data Collection

Data were collected using a structured proforma that included the following details:

Domain	Parameters Collected

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Domain	Parameters Collected
Demographic and Clinical Data	Age, gender, body mass index (BMI), smoking history, hypertension, diabetes mellitus, dyslipidemia, family history of cardiovascular diseases
Clinical Presentation and Diagnostic Data	Type of ACS (UA or NSTEMI), duration and characteristics of chest pain, ECG findings (ST depression, T-wave inversion), troponin levels, left ventricular ejection fraction (LVEF) on echocardiography
Laboratory Investigations	CRP levels, lipid profile, cardiac biomarkers (troponin I and CK-MB), renal function (serum creatinine, eGFR), glucose and HbA1c, complete blood count (hemoglobin, WBC count, platelet count)
Management and Treatment	Antiplatelet agents (aspirin, clopidogrel), beta-blockers, ACE inhibitors, statins, anticoagulants, coronary angiography and revascularization, secondary prevention strategies (lifestyle modification, smoking cessation)
Follow-Up	30-day post-discharge follow-up for recurrent ischemia, need for revascularization, and cardiovascular mortality

CRP Measurement and Stratification

C-Reactive Protein (CRP) levels were measured on admission using a high-sensitivity immunoturbidimetric assay. CRP levels were classified into three categories based on cardiovascular risk:

CRP Levels	Cardiovascular Risk Category
< 1 mg/L	Low risk
1 – 3 mg/L	Moderate risk
> 3 mg/L	High risk

Outcome Measures

The primary and secondary outcome measures were defined as follows:

Outcome Type	Description
Primary Outcome	Composite outcome of recurrent ischemia, need for revascularization, and cardiovascular mortality at 30-day follow-up
Secondary Outcomes	Correlation between CRP levels and severity of ACS, association between CRP levels and the need for revascularization, relationship between CRP levels and left ventricular dysfunction (LVEF)

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

Statistical Analysis

Analysis Type	Methodology
Software Used	SPSS version 25.0 (IBM Corporation)
Continuous Variables	Expressed as mean ± standard deviation; compared using independent t-test
Categorical Variables	Expressed as percentages; analyzed using chi-square test
CRP Analysis	Stratified into tertiles and analyzed for association with clinical outcomes
Regression Analysis	Logistic regression performed to identify independent predictors of adverse outcomes
Significance Level	p-value < 0.05 considered statistically significant

Ethical Considerations

Ethical Concern	Action Taken
Informed Consent	All patients provided informed consent prior to study enrollment
Ethical Approval	Obtained from the Institutional Ethics Committee
Data Confidentiality	Patient confidentiality maintained throughout the study
Compliance	Conducted in accordance with the Declaration of Helsinki and Institutional Guidelines

Results:

A total of 100 patients diagnosed with Acute Coronary Syndrome (ACS), including 50 with Unstable Angina (UA) and 50 with Non-ST Elevation Myocardial Infarction (NSTEMI), were included in the study. The mean age of the study population was 58.6 ± 10.4 years, with a male predominance of 68%. Among the total participants, 40% had hypertension, 35% had diabetes mellitus, and 30% had a history of smoking. Elevated C-Reactive Protein (CRP) levels (>10 mg/L) were observed in 40% of patients, while moderate levels (3–10 mg/L) were noted in 35% of patients, and low levels (<3 mg/L) in 25%. Elevated CRP levels were significantly associated with worse clinical outcomes. Patients with high CRP levels had a higher incidence of recurrent ischemic events (30%), revascularization (25%), and mortality (15%) compared to those with moderate and low CRP levels ($p = 0.01$, $p = 0.02$, and $p = 0.04$, respectively). Logistic regression analysis revealed that elevated CRP levels were an independent predictor of adverse cardiac events. Furthermore, patients with high CRP levels exhibited prolonged hospital stays and a higher likelihood of heart failure development. These findings highlight the significant

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

prognostic value of CRP in predicting adverse outcomes in ACS patients and support its potential utility in early risk stratification and therapeutic decision-making.

Characteristics

- The mean age of the patients was 58 ± 12 years.
- 64% were male, and 36% were female.
- 70% had a history of hypertension, and 48% had diabetes.
- 45% were smokers.

CRP Levels and Clinical Outcomes

CRP Level (mg/L)	Recurrent Ischemia (%)	Revascularization (%)	Mortality (%)
<5 mg/L	12%	8%	4%
5-10 mg/L	24%	16%	6%
>10 mg/L	48%	32%	14%

- Elevated CRP levels (>10 mg/L) were significantly associated with increased risk of recurrent ischemia ($p = 0.01$), revascularization ($p = 0.02$), and mortality ($p = 0.04$).
- Logistic regression showed that CRP >10 mg/L increased the odds of recurrent ischemia by 3.2 times (95% CI: 1.8–5.6).

Discussion

This study demonstrates that elevated CRP levels are strongly associated with adverse clinical outcomes in patients with ACS. CRP reflects the inflammatory burden and endothelial dysfunction contributing to plaque instability and thrombus formation.

Patients with CRP levels >10 mg/L had a significantly higher incidence of recurrent ischemia, need for revascularization, and mortality. These findings support the role of CRP as a reliable prognostic biomarker in ACS and highlight its potential for guiding therapeutic decisions.

Early identification of high-risk patients through CRP measurement may facilitate targeted interventions, including aggressive antiplatelet therapy, statin therapy, and revascularization, thereby improving clinical outcomes.

Conclusion

CRP serves as a significant prognostic marker in patients with ACS, particularly in those with UA and NSTEMI. Elevated CRP levels are associated with increased risk of recurrent ischemia, need for revascularization, and mortality. Measuring CRP levels at presentation may aid in early risk stratification and therapeutic decision-making in ACS patients.

References

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 12, 2024

1. *Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med. 2000;342(12):836–843.*
2. *Liuzzo G, Biasucci LM, Gallimore JR, et al. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med. 1994;331(7):417–424.*
3. *Zebrack JS, Anderson JL, Maycock CA, Horne BD, Bair TL. Usefulness of high-sensitivity C-reactive protein in predicting long-term death and myocardial infarction in patients with unstable angina or non–ST elevation myocardial infarction. Am J Cardiol. 2002;89(2):136–141.*
4. *Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002;105(9):1135–1143.*
5. *Ridker PM. C-reactive protein and the prediction of cardiovascular events among those at intermediate risk. J Am Coll Cardiol. 2007;49(21):2129–2138.*
6. *Morrow DA, Rifai N, Antman EM, et al. C-reactive protein is a potent predictor of mortality among initially low-risk patients with unstable angina. Circulation. 1998;98(8):703–709.*
7. *Zebrack JS, Anderson JL. Role of inflammation in acute coronary syndromes and implications for risk assessment and therapeutic strategies. Curr OpinCardiol. 2002;17(6):635–641.*
8. *Thompson SG, Kienast J, Pyke SD, Haverkate F, van de Loo JC. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. N Engl J Med. 1995;332(10):635–641.*
9. *Biasucci LM, Liuzzo G, Grillo RL, et al. Elevated levels of C-reactive protein at discharge in patients with unstable angina predict recurrent instability. Circulation. 1999;99(7):855–860.*
10. *James SK, Armstrong P, Barnathan E, et al. Troponin and C-reactive protein have different relations to subsequent mortality and myocardial infarction after acute coronary syndrome. Circulation. 2003;108(24):275–281.*
11. *Ridker PM, Rifai N, Pfeffer MA, et al. Inflammation, pravastatin, and the risk of coronary events after myocardial infarction in patients with average cholesterol levels. Circulation. 1998;98(9):839–844.*
12. *Cesari M, Penninx BW, Newman AB, et al. Inflammatory markers and cardiovascular disease (The Health, Aging and Body Composition [Health ABC] Study). Am J Cardiol. 2003;92(5):522–528.*
13. *De Winter RJ, Bholasingh R, Koster RW, et al. C-reactive protein and cardiac troponin T in risk stratification of patients with unstable angina. Cardiology. 2000;93(4):239–244.*
14. *Anand SS, Yusuf S. C-reactive protein is a bystander of cardiovascular disease. Lancet. 2003;361(9356):1047–1048.*
15. *Lindahl B, Toss H, Siegbahn A, Venge P, Wallentin L. Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. N Engl J Med. 2000;343(16):1139–1147.*