Study on levels of hs-CRP in Acute Coronary Syndrome

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KEYWORDS

angina, non-st segment elevation myocardial infarction (nstemi), st-elevation myocardial infarction (stemi), : acute coronary syndrome, hs-crp.

ABSTRACT

INTRODUCTION: CAD includes a variety of conditions resulting from sudden reduction or interruption the heart's blood flow. This spectrum includes unstable angina, NSTEMI, and STEMI. quick diagnosis and management are essential in ACS to minimize myocardial damage and improve outcomes. Among the various biomarkers used to assess ACS, Hs-CRP has emerged as a important player in evaluating cardiovascular risk and guiding treatment strategies. One is coronary heart disease, or CHD. of the leading causes of mortality and morbidity all over the world, including India. Hs-CRP is currently employed for risk assessment and primary prevention of atherosclerotic cardiovascular disease (ASCVD), there is a scarcity of information regarding the association between Hs-CRP levels in patients presenting with ACS and their association with outcomes. Studying hscrp levels in patients presenting with acute coronary syndrome is crucial for assessing inflammation's role in the condition. This investigation aids in identifying dormant markers for risk stratification and contributes to a better understanding of cardiovascular risk factors. Therefore, our research was started to evaluate the levels of hs crp in patients with acute coronary syndrome. **AIM:** To investigate the relationship between ACS patients' hs-crp levels and its relation with CAD risk factors. **OBJECTIVES:** To investigate the relationship between ACS patients' hs-crp levels .To study the demographic status of the patients presenting with ACS. To study the cardiac enzymes (creatine kinase-myocardial band, troponin I),resting 12-lead electrocardiogram of patient diagnosed with ACS. To detect the severity of ACS with laboratory parameters(CK-MB, trop I) and electrocardiogram (STEMI vs NSTEMI). **METHODOLOGY:** This Cross-Sectional Observational study conducted in single center at KIMS Deemed To Be University, Karad, Maharashtra.110 individual with CAD more than 18 years age and both sex, who were admitted in KVV and hospital ICCU and IMCU were involved in our study over a period of 18 months from 2nd September 2022 to 29th February 2024. **RESULTS:** Markers differ significantly across groups: hs-CRP levels are highest in STEMI (3.70 ± 0.69 mg/l) and NSTEMI (3.55 ± 0.86 mg/l) compared to UA (2.4 ± 0.38 mg/l) and Control (1.86 ± 0.53 mg/l), $P < 0.0001$. CK-MB is elevated in STEMI (3.35 ± 5.32 ng/ml) and NSTEMI (3.41± 6.29 ng/ml) over UA (1.52 ± 2.99 ng/ml) and Control (1.52 ± 0.99 ng/ml), $P < 0.0001$. Troponin I is highest in STEMI (4.96 ± 7.72 ng/ml) and NSTEMI (5.99 ± 8.12 ng/ml) compared to UA (0.56 ± 0.64 ng/ml) and Control (0.23 ± 0.82 ng/ml), $P = 0.003$. **Conclusion:** The study highlights hs-CRP as a valuable biomarker for diagnosing acute coronary syndrome, stratifying patient risk, and identifying those at higher risk for more intensive treatment.
Categories: Internal Medicine
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Introduction

Acute coronary syndrome:

Acute Coronary Syndrome (ACS) encompasses a spectrum of conditions arising from the sudden reduction of blood flow to the heart muscle due to the abrupt blockage of a coronary artery. ACS is a manifestation of Coronary Heart Disease (CHD) and is usually the result of plaque disruption in coronary arteries. The three principal manifestations of ACS are ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina. These conditions collectively represent a critical category within CHD, marked by distinctive clinical presentations and severity. [1] ACS is a leading cause of morbidity and mortality in developed and developing countries. Presently, India is undergoing a rapid epidemiological transition among developing nations, shifting from communicable to non-communicable diseases. This transition is notably characterized by a heightened burden of non-communicable atherothrombotic diseases. [2]

Epidemiology of coronary arterial disease:

In comparison to Western countries, the epidemiology of Coronary Arterial Disease (CAD) in India is distinguished by the premature occurrence of incidents in the younger population and a prevalence within the low-to-middle-income community.

Risk factors for cardiac disease:

Several risk factors have been related to cause cardiac disease which is divided into modifiable and non- modifiable. The major modifiable risk factors include hypertension (HTN), diabetes (DM), smoking, and hyperlipidemia, while non-modifiable risk factors consist of age, gender, and a family history of premature coronary artery disease (CAD) [3]. Clinically, patients with ACS may complain about chest pain, occasional radiation to the arm, jaw, or shoulder, lightheadedness, shortness of breath, nausea, vomiting, or dyspnea. Although, these symptoms are frequently seen among emergency department (ED) patients, the diagnosis of ACS remains challenging [4].

Inflammation and acute coronary syndrome:

In the context of CAD, inflammation plays an important role in its development, progression, and prognosis.

[5] Atherosclerosis, a key process in CAD, is influenced by inflammation at various stages. The activation of inflammatory responses is thought to significantly contribute to the instability of plaques within the arteries. This activation involves proinflammatory cells and the upregulation of adhesion molecules, resulting in increased production of cytokines and procoagulant substances. These molecular processes contribute to the thickening or rupture of atherosclerotic plaques, ultimately leading to the onset and progression of acute coronary syndrome (ACS). [6]

Diagnosis of acute coronary disease:

The diagnosis of acute coronary disease was based on clinical symptoms and cardiac marker levels. As evidence of studies showed that atherosclerosis is an inflammatory process, several plasma markers of inflammation have been evaluated as potential tools for the prediction of coronary events. These markers of inflammation include serum amyloid A, interleukin - 6, homocysteine, fibrinogen levels, fibrinolytic capacity, apolipoprotein - A, apolipoprotein B-100, lipoprotein (a), and C-reactive protein (HS-CRP). Several academic articles have revealed that high sensitivity has emerged as a valuable marker for risk stratification in acute coronary syndrome and a potent predictor of future cardiovascular risk. This is particularly evident when measured using high-sensitivity C-reactive protein assays, which boast greater analytic sensitivity and ensure reliable measurement of HS-CRP concentration within the reference range with low imprecision (5- 10%). The high-sensitivity C-reactive protein (Hs-CRP) is a biochemical test which is a highly sensitive quantification of HS-CRP.

Role of high-sensitivity C-reactive protein:

Hs C-Reactive Protein (HS-CRP) is a liver protein whose synthesis depends on several transacting cytokines of interleukin-6 (IL-6), IL-1 and tumor necrosis factor α (TNF-α). [7] Measurement of hs-CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. [8]

Initially proposed as a nonspecific marker of inflammation, hs-CRP is now suggested to play a direct pathophysiological role in the development and progression of atherosclerosis. Numerous studies have reported an independent association between hs-CRP levels and the recurrence of myocardial ischemia, as well as the occurrence of death during follow-up periods. It has been demonstrated that hs-CRP may not only serve as a biomarker of generalized inflammation; however, it may also have a direct and active role in atherogenesis and atheromatous plaque disruption.

Patient outcomes and hs-CRP levels:

Patients with ACS exhibit elevations in hs-CRP level. High sensitivity is a new modified assay which measures a low level of hs-CRP. The assessment of the risk of cardiovascular disease based on serum hs-CRP levels is categorized as follows: The normal range of hs-CRP is up to 1.0 mg/L, and levels exceeding this threshold are associated with an escalated risk of cardiovascular disease. Specifically, a level higher than 2.0 mg/L is considered indicative of high risk.

Yip et al. and Sheikh et al. demonstrated a significant elevation in hs-CRP concentrations in patients with clinical features of ACS compared to controls. Furthermore, He et al., in a meta-analysis comprising 20 longitudinal studies and 2,789 cases from 17,422 patients, quantitatively assessed the association between early blood hs-CRP after ACS and the risk of adverse outcomes. Their findings revealed that patients with higher hs-CRP levels of 3.1-10.0 mg/dL and >10.0 (mg/L) after ACS were associated with 1.4-fold and 2.18- fold higher risks of adverse outcomes when compared with the referent (hs-CRP ≤3.0 mg/L). From these studies, we understand that measuring hs-CRP at admission for patients with suspected CHD may assist in identifying those at increased risk of cardiac complications, warranting aggressive cardiac management and vigilant post-discharge monitoring.

Importance of hs-CRP in prevention:

Hs-CRP is currently employed for risk assessment and primary prevention of atherosclerotic cardiovascular disease (ASCVD). However, there is a scarcity of information regarding the association between Hs-CRP levels in patients presenting with ACS and their association with outcomes. Studying high sensitivity C- reactive protein levels in patients presenting with acute coronary syndrome is crucial for assessing inflammation's role in the condition. This investigation aids in identifying dormant markers for risk stratification and contributes to a better understanding of cardiovascular risk factors. Therefore, our research was initiated to evaluate the levels of high-sensitivity C-reactive protein in patients with acute coronary syndrome.

Materials And Methods

Study Overview:

This study was conducted at a single center, the Krishna Institute of Medical Sciences Deemed To Be University, located in Karad, Maharashtra.

Study Design:

Cross-Sectional Observational Study. Study Population:

The study comprised inpatient (IPD) patients receiving services for acute coronary syndrome in our hospital affiliated with the college.

Study Duration:

The study was organized from September 2022 to March 2024. Sampling Method:

Simple Random Sampling. Sample Size:

110 participants. Inclusion Criteria:
All patients aged more than 18 years with a diagnosis of acute coronary syndrome will be considered for enrollment in the study.
Exclusion Criteria:
Known cases of any immunocompromised state. Patients with known hepatic dysfunction. Patients with known renal dysfunction. Data Collection Procedure:
The identities of the patients will be kept strictly confidential. Data obtained will not be used for any medico-legal purposes. Cases fulfilling the inclusion and exclusion criteria and willing to provide written informed consent will be recruited for the study. Socio-demographic details of all participants will be collected.
Methodology:
A total of 110 patients with acute coronary syndrome aged more than 18 years, irrespective of sex, who were admitted to Krishna Institute of Medical Sciences and hospital ICCU (Intensive Care Unit) and IMCU (Intermediate Care Unit), were included in this study. Each of the 110 patients was subjected to a detailed history and a thorough clinical examination. The following investigations were performed:
Hemoglobin, Total Leukocyte Count (TLC) ,Differential Leukocyte Count Troponin I, Creatine Kinase-MB (CK-MB), High-Sensitivity C-Reactive Protein (hs-CRP) Electrocardiogram (ECG), NT-ProBNP, Serum Creatinine Liver Function Test 2D-Echocardiography Lipid Profile

Results

Type of cardiac events	STEMI	NSTEMI	UA	Control	Chi-square	p-value
	No. Cases (%)	No. Cases (%)	No. Cases (%)	No. Cases (%)		
NON SURVIVED						
NO	24(77.42 %)	20(76.92 %)	30(88.24 %)	24(88.89%)	2.18	0.53
YES	7(22.58 %)	6(23.08%)	4(11.76%)	3(11.11%)		
Myocardial infraction						
NO	5(14.13 %)	4(15.38%)	28(82.35 %)	27(100.00 %)	67.56	P < 0.0001
YES	26(83.87 %)	22(84.62 %)	6(17.65%)	0(0.00%)		
Recurrent unstable angina						
NO	13(41.94 %)	14(53.85 %)	13(38.24 %)	23(85.19%)	15.74	0.001
YES	18(58.06 %)	12(46.15 %)	21(61.76 %)	4(14.81%)		
Heart failure						
NO	10(32.26 %)	11(42.31 %)	30(88.24 %)	17(62.86%)	24.02	P < 0.0001
YES	21(67.74 %)	15(57.69 %)	4(11.76%)	10(37.04%)		

TABLE 1: Distribution according to type of cardiac events

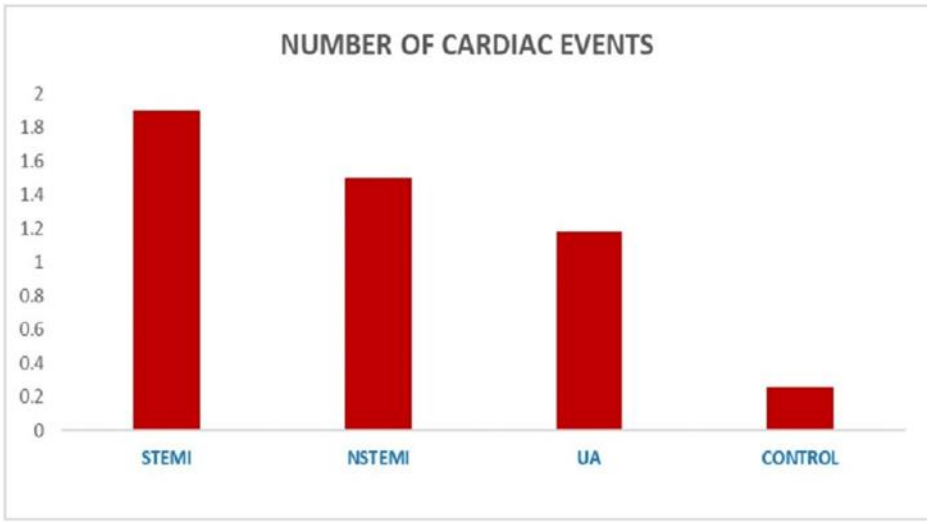

FIGURE 1: Graphical distribution according to No. of cardiac events

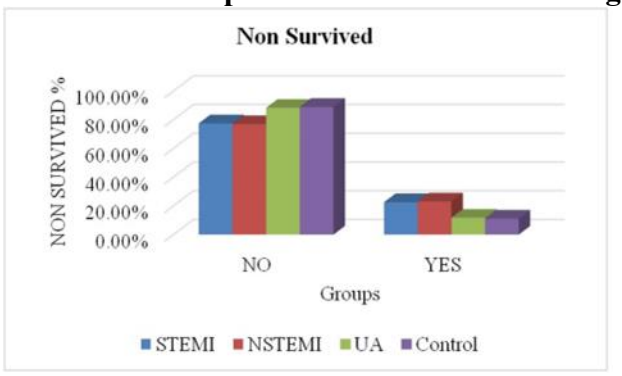

FIGURE 2: Graphical distributions according to type of cardiac events

	STEMI	NSTEMI	UA	Control	P-value
No. of cardiac events2	**No. Cases (%)**	**No. Cases (%)**	**No. Cases (%)**	**No. Cases (%)**	
	1.90 ± 0.83	**1.5 ± 0.81**	**1.18 ± 0.80**	**0.26 ± 0.44**	**P < 0.0001**

TABLE 2: Distribution according to No. of cardiac events.

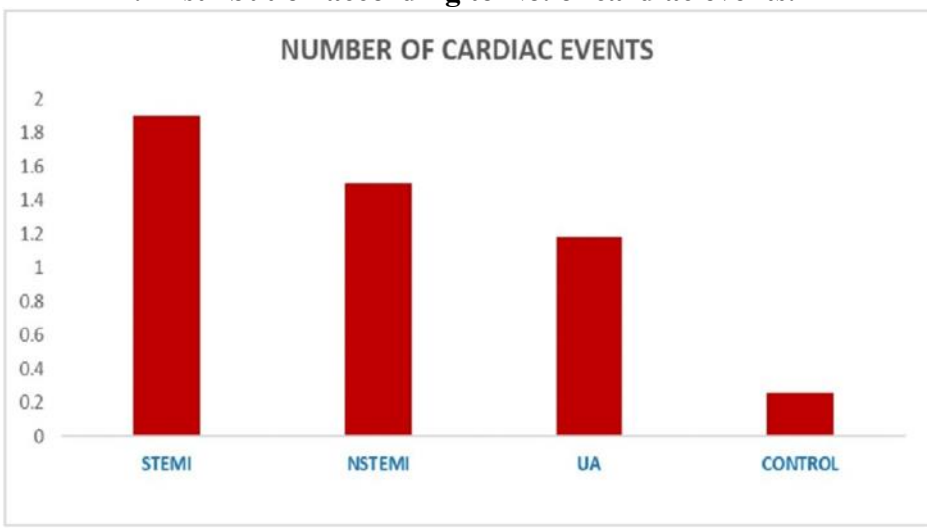

FIGURE 3: Graphical distribution according to Markers in diff group

Markers in diff group	STEMI	NSTEMI	UA	Control	P-value
	No. Cases	No. Cases	No. Cases	No. Cases	
hs-CRP (mg/l)	3.70 ± 0.69	3.55 ± 0.86	2.4 ± 0.38	1.86 ± 0.53	P < 0.0001
Creatine Kinase MB (ng/ml)	3.35 ± 5.32	3.41 ± 6.29	1.52 ± 2.99	1.52 ± 0.99	P < 0.0001
Troponin I (ng/ml)	4.96 ± 7.72	5.99 ± 8.12	0.56 ± 0.64	0.23 ± 0.82	0.003

TABLE 3: Distribution according to Markers in diff group

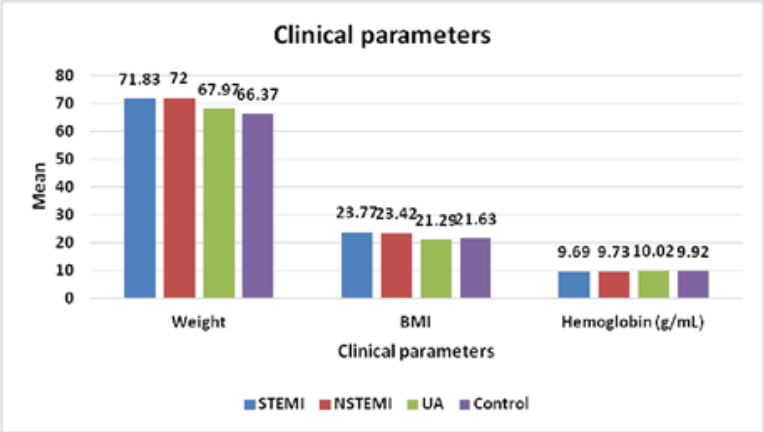

FIGURE 4: Graphical distribution according to Clinical parameters.

Clinical parameters	STEMI	NSTEMI	UA	Control	p-value
Weight(kg)	71.83 ± 16.56	72 ± 14.68	67.97 ± 14.15	66.37 ± 15.68	0.41
BMI(kg/m2)	23.77 ± 5.16	23.42 ± 5.12	21.29 ± 3.38	21.63 ±5.09	0.09
Hemoglobin (g/dl)	9.69 ± 2.08	9.73 ± 2.62	10.02 ± 2.93	9.92 ± 2.96	0.95

TABLE 4: Distribution according to Clinical parameters.

Age	STEMI	NSTEMI	UA	Control	P-value
	55.68 ± 17.29	61.07 ± 18.34	58.23 ± 18.13	44.92 ± 15.78	0.005

TABLE 5: Distribution according to Age

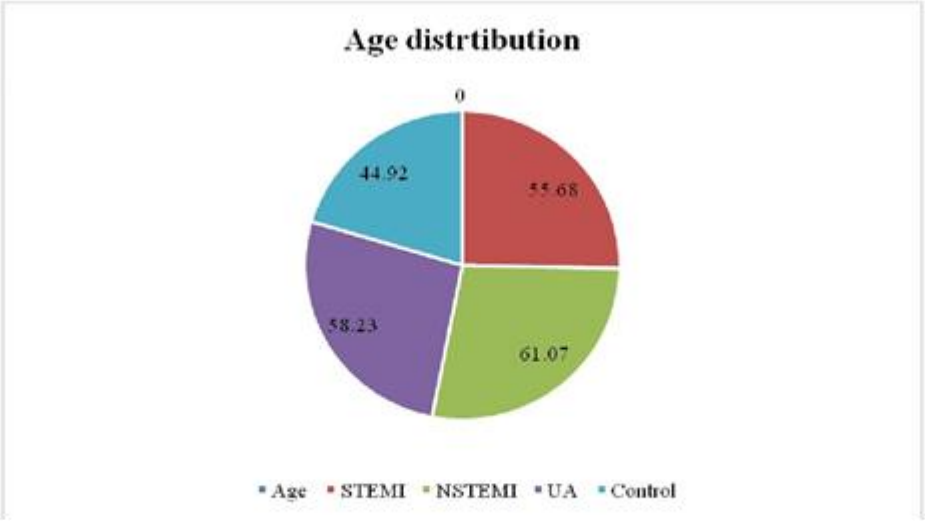

FIGURE 5: AGE DISTRIBUTION GRAPH

Gender	STEMI	NSTEMI	UA	Control	Chi-square	p-value
	No. Cases (%)	No. Cases (%)	No. Cases (%)	No. Cases (%)		
F	16(58.06 %)	12(46.15%)	12(35.29%)	11(40.74%)	3.64	0.30
M	13(41.94 %)	14(53.85%0	18(64.71%)	14(59.26%)		

TABLE 6: Distribution according to Gender

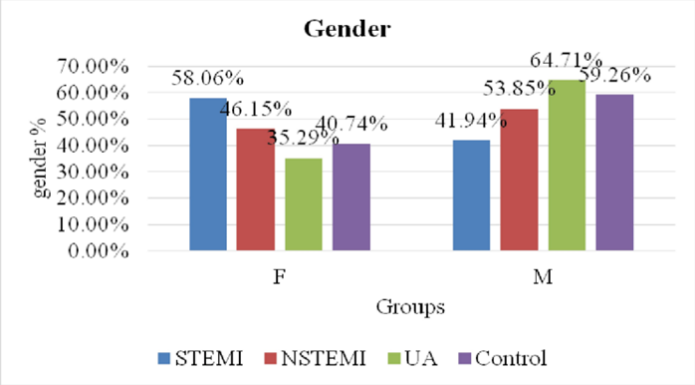

FIGURE 6: Graphical distribution according to Gender

Discussion

C-Reactive Protein (CRP) Overview

C-Reactive Protein (CRP) is a liver protein synthesized in response to several cytokines, including interleukin-6 (IL-6), IL-1, and tumor necrosis factor α (TNF-α). The measurement of high-sensitivity CRP (hs-CRP) levels is valuable for detecting and evaluating infections, tissue injuries, inflammatory disorders, and related diseases. Numerous studies have demonstrated that serum hs-CRP levels serve as an independent predictor of both short-term and long-term outcomes in patients experiencing coronary events or acute myocardial infarction.

Role of hs-CRP in Acute Coronary Syndrome (ACS)

Elevated hs-CRP levels in patients with acute coronary syndrome (ACS) at the time of hospital admission may indicate persistent inflammation and predict poor short-term prognosis. This finding underscores the role of inflammation in the pathophysiology of ACS and emphasizes

the importance of hs-CRP as a biomarker in assessing patient risk for cardiovascular disease (CVD), heart failure, and mortality.

Study Population and Findings

In the present study, 110 patients presenting with ACS were enrolled. Among these patients: ST-Elevation Myocardial Infarction (STEMI): 26.36% (29 cases)

Non-ST-Elevation Myocardial Infarction (NSTEMI): 23.63% (26 cases) Unstable Angina (UA): 27.12% (30 cases)

Control Group: 22.72% (25 cases)

The mean ages for patients diagnosed with, respectively:

STEMI: 55.68 ± 17.29 years

NSTEMI: 61.07 ± 18.34 years

UA: 44.92 ± 15.78 years

A statistically significant p-value of 0.05 was found, aligning with the study conducted by in India, highlighting a prevalence rate of ACS among patients aged above 40 years.

Age and Gender Distribution

The study found slightly higher mean ages for NSTEMI (61.07 years) and UA (58.2 years) compared to STEMI (55.6 years), with a statistically significant p-value of 0.05. Gender distribution in our study revealed:

Unstable Angina (UA): 64.71% (18 cases) male NSTEMI: 53.85% (14 cases) male

This aligns with findings from]a study, who reported that 63.1% of their ACS patients were male. Risk Factors Associated with ACS

In our study, common risk factors including Diabetes Mellitus: Highest statistically significant p-value < 0.0001

Hypertension: Present in several cases Smoking: Identified as a risk factor.

Family history of coronary heart disease (CHD) and its association with ACS showed no strong correlation (p= 0.69), consistent with findings. hs-CRP Levels in Patients

Significantly higher serum concentrations of hs-CRP were observed in ACS patients compared to the control group:

STEMI: 3.70 ± 0.69 mg/l

NSTEMI: 3.55 ± 0.86 mg/l

UA: 2.4 ± 0.38 mg/l

Controls: 1.86 ± 0.53 mg/l

These findings indicate that elevated hs-CRP levels are associated with myocardial damage, consistent with previous studies.

Biomarkers and Clinical Outcomes

Our study noted significant differences in other biomarkers:

Creatine Kinase MB (CK-MB): Highest in STEMI and NSTEMI compared to UA and controls ($p < 0.0001$). Troponin I Levels: Significantly elevated in STEMI and NSTEMI compared to UA and controls ($p = 0.003$).

A significant majority of STEMI (83.87%) and NSTEMI (84.62%) patients experienced myocardial infarction, while none from the control group did.

Recurrent Events in ACS Patients

Recurrent unstable angina was notable, with 58.06% of STEMI, 46.15% of NSTEMI, and 61.76% of UA patients experiencing it. These findings align with those reported by other studies, underscoring a persistent ischemic risk in ACS patients.

Study Limitations

The present study was conducted at a single center and included a limited sample size. It is recommended that further detailed multicenter studies be conducted in this area with a larger sample size to confirm these results and implement preventive measures for societal benefit.

Study Design: This cross-sectional observational study was conducted at the Krishna Institute of Medical Sciences Deemed To Be University, Karad, Maharashtra.
Ethical Considerations:
Prior to the study, institutional ethical committee approval was obtained. Study Population
A total of 110 patients, aged over 18 and of both sexes, were enrolled in the study. Based on clinical examination and the type of acute coronary syndrome (ACS), the patients were divided into four groups:
STEMI (ST-Elevation Myocardial Infarction): 29 patients NSTEMI (Non-ST-Elevation Myocardial Infarction): 26 patients UA (Unstable Angina): 30 patients
Control Group: 25 patients Methodology
Upon admission, venous blood samples were taken from all patients for analysis of the following biomarkers:
High-Sensitivity C-Reactive Protein (hs-CRP) Creatine Kinase-MB (CK-MB)
Troponin I levels Study Results
hs-CRP Levels:
STEMI: 3.70 ± 0.69 mg/l
NSTEMI: 3.55 ± 0.86 mg/l
UA: 2.4 ± 0.38 mg/l
Controls: 1.86 ± 0.53 mg/l
The study found that hs-CRP levels were significantly higher in ACS patients compared to the control group. CK-MB Levels:
STEMI: 3.35 ± 5.32 ng/ml
NSTEMI: 3.41 ± 6.29 ng/ml
UA: 1.52 ± 2.99 ng/ml
Controls: 1.52 ± 0.99 ng/ml
All differences in CK-MB levels were statistically significant ($p < 0.0001$). Clinical Outcomes: Significant associations were found between STEMI and NSTEMI with higher rates of myocardial infarction and heart failure, both having a p-value of < 0.0001, indicating a relationship to severity.

Conclusion

The study concludes that hs-CRP is a valuable biomarker that aids in diagnosing acute coronary syndrome by indicating inflammation associated with coronary artery disease. Additionally, it assists in stratifying patient risk and identifying individuals at higher risk who may require more intensive treatment and monitoring.