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High Sensitivity C - Reactive Protein Prognostic Role In Patients With Acute Myocardial Infarction.

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ABSTRACT

Acute Myocardial Infarction (AMI), also known as a heart attack, is a medical emergency that is the leading cause of death for men and women worldwide. Acute coronary syndromes include unstable angina and acute myocardial infarction, both of which are caused by myocardial ischemia and or necrosis, which causes inflammation and subsequent repair processes. Chronic inflammatory responses and oxidative stress play a mysterious role in the initiation and progression of acute coronary syndromes (ACS). Acute myocardial infarction is a serious cardiovascular event that is associated with significant morbidity and mortality. This study aims to study the levels of serum highly sensitive C-reactive protein in patients with AMI as compared to the control. The major purpose of this study is to assess serum high sensitive C-reactive protein levels in AMI patients and to connect serum high sensitive C-reactive protein levels with AMI-related mortality. The secondary purpose is to predict AMI early diagnosis, improved management and therapy, and prognosis. The present study was carried out in the Department of Biochemistry and Central Investigation Laboratory in collaboration with the Department of Medicine, Intense cardiac care units, medical intensive care units, and emergency and private hospitals. The study was approved by Institutional Ethical and Research Committee to use human subjects in the research study. Informed consent was taken from patient and control subjects. Out of 100 subjects, 50 were acute myocardial infarction patients and 50 were age matched healthy controls. The study was conducted from January 2020 to December 2021. The Microlab 300 analyzers (semi-autoanalyzer) were used to assess highly Sensitive C - reactive protein concentrations, and the comparisons between the two groups were examined using an unpaired *t*-test. A $P < 0.05$ was deemed statistically significant. There was a substantial elevated in the mean serum highly sensitive C-reactive protein in cases on 0, 3rd and 7th day were 7.0±2.92 mg/dl, 5.95±2.32 mg/dl, 3.46±2.70 mg/dl day respectively which were higher than controls group (2.45±1.34 mg/dl). Comparison between control and serum highly sensitive C-reactive protein on 0 and 3rd day was found to be more significant than that of 7th day. Unpaired *t*-test showed that there was significant increase in serum highly sensitive C-reactive protein level in cases as compared to controls ($p<0.005$). As a result, the study concludes that serum high sensitivity C-reactive protein levels play an important role in the diagnosis and treatment of AMI.

Keywords: Acute Myocardial Infarction, High Sensitive C - reactive protein, Acute Coronary Syndromes and Mortality.

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INTRODUCTION

Acute Myocardial Infarction (AMI), also known as a heart attack, is a medical emergency that is the leading cause of death for men and women worldwide [1, 12]. Acute coronary syndromes include unstable angina and acute myocardial infarction, both of which are caused by myocardial ischemia and/or necrosis, which causes inflammation and subsequent repair processes. Chronic inflammatory responses and oxidative stress play a mysterious role in the initiation and progression of acute coronary syndromes (ACS) [2].

Acute myocardial infarction is a serious cardiovascular event that is associated with significant morbidity and mortality. In patients with coronary artery disease, total white blood cell (WBC) count has been identified as an independent predictor of death or myocardial infarction [3].

The classic acute phase reactant is high sensitive C-reactive protein, the serum level of which has long been known to rise in AMI [4]. The high-sensitivity C-reactive protein assay is a quantitative analysis test that is increasingly being used as a marker for assessing cardiac risk as well as a prognostic tool in heart disease. Recent evidence suggests that the role of hs-CRP measurement in distinguishing ischemia and non-ischemic situations, as well as its correlation with various myocardial infarctions, is important [5].

Although high sensitive-CRP has been proven to have predictive significance in individuals with acute coronary syndromes, its most promising application has been in primary prevention. High sensitive-CRP may be a sign of low grade chronic systemic inflammation as well as a direct contributor to atherosclerosis [6].

CRP has been identified as an important marker of endothelial dysfunction and future CVD risk. CRP has emerged as a good biomarker for vascular inflammation linked to atherosclerosis, and it may directly drive atherosclerotic processes [7]. CRP is involved in the development of atherosclerosis. CRP's role as a marker of coronary artery disease is well established [8, 9].

The current investigation is being conducted to investigate if CRP is an acute phase protein generated in the liver in response to inflammatory mediators and is referred to be a classical short pentraxin. The link between a modestly raised CRP level and an increased risk of a cardiovascular incident is well recognised [10].

METHODS

The present study was carried out in the Department of Biochemistry and Central Investigation Laboratory in collaboration with the Department of Medicine. The study was approved by Institutional Ethical and Research Committee to use human subjects in the research study. Informed consent was taken from patient and control subjects. The study was conducted from January 2020 to December 2021. The acute myocardial infarction patients and healthy controls subject participated in the study.

Subjects

A total 100 subjects were selected for the present study based on inclusion and exclusion criteria. Out of 100 subjects, 50 were acute myocardial infarction patients and 50 were age matched healthy controls.

Inclusion Criteria

Cases

The study includes acute myocardial infarction patients of age group 30-75 years, referred by various intensive cardiac care units (ICCU), medical intensive care units (MICU), emergency and private hospitals to our institute.

Criteria for myocardial infarction refer (at least 2 must be present) [11, 12]

- Typical (ischemic) symptoms of prolonged chest pain
- Serial electro cardio grams (ECG) changes:
  - Progression from no Q wave to a definite Q wave
  - A lesser Q wave progression combined with progressive ST-segment depression, developing ST-segment elevation.
  - Persistent ST-segment elevation with progressive T-wave inversion in sequential daily electro cardio grams (ECG).

- Cardiac enzyme levels CK-MB twice the limit of normal.

Exclusion criteria

Following patients will be excluded from the study

- Patients with sexually transmitted diseases (STDs).
- Patients with Rheumatoid Arthritis.
- Patients with rheumatic fever.
- Patients with inflammatory bowel disease.
- Patients with neoplastic disease.
- Patients with renal failure.
- Patients with gout and bacterial infection

Collection of Blood Sample

About 3-5 ml of venous blood was collected in vacutainer by means of sterile needle, from anterior anticubital vein. It was allowed to clot for few minutes and was subjected to centrifugation for 10 minutes at 3000 rpm to separate the serum and kept at -20^0C until analysis was carried out. Estimation of serum high sensitive C-reactive protein.

Concentration measured on 0, 3rd and 7th day of Acute Myocardial infarction by microlab 300 analyzer (semi autoanalyzer) using the kits supplied by Siemens where as serum high sensitive C-reactive protein (hs-CRP) will be measured by Turbidimetric immunoassay method on microlab 300 using the kits supplied by Quantia CRP.

Statistical analysis

Mean and standard deviation were worked out for estimating the levels of serum high sensitive C-reactive protein (hs-CRP) in patients of AMI and age matched controls. In order to compare these parameters between patients and controls, student's t-test was applied and the results were presented in tabular and graphical presentation.

Using the student's *t*-test values, the '*p*' values (probability values) were obtained. *'p'* value less than 0.05 was considered as significant.

RESULTS

Present study was carried out in the Department of Biochemistry of Tertiary Hospital. The total 60 subjects were studied of which 50 cases were served as cases who were the patients of acute myocardial infarction and 50 cases were (age matched) served as controls. They were from 30-75 years. The youngest patient was of 31 years and oldest was 69 years. Case group was further divided into three subgroups as per the 0 day, 3rd day and 7th days.

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Table 1: Distribution of patients according to gender.

Gender	Case		Control	
	No.	%	No.	%
Male	36	72%	32	64%
Female	14	28%	18	36%
Total	50	100.0%	50	100.0%

Table no 1: Present study comprise of 50 cases and 50 controls. Among cases, 36 were male (72 %), 14 were female (28%). Out of 50 controls 32 were male (64 %) and 18 were female (36%).

Table 2: Age group mean value of case & control.

	Case	Control	
	Mean±SD	Mean±SD	*p* value
Age (years)	56.84±8.29	54.36 ± 10.89	$p<0.01$

Table no-2: The mean age of cases and controls were 56.84±8.29 years and 54.36 ± 10.89 years respectively. This is not statistically significant.

Table 3: Risk Factors for Acute Myocardial Infarction (n=50).

Characteristics	Number of patients	Percentage
Hypertension	15	48.39 %
Diabetes mellitus	10	32.26 %
Smoking	06	19.35 %
Total	31	100.00%

Table no-3: In the present study, out of 50 AMI cases 31 (62%) had hypertension, diabetes mellitus and smoking habit. Maximum i.e. 15 cases (48.39%) had hypertension followed by diabetes 10 cases (32.26%) smoking 6 cases (19.35%). 19 cases (38%) had no hypertension, diabetes mellitus and smoking habit.

Table 4: Age and sex wise distribution.

Age in years	Cases group (n=50)		Control group (n=50)	
	male	Female	Male	Female
	No. (%)	No. (%)	No. (%)	No. (%)
30-40	06(12%)	1(2 %)	7(14 %)	1(2 %)
41-50	10(20%)	4(8%)	13(26 %)	4 (8 %)
51-60	12(24%)	7(14%)	11(22 %)	6 (12 %)
61& above	7(14%)	3(6%)	06(12%)	2 (4 %)
Total	35(70%)	15(30%)	37(74%)	13(23.3%)

Table no -4: The most men 12 (24%) were in the age groups 51-60 years, followed by 10 (20%) in the age groups 41-50 years, and 7 (14%) in the age groups over 61 years. The majority of the males in the 6(12%) case group were between the ages of 30 and 40. In some cases, 7 (14%) of the females were 51-60 years old, followed by 4(8%) females 41-50 years old. While 1 (2%) of females were between the ages of 30 and 40, and 3 (6%) were over the age of 61 years.

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Table 5: Mortality of patients according to day in case groups.

Mortality	No. of patients	Percentage (%)
Day (0)	4	8 %
Day 3rd	3	6 %
Day 7th	2	4 %
Total	9	18 %

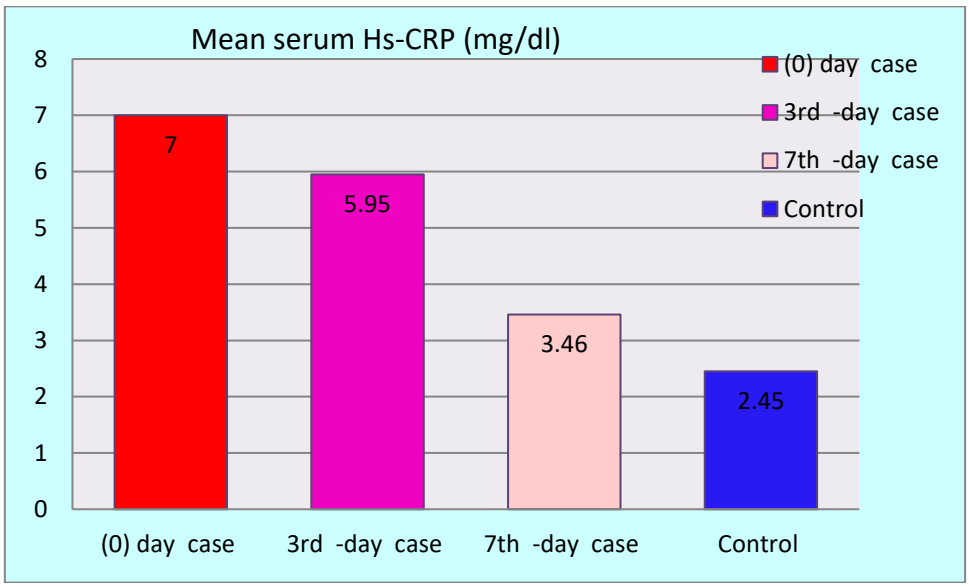
Table no 5: In the present study, mortality of patients according to day in case groups. Here cases on (0) day, 4 patients death, 3rd day three patients death and 7th day, 2 patients death in case group.

Table 6: Comparison of serum high sensitive C-reactive protein (hs-CRP) at 0 day, 3rd day and 7th day in case and control group (unpaired t-Test).

Serum hs-CRP	Mean	SD	t- value	p-value
(0) day case	7.00	2.93	t= 9.96	*p* <0.01
3rd -day case	5.95	2.32	t= 6.89	*p*< 0.01
7th -day case	3.46	2.70	t= 2.36	*p< 0.01*
Control	2.45	1.34		

As shown in table No. 6, mean serum high sensitive C-reactive protein in cases on 0, 3rd and 7th day were 7.0±2.92 mg/dl, 5.95±2.32 mg/dl, 3.46±2.70 mg/dl day respectively which were higher than controls group (2.45±1.34 mg/dl). Comparison between control and serum high sensitive C-reactive protein on 0 and 3rd day was found to be more significant than that of 7th day. Unpaired *t*-test showed that there was significant increase in serum high sensitive C-reactive protein level in cases as compared to controls (p<0.005).

The comparison of mean serum high sensitive C-reactive protein level between controls and cases was also presented graphically in Bar Diagram No.8.



Bar Diagram 1: Mean serum high sensitive C-reactive protein in cases and controls.

The mean level of cases for high sensitive C-reactive protein is decreasing from 0 day to 3rd day, 3rd day to 7th day. Lowest level was observed on 7th day.

DISCUSSION

Acute myocardial infarction may be the first manifestation of coronary artery disease, or it may occur, repeatedly, in patients with established disease. Information on myocardial infarction attack rates can provide useful data regarding the burden of coronary artery disease [13].

As shown in Table no 1: The current study included 50 patients and 50 controls. There were 36 males (72%), and 14 females (28%). Out of 50 controls, 32 were male (64%) and 18 were female (36%).

Table no-2: The mean age of cases and controls were 56.84±8.29 years and 54.36 ± 10.89 years respectively. This is not statistically significant. Our result correlated well with finding showed by Nadkar et al. (2008) [14] Chaithra S.P et al (2013) [15], Badiger et al (2014) [16].

Table no-3: In the current study, 31 (62%) of the 50 AMI patients had hypertension, diabetes, and a smoking habit. The greatest number of patients (48.39%) had hypertension, followed by diabetes (10 instances (32.26%), and smoking (6 cases (19.35%). 19 instances (38%) did not have hypertension, diabetes, or a smoking habit., Our result correlated well with finding showed by Mishra D.N. (2023) [12] Shin et al (2012) [17], Kulkarni MR.(2020) [18].

Table no -4: the majority of males 12 (24%) were 51-60 years old, 10 (20%) were 41-50 years old, and 7 (14%) were above 61 years old. The 6(12%) case group's males were mostly between the ages of 30 and 40. In certain situations, 7 (14% of the females) were 51-60 years old, with 4 (8% of the females) being 41-50 years old. While 1 (2%) of females were aged 30 to 40, 3 (6%) were above the age of 61. Our result correlated well with finding showed by Mishra D.N.(2023)[12] Kulkarni MR.(2020) [18].

With respect to mortality, some previous epidemiologic studies in initially healthy populations have also shown that CRP levels may be associated with cardiovascular morbidity and death [19, 20, 22]. Some studies found that elevated CRP at presentation after ACS were associated with risk for all-cause death [21, 22]. Table no 5: In the present study, mortality of patients according to day in case groups. Here cases on (0) day, 4 patients death, 3rd day three patients death and 7th day, 2 patients death in case group. Our result correlated well with finding showed by Mishra D.N.(2023)[12] Zhang X(2021) [22].

As shown in table No. 6, the mean serum high sensitive C-reactive protein in cases on 0, 3rd and 7th day were 7.0±2.92 mg/dl, 5.95±2.32 mg/dl, 3.46±2.70 mg/dl day respectively which were higher than controls group (2.45±1.34 mg/dl). Comparison between control and serum high sensitive C-reactive protein on 0 and 3rd day was found to be more significant than that of 7th day. Unpaired *t*-test showed that there was significant increase in serum high sensitive C- reactive protein level in cases as compared to controls (p<0.005). Our result correlated well with finding showed by Baruah et al (2012) [23], Badiger et al (2014) [24], Pietila et al (1996) [25].

Previous research found that blood CRP levels in AMI patients were considerably higher than in control participants (p< 0.01) on day 1, day 3, day 5, and at the time of discharge. Correlate with Baruah et al (2012) [23]. Another study discovered significantly greater hs-CRP in acute ST-segment elevation myocardial infarction on the first and third day in individuals who developed heart failure. according to Pietila et al (1996) [25].

Inflammation is one of the primary factors in the pathophysiology of atherosclerosis, and there is growing interest in evaluating inflammatory biomarkers in coronary artery disease (CAD) [26, 27].

Patients with AMI who had greater hs-CRP levels upon admission were older, had higher baseline creatinine levels, and were at a higher risk of developing heart failure in the long run [26, 28]. As a result, there are variable degrees of ischemia in AMI as the time increases. This might result in varying amounts of Hs-CRP.

CONCLUSION

Thus, the study concludes that evaluation of serum high sensitive C-reactive protein in serum play an important role in the diagnostic marker and management of Acute Myocardial Infarction.

Abbreviations

Hs-CRP= High Sensitive- C Reactive Protein	**ICCU =** Intensive Cardiac Care Units
MI= Myocardial Infraction	**MICU=** Medical Intensive Care Units
AMI= Acute Myocardial Infraction	**ACS =** Acute Coronary Syndromes.
CVS= Acute Coronary Syndromes	**CK-MB=** Creatine Kinase-Myoglobin Binding
ECG = Electro Cardio Grams	

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