Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/173

Original Article

Level of High-Sensitivity C-Reactive Protein Assay to Evaluate Risk in Follow-Up Patients with Acute Coronary Syndrome

Himanshu Mathur[1], Jitendra Kumar Jatav[2]

[1]Assistant Professor, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India, [2]Associate Professor, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India

Abstract

Introduction: Among currently recognized inflammatory markers numbers of considerations favor high-sensitivity C-reactive protein (Hs-CRP) as a potentially useful predictor of prevalence and incidence of cardiovascular diseases. Clinical interest in these markers has also focused on their potential utility in predicting future cardiovascular events and thereby in patient's management.

Purpose of study: The purpose of the study was to determine the mean level of Hs-CRP assay in patients of acute coronary syndromes and corelation of Hs-CRP with two or more major risk factors and to correlate the level of Hs-CRP and cardiac events in patients of acute coronary syndromes during follow-up of a specified period of 6 months.

Materials and Methods: Present study had been carried out in the Department of Medicine, Gajra Raja Medical College and associated Hospital, Gwalior, Madhya Pradesh, India, from January 2004 to September 2005. This was a prospective observational study. The targeted populations were 30 cases with acute coronary syndromes of both sexes.

Results: The study was statistically insignificant in reference to various major cardiac events compared to various levels of Hs-CRP. ST elevation myocardial infarction (MI) was the most prevalent acute coronary syndrome. Most of the risk factors show their association with the moderate risk level of Hs-CRP, i.e., 1.0–3.0 mg/L, followed by high-risk levels, i.e., >3.0 mg/L, followed by low-risk levels, i.e., <1.0 mg/L. Post MI/angina was the major cardiac event that highest number of patients developed, during the follow-up period of 6 months.

Conclusion: No statistically significant association of various risk factors with Hs-CRP was observed in patients of acute coronary syndromes. No statistically significant association of Hs-CRP levels with major cardiac events was appreciable in patients of acute coronary syndrome in a follow-up period of 6 months.

Key words: Coronary syndrome, C-reactive protein, Myocardial infarction, Risk factor, Unstable angina

INTRODUCTION

In the current era, cardiovascular diseases (CVD) remain the leading cause of death worldwide.[1] Although we do not have exact national data on ischemic heart disease (IHD), it was found that the prevalence of CVD is increasing day by day, predominantly the incidence of coronary artery disease (CAD). The significance of the contribution of laboratory methods in clinical cardiology has grown in importance over the years. In recent time, the incorporation of biomarkers plays a major role for making new international guidelines and in the redefinition of myocardial infarction (MI). There are mainly two classes of indicators or markers of early cardiac cell injury and/or ischemia and marker of inflammation and coronary plaque instability and disruption.[2]

Access this article online

www.ijss-sn.com

Month of Submission : 04-2018
Month of Peer Review : 05-2018
Month of Acceptance : 06-2018
Month of Publishing : 06-2018

Corresponding Author: Dr. Jitendra Kumar Jatav, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur – 482 003, Madhya Pradesh, India. Phone: +91-9993010708. E-mail: jkjgrmc@gmail.com

There are various serum cardiac biomarkers which associated with the acute coronary syndrome (ACS). The clinical application of cardiac biomarkers in ACS is no longer limited to establishing or refuting the diagnosis of myocardial necrosis. In association with electrocardiography (ECG) and clinical criteria, the cardiac biomarkers provide a convenient and non-invasive means to gain insights into the underlying causes and consequences of acute coronary syndrome that mediate the risk of recurrent events and may be targeted for specific treatment.[2]

Biochemical cardiac markers play a major role for risk assessment in patients with an ongoing non-STsegment elevation ACS. Although the cardiac troponin-T, in particular, is generally recognized as an important risk indicator of underlying cardiac tissue damage, other markers of left ventricular performance (i.e., N-terminal pro-brain natriuretic peptide), inflammation (i.e., C- reactive protein), and renal function, i.e., estimated glomerular filtration rate are equally important in providing strong prognostic significance.[3,4]

Since vascular inflammatory changes can hardly be evaluated using cardiac imaging methods, the role of inflammation biomarkers testing in peripheral blood is increasing, with the high sensitivity C-reactive protein (Hs-CRP) being the most profoundly studied in CVD. It remains stable in samples over long periods of time and can be quite simply, rapidly, and cheaply tested.[1]

Multiple prospective cohort studies have shown the association between increased CRP levels and increased CVD event risk in patients with established disease, and the incidence of first cardiovascular events in individuals at risk for atherosclerosis.[5]

It makes Hs-CRP testing valuable in both, primary and secondary CVD prophylaxis and for those, who already suffer from CVD. This test is useful in the evaluation of disease severity, treatment efficacy, and outcome prognosis.[6,7]

MATERIALS AND METHODS

Place of Study

The present study had been carried out in the Department of Medicine, Gajra Raja Medical College and J.A group of Hospital, Gwalior, in the state of Madhya Pradesh, India, between the periods of January 2004–September 2005.

Aims and Objectives of the Study

The objectives are as follows:

1. To study the risk factors in patients of acute coronary syndromes.
2. To determine the mean level of Hs-CRP assay in patients of acute coronary syndromes.
3. To determine the corelation of Hs-CRP with two or more major risk factors.
4. To correlate the level of Hs-CRP and major cardiac events in patients of acute coronary syndromes, during follow-up of a specified period of 6 months.

Inclusion Criteria

The present study was included 30 cases of acute coronary syndromes, i.e., Unstable angina (UA), Non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). All the cases selected for the study were taken from the intensive care unit (ICU) of the Department of Medicine and J.A. Group of Hospitals at Gajra Raja Medical College, Gwalior, in the state of Madhya Pradesh, India.

Eligible patients had admitted with a typical history and chief complaint of anterior chest pain mainly at the retrosternal area which may radiate toward the left lateral side of chest and arm. Cases may have associated complaint of vomiting, breathlessness, palpitations, and sweating, etc. Cases were found positive for at least one cardiac marker of injuries such as CPK-MB or cardiac troponin-T (by Trop-T kit method) for NSTEMI and STEMI along with the typical ECG changes in support of CAD.

Exclusion Criteria

Following patients were excluded from the present study:

1. Patients taking estrogens/hormonal medications.
2. Patients with acute or chronic inflammatory conditions such as gingivitis, bronchitis, pneumonia, pancreatitis, and arthritis.
3. Patients already on aspirin, beta-blockers, niacin, and various statins therapy.
4. Patients on increased activity or endurance exercises.
5. Recent history of chest trauma.
6. Patients with valvular heart disease like rheumatic heart disease.
7. Cardiomyopathies and pericardial inflammatory diseases.

Laboratory Tests

All the relevant investigations have been done in the Department of Pathology, Radiology, and Cardiology, etc., of Gajra Raja Medical College and J.A group of Hospital, Gwalior, in the state of Madhya Pradesh, India.

1. Data from the clinical history, physical examination and ECG were recorded according to a fixed protocol.
2. The Hs-CRP estimation was done at the time of presentation, and the analysis was performed by turbidimetry immunoassay using QUANTA Reagent kit

(latex) manufactured by Tulip corporation, USA. Values of ≤1 mg/L, 1–3 mg/L, and >3 mg/L were labeled as low risk, intermediate risk, and high risk, respectively.
3. Complete blood picture,
4. Lipid profile.
5. Blood urea.
6. Serum creatinine.
7. Urine R/M.
8. X-Ray chest
9. 2-D Echo study.

All above-mentioned investigations were carried out by standard methods.

Patient's Diagnostic Criteria and Data Collection Method

STEMI

1. Qualitative assay of cardiac troponin-T or CPK-MB positivity.
2. ECG showing pathological Q waves (> or = 0.04 s in duration) and at least 20% reduction in amplitude of the following R wave.
3. ST-segment elevation of >l mm in the limb leads or >2 mm in the precordial leads in at least 2 or more contiguous leads in a clinical setting of acute coronary syndromes.

UA and/or NSTEMI

TIMI-II Cass-A and B criteria for UA and Class-C for NSTEMI were followed which is as below:

1. Resting angina of at least 5 min duration, ST deviation ≥0.5 mm, and increased cardiac markers in case of NSTEMI.
2. New onset angina of at least Canadian cardiovascular classification Class III severity with onset within 2 months of presentation.
3. Previously diagnosed angina that became distinctly more frequent, longer in duration or lower in the threshold.

Major Cardiac Events were Recorded

1. Post-MI/ischemia angina.
2. Ventricular tachycardia (VT).
3. Re-myocardial infarction (Re-MI).
4. Atrioventricuar blocks (AV-block).
5. Mortality.

All patients admitted in ICU with the fulfillment of above diagnostic criteria for acute coronary syndromes were investigated thoroughly at the time of admission with all above-mentioned investigations including Hs-CRP. Patients were also inquired about other associated medical illnesses such as diabetes mellitus (DM), hypertension (HTn), cigarette smoking, and family history of cardiovascular events and obesity.

After discharge, all patients were kept in strict follow-up individually, for a specified period of 6 months from the date of discharge. Patients were asked to report from time to time and as and when needed strictly in person. Any major events from the above list were emphasized and if present, noted.

Statistical Analyses

The present study was a prospective observational study. Study data have been recorded using structured schedule (case report form) and entered for tabulation in Microsoft Excel Sheet. Statistical data were analyzed using statistical analysis system (SAS) for window version 9.1; SAS Institute North Carolina State University software. Statistical data were calculated by the frequency, percentage and mean ± standard deviation and level of statistical significance were calculated with *P*-value (<0.05 significance) consideration.

RESULTS

Out of total $n = 30$ patients, $n^1 = 22$ cases were found male and remained $n^1 = 8$ cases female. The percentage of male patients was approximately $n = 22/30$, (73.33%) and that of females was $n = 8/30$, (26.67%). This data show the preponderance of male gender, which is consistent with the fact that it is male gender which is more susceptible to cardiovascular events. None of the patients was lost during follow-up period.

Age and Sex Distribution [Table 1]

The prevalence of acute coronary syndromes in various age groups in both males and females was as follows:

In Males

In the present study $n = 6/22$, 27.27% of male patients were belong to age group of 50–59 years which were followed by $n = 5/22$, 22.73% patients of age group between 40 and 49 years, this was subsequently followed by $n = 4/22$, 18.18% patients of age group 60–69 years,

Table 1: Age and sex distribution in cases of acute coronary syndromes

Sex (*n*=30)	Age in years (*n*=30)						
	0–29	30–39	40–49	50–59	60–69	70–79	80 and more
Male (n^1=22) (%)	0 (0)	3 (13.64)	5 (22.73)	6 (27.27)	4 (18.18)	3 (13.64)	1 (4.55)
Female (n^1=8) (%)	0 (0)	0 (12.5)	2 (25)	2 (25)	3 (37.5)	0 (0)	0 (0)

n: Total number of cases, n^1: Number of cases according to sex

this, in turn, followed by n = 3/22, 13.64% patients of 70–79 years of age group, and n = 3/22, 13.64% patients belong to 30–39 years of age group. The second last prevalence was seen in n = 1/22, 4.55% patients in "80 and more" age group, ultimately followed by 0% patients in 0–29 years of age group.

In Females

The maximum percentage of the female patients n = 3/8, 37.50% belong to age group of 60–69 years which were followed by two groups simultaneously with equal prevalence n = 2/8, 25% in both 40–49 and 50–59 years age group, this was subsequently followed by n = 1/8, 12.5% patients from age group 30 to 39 years.

From Overall Patients

- Patients presented with UA - n=8/30, (26.67%).
- Patients presented with NSTEMI –n=6/30, (20%).
- Patients presented with STEMI – n=16/30, (53.33%).

The above results show that the maximum patients were presented with STEMI followed by UA which, in turn, followed by NSTEMI.

Symptomatology [Tables 2 and 3]

Chest pain described as most of the patients have retro-sternal and left-sided chest pain, few patients complaining radiation to the back also. Nitrates typically relieved the pain.

Males

Out of five presenting symptoms considered in the study, chest pain was the most prevalent symptom in males n = 21/22, (95.45%) which followed by palpitation n = 15/22, (68.18%) then by sweating n = 15/22, (68.18%), breathlessness n = 11/22, (50%) and ultimately vomiting n = 6/22, (27.27%).

Female

Out of five presenting symptoms the most prevalent symptom in females was chest pain n = 7/8, (87.50%), followed by palpitation n = 6/8, (75%) and sweating n = 3/8, (37.50%) which, in turn, followed by vomiting and breathlessness with n = 2/8, (25%) and n = 1/8, (12.50%), respectively.

- Total number of patients with chest pain – n = 28/30.
- Total number of patients with palpitation –n = 21/30.
- Total number of patients with sweating –n = 18/30.
- Total number of patients with breathlessness – n = 12/30.
- Total number of patients with vomiting –n = 8/30

Overall, chest pain was the most common presenting symptom in all three classes of acute coronary syndrome n = 8/30, (87.5%) in UA, n = 6/30, (99.99%) in NSTEMI, and n = 16/30, (93.75%) in STEMI with mean value percentage (93.75%).

Hs-CRP level [Table 4]

- Total patients in low-risk group (<1 mg/L Hs-CRP level) – n = 6/30 (20%).
- Total patients in moderate risk group (1–3 mg/L Hs-CRP level) – n = 14/30 (46.67%).
- Total patients in high-risk group (>3 mg/L Hs-CRP level) – n = 10/30 (33.33).

Male

In present study n = 10/22 (45.46%) of males showed moderate risk Hs-CRP levels followed by n = 8/22 (36.37%) patients were showing high-risk Hs-CRP levels and finally n = 6/30 (18.18%) of patients showing low-risk Hs-CRP levels.

Female

In present study n = 4/8, (50%) of females showed moderate risk Hs-CRP levels followed by patients showing high-risk and low-risk Hs-CRP levels n = 2/8, (25%) each.

Major risk factors [Table 5]

In the present study, following were the percentages wise distribution of the various major risk factors in overall acute coronary syndrome, as patients presented with more than one risk factor.

DM	16.67% (n=5)
HTn	23.33% (n=7)
Smoking	36.67% (n=11)
Hyperiipidemia	26.67% (n=8)
Family history	10% (n=3)
Obesity	13.33% (n=4)

Table 2: Incidence of various symptoms in patients with acute coronary syndromes

Sex (n=30)	Symptoms				
	Chest pain	Palpitation	Sweating	Breathlessness	Vomiting
Male (n^1=22)	21 (95.45)	15 (68.18)	15 (68.18)	11 (50)	6 (27.27)
Female (n^1=8)	7 (87.50)	6 (75)	3 (37.5)	1 (12.5)	2 (25)

n=total number of cases, n^1=number of cases according to sex

In the present study, no statistically significant association of various major risk factors was observed with all three acute coronary syndromes mainly UA, NSTEMI, and STEMI, *P*- value of the risk factors was found statistically non-significant.

In the evaluation of the association of major risk factors with low, moderate, and high-risk levels of Hs-CRP following results were drawn out

DM

DM (n = 5) showed equal association with moderate and high-risk groups, i.e., n=2/5, 40% patients falling in each group, followed by n = 1/5, 20% patients in a low-risk group.

HTn

HTn (n = 7) showed maximum association with moderate risk group n = 4/7, (57.14%); followed by high-risk group n = 3/7, (42.80%) and finally the low-risk group n = 2/7, (28.57%).

Smoking

Smoking (n = 11) showed maximum association with moderate risk group with n = 6/11, 54.55% patients followed by high-risk group with n = 4/11, (36.36%) and finally followed by low-risk group with n = 1/11, (9.09%).

Table 3: Frequency of various symptoms in different acute coronary events

Symptomatology (*n*=30)	UA (*n*=8)	STEMI (*n*=16)	NSTEMI (*n*=6)	MEAN %
Chest Pain	7 (87.5)	15 (93.75)	6 (99.99)	93.75
Palpitation	5 (62.5)	2 (68.75)	5 (83.35)	71.53
Sweating	5 (62.5)	2 (68.75)	2 (33.34)	54.86
Breathlessness	3 (37.50)	7 (43.75)	2 (33.34)	38.20
Vomiting	1 (12.5)	3 (18.75)	4 (66.67)	33.64

UA: Unstable angina, STEMI :ST-elevation myocardial infarction, NSTEMI :Non-ST-elevation myocardial infarction

Table 4: Risk wise distribution of Hs-CRP assay in patients of acute coronary syndrome

Sex (*n*=30)	Hs-CRP		
	Low-risk <1 mg/L (*n*=6)	Moderate risk 1–3 mg/L (*n*=14)	High-risk >3 mg/L (*n*=10)
Male (n^1=22)	4 (18.18)	10 (45.46)	8 (36.37)
Female (n^1=8)	2 (25)	4 (50)	2 (25)

n=total number of cases, n^1=number of cases according to sex. Hs-CRP: High-sensitivity C-reactive protein

Family History

The scenario with family history (n = 3) was different from other risk factors. In our study, it showed equal association with all three risk groups of Hs-CRP levels, i.e., n = 1/3, 33.34% patients in all three groups.

Obesity

The maximum association of obesity (n = 4) was observed with moderate risk group, i.e. n = 2/4, 50% patients followed by both low-risk group and high-risk group with n = 1/4, 25% patients each. "*P*" value (the value of significance) was more than 0.05 for all major risk factors, namely DM, HTn, smoking, family history, and obesity, which signifies that association of all Hs-CRP levels with all major risk factors was statistically insignificant, attributable largely to small study cohort, and short period of follow-up.

Major Cardiac Events [Table 6]

Post-MI/ischemia angina

Post-MI/ischemia was the most occurring major cardiac event in overall patients of the acute coronary syndrome (13.33%).

Incidence of post-MI/ischemia angina (n = 4) was the highest in high-risk group of Hs-CRP level with n = 2/10, 20% patients followed by n = 1/6, 16.67% patients in low-risk group and then ultimately moderate risk group with n = 1/14, 7.14% patients.

VT

There was virtually no incidence of VT in any risk groups of Hs-CRP levels.

Re-MI

In our study, 6.67% of overall patients of acute coronary syndrome developed Re-MI during the follow-up period of 6 months with equal incidence in both high-risk and low-risk groups.

Table 5: Significance of post-infarct/ischemic events with special reference to the levels of Hs-CRP

Cardiac Events	Mild Risk (*n*=6)<1 mg/L	Moderate Risk (*n*=14)1-3 mg/L	High-Risk (*n*=10)>3 mg/L	*P*	Overall Incidence
Post-MI/ischemia angina	1 (16.67)	1 (7.14)	2 (20)	0.635	13.37
VT	0 (0)	0 (0)	0 (0)	-	0 (0)
Re-MI	0 (0)	1 (7.14)	1 (10)	0.73	6.67
Blocks	0 (0)	0 (0)	2 (20)	0.117	6.67
Mortality	0 (0)	1 (7.14)	1 (10)	0.736	6.67

Total number of patients having major cardiac events=10 (33.37%). Total number of patients having no major cardiac events=20 (66.67%). Hs-CRP: High-sensitivity C-reactive protein

Table 6: Distribution of major cardiac events in the follow-up period of 6 months in the patients of acute coronary syndromes

Sex (*n*=30)	Major Cardiac Events during 6 months follow-up period				
	Post-MI/ Ischemia Angina	VT	Re-MI	Blocks	Mortality
Male (n^1=22)	3 (13.64)	0 (0)	2 (9.09)	1 (4.55)	2 (9.09)
Female (n^1=8)	1 (12.5)	0 (0)	0 (0)	1 (12.5)	0 (0)

n=total number of cases, n^1=number of cases according to sex. VT: Ventricular tachycardia, Re-MI: Re-myocardial infarction, Post-MI: Post-myocardial infarction

Mortality

Two cases among overall 30 patients suffered mortality; one case was from moderate risk group and another from high-risk group.

The overall incidence of mortality among all patients of the acute coronary syndrome was 6.67%.

Major cardiac events and corresponding Hs-CRP

Following results were drawn out:

Type of cardiac event	Mean Hs-CRP values (mg/L)
Post-MI/ischemic angina	2.50
Re-MI	2.865
AV-Blocks	3.68
Mortality	4.0

The mean value of Hs-CRP in major cardiac events group was 3.26 (mg/L) which is higher compared to the mean of no major cardiac events group 1.73 (mg/L); however, it is statistically insignificant ($P > 0.05$).

Taking the cutoff value 1 mg/L of hs-CRP we found that the

Sensitivity = 90% and Specificity = 25%

If taking the cutoff value of 3 mg/L of hs-CRP we found that the

Sensitivity = 40% and Specificity = 80%.

DISCUSSION

A total of total 30 patients, 22 cases were found male and remained 8 cases female. The percentage of males was approximately n = 22/30, (73.33%) and that of females n = 8/30, (26.67%). This data show the preponderance of male gender, which is consistent with the fact that it is male gender which is more susceptible to cardiovascular events. The maximum numbers of cases n = 6/22, 27.27% of males were belong to age group of 50–59 years.

Sharma *et al.* have been found in their study that from total 955 of patients those were admitted with a history of MI in 2 years of study periods, of which only 37 patients (3.9 %) fulfilled the inclusion criteria. The mean age was found 36.14 years, Male:female ratio was found to be 8:1, this data consistent with the present study.[8]

Singh *et al.* have been observed in their study that, the highest number of cases was among 51–60 years (34.21%) and mean age of survived cases was 56.75 ± 10.47. These findings were comparable to create registry and other two studies reported from Pakistan and Chennai study. The percentage of males was 76.58%, with male:female ratio 3.3:1 in this study. South Indian study noted that maximum anterior wall MI occurred among males (82%) with the male:female ratio 4.5:1. In North Bengal study, higher prevalence of CAD was noted among males. Male preponderance among STEMI cases in all age groups was observed in North India study.[9]

Present study results show that the maximum patients were presented with STEMI followed by UA which, in turn, followed by NSTEMI.

T. Ohira, H studied that the acute coronary syndrome is now a leading cause of mortality in the Asia-Pacific region, accounting for around half of the global burden.[10]

Xavier *et al.* have been found that the Indian patients with the acute coronary syndrome have a higher rate of STEMI (61%) than do patients in high-income countries (15-25%). India has the highest burden of ACS in the world and the create registry has provided contemporary data on 20,468 patients from 89 centers from 10 regions and 50 cities in India.[11]

In the present study, maximum numbers of patients have associated risk factor as smoking followed by hyperlipidemia, HTn, DM, obesity, and family history. Our study results were consistent with the study of Sharma *et al.*[8] as they have also been found the risk factors in their study patients as dyslipidemia, smoking, diabetes and HTn, and family history.

International Research Groups noted smoking or smokeless tobacco as a major risk factor for STEMI. In North Bengal study, the prevalence of IHD among smokers was significantly higher than in nonsmokers. Other published literature correlated smoking to be an important risk factor for CAD in Indian population.[9]

Researchers from India reported less (7%) family history of among anterior wall myocardial infarction (AMI) cases. The rising incidence of ACS in Indians may be related to familial hereditary factors acting on modifiable risk factors, an important independent risk factor for CAD in younger cases.[9]

Our study showed silent infarction in some patients with DM, although total percentage of DM was found to be 16.67%, the whole fact goes well. Rachel Hajar has also concluded that the DM patient has a high risk for cardiovascular disease development.[12]

We have observed that the most common presenting symptoms in ACS cases were chest pain, palpitation, sweating, breathlessness, and vomiting, respectively. Chest pain among these found to be the most prevalent (93.75%), which was consistent with the study results of Cervellin and Rastelli.[13]

In the present study, mean Hs-CRP level for major cardiac events group was 3.26 mg/L, which was much higher compared to l.73% in the no major cardiac events group. Elevated Hs-CRP levels have been related to increased risk of death and MI. It was noted in present study that level of Hs-CRP was more with the aged patients, which were more susceptible to cardiovascular events, so there could be an indirect relation between Hs-CRP and cardiovascular events.

Patients having Hs-CRP value <l mg/L were said to be at low risk, between 1 and 3 mg/L moderate risk and >3 mg/L are high-risk groups. Elevated levels of CRP in patients of acute coronary syndromes are approximately 5 times higher than stable individuals. In our study, being a noncomparative one did not measure the Hs-CRP level in normal patients; moreover, size of the cohort and small duration of follow-up was unlikely to give any significant results.

Karki *et al.* have been studied that the hs-CRP levels of >5 mg/L were found highly significant for predicting mortality during the hospital stay and at 6 weeks. In the GRACE registry, 12% of patients with STEMI, 13% with NSTEMI, and 8% with UA were expected to die in 6 months within the onset of symptoms. There have been a number of studies done which also found the prognostic significance of hs-CRP. Most of the studies were done in stable CAD. The JUPITER trial, which was restricted to participants with CRP levels >2 mg/L, found that treating the patients with rosuvastatin decreased the hs-CRP and low-density lipoprotein levels and finally the cardiovascular outcomes.[14]

In our study, elevated levels of Hs-CRP were also noted with increasing age especially after 4th decade. Stone *et al.* have been also observed that the increased age has been shown to be associated with a significant increase in adverse outcomes in patients of UA/NSTEMI.[15]

Ridker has observed that the acute phase reactant CRP as a simple downstream marker of inflammation has now emerged as a major cardiovascular risk factor.[16]

Calabro *et al.* have been shown that CRP is composed of 523kD subunits and it is a circulating marker of pentraxin family that plays a major role in the human immune system. Although it is primarily derived from liver, recent data indicate that cells within human coronary arteries particularly in the atherosclerotic intima can elaborate CRP.[17]

Raised levels of CRP have been reported with poor prognosis in cases of UA in other study[16] also, but in the present study no such association could be established along with this and there has been no statistically significant association of various risk factors, namely DM, HTn, smoking, obesity, hyperlipidemia, and family history with any of the acute coronary syndromes. Both these observations are largely attributable probably to the small-sized cohort and a very short period of follow-up.

The similar observations were noted by the Adukauskiene *et al.* in association of specified Hs-CRP levels with major cardiac events during the follow-up period; however, the mean Hs-CRP level of the patients suffering major cardiac events was higher than those who had no major cardiac events, but statistical significance is still lacking, probably again attributable largely to small cohort and short follow-up period.[18]

So as a whole we know that Hs-CRP is a noble marker for prediction of risk because of its outstanding characteristics, this can be used as a routine tool for future risk estimation with excellent accuracy, as evidenced by Framingham Heart Study,[19] but the present study does not support these findings, reasons are many but small-sized cohort and short follow-up period seem to be the most obvious culprits.

CONCLUSION

Here, finally, we concluded that:

1. The study was found statistically insignificant in reference to various major cardiac events compared to various levels of Hs-CRP.
2. The study was again found to be statistically insignificant in reference to different risk factors such as DM, HTn, smoking, hyperlipidemia, positive family history, and obesity compared to different acute coronary syndromes.
3. There was definitive male preponderance in the overall patients of various acute coronary syndromes.
4. The maximum numbers of patients were from 40 to 70 years age group both for the males and females.
5. Chest pain has been the most consistent symptom in overall patients, at the time of presentation to the ICU, both in males and females as well.
6. Smoking was the most consistent major risk factor associated with all acute coronary syndromes at the time of presentation.
7. Smoking was the major risk factor, which shows the maximum association with various levels of Hs-CRP.

8. In the present study, STEMI was the most prevalent acute coronary syndrome followed by UA and then by NSTEMI, among overall patients at the time of presentation.
9. Most of the risk factors had shown their association with the moderate risk level of Hs-CRP, i.e., 1.0 to 3.0 mg/L, followed by high-risk levels, i.e., >3.0 mg/L, and followed by low-risk levels, i.e., <1.0 mg/L.
10. Post-MI/ischemia angina was the major cardiac event that highest number of patients developed, during the follow-up period of 6 months. This was true for both males and females.
11. Total percentage of males developing major cardiac events, among overall patients were 26.67%, while total percentage of females developing major cardiac events among overall patients was 6.67%.
12. Among all major cardiac events, mortality was associated with highest concentrations of Hs-CRP.
13. The mean of Hs-CRP level of major cardiac events group was much higher than the mean of no major cardiac events group. The range of Hs-CRP levels from 0.14 to 5.1 mg/L; mean value = 2.23 mg/L.
14. No statistically significant association of various risk factors with Hs-CRP was observed in patients of acute coronary syndromes.
15. No statistically significant association of Hs-CRP levels with major cardiac events was appreciable in patients of the acute coronary syndrome in a follow-up period of 6 months.

Limitation of Study

The statistical insignificance in above study was probably attributable to small cohort under study and short duration of follow-up. This was a single center study with our limited resources.

Ethical Issues

The present study work has been conducted in the Department of Medicine and J.A. Group of Hospitals at Gajra Raja Medical College, Gwalior, in the state of Madhya Pradesh, India. The study work has been approved by the Institutional Ethics Committee.

ACKNOWLEDGMENT

We would like to acknowledge this article to our all senior consultants our parents and friends for enabling us to complete the present thesis work by providing the knowledge and necessary inspiration.

REFERENCES

1. Salazar J, Martínez MS, Chávez M, Toledo A, Añez R, Torres Y, *et al.* C-reactive protein: Clinical and epidemiological perspectives. Cardiol Res Pract 2014;2014:605810.
2. Panteghini M. Role and importance of biochemical markers in clinical cardiology. Euro Heart J 2004;25:1187-96.
3. Heeschen C. Predictive value of C-reactive protein and troponin T in patients with unstable angina: A comparative analysis. J A Coll Cardiol 2000;35:1535-42.
4. James SK, Lindahl B, Siegbahn A, Stridsberg M, Venge P, Armstrong P, *et al.* N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: A Global utilization of strategies to open occluded arteries (GUSTO)-IV substudy. Circulation 2003;108:275-81.
5. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, *et al.* 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: Executive summary: A report of the American college of cardiology foundation/American heart association task force on practice guidelines. Circulation 2010;122:2748-64.
6. Araujo JP, Lourenc P, Zevedo A, Friores F, Rocha-Goncalves F, Ferreira A, *et al*. Prognostic value of high-sensitivity C-reactive protein in heart failure: A systematic review. J Cardiac Fail 2009;15:256-66.
7. Alyan O, Metin F, Kacmaz F, Ozdemir O, Maden O, Topaloglu S, *et al*. High levels of high sensitivity C-reactive protein predict the progression of chronic rheumatic mitral stenosis. J Thromb Thrombolysis 2009;28:63-9.
8. Sharma A, Chomayil Y, Karim FA, Parambil VP. Incidence and risk factors of acute coronary syndrome in younger age groups. Int J Emerg Med 2015;8 Suppl 1:P4.
9. Singh SS, Paul SK, Pal R, Thatkar PV. Acute coronary syndrome-related mortality audit in a teaching hospital at Port Blair. India J Fam Med Prim Care 2017;6:502-8.
10. Ohira T, Iso H. Cardiovascular disease epidemiology in Asia: An overview. Circ J 2013;77:1646-52.
11. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, *et al.* Treatment and outcomes of acute coronary syndromes in India (CREATE): A prospective analysis of registry data. Lancet 2008;371:1435-42.
12. Hajar R. Diabetes as coronary artery disease risk equivalent: A Historical perspective. Heart Views 2017;18:34-7.
13. Cervellin G, Rastelli G. The clinics of acute coronary syndrome. Ann Transl Med 2016;4:191.
14. Karki P, Agrawaal KK, Lamsal M, Shrestha NR. Predicting outcomes in acute coronary syndrome using biochemical markers. Indian Heart J 2015;67:529-53.
15. Stone PH, Thompson B, Anderson HV, Kronenberg MW, Gibson RS, Rogers WJ, *et al.* Influence of race, sex, and age on management of unstable angina and non-Q-wave myocardial infarction: The TIMI III registry. JAMA 1996;275:1104-12.
16. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation 2003;107:363-9.
17. Calabró P, Willerson JT, Yeh ET. Inflammatory cytokines stimulated C-reactive protein production by human coronary artery smooth muscle cells. Circulation 2003;108:1930-2.
18. Adukauskienė D, Čiginskienė A, Adukauskaitė A, Pentiokinienė D, Šlapikas R, Čeponienė I, *et al.* Clinical relevance of high sensitivity C-reactive protein in cardiology. Medicina (Kaunas) 2016;52:1-0.
19. Wilson PW, Pencina M, Jacques P, Selhub J, D'Agostino R Sr, O'Donnell CJ, *et al.* C-reactive protein and reclassification of cardiovascular risk in the Framingham heart study. Circ Cardiovasc Qual Outcomes 2008;1:92-7.

How to cite this article: Mathur H, Jatav JK. Level of High-Sensitivity C-Reactive Protein Assay to Evaluate Risk in Follow-Up Patients with Acute Coronary Syndrome. Int J Sci Stud 2018;6(3):36-43.

Source of Support: Nil, **Conflict of Interest:** None declared.