

Original Research Article

A STUDY OF hs-CRP AND MEAN PLATELET VOLUME IN ACUTE MYOCARDIAL INFARCTION

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Received : 01/08/2024
Received in revised form : 08/08/2024
Accepted : 13/08/2024

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DOI: 10.5530/ijmedph.2024.2.183

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

Int J Med Pub Health
2024; 14 (2); 946-953

ABSTRACT

Background: To study the association of high sensitivity c-reactive protein and mean platelet volume with severity of coronary atherosclerosis in cases of acute myocardial infarction.

Materials and Methods: A Prospective, single center, observational study was carried out from September 2016 to September 2018 at Kasturba medical hospital and a total of 168 patients who presented with ACS were included after complying with the inclusion and exclusion criteria following approval by the Institutional Ethics Committee. All patients presenting with first episode of ACS were included.

Results: In the present study, There is a significant association between the hs-CRP and angiographic severity of coronary atherosclerosis as assessed by Gensini score. There is no significant association between the mean platelet volume and angiographic severity of coronary atherosclerosis as assessed by Gensini score.

Conclusion: Hence hs-CRP and mean platelet volume can be termed as a simple but a novel biochemical marker which helps us to assess the spectrum of the patient presenting with acute coronary syndrome and may help in deciding the need for adjunctive therapy to improve the outcome.

Keywords: hs-CRP, Gensini score, Coronary Artery, Angiographic, Platelet.

INTRODUCTION

Coronary Artery Disease (CAD) is a well-recognized cause of mortality worldwide,^[1] and by the year 2020, will be first in the main causes of disability.^[2] While there is decline in death rate in west in the last three decades, in India it shows a increasing trend. In the past three decades, there is increase in coronary artery disease prevalence which was increased to 7.5% from 1.1%, where as in rural population it was increased to 3.7% from 2.1%.^[3] Coronary artery disease still remains the prime cause of death in spite of improvement in treatment in most of the developed and developing countries.^[4] Even before myocardial infarct individuals reach the hospital there is mortality of 50%.^[5]

Traditional risk factors for coronary disease such as hypertension, dyslipidemia, diabetes, insulin resistance are well known, however in recent times more importance is given to novel inflammatory markers.^[2,3] Recent studies show that there is inflammatory role in coronary artery disease, hence

the risk of cardiovascular events can be determined by measuring inflammatory markers in patients with coronary artery disease.^[6] The hs-CRP (C-reactive protein) is one of such inflammatory marker that is elevated in individuals with myocardial infarction and is positively associated with atherosclerosis severity.^[7] CRP is the most potent prognosticator of future risk in patients of coronary artery disease. CRP's predictive power resides between 0.1-0.5mg/dl – which is present in most of the normal subjects, but hs-CRP values can be measured as low as 0.3 mg/L. Hence, even low grade of inflammation can be detected by hs-CRP.

Acute coronary syndrome results from plaque rupture, followed by a platelet adhesion, activation and aggregation, finally resulting in formation of thrombus. Platelets have different sizes and densities. Large platelets are usually more dense and have more faster aggregation rate, have more granules and can secrete more thromboxane A₂, they have more receptors of glycoprotein which will again aid in aggregation of platelets resulting in thrombus

formation.^[8] Larger platelets increases thrombosis, and chances of myocardial infarction compared to individuals with smaller platelet. Studies done previously showed that large platelets have relation with myocardial injury and have more mortality at follow up in individuals of acute coronary syndrome.^[9]

Aim and Objectives

Aim

To study the association of high sensitivity c-reactive protein and mean platelet volume with severity of coronary atherosclerosis in cases of acute myocardial infarction.

Objectives

1. To study the association of hs-CRP and severity of coronary atherosclerosis as assessed by gensini score in patients with diagnosis of acute myocardial infarction.
2. To study the association of mean platelet volume and severity of coronary atherosclerosis as assessed by gensini score in patients with diagnosis of acute myocardial infarction.
3. To predict in hospital complications and mortality in patients with acute myocardial infarction with respect to serum hs-CRP level.
4. To predict in hospital complications and mortality in patients with acute myocardial infarction with respect to mean platelet volume.
5. To predict outcome in relation to morbidity and mortality at the end of 3 months with respect to baseline hs-CRP and mean platelet volume.

MATERIAL AND METHODS

A Prospective, single center, observational study was carried out from September 2016 to September 2018 at Kasturba medical hospital and a total of 168 patients who presented with ACS were included after complying with the inclusion and exclusion criteria following approval by the Institutional Ethics Committee. All patients presenting with first episode of ACS were included and the following assessment were done:

Inclusion Criteria

All patients presented to casualty or outpatient department with acute myocardial infarction (as per ESC and ACC criteria) will be included in study.

Exclusion Criteria

Patients with any of following in last 3 weeks

1. Infection
2. Inflammatory condition
3. Tissue necrosis
4. Malignancy
5. Liver failure
6. Trauma
7. Pregnancy
8. Drugs- steroids / immunosuppressants, oral contraceptives, hormone replacement therapy, antiplatelet, statins.
9. Iron deficiency anemia, megaloblastic anemia

10. HIV illness
11. Other cardiac problems- congenital heart disease,
12. Known cases of bleeding or clotting disorders
13. Known cases of any platelet disorders

Statistical Analysis

“An expert statistical advice was taken for Statistical analyses and analyses was done using SPSS version 20.0. Mean±standard deviation is used to represent continuous variables for normal distributed data, median with interquartile range for skewed data, and categorical variables as percentages. Kruskal Wallis test and Mann-Whitney test was used to compare skewed data. The association between two continuous data was determined using spearman’s correlation test. To determine the association between two categorical data, chi-square was used. A p-value of < 0.05 (5%) was taken as statistically significant”.

RESULTS

Distribution of patients based on diagnosis: A total of 168 patients were included in the study, 130 had STEMI, 38 had NSTEMI [Figure.12].

Age distribution: The most common age group of the patients who presented with first episode of ACS was between 60-79 years [Figure.13].

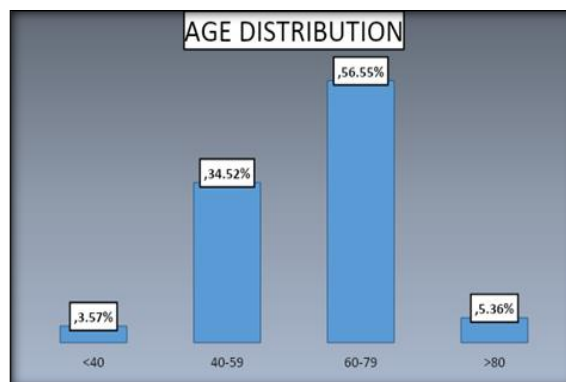


Figure 1: Age distribution

1. **Sex distribution:** Out of the 168 patients, 119[70.8%] were males and 49[29.1%] were females [Figure.14].
2. **CAD risk factor profile:** CAD risk factor analysis showed 151 patients were aged equal to or greater than 45yrs and 55yrs in males and females respectively. Hypertension was detected in 85 patients, diabetes in 57 patients, history of smoking was present in 41 patients, history of alcohol consumption was present in 32 patients, family history of premature CAD [male first degree relative <55years, female first degree relative <65years] was present in 22 patients [Figure.15].

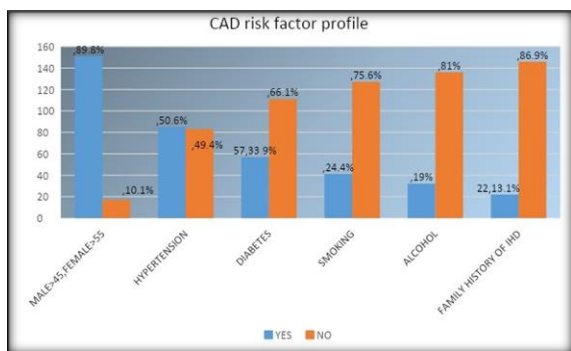


Figure 2: CAD risk factor profile

Correlation between hs-CRP and angiographic Gensini score

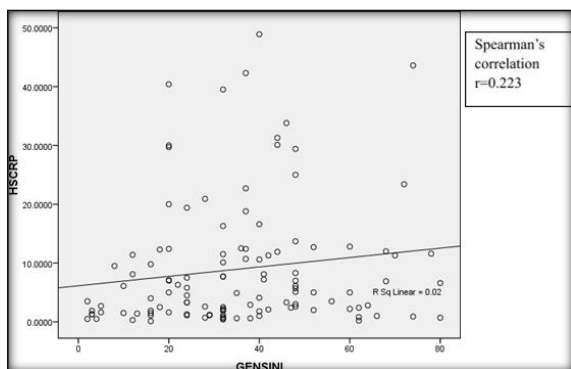
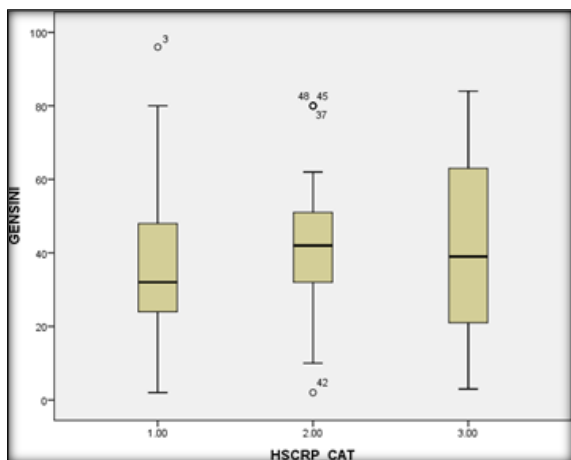


Figure 3: scatter plot between hs-CRP and Gensini score

Spearman's correlation coefficient between hs-CRP and angiographic Gensini score was $r=0.223$. Median Gensini scores were calculated, as data is skewed it was interpreted as median and interquartile range. Patients who were in low hs-CRP risk group had a median angiographic Gensini score of 32, whereas moderate risk group is 39, and in high risk group it is 32 [Table.1]. Kruskal-Wallis analysis showed no significance difference in median Gensini scores between low, moderate and high hs-CRP groups ($p=0.397$).



Correlation between mean platelet volume and angiographic Gensini score

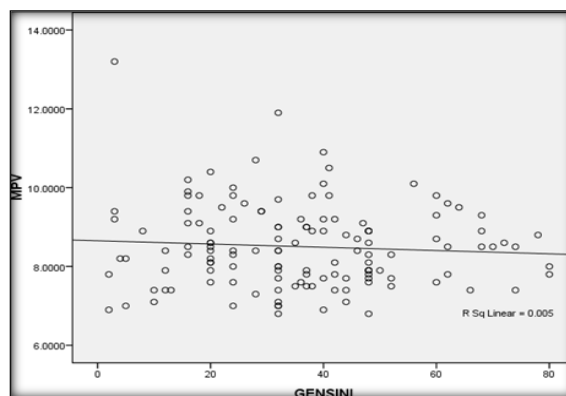


Figure 4: Scatter plot between mean platelet volume and Gensini score

Spearman's correlation coefficient between MPV and angiographic Gensini score was $r=-0.048$. Since the data was skewed it was interpreted as median and interquartile range. Patients who were in low MPV risk group had a median angiographic Gensini score of 36.5, and high risk group 32 [Table.2]. Mann-Whitney U test showed no significance difference in median Gensini scores between lower and higher mean platelet volume risk groups ($p=0.31$).

In hospital complications

hs-CRP in patients with and without complications: Table 3: hs-CRP in patients with and without complications.

Out of the 107[63.6%] patients who had hs-CRP $>3\text{mg/L}$, 45[26.7%] patients had complications. Of the 61 [36.4%] of patients with hs-CRP $<3\text{mg/L}$, 21[12.6%] had complications [Table.3]. Statistical analysis by chi square test showed a p value of 0.33, which is not statistically significant.

Out of the 122[72.6%] patients who had MPV $<9.0\text{fl}$, 24[14.3%] patients had complications. Of the 46 [27.4%] of patients with MPV $\geq 9.0\text{fl}$, 42[25%] had complications [Table.4].

Statistical analysis by chi square test showed a p value of 0.001 which is statistically significant.

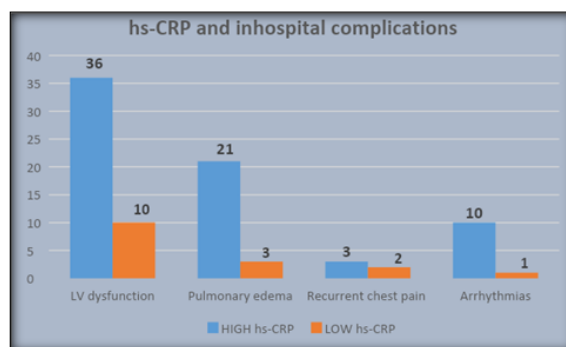


Figure 5: hs-CRP and in hospital complications

Left ventricular dysfunction is seen in 46[27.4%] patients, of which 36[21.4%] were in the high hs-CRP group, 10[5.9%] were in the moderate and low hs-CRP group [Table.5]. Statistical analysis of association by Chi-square test showed a p value of

0.01 which is significant. Left ventricular dysfunction is seen in 46[27.4%] patients, of which 17[10.1%] were in low MPV group and 29[17.2%] were in high MPV group [Table.6]. Statistical analysis of association by Chi-square test showed a p value of 0.001 which is significant.

hs-CRP and pulmonary edema

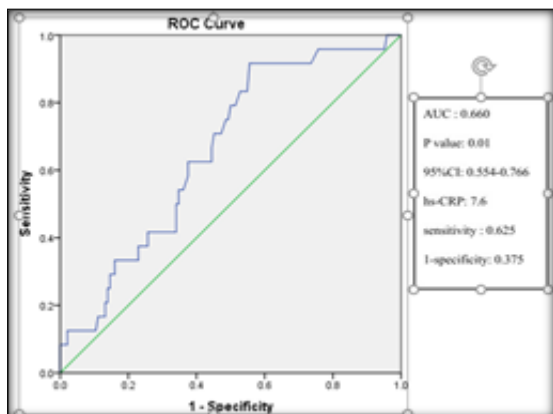


Figure 7: ROC curve between hs-CRP and arrhythmias

Using ROC curve, a cut off was obtained above which levels of hs-CRP were considered to be associated with pulmonary edema [Figure.23]. This value in our study was 7.6mg/dl.

Area under ROC curve was 0.615 (p = 0.203, 95%CI: 0.457 - 0.773) [Figure.24].

Mean platelet volume and left ventricular dysfunction.

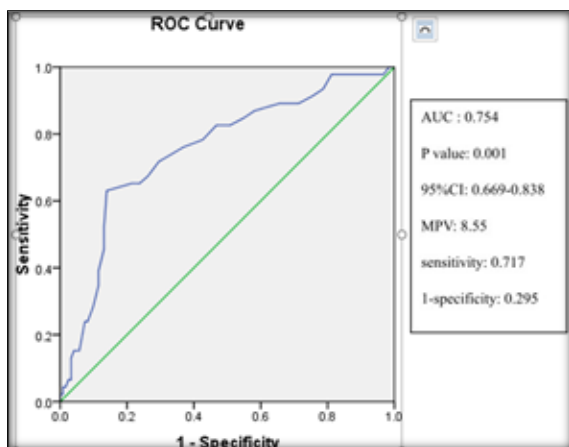


Figure 8: ROC curve between mean platelet volume and left ventricular dysfunction

Using ROC curve, a cut off was obtained above which levels of MPV were considered to be associated with left ventricular dysfunction [Figure.25]. This value in our study was 8.55fl.

Major Adverse Cardiac Events (MACE) at 3 months follow up

Statistical analysis by chi-square test showed a p value of 0.001 which is statistically significant [Table.7].

Statistical analysis by chi-square test showed a p value of 0.001 which is statistically significant [Table.8].

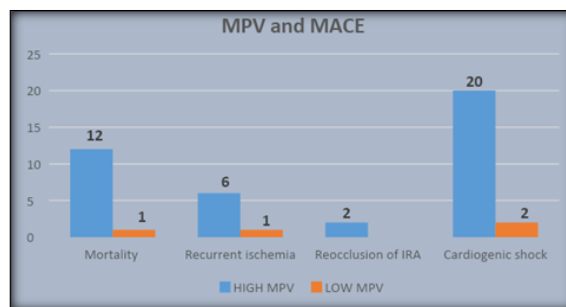


Figure 9: Relation between MPV level and MACE

There was an observed mortality in 12[7.1%], recurrent ischemia in 6[3.6%], reocclusion of infarct related artery in 2[1.1%] and cardiogenic shock in 20[11.9%] patients in high MPV group on follow up for 3months; observed mortality of 1[0.5%], recurrent ischemia in 1[0.5%], with no reocclusion of infarct related artery and cardiogenic shock in 2[1.1%] patients in MPV group[Table.10]. Each component of the primary end point was more prevalent in high MPV group.

hs-CRP and mortality

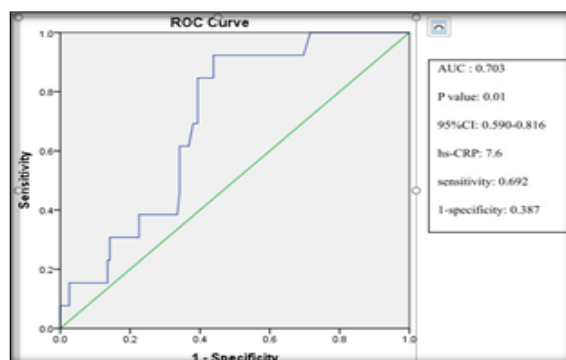


Figure 10: ROC curve between hs-CRP and mortality

Using ROC curve, a cut off was obtained above which levels of hs-CRP were considered to be associated with mortality [Figure.30]. This value in our study was 7.6mg/dl.

hs-CRP and recurrent ischemia

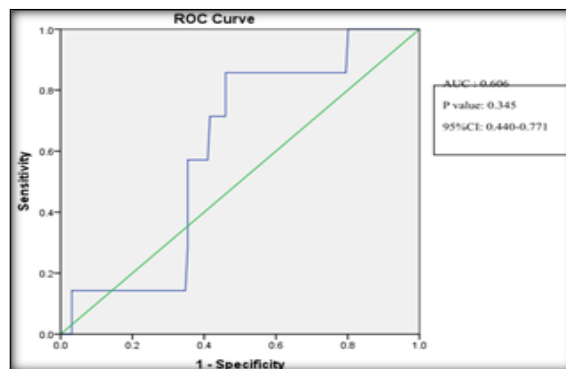


Figure 11: ROC curve between hs-CRP and recurrent ischemia

Area under ROC curve was 0.606 (p = 0.345, 95% CI: 0.440 - 0.771) [Figure.31].

hs-CRP and cardiogenic shock

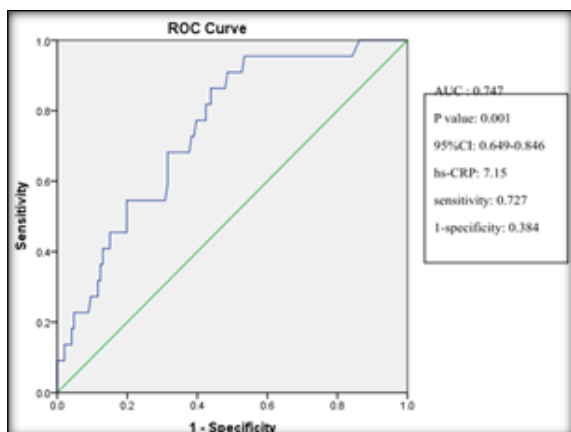


Figure 12: ROC curve between hs-CRP and cardiogenic shock

Using ROC curve, a cut off was obtained above which levels of hs-CRP were considered to be associated with cardiogenic shock [Figure.32]. This value in our study was 7.15mg/dl.

Mean platelet volume and mortality

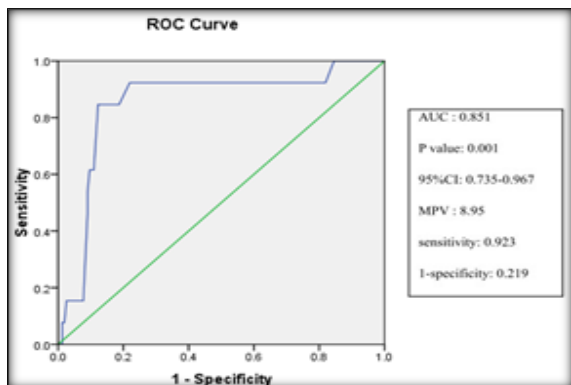


Figure 13: ROC curve between mean platelet volume and mortality

Using ROC curve, a cut off was obtained above which levels of MPV were considered to be associated with mortality [Figure.33]. This value in our study was 8.95fl.

Table 1: hs-CRP and angiographic Gensini score

hs-CRP		Gensini score
		Median (IQR)
Low	<1mg/L	32 (12,44)
Moderate 1-3mg/L		39 (32,48)
High ≥3mg/L		32 (20,48)

Table 2: Mean platelet volume and angiographic Gensini score

MPV		Gensini score	
		Median(IQR)	
low	<9.0fl	36.5 (20,48)	
high	≥9.0fl	32	(20,48)

Mean platelet volume and recurrent ischemia

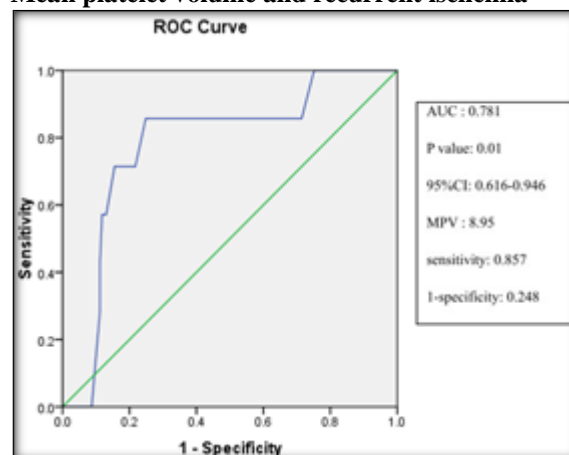


Figure 14: ROC curve between mean platelet volume and recurrent ischemia

Using ROC curve, a cut off was obtained above which levels of MPV were considered to be associated with recurrent ischemia [Figure.34]. This value in our study was 8.95fl.

Mean platelet volume and cardiogenic shock

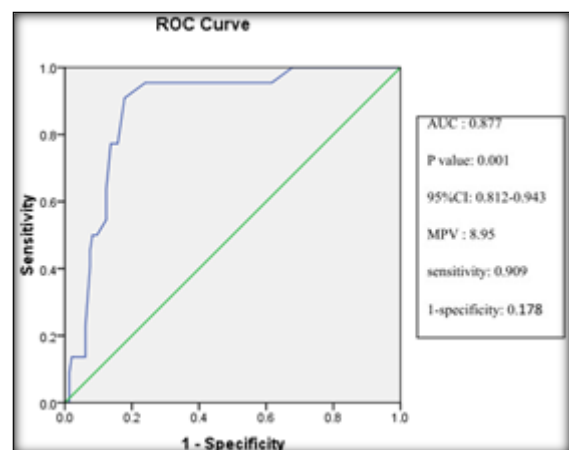


Figure 15: ROC curve between mean platelet volume and cardiogenic shock

Using ROC curve, a cut off was obtained above which levels of MPV were considered to be associated with cardiogenic shock [Figure.35]. This value in our study was 8.95fl

Table 3: hs-CRP in patients with and without complications

hs-CRP	ACS with complications	ACS without complications
<3 (n=61)	21	40
≥3 (n=107)	45	62

Table 4: MPV in patients with and without complications

MPV	ACS with complications	ACS without complications
<9.0 (n=122)	24	98
≥9.0 (n=46)	42	4
		P value=0.001

Table 5: Relation between hs-CRP level and in hospital complications

Complication	High hs-CRP group (n=107)	Moderate and low hs-CRP group(n=61)	P value
LV dysfunction	36	10	0.01
Pulmonary edema	21	3	0.001
Recurrent chest pain	3	2	0.86
Arrhythmias	10	1	0.05

Table 6: Relation between MPV level and in hospital complications

Complication	High MPV group (n=46)	Low MPV group (n=122)	P value
LV dysfunction	29	17	0.001
Pulmonary edema	17	7	0.001
Recurrent chest pain	3	2	0.09
Arrhythmias	8	3	0.001

Table 7: hs-CRP in patients with and without MACE

hs-CRP	ACS with MACE	ACS without MACE
<3 (n=61)	4	57
≥3 (n=107)	29	78
		P value: 0.001

Table 8: MPV in patients with and without MACE

MPV	ACS with MACE	ACS without MACE
<9.0 (n=122)	9	113
≥9.0 (n=46)	24	22
		P value: 0.001

Table 9: Relation between MPV level and MACE

Complication	High MPV group (n=46)	Low MPV group (n=122)	P value
Mortality	12	1	0.001
Recurrent ischemia	6	1	0.001
Reocclusion of IRA	2	0	0.12
Cardiogenic shock	20	2	0.001

DISCUSSION

In our study among 168 patients, 130 had STEMI, and 38 had NSTEMI with the mean age of the patients being 61.52 years. It is a known fact that chance of ACS in Indian sub-continent is a decade prior than in western population. In studies done by Suleiman et al,^[10] and Foussas et al,^[11] ACS was seen in seventh decade.

Among 168 patients, 119 were males and 49 were females which indicates a significant prevalence of acute coronary syndrome in males. These results are consistent with several population studies which have identified male gender as a risk factor for higher rates of CHD.^[12] Protection against CAD in

premenopausal women derives from their relatively higher HDL levels.

RISK FACTORS

Hypertension: it is a known risk factor for adverse cardiovascular outcomes including death from coronary artery disease. In our study 50.6% of the patients had hypertension. In the study done by Foussas et al,^[11] hypertension was seen in 51% patients, and in the study done by Suleiman et al,^[10] hypertension was seen in 53% patients.

Both systolic and diastolic levels are important in increasing risk. Recent studies also show a reduction in CHD risk by antihypertensive therapy, particularly interruption of renin-angiotensin system,^[13]

Diabetes: Insulin resistance, hyperinsulinemia, and elevated blood glucose are related to atherosclerotic cardiovascular disease. In our study 33.93% patients had diabetes as the risk factor which was consistent with various other studies. In Foussas et al,^[11] study diabetes was seen in 31% of patients and in Suleiman et al,^[10] study diabetes was present in 30% of patients. The 2002 National Cholesterol Education Programme report labelled diabetes as a CHD risk correspondent, thereby uplifting it to the highest risk category.

Smoking: In our study 24.4% of patients were smokers, in Foussas et al,^[145] study smoking was observed in 57% of patients, in Suleiman et al,^[10] study smoking was observed in 40% of patients. Cigarette smoking is an reversible risk factor for coronary artery disease. There is 6-fold increase in acute coronary event in women and 3 fold increase in men who smoke at least 20 cigars per day in comparison with individuals who had never smoked.^[14,15]

hs-CRP and Gensini score: In our study spearman's correlation coefficient between hs-CRP and angiographic gensini score was $r= 0.223$, indicating moderate correlation. There is statistical correlation exists between angiographic severity gensini score and hs-CRP. Higher hs-CRP were associated with higher gensini score in ACS patients. However Kruskal -Wallis analysis showed no significance difference in median gensini scores between low, moderate and high hs-CRP groups ($p=0.397$).

In a study done by Tenzin nyandak, Arun gogna, Sandeep bansal,^[16] showed that higher CRP levels were associated with higher stenosis score in CAD patients. Stenosis score used was a modified gensini score. Spearman's correlation coefficient between hs-CRP and angiographic stenosis score was $r=0.316$. However study done by JIA En-Zhi et al,^[17] in which 506 patients were included and their study specified that the severity of coronary atherosclerosis was significantly associated with the concentration of plasma hs-CRP in Kruskal -Wallis analysis ($p=0.017$).

In our study there was significant correlation observed between the extent of coronary artery disease and hs-CRP levels. This shows that hs-CRP level also has correlation with the disease burden apart from being a well-known indicator of the presence of ACS. It therefore suggests that inflammation is not only an important trigger mechanism of acute coronary syndrome related to plaque rupture, but also a promoter of atherosclerosis, as proposed that CRP might play an atherogenic role through interaction with low density lipoproteins.^[19]

MPV and Gensini score: In our study, spearman's correlation coefficient between mean platelet volume and angiographic gensini score was $r= -0.048$. There is no statistically significant correlation between angiographic severity gensini score and mean platelet volume levels. Mann Whitney U test showed no significance difference in median gensini scores

between lower and higher mean platelet volume risk groups ($p=0.31$).

However study done by Sani Namik Murat et al,^[18] in which 520 patients were included, their study showed high mean platelet volume group has high syntax and gensini scores and has more critical lesions.

In hospital Complications

a. Left ventricular dysfunction was seen in 46[27.4%] patients of which 36[21.4%] were in the high hs-CRP group, 10[5.9%] were in the moderate hs-CRP group and low hs-CRP group. Statistical analysis of association by chi-square showed a p value of 0.01, which is statistically significant. 17[10.1%] were in low MPV group and 29[17.2%] were in high MPV group. Statistical analysis of association by Chi-square test showed a p value of 0.001 which is significant.

b. Other complications

- A total of 24 patients had pulmonary edema, of which 3 were in the moderate hs-CRP level group, 21 were in the high hs-CRP level group, 7 were in low MPV group and 17 were in high MPV group.
- 5 patients had recurrent chest pain, of which 2 were in the moderate hs-CRP group, 3 were in the high hs-CRP group, 2 were in low MPV group and 3 were in high MPV group.
- 11 patients had arrhythmias, of which 10 were in the high hs-CRP group, 1 was in moderate hs-CRP group, 8 were in low MPV group and 3 were in high MPV group.

In current study out of the 107[63.6%] patients who had hs-CRP $>3\text{mg/L}$, 45[26.7%] patients had complications. Of the 61 [36.4%] of patients with hs-CRP $<3\text{mg/L}$, 21[12.6%] had complications.

Major Adverse Cardiac Events (MACE) at 3 months follow up: The 3 months MACE occurred in 29[17.2%] high hs-CRP group patients, 4 [2.4%] in moderate hs-CRP group patients, 24[14.3%] in high MPV group and 9[5.4%] in low MPV group. Statistical analysis by chi-square test showed a p value of 0.001 which is statistically significant.

In a study done by Yip HK et al (20), the 30 day MACE occurred in 23.3% of high hs-CRP group patients and in 4.1% of low hs-CRP group patients. There was mortality in 15%, recurrent ischemia in 2.7%, reocclusion of infarct related artery in 5.5%, cardiogenic shock in 11% of patients in the high hs-CRP group; mortality in 4.1%, cardiogenic shock in 6.4%, no reocclusion of infarct related artery and recurrent ischemia in patients with low hs-CRP levels.

In our study, there was an observed mortality in 12[7.1%], recurrent ischemia in 6[3.6%], reocclusion of infarct related artery in 2[1.1%] and cardiogenic shock in 20[11.9%] patients in high MPV group on follow up for 3months; observed mortality of 1[0.5%], recurrent ischemia in 1[0.5%], with no reocclusion of infarct related artery and cardiogenic shock in 2[1.1%] patients in MPV group. Each

component of the primary end point was more prevailing in high MPV group.

CONCLUSION

1. There is a significant association between the hs-CRP and angiographic severity of coronary atherosclerosis as assessed by Gensini score.
2. There is no significant association between the mean platelet volume and angiographic severity of coronary atherosclerosis as assessed by Gensini score.
3. In patients presenting with the first episode of acute coronary syndrome elevated hs-CRP level and mean platelet volume both are associated with higher rate of in hospital complications and other complications including mortality at 3 months follow up.

Hence hs-CRP and mean platelet volume can be termed as a simple but a novel biochemical marker which helps us to assess the spectrum of the patient presenting with acute coronary syndrome and may help in deciding the need for adjunctive therapy to improve the outcome.

Limitations

1. The coronary angiographic assessment is based upon luminal assessment and lacks plaque visualization.
2. Angiographic techniques do not demonstrate vessels of which the luminal diameter is 100mm or less.

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