Original Research Article

Mean platelet volume as a predictor of clinical outcomes in patients of acute myocardial infarction

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ABSTRACT

Background: High levels of mean platelet volume (MPV), as an indicator of larger, more reactive platelets resulting from an increased platelet turnover, may represent a risk factor for overall vascular mortality and other cardiovascular events, including myocardial infarction (MI). The present study was undertaken to see the predictive value of MPV in accessing the clinical outcomes in acute myocardial infarction, (AMI).
Methods: Total consecutive 114 cases of AMI admitted to intensive care unit were enrolled in the study and were compared with the equal number of age and gender-matched controls. The clinical evaluation of cases was done at admission and on day 7 in terms of a) Cardiogenic shock, b) Arrhythmia and c) Effect of thrombolysis. Patients were classified according to tertile of baseline MPV.
Results: The mean age of cases was 55.56±12.19 years. Males (66.67%) were outnumbering females (33.33%) in cases and controls showing male to female ratio of 2:1. Mean MPV was 10.2±1.27fl in cases and 7.26±0.79fl in controls which was statistically significant. Correlation of MPV with cardiogenic shock, arrhythmia and mortality was significant. Correlation of MPV with risk factor shows that diabetes was the only risk factor significant in AMI. Multiple logistic regression of risk factors with mortality in AMI shows that high MPV and obesity was found to be independently associated with mortality in AMI.
Conclusions: Mean platelet volume is simple, easily available and cheap method. Serial estimation of MPV is a predictor of adverse clinical outcome in AMI so treating doctor can be more vigilant.

Keywords: Arrhythmia, Mortality, Myocardial infarction, Platelet, Risk factor

INTRODUCTION

Platelets are heterogeneous blood elements with diverse sizes and densities. It has been shown that platelet size when measured as mean platelet volume (MPV) is a marker of platelet function and is positively associated with indicators of platelet activity. However, the increase of platelet volume may contribute to increased prothrombotic tendency of atherosclerotic plaque in acute coronary syndrome and increased risk of intracoronary thrombus formation in AMI cases. In addition, it has been demonstrated that the platelet count is inversely associated with MPV, suggesting that platelet consumption during acute coronary events can lead to the production of bigger one by megakaryocyte activity and consequent elevated MPV value.[1] Previous studies have shown MPV as an independent variable for prognosis in patients with cardiovascular diseases such as myocardial infarction (MI), heart failure or stroke, and also in patients undergoing coronary bypass surgery or coronary angioplasty.[2-8]

The effective screening of patients at the emergency room for acute myocardial infarction remains a challenge. The association of increased MPV with a critical disease like AMI may possibly emerge this measurement as a simple and accessible test to estimate platelet activity. This will further help to stratify cardiovascular risk among patients with acute coronary syndromes.[9] Currently, cardiac coronary related diseases continue to be the leading cause of morbidity and mortality in India. There are limited studies in regards to Indian population of mean platelet volume in association with acute myocardial infarction.

So, present study was undertaken to see the association of mean platelet volume at admission on clinical outcome in patients with AMI in terms of a) cardiogenic shock b) successful thrombolysis and c) arrhythmia. Also, see in-hospital mortality in acute myocardial infarction with relation to mean platelet volume within 7 days. Last but not least to see correlation of mean platelet volume with established (Traditional) risk factors for acute myocardial infarction.

METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from all the participants, this cross sectional observational study was conducted in total consecutive 114 cases of AMI admitted to the coronary care unit of tertiary care centre during the period of November 2015 to December 2017. The diagnosis of AMI was as per criteria laid down in consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction.[10] The cases with severe hepatic or renal impairment, patients taking oral anticoagulation medicine, patients with myeloproliferative disorders, malignancy, thyroid disorders, sepsis, inflammatory diseases (like rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease etc.) pregnant women and recent history of blood transfusion were excluded from the study.

All these selected cases were compared with an equal number of age and gender-matched controls. Subjects attending outpatient department of the hospital for minor ailments or routine medical check-up, subjects from the community (population-based) accompanying patients (other than ischemic heart disease) or amongst office working staff from the various department of this institution without having any evidence of acute or chronic heart disease were included as controls. Subjects diagnosed to have myocardial infarction at any time in the past and those failures to obtain consent were excluded from the study. The other exclusion criteria were same for controls as that for cases.

Cases and controls were investigated for conventional risk factors (BMI, blood sugar, lipid profile). ECG, serum CK-MB, height and weight was recorded. History of smoking and alcohol consumption were noted in detail. Estimation of platelet count and MPV was performed in all subjects. Blood Sample was collected within 6hours on arrival at ICU into tubes containing EDTA who were subsequently diagnosed having AMI. For measurement of platelet count (PLC), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT), samples were analyzed by automated flow meter (Erma INC PCE210 automated flow meter). Normal MPV ranges 7.0-11.0fl.[11] After the determination of baseline MPV values, the study population was divided into tertiles (first tertile: <9.7fl; second tertile: 9.7 to 10.2fl; third tertile: ≥10.3fl). A high MPV was defined as a value in the third tertile (≥10.3fl), and a low MPV was defined as a value in the lower two tertiles (<10.3fl).[12]

Complications were studied. The clinical evaluation of cases was done at admission and on day 7 in terms of 1) Cardiogenic shock, 2) Arrhythmia, 3) Effect of thrombolysis: i) Reperfusion arrhythmia, ii) Decrease in ST elevation. The primary outcome for this study was an estimation of mean platelet volume and adverse clinical outcomes in AMI cases.

Statistical analysis

It included the usual descriptive and univariate analysis. Discrete (categorical) variables were compared by Pearson CHI- Square test and for a continuous variable, student t-test was used. Unadjusted odds ratio with 95% confidence intervals (CI) was calculated and P values <0.05 was considered statistically significant. The Pearson correlation test was used to assess the correlation between the continuous variables.

In order to determine the independent association of MPV with AMI in multivariate analysis, we performed multiple logistic regressions after adjusting for conventional risk factors and adjusted OR and 95% CI was computed using STATA statistical software version 10.1 2011 on a personal computer.

RESULTS

Total 114 cases of acute myocardial infarction and equal number of age and gender match healthy controls were enrolled in study. The age of participants was ranged from 26 to 76 years. The maximum number of cases and controls were in age group of 61 to 70 years i.e. 39 (34.21%) and 42 (36.84%) respectively. The mean age at the time of presentation was 55.56±12.19 years in cases and 55.53±12.14 years in controls. Males (66.67%) were outnumbering females (33.33%) in this study showing male to female ratio of 2:1.

On admission, the mean MPV was 10.2±1.27fl in cases and 7.26±0.79 in controls which was statistically significant. Out of 114 cases, 29 (25.44%) cases had high MPV i.e. >11fl while all controls had normal MPV, this difference was statistically highly significant, (p=0.0001).

The other platelet indices i.e. platelet distribution width (PDW) and plateletcrit (PCT) were also increased in cases (13.51±1.88) and (0.24±0.06) respectively compared with controls (10.31±1.04) and (0.12±0.04). Maximum number of cases 53 (46.50%) were in third tertile having MPV≥103 (Table 1).

Table 1: Distribution of MPV in tertile among cases and controls.

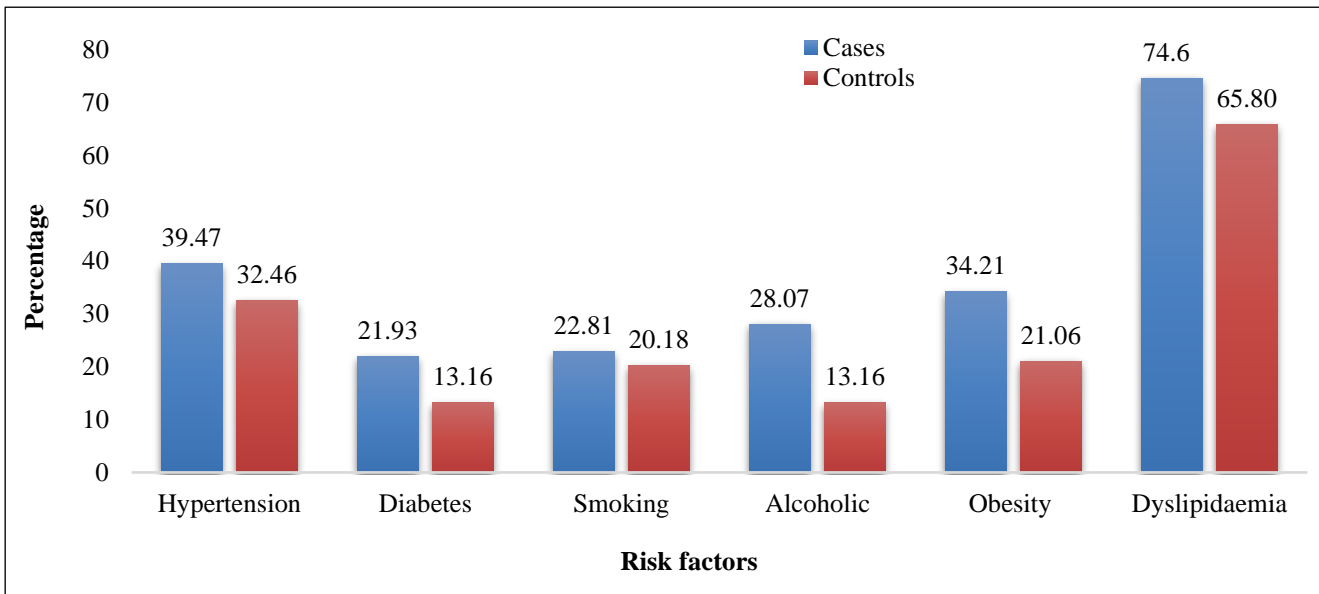| MPV (fl)	Cases (n=114)		Controls (n=114)	
	No. (%)	Mean±SD	No. (%)	Mean±SD
First Tertile (≤9.7)	38 (33.33)	8.99±0.67	110 (96.50)	7.22±0.77
Second Tertile (9.8-10.2)	23 (20.17)	10.05±0.19	4 (3.50)	9.93±0.13
Third Tertile (≥10.3)	53 (46.50)	11.44±0.86	0 (0.00)	0

Figure 1: Distribution of risk factors among study subjects.

The incidence of hypertension, diabetes, smoking, alcohol, obesity and dyslipidemia were more in cases than controls amongst which diabetes, alcohol, obesity was statistically significant, (Figure 1).

Amongst the type of infarct on ECG anterior wall infarct 47 cases (41.23%) was most common type involved. Next common was inferior wall MI 36 (31.57%) and extensive anterior wall MI was seen in 20 (17.54%) cases. Maximum number of cases 76 (66.67%) were in Killip's class 1 while 16 (14.03%) cases were in Killip's class 2, only 4 (3.51%) cases were in Killips class 3 and 18 (15.79%) cases were in Killip's class 4.

In evaluation of cases for complications, arrythmias were the most common complication observed in 23 (20.18) cases and the next common was cardiogenic shock 18 (15.79 %), (Table 2). 69 cases (60.52%) did not show any complications.

Table 2: Distribution of cases as per complications.

Complication	Cases in No. (%)
Cardiogenic shock	18 (15.79)
Arrhythmia	23 (20.18)
Reinfarction	0
Cerebrovascular episodes	0
Major/Minor bleeding	4 (3.51)
No complication	69 (60.52)

Around 61 (78.21%) cases were successfully thrombolysed (showing >50% decrease in ST elevation with reperfusion arrhythmia) after myocardial infarction. There was mortality in 26 (22.81%) cases of acute myocardial infarction, 10 died of arrhythmia and 16 died due to cardiogenic shock. 8 cases died within 24hours of presentation while 18 cases died within 24hours to 7 days of hospital stay. 15 mortalities had high MPV values in cases i.e. MPV ≥11 which was significant compared to 11 mortalities in low MPV values i.e. MPV<11.

Table 3: Correlation of MPV with clinical outcomes.

Parameters	No. of cases	MPV on admission Mean±SD	P-Value
Cardiogenic shock	18	11.51±1.61	0.0001
successful thrombolysis	61	10.46±1.35	0.1105
Arrhythmia	23	10.57±1.27	0.0121
Mortality	26	11.34±1.37	0.0001

When mean MPV was correlated with clinical outcomes, cardiogenic shock showed positive correlation (MPV was more) which was statistically significant. Cases with arrhythmias did not show significant correlation with MPV. Overall mortality was 22.81% in 26 cases. 15 cases out of 26 amongst total deaths had MPV>11 which was statistically significant, (Table 3).

In univariate analysis, correlated MPV with risk factor diabetes was significantly associated with high MPV in cases while hypertension/DM and alcohol intake were significantly associated with high MPV in controls, (Table 4).

Multiple logistic regression of risk factors with mortality in acute myocardial infarction shows that high MPV (p = 0.0001, adjusted odds ratio 7.55, 95% CI 2.71-21.01) and obesity (p = 0.036, adjusted odds ratio 0.15, 95% CI 0.01-0.85) was found to be independently associated with mortality irrespective of risk factors in acute myocardial infarction.

Table 4: Univariate analysis of MPV with risk factors among cases and controls.

Risk Factors	Cases/Controls	Present/Absent	Observation	Mean±SD	P value
Hypertension	Cases	Present	45	10.52±1.26	0.1322
		Absent	69	10.14±1.25	
	Controls	Present	37	7.57±0.89	0.0035
		Absent	77	7.12±0.70	
Diabetes	Cases	Present	25	10.80±1.81	0.0207
		Absent	69	10.14±1.30	
	Controls	Present	15	7.85±0.72	0.0019
		Absent	99	7.18±0.77	
Smoking	Cases	Yes	26	9.87±1.39	0.0591
		No	88	10.40±1.21	
	Controls	Yes	23	7.14±0.92	0.4126
		No	91	7.30±0.76	
Alcohol	Cases	Yes	32	10.18±1.26	0.5914
		No	82	10.32±1.28	
	Controls	Yes	15	7.66±1.01	0.0374
		No	99	7.21±0.74	
Obesity (BMI)	Cases	Present	39	10.50±1.5	0.1837
		Absent	75	10.17±1.21	
	Controls	Present	24	7.53±0.74	0.0698
		Absent	90	7.20±0.79	
Dyslipidaemia	Cases	Present	85	10.37±1.32	0.1840
		Absent	29	10.01±1.06	
	Controls	Present	75	7.22±0.76	0.3625
		Absent	39	7.36±0.86	

DISCUSSION

Mean platelet volume is a simple and accurate marker of the functional status of platelets. Platelets are known to have a major effect on the formation of atherosclerotic plaques and therefore play an essential role in the pathogenesis of atherothrombosis. As described previously, larger platelets are more reactive. Platelet size is determined at the level of the progenitor cell (i.e., the megakaryocyte), and studies have reported that cytokines, such as interleukin-3 or interleukin-6, influence megakaryocyte ploidy and can lead to the production of more reactive, larger platelets.[13] Thus, platelet volume has been proposed as an indirect marker of increased platelet reactivity. MPV levels were associated with overall increased vascular mortality and other cardiovascular events, including MI. Therefore, MPV has been suggested as a simple marker of the functional

status of platelets and may represent a risk factor for vascular adverse events.

From the current study, it was evident that the risk of myocardial infarction (MI) increases progressively in older men, especially after the age of 43 years predominantly in old age (greater than 55 years). The demographic data (Age and sex) of the study were well correlating with the study carried out by Saleh et al.[14] MPV and other platelet indices such as PCT and PDW were significantly higher in patients with AMI in comparison to the control subjects. This finding was in accordance with the observation by other studies.[8,15] Anterior wall MI was the commonest type of AMI, the next common group was inferior wall myocardial infarction followed by extensive anterior wall myocardial infarction, very few cases were observed in lateral wall myocardial infarction, anterior lateral wall myocardial infarction and inferior lateral wall myocardial infarction. Present study was in accordance with incidence of anterior wall myocardial infarction among other types acute myocardial infarction with previous studies.[16,17]

Among the complication in current study 18(15.79%) cases had cardiogenic shock i.e. Killip's class 4 out of which 2 cases recovered but 16 cases died of cardiac arrest. Mean MPV was 11.51±1.61 which was significant (p=0.0001). These observations were similar compared to the study carried out by Supel K et al.[18] We evaluated the prognostic value of MPV in AMI complicated by cardiogenic shock. Such an analysis in patients with the most serious and fatal complication of ACS has not been performed so far. Mean MPV was significantly higher in patients with cardiogenic shock. Cardiogenic shock was responsible for the majority of mortality in AMI. Thus, cases with high MPV in AMI complicated by cardiogenic shock had worst outcome. Arrhythmia was most common complication in 23 (20.18%) of which 13 cases recovered but 10 cases died of cardiac arrest. Mean MPV was 10.57±1.27fl which was significant (p=0.0121). Similar kind of study done by Ocak et al reported ventricular tachycardia in 26.09% and CHB in 21.71%.[19] Cardiogenic shock parameter wasn't considered in above study and sample size was very small i.e. 23 cases only. Out of 114 cases, 78 (68.42%) cases had reperfusion arrhythmia whereas 36 (31.58%) had no reperfusion arrhythmia during thrombolysis. There is limited data available up till now regarding the correlation of MPV with arrhythmias.

Present study highlighted the significant correlation of MPV with arrhythmias. Overall mortality was 22.81% in the present study. The incidence of major adverse mortality event was significantly higher in patients with higher MPV as compared with patients with lower MPV. It indicates that high MPV is a predictor of the mortality in acute myocardial infarction.

The incidence of AMI was significant in alcoholics, obese, deranged triglycerides, total cholesterol, HDL but

after correlating MPV with risk factors diabetes was the only risk factor which showed significant correlation with raised MPV. MPV in relation to smoking was near to the significant value and might be significant in larger sample size studies than our study.

Thus, present study corroborates with other studies observations that MPV is higher in cases of acute myocardial infarction and increase in MPV associated with cardiogenic shock, arrhythmia, and mortality but still, it is not yet clear whether the increase in MPV is the cause or effect of coronary artery occlusion.[20-23]

There are some limitations of the study which includes: 1) Study was carried out in single institute it may not represent the exact global population, 2) The complication developed after 7 days was missing due to limited duration of follow up, 3) Serial estimation of MPV could not be done because of financial constraints, so further complication beyond 7 days could not be assessed.

CONCLUSION

The increased mean platelet volume is present in acute myocardial infarction and it is associated with complications like cardiogenic shock, arrhythmias and higher mortality in acute myocardial infarction. Also, MPV is a very low-cost investigation available easily in most healthcare settings. Causal relationship of increased mean platelet volume and acute myocardial infarction could not be established. The present study suggested that the mean platelet volume is simple, easily available and cheap method. Serial estimation of MPV is a predictor of adverse clinical outcome in AMI so treating doctor can be more vigilant.

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