Original Article

Elevated mean platelet volume is a marker of acute coronary syndrome

Pervin S[1], Ferdousy S[2], Hossain M[3], Joarder AI[4], Sultana T[5]

Abstract

Acute coronary syndrome (ACS) is a set of signs and symptoms due to rupture of a plaque and are a consequence of platelet rich coronary thrombus formation. Platelet parameters especially MPV could be an important and reliable markers in early detection of ACS when other markers are not available. This quasi- experimental study was conducted from September 2011 to August 2012 in the Department of Clinical Pathology, BSMMU, in collaboration with Department of Cardiology, BSMMU and BIRDEM on 79 patients with ACS diagnosed on the basis of clinical history, Electrocardiographic changes and increased cardiac markers especially troponin I with 63 subjects enrolled as control. For determination of platelet parameters, the blood sample was obtained from all patients of ACS before anti-platelet therapy when patient attended in the Cardiac emergency department and on 5th day of ongoing anti-platelet therapy in coronary care unit. The sensitivity, specificity, accuracy, positive and negative predictive value of platelet counts and MPV were 83%, 28.1%, 42.3%, 37.6%, 64% and 90.6%, 49.4%, 64.8%, 51.6%, 89.8% respectively. In our study, we found that MPV had higher sensitivity and specificity in contrast to platelet count. MPV may used as predictor for early detection of ACS and risk stratification when other cardiac biomarkers are negative.

Key words: Mean platelet volume, acute coronary syndrome, platelet count

1. Dr Silpi Pervin, Assistant professor, Department of Pathology, MH Samorita Medical College, Dhaka
2. *Dr Sheuly Ferdoushi, Medical officer, Department of Gastroenterology, BSMMU, Dhaka
3. Dr Mosharaf Hossain, Department of Medicine, ShSMC, Dhaka
4. Dr Ariful Islam Joarder, Consultant, Department of Cardiology, BSMMU, Dhaka
5. Dr Tuhin Sultana, Associate Professor, Department of Clinical Pathology, BSMMU, Dhaka

**For correspondence*

Introduction

Acute coronary syndrome (ACS) is a set of signs and symptoms due to rupture of a plaque and are a consequence of platelet rich coronary thrombus formation.[1] Platelets have a major role in the pathogenesis of acute coronary syndrome (ACS), where plaque rupture is followed by platelet activation and thrombus formation.[2] Platelet activation is the key step of pathogenesis of acute coronary syndrome.[3] Activated platelets are larger in size, which can be measured by mean platelet volume (MPV). Larger platelets are more adhesive and tend to aggregate more as they more dense granules. They are metabolically and enzymatically more active than small platelets and produce more thromboxane A2.[4,5,6] Increased platelet volume will increase the tendency for coronary thrombus formation in ACS patients.[7] The activated platelet is the major biological risk factor for pathogenesis of ACS, soinhibition of this process could play an important role in prevention of ACS.[8] That's why anti-platelet therapy like aspirin and clopidogrel are used to prevent platelet activity.

The diagnostic criteria of ACS are clinical presentation, biochemical markers of acute ischemic injury, and electrocardiographic findings.[9,10] The present cardiac markers are not sufficiently sensitive at an early stage of ACS. That's why an early and reliable marker is needed for accurate diagnosis of ACS when patients will attend in cardiac emergency department. Platelet parameters especially MPV could be an important and reliable markers in early detection of ACS when other markers are not available. This could lower the morbidity and mortality rates.

Methods

This interventional quasi-experimental study was conducted in Department of Clinical Pathology, in collaboration with Department of Cardiology, BSMMU and BIRDEM from September 2011 to August 2012. Total 142 adult (18 years above) patients with clinically suspected acute coronary syndrome who attended in cardiac emergency and admitted in coronary care unit (CCU) in the department of Cardiology, BSMMU, and BIRDEM, Dhaka were enrolled in this study. Among them 79 patients had ECG changes (ST-elevation, ST-depression, T-inversion, appearance of Q-wave) with or without elevated troponin I and treated with anti-platelet drugs. They were considered as cases(group I). The rest 63

patients had normal ECG findings, normal cardiac troponin I and did not receive anti-platelet therapy. They were comsidered as as controls (group II). Clinical history, medical reports, findings and information were documented in a pre-designed data sheet with informed and written consent. Blood was collected aseptically for CBC and MPV with EDTA tube and determined by automated Haematology analyzer (Sysmex XT-4000i) on 1st day when patient admitted in emergency unit and ongoing 5th day in CCU.

Data were processed and analyzed by using computer software SPSS (Statistical package for social sciences version 16) by applying appropriate formula. Data were analysed by mean with standard deviation (SD), t-test, and Chi-square test with 95% confidence interval. Test of validity was calculated by receiver operative characteristic analysis curves.

Data were processed and analyzed by using computer software SPSS (Statistical package for social sciences version 16) by applying appropriate formula. The test statistics used to analyze the data was experimental statistics, mean ± standard deviation (SD), t-test, and Chi-square test with 95% confidence interval. Test of validity done by receiver operative characteristic analysis curves.

Results

Total 142 patients were included in this study. Maximum 33 (41.8%) patients belonged to 51-60 years age group in group I and 22 (34.9%) patients age belonged to 41-50 years age in group II. The mean age was found 55.05±10.73 years in group I and 48.4±10.39 years in group II. (Table -I)

Table I: Age distribution of the study patients (n=142)

Age (in years)	Group I (n=79)		Group II (n=63)		P value
	n	%	n	%	
≤30	0	0.0	5	7.9	
31 - 40	9	11.4	12	19.0	
41 - 50	17	21.5	22	34.9	
51 - 60	33	41.8	16	25.4	
61 - 70	14	17.7	8	12.7	
>70	6	7.6	0	0.0	
Mean ± SD	55.05 ±10.73		48.4 ±10.39		0.001[s]
Range (min-max)	(31-80)		(28-70)		

Group I: Patients having acute coronary syndrome, Group II: Patients without acute coronary syndrome, s= significant, P value reached from unpaired t-test

In present study males were predominant in both groups, 57(72.2%) in group I, and 44 (69.8%) in group II. (Figure-1) In 1st sample, the mean (±SD) platelet count on admission before anti-platelet therapy was 273.1(±50.15) 109/L and 290.78(±74.86) 109/L in group I and group II respectively. Difference between two groups was not statistically significant (P=0.096). In 2nd sample, on 5th day of treatment, the mean (±SD) platelet count was 284.56(±41.93) 109/L in group I. In-group I, the mean platelet count difference in 1st& 2nd samples was not statistically significant (P=0.052).

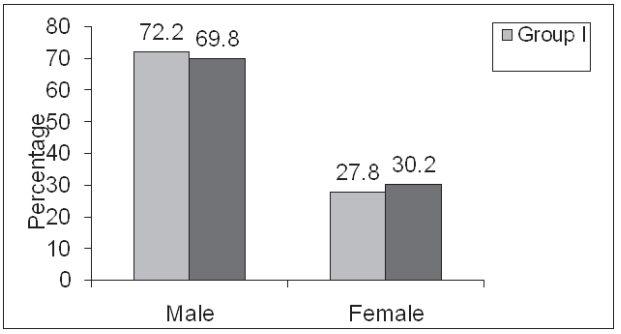

Figure-1: *Showing distribution of sex.*

Table II: Mean platelet parameters before and after anti-platelet therapy of the study patients (n=142).

Variables	Group I (n=79)	Group II (n=63)	P^avalue
	Mean±SD	Mean±SD	
Platelet count (10^9/L)			
Before (1st sample)	273.1 ±50.15	290.78 ±74.86	0.096^{ns}
After (2nd sample)	284.56 ±41.93	323.57 ±69.2	0.001^s
MPV (fl)			
Before (1st sample)	12.48 ±1.17	10.45 ±0.66	0.001^s
After (2nd sample)	11.55 ±1.08	10.17 ±0.76	0.001^s
P^bvalue	0.001^s		

s= significant, ns= not significant, P^a= value reached from unpaired t-test, P^b= value reached from paired t-test

Receiver-operator characteristic (ROC) curves were constructed using MPV value of the patients between two groups, which gave cut off value of >10.7 fl as the value with a best combination of sensitivity and specificity for acute coronary syndrome. MPV had the best area under curve compared to platelet counts.Platelet count cut-off value was>225X109/L showed sensitivity 83.0% and specificity 28.1% in the diagnosis of acute coronary syndrome where MPV showed sensitivity 90.6% and specificity 49.4% in the diagnosis of acute coronary syndrome.

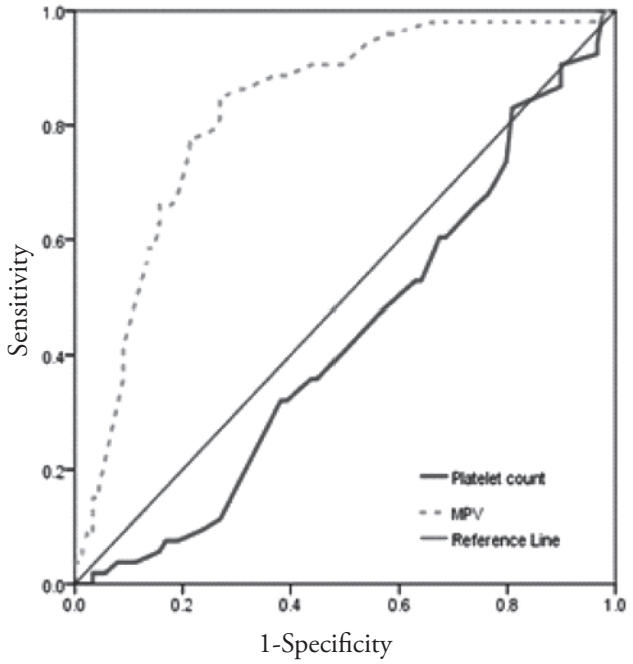

Figure-2: *Receiver-operator characteristic curves of platelet count and MPV.*

Discussion

Acute coronary syndrome occurs at any adult age, but it is the disease of middle & old age. The disease process usually starts in young age. In our study there was significant differences found between cases and controls in respectof age. The mean age of the patients with ACS was 55.05±10.73 years as compared to 56.59±13.63 years, 58.01±12.9 years, 52.0±8.6 years and 56.6 years in studies done by AS Assiriet al,[10] SM VAl-Saif et al,[11] MA Siddique et al[12] and by M Ullah et al.[13] It also correlates with the study done by MAK Akandaet al,[14] MaqboolJafary et al[15] and J Rumi et al[16] where the mean age was 50.15±8.8 years, 58±11 years and 60±11 years respectively. Gender variations in ACS are also significant. There was clear male predominance in this study, 72.2% and 69.8% in group I and group II respectively. However, the variation was not statistically significant between the groups. Our study is consistent with findings of study done by Khan AR and Majumder AAS,[17] AFMS Haqueet al,[18] MA Sayeed et al,[19] R Paudel et al,[20] P Joshi.[21] This may be due to prevalence of current and former smoking, and higher alcohol consumption in male than female in Bangladesh.

In our study, we found that ACS was associated with abnormal platelet parameters. The study reveals that the mean (±SD) value of total platelet count was lower in cases than controls where as MPVwas significantly higher in group I than group II. In our study, total platelet count was 273.1±50.15 X 109/L in ACS and 290.78 X 109/L in control groups. Similarly MPV was 12.48±1.17 fl and 10.45±0.66 fl respectively. MPV was significantly higher in patients with ACS compared to non-ACS. Our results are consistent with the results of A Mathuret al[22] and AS Assiri et al.[10] They found mean (±SD) value of total platelet

count was slightly lower in ACS group than control subjects. MPV were significantly higher in ACS groups in compared to control groups. They described platelets parameters mainly MPV was raised in ACS compared to controls.

A study done by S Nandwani et al[23] in India found that platelet volume indices were raised in patients with ACS compared with controls. MPV was 10.78 µm 3 in acute myocardial infarction and 11.73 µm3 in unstable angina. Another study done in India conducted by MM Khandekar et al[24] suggested that all platelet volume indices were increased significantly in patients with acute myocardial infarction and unstable angina compared to subjects of stable coronary artery disease. The authors found platelet volume indices especially, MPVwas 10.43±1.03 fl. Our findings are consistent with these studies. The findings of platelet count and MPV also consistent with a number of studies, done by E Varol et al,[25] R Cemin et al[26] and Yilmaz et al.[27] They found that MPV was significantly higher in patients with ACS groups than controls, along with reverse changes in platelet count. E Varol et al[25] found, platelet count 291±16.2 X 109/L and MPV 9.9±1.8 fl. Yilmaz et al[27] shown, 248±48 x 109/Land MPV were 10.7±0.7 fl in UA groups and 10.4±0.6 fl in MI groups. L Pizzuli et al,[28] R Mercan et al[4] and MP Ranjith et al[29] found platelet counts were significantly lower in the ACS groups as compared to control subjects, but MPV was significantly higher in ACS. R Sewell et al[30] described in their study that high MPV after MI was associated with consumption of small platelet and release of young platelet from bone marrow. Our study is consistent with study done by other authors.

Platelets are heterogeneous cells with size, density and activity.[31] Platelet volume is an important indicator for platelet function and activation. There are many studies reported where platelet volume had association with ACS. Independent association of MPV in AMI was shown by G Endler et al.[2] They also showed that higher the MPV (>11.6 fl) higher the risk of MI. Park et al[32] considered increased MPV to be a risk factor for platelet activation. Z Huczek et al,[7] AS Yasar et al,[33] Y Kucukardali et al[34] and A Kenneth et al[35] observed in their studies that increased MPV (>9.8±1.5 fl, >10.3fl and >10.7 fl) on admission predicts impaired reperfusion, where there is activation of platelet before AMI begins, and consequently, there are more death occur in those patients after thrombolytic therapy. The MPV remain increased upto 5/6 days suggest that the activity of platelets remain constant. SG Chu et al[36] found that MPV was associated with patients AMI by a systemic review and Meta analysis. They observed increased MPV (>9.42 fl) in AMI were 14 studies among 16 studies. They described MPV as a risk factor and prognostic indicator in cardiovascular disease. Similar fingings were obtained by RE Ulusoy et al[37] in STEMI, where the platelet count was low.

In present study, sensitivity and specificity of MPV were 90.6% and 49.4% respectively. Hsin Chu et al[1] and AS Yasar et al[33] observed in their studies that MPV was significantly higher in patients with acute myocardial infarction and unstable angina in comparison to control subjects. They found that in patients with ACS, the best cut off value of MPV was 10.35 fl and 8.88 fl. Sensitivity and specificity were 78.3% & 70.4% and 74.6% & 66.1% respectively. In our study, the sensitivity and specificity of platelets counts were 83% and 28.1% respectively. The positive and negative predictive values were 37.6% and 64%.

The sensitivity, specificity, positive and negative predictive values were determined through ROC curves against troponin I. In our study among the 79 cases, 53 were troponin I positive and 26 were negative. All of the control subjects were troponin I negative. According to diagnostic criteria 67 cases were diagnosed as AMI and 12 cases were UA where troponin I was negative. Among 67 AMI cases, only 53 cases were troponin I positive in 1st sample and 14 cases were initially troponin I negative and became positive later. That is why specificity was low in our study in compared to study done by Hsin Chu et al[1] and AS Yasar et al.[33] Because there was similar result of platelet parameters found in troponin I positive and negative subjects in group I.

In present study, total counts of platelet in group I before and after anti-platelet therapy were 273.1±50.15x109/L and 284.56±41.93x109/L respectively. This denotes no significant differences between the samples. Considering MPV, we found significant differences before and after anti-platelet therapy, but not below the cut off values. There are two hypotheses that described the increased platelet volume. First, when platelets are activated they change their size and shape (metamorphosis). Second, after platelet activation aggregation of more platelet this leads to release of younger platelet from bone marrow. These suggest that MPV is indirect indicators of platelet activation and its association with ACS. After anti-platelet therapy, MPV was decreased, due to inhibition of platelet activation and aggregation.

These findings lead to the hypothesis that larger platelets as determined by their volumes (MPV) may be useful markers in patients with ACS. Our data indicate that, higher MPV may become useful marker for early detection of ACS along with other biomarkers. Larger platelets are haemostatically more active and carry risk for developing coronary thrombosis leading to ACS. Patients with increased MPV could be easily identified during routine haematological analysis. It could play an important role in early detection of acute coronary syndrome (ACS) and beneficial for preventive treatment. It could be used as a screening test to differentiate the origin of chest pain along with other cardiac biomarkers.

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