Study of platelet parameters in patients with acute coronary syndrome

Manish Barnawal[1], Nanda J Patil[2*], Sujata R. Kanetkar[3], Shefali Mishra[4]

Abstract

Background and Objectives: Platelet indices play a significant role in the pathogenesis of acute coronary syndrome (ACS), where rupture of plaque is followed by platelet activation and thrombus formation. The present study aimed to evaluate the platelet indices in patients with ACS syndrome.

Materials and Method: This case control study was conducted in 300 patients consisting of 150 ACS cases and 150 age- and sex-matched controls without any history of ACS. Blood samples of both the groups were analyzed for the association of indices [mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC)] with ACS and compared with controls. Also, correlation of MPV with cardiac biomarkers like troponin (Tn) and creatine kinase-MB (CKMB) was assessed. Student's t test was used to test the significance between the two groups. P value of <0.05 was considered as significant.

Results: Significantly higher levels of MPV, PDW ($p<0.01$), and PC ($p<0.002$) were observed in cases as compared to controls. Comparison of MPV and PDW showed a significant increase in myocardial infarction (MI) cases ($p<0.001$ and $p=0.008$) and unstable angina (UA) cases ($p<0.001$) as compared to controls. The mean value of MPV was found to be significantly higher in Tn+ve ACS cases ($p<0.0001$) and CKMB +ve ACS cases ($p<0.01$) as compared to Tn-ve, CKMB-ve cases, and controls.

Conclusion: Platelet indices showed a significant variation in patients with ACS. Therefore, it can be considered as an economic marker for acute coronary event.

KeyWords: Acute coronary syndrome, Creatinine, Mean platelet volume, Myocardial infarction, Troponin, Thrombosis, Unstable angina

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Introduction

Acute coronary syndrome (ACS) is one of the leading causes of death and also the major cause of mortality and morbidity in developed as well as developing countries.1 The signs and symptoms of ACS are caused by the rupture of plaque and platelet-rich coronary thrombus formation.2 The thrombus further leads to partial or complete coronary artery occlusion and a variety of clinical manifestations ranging from unstable angina (UA) to myocardial infarction (MI).3

Platelet hyperactivity and local platelet activation have been found to play a major role in acute coronary events.4,5 Larger platelets in the form of elevated mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC) are observed to be enzymatically and metabolically more active than smaller platelets.6 Larger platelets are denser and aggregate more rapidly with subendothelial collagen to produce thromboxane A2 and express more glycoprotein Ib and glycoprotein IIb/IIIA receptors.7 Mean platelet volume is the average size of the platelets circulating in blood.8 Platelet width distribution is a quantitative measure of platelet size variation and could be a predictor of platelet activation and turnover.

Corresponding author: Nanda J Patil
Address: [1]Student, Department of Pathology, Krishna Institute of Medical Sciences "Deemed to be University", Karad, Maharashtra, India – 415110. [2]Professor, Department of Pathology, Krishna Institute of Medical Sciences "Deemed to be University", Karad, Maharashtra, India – 415110,[3]Professor and Head, Department of Pathology, Krishna Institute of Medical Sciences "Deemed to be University", Karad, Maharashtra, India - 415110. [4]Senior Resident, Department of Pathology, Krishna Institute of Medical Sciences deemed to be university, Karad, Maharashtra, India- 415539

9 Mean platelet count denotes the refractive index of platelets. It is linearly associated with platelet

intensity and is decreased when platelets degranulate indicating that they have undergone activation.10

Diagnosis of ACS poses a challenge despite the availability of various diagnostic modalities. Biochemical markers of acute ischemic injury, clinical presentation, and electrocardiographic findings are used in the diagnosis of ACS.11,12 Most of these events are biochemically undetectable or clinically unrecognizable until the onset of necrosis. The cardiac markers troponin (Tn) and creatine kinase-MB (CKMB) are not sensitive enough during the early stages of ACS though they have greater sensitivity.13 In spite of this greater diagnostic sensitivity feature of troponins and CK-MB, early diagnosis could not be achieved due to its slow release kinetics from damaged myocardium.13 Also, diagnosis of ACS with biochemical markers is expensive and their availability and usage in a rural set-up is limited due to poor laboratory facilities. Hence, there is a need for a reliable and inexpensive marker for accurate diagnosis of ACS. Platelet parameters, especially MPV and PDW, could be a potential marker in early detection of ACS when patients attend the Cardiac emergency department.14

Platelet parameters are easily obtained routinely with complete blood count (CBC) in fully automated hematology analyzer without any extra cost, time, and extra sample. Increased MPV might become a useful biomarker for early detection of ACS along with other biomarkers like cardiac troponins and brain natriuretic peptide/N-terminal pro b-type natriuretic peptide (BNP/NT-proBNP). Identifying the risk factors for ACS is important for both diagnostic and prognostic purposes. Study on the evaluation of platelet parameters in patients with ACS compared to controls in a tertiary care center is limited in India. Hence, an attempt has been made to study the platelet parameters in patients with ACS with age- and sex-matched controls in a tertiary care center.

Materials and Methods

Study design

This case-control study was conducted on adult patients with clinically suspected ACS and compared with age- and sex-matched controls at Karad, Maharashtra, India, from May 2014 to April 2016. A total of 300 patients with ACS and controls were selected following a written informed consent. The study was carried out after approval from the institutional ethics committee. The sample size was calculated based on student's t-test with 95% level of significance and 90% power to obtain a minimum sample size of 146 subjects for each group. All clinically suspected as well as diagnosed patients with ACS, including MI as well as UA admitted due to chest pain in the hospital's Casualty center were included as cases. Age- and sex-matched patients recently admitted for elective surgical procedures with normal ECG and without any history of ACS in the previous 2 years were included as controls while patients who were on anti-platelet therapy and those with comorbid conditions like diabetes, hypertension, use of tobacco and alcohol, and obesity were excluded.

Demographic characteristics and previous history of the cases were recorded. Blood samples of the cases and controls were collected within 24 h of onset of ACS symptoms. The samples were collected aseptically in ethylenediaminetetraacetic acid (EDTA) vacutainers and analyzed using a 5-part automated hematology analyzer within 30 min of sample collection. The platelet parameters of both the groups were analyzed immediately. Correlation of MPV with cardiac biomarkers like Tn and CKMB was also assessed. The results of MPV, PDW, and PC were confirmed with peripheral smear.

Statistical analysis

Data was analyzed using GraphPad software. Percentage, mean, and standard deviation (SD) were used to present the data which was compared between cases and controls. The student's t-test and ANOVA were used to assess the difference between the groups. P value of <0.05 was considered as significant.

Results

The demographic characteristics are presented in Table 1. Majority (40%) of the cases were in the 51-60-year age group with a mean age of 56.48 ± 9.75 years. Male predominance was observed in the study with 68% males versus 32% females. The most common risk factors in majority of the patients were tobacco/smoking (72%), alcohol (42%), and diabetes (34%).

With regard to the symptoms, most of the ACS patients had chest pain (62%), sweating (60.67%), breathlessness (54%), giddiness (34%), vomiting (22%), and palpitation (21.33%) (Table 2).

Considering the platelet volume indices with respect to gender, the MPV was observed to be higher in females (11.53±1.38) when compared to

males (9.09±1.08). In terms of comparison of MPV between post-menopausal and pre-menopausal women, post-menopausal women showed higher levels of MPV (11.61±1.54) than pre-menopausal women (10.83±1.58).

Table 3 shows the comparison of various hematological parameters between the cases and control groups. Significantly higher levels of MPV, PDW ($p<0.01$), and PC ($p=0.002$) were observed in the cases when compared to controls.

Comparison of MPV and PDW between MI and controls ($p<0.001$ and $p=0.008$) and also between UA and controls ($p<0.001$) showed a statistically significant increase in both the platelet parameters in MI and UA cases, respectively, compared to controls. With respect to PC, there was no statistically significant difference observed when MI and UA cases were compared with controls. Also, comparison of platelet parameters between MI and UA cases was statistically insignificant (Table 4).

Among the ACS cases, most of the patients showed increase in cardiac biomarkers. The mean value of MPV was found to be higher in Tn+ve ACS cases as compared to Tn-ve cases and controls, and the difference was statistically significant ($p<0.0001$). Similarly, the mean value of MPV was higher in CKMB+ve ACS cases than in CKMB-ve cases and controls, and the difference was statistically significant ($p<0.01$)(Table 4).

Discussion

The factors causing ACS include coronary plaque rupture, platelet aggregation, and thrombus formation. MPV reflects the degree of activation of platelets to a certain limit and is considered an important marker of cardiovascular disease.15 Moreover, it can be used in risk prediction, diagnosis, and prognostic assessment of cardiovascular diseases.16,17

In the present study, significantly higher levels ($p<0.01$) of MPV were observed in ACS cases as compared to controls. These results were in agreement with the study conducted by Hassan et al which reported significantly higher MPV levels ($p<0.001$) in ACS cases as compared to healthy controls.18 A few other studies have also reported similar results.19-21 With regard to the mean value of PDW in ACS cases compared to that of controls in our study, a significantly higher value ($p<0.01$) was reported in ACS cases compared to controls. These results were in concordance with various other studies which also reported significantly higher mean value of PDW in ACS cases compared to controls.19,20,22 These findings could lead to the hypothesis that larger platelets as determined by their volumes, MPV and PDW, could be useful markers in patients with ACS. It also indicates that increased MPV and PDW might become useful markers for early detection of ACS along with other biomarkers. In contrast, a study conducted by Paramjit et al reported no significant changes in MPV and PDW in ACS cases as compared to controls. The reason for the insignificance in that study could be due to smaller size of the study group or due to other regional or cultural factors.

In terms of platelet count, the present study revealed significantly lower PC in cases compared to controls ($p<0.002$). This is in accordance with the study carried out by Yaghoubi et al which also reported significantly lower PC ($p<0.001$) as compared to controls.21 These findings imply that a decline in the platelet count may ensue along with disease progression in acute coronary events. In contrast, various studies reported no significant difference between ACS cases and controls with respect to the PC.12,13,20

With respect to the comparison of MPV and PDW between AMI cases and controls, significantly higher MPV and PDW was observed in cases versus controls in the present study. Likewise, comparison of MPV and PDW between UA cases and controls also showed similar results. These results were in concordance with the studies conducted by Biradar et al and Assiri et al.12,19 These findings could be attributed to the fact that high MPV and PDW are hemostatically active and act as risk factors for developing coronary thrombosis leading to MI and UA. These indices can further provide a signature for the prethrombotic state in ischemic heart disease.

Comparison of MPV with various cardiac biomarkers in the present study showed a significantly higher mean values of MPV ($p<0.0001$) in Tn +ve ACS cases compared to Tn -ve ACS cases and controls. El-Dosouky et al also reported similar results with significant MPV values compared to controls.23 This could be due to sample collection being done immediately after admission, and Troponin I level usually increased 6-8 h after the onset of symptoms in the current study. With respect to CKMB markers, a significantly higher MPV levels ($p<0.01$) were observed in CKMB+ve ACS cases than in CKMB-ve cases and controls. These results were consistent with the study conducted by Costa et al which also reported a

significant positive correlation between MPV and CKMB levels ($p<0.05$) suggesting that MPV analysis could be an additional tool for diagnostic investigation of MI risk when CKMB levels are above normal.24

Based on the overall findings, it can be concluded that larger platelet volume and distribution width constitute a significant risk for acute coronary syndrome and ischemic complications. Hence, the use of platelet indices in laboratory routine could be an important complement in the assessment and follow-up of cardiac patients since these indices are easily provided by an automated equipment when a complete blood count is requested by an attending physician. However, this study had a few limitations. The sample size was too small to be extrapolated to the general population. Serum MPV, PDW, and platelet count was measured only once. Therefore, their variability as time passed was not studied which cannot be accounted for intra-individual variability. Also, patients with non-cardiac chest pain might have UA in the absence of electrocardiographic changes, and cardiac troponin positivity could have resulted in selection bias. Further studies on larger cohorts are warranted in patients with ACS with more appropriate design to confirm its value as a diagnostic marker.

Conclusion

Platelet parameters in patients with ACS were significantly increased when compared to controls. The present study also showed a significant increase in MI and UA cases with increase in MPV and PDW. Hence, MPV and PDW could be utilized with other investigational tools in future to screen patients presenting to the emergency room with chest pain and are suspected to have ACS.

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Table 1: Demographic characteristics

Variables	Number of cases n (%)
Age (in years)	
≤30	0 (0.0)
31-40	14 (9.3)
41-50	23 (15.3)
51-60	60 (40)
61-70	46 (30.7)
>70	7 (4.7)
Gender	
Males	102 (68)
Females	48 (32)
Risk factors	
Positive family history	8 (5)
Tobacco (including smoking)	108 (72)
Alcohol	64 (42)
Diabetes	51 (34)
Hypertension	33 (23)
Others	30 (13)

Table 2: Distribution of presenting symptoms in the cases group

Symptoms	Count n (%)
Chest pain	93 (62)
Sweating	91 (60.67)
Breathlessness	81 (54)
Giddiness	51 (34)
Palpitation	32 (21.33)
Vomiting	33 (22)

Table 3: Comparison of various hematological parameters between cases and controls

Parameters	Cases (n=150) mean±SD	Controls (n=150) mean±SD	P value
MPV (in fL)	11.52±1.38	9.09±1.08	<0.01*
PDW (in fL)	10.45±1.31	9.92±1.02	<0.01*
PC (in lacs/cu.mm.)	2.59±0.64	2.84±0.84	0.002*

fL: femtoliter; MPV: Mean platelet volume; PC: Platelet count; PDW: Platelet distribution width
*p<0.05 considered statistically significant

Table 4: Comparison of platelet parameters between myocardial infarction and unstable angina cases with controls

Parameters	MI (n=98) mean±SD	Controls (n=150) mean±SD	P value	UA (n=52)	Controls (n=150)	P value
MPV (fL)	11.52±1.35	9.09±1.08	<0.001*	11.54±1.44	9.09±1.08	<0.001*
PDW (fL)	10.43±1.33	9.92±1.02	0.008*	10.49±1.27	9.92±1.02	<0.001*
PC (in lacs/cu.mm.)	2.61±0.68	2.73±0.81	0.228	2.52±0.54	2.73±0.81	0.838

MI: Myocardial infarction; MPV: Mean platelet volume; PC: Platelet count; PDW: Platelet distribution width; UA: Unstable angina
*p<0.05 considered statistically significant

Table 5: Comparison of mean platelet volume with various cardiac biomarkers

Variables	Cases		Controls (n=150)	P value
	Tn+ve (n=61) mean ±SD	Tn-ve (n=89) mean±SD		
MPV (in fL)	12.20±1.04	11.06±1.39	9.09±1.08	<0.0001
	CKMB+ve (n=98) mean±SD	CKMB-ve (n=52) mean±SD	Controls (n=150)	P value
	11.7±1.35	11.3±1.41	9.09±1.09	<0.01

CKMB: Creatine kinase-MB; MPV: Mean platelet volume; Tn: Troponin
*p<0.05 considered statistically significant