Original Research Article

Mean Platelet Volume in patients with Acute Coronary Syndrome

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Abstract

Background: Acute coronary syndrome (ACS) including acute myocardial infarction and unstable angina is becoming more prevalent worldwide. Activated platelets play an important role in the pathogenesis of atherosclerotic lesions and their complications. Platelet indices including Mean Platelet Volume (MPV), Platelet large cell ratio (PLCR) and Platelet distribution width (PDW) are indirect measures of activated platelets. Previous studies have shown MPV as an independent variable for prognosis in patients with acute coronary syndrome. **Objective**: To evaluate the platelet count and platelet volume indices in patients with acute myocardial infarction and unstable angina and study their usefulness as predictive factors for risk of ACS. **Material & Methods:** A case control comparative study was conducted including 87 patients of Acute coronary syndrome and 90 age and sex matched normal healthy controls. Platelet count and platelet volume indices including MPV, PLCR, PDW of both the groups were estimated by SYSMEX KX21 hematology autoanalyzer. Results were tabulated and Statistical analysis was done using SPSS16 version statistical software. **Results**: MPV of 10.03±1.04fL, Platelet count of 250±89x10^9/L, LCR of 26.4±8.9, PDW of 12.9±2.7 were observed in ACS group. Statistically significant difference was observed for MPV of ACS and control groups with p value of 0.025. There was no significant difference of Platelet count, P-LCR and PDW among study and control groups. **Conclusions**: MPV is significantly higher in ACS patients than controls. MPV is simple, cost-effective tool that can be done along with biochemical cardiac markers to predict an impending adverse event in cardiovascular diseases.

Keywords: Acute coronary syndrome, platelet indices, mean platelet volume

Introduction

Acute coronary syndrome (ACS) is one of the leading causes of mortality and morbidity worldwide. Atherosclerosis with plaque disruption and superimposed thrombosis is the common underlying cause. Coronary artery occlusion leads to clinical manifestations of unstable angina (UA) or acute myocardial infarction (AMI).

Platelets are the small anucleate cytoplasmic fragments derived from megakaryocytes in bone marrow. They measure 1.5 – 3.0µm in diameter with a volume of ~ 7fL. Platelets are directly released into the circulation by fragmentation of cytoplasm. They have a lifespan of 8-12 days and an estimated turnover of 1.2-1.5x10^{11}/day. Platelets contain several organelles like mitochondria and glycogen stores, lysosomes, alpha (α) granules and dense (δ) granules. Calcium, ATP, ADP, magnesium and serotonin are present in δ granules. The α granules contain numerous proteins, including β - thromboglobulin and platelet factor 4, several coagulation factors, Von Willebrand factor (vWF) and certain growth factors.

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Platelets secrete many substances that are important mediators of coagulation, thrombosis, inflammation and atherosclerosis[1,2]. Hyperactive and larger platelets are implicated in acute coronary syndrome. Larger platelets have more prothrombotic property, increased metabolic and enzymatic activity due to increased dense granules and thromboxane A2 synthesis[3,4,5]. Platelet volume indices including Mean Platelet volume (MPV), Platelet large cell ratio (PLCR), Platelet distribution width (PDW) are the measures of platelet size and activity. Platelet volume parameters provided by hematology analysers indicate the activation of platelets and hence can be utilized to know the risk and early identification of ACS. Previous studies have found that mean platelet volume is elevated in ACS and is an independent variable for prognosis in patients with cardiovascular diseases[6]. Studies have been done to evaluate MPV in myocardial infarction, heart failure, stroke. Few studies have shown no association between MPV and myocardial infarction[7]. The present study was conducted to evaluate the Mean Platelet Volume in patients with acute coronary syndrome and normal controls, and study its usefulness as predictive factor for risk of acute coronary syndrome.

Materials and Methods

A case control study was conducted at tertiary care hospital, Shivamogga Institute of Medical Sciences, over a period of 6 months. Study was conducted after approval by the Institutional Ethical

committee. It was conducted on 177 subjects after taking informed consent. It included two study groups.

1. Acute coronary syndrome (Myocardial infarction and Unstable angina) – 87 patients.
2. Age and sex matched healthy controls- 90.

Diagnosis of myocardial infarction and unstable angina was based on Clinical presentation, ECG and cardiac biomarkers.

Inclusion criteria

Patients above 20 years of age, with history of chest pain, ECG changes, and elevated cardiac biomarkers were included in the study.

Age and sex matched healthy controls were selected from the blood donors visiting the Blood Bank and also from healthy relatives visiting the patients in the hospital. Any cardiac illness was excluded by history.

Exclusion criteria

Patients with previous history of myocardial infarction, platelet disorder, major surgery, malignancies and terminal illness were excluded. After taking consent, 2 ml of venous blood was collected in EDTA anticoagulated tubes, under aseptic precautions. In the ACS patient group, venous blood was collected before initiation of antiplatelet therapy. Platelet count, platelet volume indices including Mean Platelet volume, Platelet large cell ratio, Platelet distribution width were estimated by SYSMEX KX21 hematology autoanalyser, within 1 hour of blood collection. Quality control measures were strictly followed.

Statistical Analysis

Results were tabulated and Statistical analysis was done using SPSS16 version statistical software. As the data showed asymmetric distribution, Mann Whitney test was done to compare the median and the inter quartile range of two study groups. P value <0.05 was considered significant.

Results

A total of 177 cases were analysed. Age and sex wise distribution of cases is as shown in Table 1. Study included 90 healthy controls with a mean age of 40 years (±11.8) and 87 acute coronary syndrome patients with a mean age of 55 years (±15.2). Among the ACS group 57.4% were males and 42.6% were females. In the control group, 61.1% were males and 38.9% were females.

Table 1: Distribution of Study population

Study population	Sex	Number (Percentage)	Age (Mean±SD)
Acute coronary syndrome	Male	50(57.4%)	54±14.6
	Female	37(42.6%)	56±16.2
Controls	Male	55(61.1%)	43±11.5
	Female	35(38.9%)	45±11.6

Table 2: Platelet parameters in ACS and control groups

Parameters		Mean±SD	Median	Interquartile Range	P value
Platelet Count ($x10^9$/L)	ACS	250±89	241	128	0.126
	Control	260±87	258	36	
MPV (fL)	ACS	10.03±1.04	10	1.4	0.025*
	Control	9.7±0.79	9.6	1.2	
P-LCR	ACS	26.4±8.9	25.8	10.1	0.225
	Control	24.65±6.4	24.3	9.9	
PDW	ACS	12.9±2.7	12.4	2.7	0.340
	Control	12.36±1.7	12.1	2.5	

*Significant

Statistical analysis was done using SPSS16 version statistical software. Results of platelet count and platelet volume indices are as shown in Table 2. As the data showed asymmetric distribution, Mann Whitney test was done to compare the median and the inter quartile range of two study groups. Analysis showed a statistically significant difference between MPV of ACS and control group with a Mann-Whitney Test U value of 3149.5, Z value of -2.24 and p value of 0.025. There was no significant difference of Platelet count, P-LCR and PDW among study and control groups.

Discussion

Platelets play a major role in initiation of atherosclerosis and its complications. They are activated in response to disruption of plaque, leading to occlusive thrombosis of coronary artery and acute myocardial infarction. Secretion of storage granules cause platelet aggregation. As platelet aggregation increases, larger and more reactive platelets are released from the bone marrow[5,8].In the present study, we found that Mean platelet volume was increased in patients with acute coronary syndrome compared with the healthy controls. We observed MPV of 10.03±1.04fL, Platelet count of 250±89x10^9/L, LCR of 26.4±8.9, PDW of 12.9±2.7 in ACS group. In Control group, MPV of 9.7±0.79fL, Platelet count of 260±87x10^9/L, LCR of 24.65±6.4, PDW of 12.36±1.7 was observed. Among these, statistically significant difference was observed only for MPV of ACS and control group. LCR, PDW and platelet count of ACS and control groups did not show statistically significant difference. The finding of elevated MPV is similar to the other studies findings.

Table 3: Comparison of Mean platelet volume in ACS and control groups in different studies

Study	MPV (fL) in ACS		MPV (fL) in Controls		P value
Khode et al [9]	9.65 ± 0.96	n=39	9.21 ± 0.58	n=65	0.025
Khandekar et al [10]	10.43 ± 1.03	n=94	9.2 ± 0.91	n=30	<0.001
Gupta et al [11]	8.49+2.10	n=40	7.10 ±1.60	n=40	<0.001
Agrawal BK et al [12]	11.0±2.2	n=50	7.8±1.3	n=50	0.000
ChetanSagar S et al [13]	8.26 ± 0.56	n=107	7.93±0.869	n=100	0.002
Senaran H et al [14]	8.2 ± 0.8	n=20	6.6 ± 0.6	n=20	<0.001
Bilagi UR et al[15]	9.722±0.7517	n=50	7.896±0.5002	n=50	<0.00001
Gururajaprasad et al [16]	10.45 ± 0.76	n=100	10.21 ± 0.87	n=100	0.000
Present Study	10.03±1.04	n=87	9.7±0.79	n=90	0.025

n – sample size.

Studies by Khandekar et al, Gupta et al, ChetanSagar et al, Bilagi et al, Lippi G et al observed higher MPV values in ACS cases compared to controls[10,11,13,15,17]. Studies by Khode et al, Senaran et al and Gururajprasad et al also showed elevated MPV in AMI cases when compared to controls [9,14,16]. Study by Amraotkar et al showed that MPV was higher in acute MI (9.18±1.21) compared to stable coronary

artery disease group (8.13±0.66) with a P =0.003, in the acute phase. No statistically significant difference was noted in MPV of stable coronary artery disease group and MI group, when MPV was measured 3 months post MI, in quiescent phase[18]. Study by Chu et al suggested that MPV is higher in patients with AMI and in patients who develop restenosis following coronary angioplasty[5]. Klovaite J et al studied Platelet indices in 39,531men and woman from the general population, of whom 1300 developed MI. Study showed that risk of MI increased with increasing MPV independently of known cardiovascular risk factors[6]. Study by Avci et all showed that high MPV was associated with long-term mortality in myocardial infarction patients[19]. In the study by Jayaganesh et al on Coronary Artery Disease (CAD) patients and controls. MPV and PDW showed significant increase in CAD group compared with control group. Difference in MPV was statistically significant among three angiogram groups including single vessel disease, double vessel disease, triple vessel disease and controls[20].Platelet distribution width measures the extent of variation of the size of platelets. High PDW values are due to increased production of larger reticulated platelets. In the study by Khode et al, there was no significant increase in PDW and P- LCR in ACS and controls[9]. In the present study also, no statistically significant increase of PDW and P-LCR among the ACS and control groups was observed. Khandekar et al have reported higher PDW and P-LCR in ACS patients when compared with that of controls[10].Platelet activation has been observed in acute coronary syndromes. Increased platelet consumption at the coronary artery thrombosis site stimulates the bone marrow to release larger activated platelets. Activated platelets have large size, more granules, more adhesion receptors and high thrombotic potential. Hyperactivity can be attributed to the increased concentrations of substances like thromboxane, P Selectin, Platelet Factor 4 and increased expression of the adhesive receptors like Glycoprotein IIB/IIIA. Aging, increasing body fat, high blood pressure, diabetes, tobacco derived toxins, myocardial infarction can cause changes in secretion of such substances. This variation is also observed post coronary bypass surgery or coronary angioplasty[5,6].

The cause for the enlarged circulating platelets is the newly generated larger platelets derived from bone morrow megakaryocyte. As megakaryocyte differentiation and maturation occurs over 4-5 days period, elevated MPV cannot be attributed only to new platelets from marrow. The human spleen could be reservoir for the large platelets, which have 20% greater MPV than that of circulating platelets. Therefore, release of larger platelets from spleen could also be a factor responsible for sudden increase in number of circulating large platelets and elevated MPV during stress including intense exercise and stimulation by cytokines or catecholamines[19-21].MPV could be a valuable indicator of platelet activity in cardiovascular events. Elevated MPV could serve as a reliable marker of adverse event in such patients. The limitations include cut-off point of MPV useful for predicting cardiovascular events still needs to be established. Blood sample collection, calibration of hematology analysers, time of sample collection and test measurement have to be considered. EDTA, the commonly used anticoagulant is known to cause platelet swelling with time. Increase in MPV has been reported to be 7.9% within 30min and 13.4% over 24 hours. Analysers utilize different technologies for assessment of various tests. Increase in MPV overtime has been reported when MPV assessment is done by impedance method. But MPV decreased when assessment was done by optical method because platelet swelling caused reduced platelet density[22,23]. Elevation in MPV attributable to other multifactorial risk factors of ACS also have to be considered.

Conclusion

MPV is significantly higher in ACS patients than controls. Larger platelets can easily be identified during routine haematological analysis in patients with coronary artery disease. MPV is simple, practical and cost-effective tool that can be done along with biochemical cardiac markers to predict an impending adverse event in cardiovascular diseases.

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