



COMPARISON OF PLATELET DISTRIBUTION WIDTH IN STABLE CORONARY ARTERY DISEASE AND ACUTE MYOCARDIAL INFARCTION

Pathology

Dr. Rabia Parveen Siddiqui	Associate Professor, Department of Pathology, Pt. JNM Medical College Raipur (Chhattisgarh)
Dr. Gayatri Sahu*	Postgraduate student, Department of Pathology, Pt. JNM Medical College Raipur (Chhattisgarh) *Corresponding Author
Dr. Shruti Srivastava	Associate Professor, Department of Pathology, Government Medical College Rajnanadgaon (Chhattisgarh)
Dr. Renuka Gahine	Director Professor and Head of the Department, Department of Pathology, Pt. JNM Medical College Raipur (Chhattisgarh)

ABSTRACT

Background: Coronary artery disease is mainly caused by atherosclerosis and its complications. Platelets and their activity have an important role in initiation of atherosclerotic lesions and coronary thrombus formation. Larger platelets are enzymatically and metabolically more active and have a higher potential thrombotic ability as compared with smaller platelets. Variation in platelet size (anisocytosis) can be measured by Platelet distribution width.

Aim: To study the changes in platelet distribution width in patients with stable coronary artery disease and acute myocardial infarction.

Material and method: A total of 200 cases were studied, 100 patients were of acute myocardial infarction (AMI) and 100 patients were of stable coronary artery disease consisting of those who were either admitted for coronary angiography or who had AMI at least 5 weeks prior. Venous samples were drawn and collected in standardized EDTA sample tubes. Platelet count and platelet volume indices were assayed using BECKMAN COULTER (USA) LH-750 auto-analyzer with regular quality control and the results were analyzed using appropriate statistics.

Results: Platelet distribution width (PDW) and Mean platelet volume (MPV) were found to be increased in AMI patients (17.89±0.61fl and 9.86±1.27 fl respectively) as compared to stable CAD patients (16.51±0.34fl and 8.55±0.81fl respectively). The difference was found to be statistically significant for PDW and MPV among the two groups.

Conclusion: The study concludes that Platelet Indices especially MPV & PDW is raised in patients suffering from AMI as compared to stable CAD patients and they can be used for predicting impending acute coronary events.

KEYWORDS

Acute myocardial infarction, stable coronary artery disease, platelet distribution width

INTRODUCTION

In the new millennium, coronary artery disease (CAD) is looming large as the new epidemic afflicting Indians. Cardiovascular disease is a global public health problem contributing to 30% of global mortality and 10% of the global disease burden.^{1,2}

Acute coronary syndrome (ACS) is a unifying term representing a common end result, acute myocardial ischemia. Acute ischemia is usually, but not always, caused by atherosclerotic plaque rupture, fissuring, erosion, or a combination with superimposed intracoronary thrombosis and is associated with an increased risk of cardiac death and myonecrosis.³

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. Larger and hyperreactive platelets accelerate the formation of an intracoronary thrombus, leading to a cascade of clinical events, such as acute coronary syndrome. Large platelets are more adhesive and tend to aggregate more than smaller ones.⁴

Platelet distribution width (PDW) is a quantitative measure of platelet size variation. An increased PDW indicate more variation of size (anisocytosis) which result from formation of pseudopodia and may be the predictor of platelet activation and turnover.⁵

Platelet indices such as PDW and MPV may be useful to show the association between platelet size and ischemic events.⁶ PDW is more sensitive and specific than MPV in terms of platelet reactivity.⁷

We currently lack understanding of the predictive accuracy of PDW for spectrum of CAD. Our aim was to compare PDW and other platelet indices in AMI and stable CAD patients and to find predictive value of PDW in spectrum of CAD.

MATERIALS AND METHODS

This hospital-based observational study was designed to assess whether platelet distribution width (PDW) show variation among

patients with acute myocardial infarction and stable coronary artery disease. The study protocol was approved by the Institutional Ethics Committee. Sample size was calculated based on standard error obtained in pilot study.⁸ Sample size was calculated to allow detection of a 30% difference in PDW between different groups and with α of 0.05 and power of 0.80. As per sample size calculation, a total of 200 subjects were studied divided equally in to two groups.

Group 1 had patients with AMI on admission.

Group 2 had patients of coronary artery disease who had AMI at least 5 weeks prior admitted for angiography without chest pain or with any other complain.

The enrolment period was between March 2017 and October 2017.

Following patients were excluded from the study: Patients with severe hepatic or renal impairment, Myeloproliferative disorders and malignancy, Thyroid disorders, Pregnant women, Inflammatory diseases (like rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease etc.), Sepsis, Recent history of Blood Transfusion, Thrombotic thrombocytopenic purpura (TTP) and idiopathic thrombocytopenic purpura.

Blood sample of patients diagnosed as AMI on admission was taken in EDTA containing tubes within 6 hours of arrival. Blood sample of stable CAD patients, who previously had AMI was taken in EDTA containing tubes within 12-24 hours of arrival.

Blood samples are drawn using a 19-G needle, approximately 2-ml from each patient was collected into a vacuum tube (purple cap) containing 2.0 mg/ml EDTA-2K and preserved at 37°C for platelet analysis.

For measurement of platelet distribution width (PDW), mean platelet volume (MPV) and plateletcrit (PCT), samples were analyzed within 30 minutes of collection with automated flow meter (BECKMAN COULTER Lx-750, USA).

The volume of platelets remains unchanged for about 1-2 hours but increases thereafter, so it is best to minimize the delay between collection and counting.

STATISTICAL ANALYSIS

Data were entered in excel and analyzed with recent available software. Results were presented as frequency, percentage, mean ± SD, median and analyzed using SPSS version 16.0. Categorical variables were analyzed by chi-square test and the continuous variables with ANOVA between the groups. The student t-test was used to assess whether the means of two groups are statistically different from each other. The chosen level of significance was 5%. The areas under the receiver operating characteristic (ROC) curve for assessing the predictive values of MPV, PDW and PLCR in predicting the occurrence of acute coronary syndromes were constructed by plotting the sensitivities for all individual cut-off values versus the corresponding (1-specificity). A P value < 0.05 was considered statistically significant.

The data was statistically analyzed for various parameters like age, sex incidence, mean PDW, mean platelet count, mean MPV, and mean plateletcrit and compared among group 1 and group 2.

RESULTS

A detailed clinical examination revealed that 70% (140) of study patients out of 200 were hypertensive, which is one of the major risk factors for MI. Tobacco use was seen in 58% (116) of the study patients accounting for the second most common risk factor in our study. Diabetes mellitus constitutes 38.5% (77) of all study patients. History of smoking was present in 35% (70) of study patients.

In our study, the mean age of patients with ACS (MI) was found to be 58.84 years, patients of age ranging more than 60 year were maximum followed by 51 to 60 year age group. Least affected age groups in our study were patients of less than 30 year and more than 70 year. Males are at more risk for AMI than females. In our study, 74.5% were males while 25.5% of cases were females clearly showing male predominance with male: female ratio is 2.92:1

Figure 1 : Age and Gender distribution in study subjects:

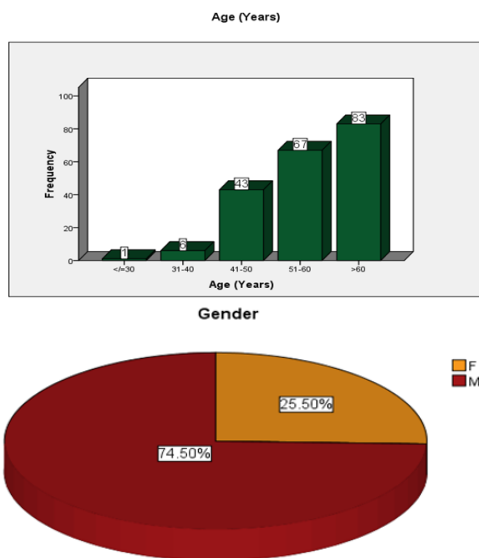


Table 1 : Comparison of platelet indices between Study group :

Characteristics	Study group	N	Mean	Std. Deviation	Std. Error Mean	T	P value
PDW (fL)	ACUTE MI	100	17.89	0.61	0.06	19.80	<0.0001
	STABLE CAD	100	16.51	0.34	0.03		
MPV	ACUTE MI	100	9.86	1.27	0.13	8.73	<0.0001
	STABLE CAD	100	8.55	0.81	0.08		
PCT	ACUTE MI	100	0.21	0.07	0.01	-1.64	0.10
	STABLE CAD	100	0.22	0.07	0.01		

Comparison of platelet indices between Study group was performed using Student's t test. Significant difference was found between two

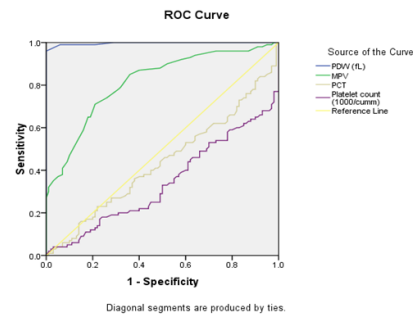
groups for PDW and MPV indicating significantly higher MPV and PDW in subjects with Acute MI. No significant difference was detected between two groups for PCT.

Table 2 : Association of PDW with MI:

			Study group		Total	P Value
			Acute MI	Stable CAD		
PDW (fL)	<=17.05	Count	4	100	104	<0.0001
		% within Study group	4.0%	100.0%	52.0%	
	>17.05	Count	96	0	96	
		% within Study group	96.0%	.0%	48.0%	
Total		Count	100	100	200	
		% within Study group	100.0%	100.0%	100.0%	

Our study revealed that mean PDW in AMI group was 17.89±0.61 fL and in stable CAD patients it was 16.51±0.34 fL. We found that the difference was statistically significant between the two groups with a p-value of <0.001.

Figure 2 : ROC curve for prediction of AMI :



Test Result Variable (s)	Area	Std. Error ^a	P Value. ^b	Asymptotic 95% Confidence Interval		Diagnostic cut off	Sensitivity (%)	Specificity (%)
				Lower Bound	Upper Bound			
				PDW (fL)	.997			
MPV (fL)	.814	.030	.000	.756	.873	9.15	79	71
PCT (%)	.564	.041	.120	.484	.643	0.168	81	34
Platelet count (1000/cumm)	.659	.038	.000	.583	.734	149.5	97	31

The sensitivity, specificity, positive and negative predictive values were determined through ROC curve. PDW was found to be 88% sensitive and 100% specific whereas MPV was 79% sensitive and 71% specific as an early indicator in the prediction of impending acute coronary event.

DISCUSSION

The findings of our study clearly indicate that MPV and PDW at admission are significantly higher in patients with diagnosed AMI as compared to the patients with stable coronary disease. Patients with increased PDW could be identified easily and play an important role in early initiation of anti-platelet therapy, thereby preventing development of full blown ACS. It can be used as a screening test of ACS. The findings of PDW and MPV in our study will enrich diagnostic modalities in patients with ACS.

As our study was cross-sectional with relatively less sample size we suggest further studies to assess whether PDW provide beneficial role to identify patients at early stages of ACS, clinical risk and whether therapeutic modification of this marker may lead to improved cardiovascular risk.

Table 3: Comparison of age in various studies:

Author	Year	Mean age in years	
		ACS	Stable CAD
Vitthal Khode et al ⁸	2012	54.77±9.09	55.75±11.06
Ugur Turk et al ⁹	2013	59.9±10.8	60.7±11.0
Jaya Manchanda et al ¹⁰	2015	57.76±13.19	-
Mohamed Abdirahman Abdinur et al ¹¹	2017	65.19±10.95	62.84±9.14
Present study	2017	58.84±9.74	59.00±11.17

Table 4 : Comparison of PDW in various studies:

AUTHOR	YEAR	PDW (fL)			P- VALUE
		ACS(MI)	STABLE CAD	CONTROL	
M.M.Khandekar et al ¹²	2006	13.19±2.34	11.35±1.95	10.75±1.42	<0.001
Abdullah S.Assiri et al ¹³	2011	15.88±1.5		11.96±1.8	0.001
Sajal Gupta et al ¹⁴	2012	17.67±1.41		16.97±1.67	<0.05
Vitthal Khode et al ⁸	2012	10.84±2.2	10.65±1.7	10.35±1.3	0.376
Silpi Pervin et al ⁵	2013	16.23±2.56		11.89±1.42	0.001
Salim R.Hamudi Al-Obeidi et al ¹⁵	2013	21.6%±1.5%		15%±2.3%	<0.001
Neelam Bharihoke et al ¹⁶	2014	16.45±0.79	16.03±2.46	15.63±0.70	0.0002
Jaya Manchanda et al ¹⁰	2015	13.49±3.67	-	12.23±3.13	0.018
Awad Elkareem Abass et al ¹⁷	2016	15.9	13.1	12.2	0.01
Satish Basanagouda et al ¹⁸	2016	11.3±1.5		10.2±1.5	0.000
Mohamed A.A. et al ¹¹	2017	13.89±2.16	13.85±2.68	12.58±2.11	0.010
Present study	2017	17.89±0.61	16.51±0.34		<0.001

Our study revealed that mean PDW in AMI group was 17.89±0.61fL and in stable CAD patients it was 16.51±0.34 fL. **Silpi Pervin et al (2013)** ⁵ found that among the platelet parameters, PDW was more significant than MPV and suggested that higher PDW may become useful marker for early detection of ACS along with other biomarkers. **Smith NM** ¹⁹ observed increase PDW and MPV are index of platelet size and correlates with platelet activation, and also a reliable index of platelet activation. It may be a potentially useful marker in cardiovascular risk stratification. However **Vitthal Khode et al (2012)** ⁸ in a study of 128 patients including 39 patients with AMI, 24 patients with stable CAD and 65 controls found that the difference in PDW among the three groups was not statistically significant.

Our study showed higher mean platelet volume (MPV) in AMI patients (9.86±1.27 fL) as compared to stable CAD patients who had mean MPV of 8.55±0.81fL. The difference among the two groups was statistically significant with a p-value of <0.001. This finding is in concordance with the findings of **M.M.Khandekar et al** ¹², **Vitthal Khode et al** ⁸, **Neelam Bharihoke et al** ¹⁶ and **Chu et al** ²⁰.

The mean platelet count in AMI patients was 216.13±92.74 ($\times 10^9/L$) whereas in stable CAD patients it was 261.20±77.30 ($\times 10^9/L$). Platelet count in AMI patients was found lower than that in stable CAD patients and the difference was statistically significant. The finding was in concordance with **M.M.Khandekar et al** ¹², **Neelam Bharihoke et al** ¹⁶ and **Deepshikha Sharma et al** ²¹. However **Awad-Elkareem Abass et al (2016)** ¹⁷ found that there was no significant difference in platelet counts in ACS patients as compared to stable CAD patients. Also **Abdullah S. Assiri et al (2011)** ¹³ did not detect a statistically significant difference regarding the platelet count (PC) among the three groups (i.e. MI, unstable angina and control group).

This discrepancy in findings regarding the Platelet Count and agreement on findings regarding the platelet volume parameters among different studies in ACS patients might indicate that the platelet volume indices rather than the platelet count are more important in determining the risk of developing ACS. ¹³

We found that plateletcrit was slightly higher in stable CAD patients than in AMI patients and the difference was not statistically significant. Plateletcrit failed to prove its significance due to conflicting results obtained in various studies.

The sensitivity, specificity, positive and negative predictive values were determined through ROC curve. PDW was found to be 88% sensitive and 100% specific whereas MPV was 79% sensitive and 71% specific as an early indicator in the prediction of impending acute coronary event.

CONCLUSION

The metamorphic platelets are haemostatically more active and are a risk factor for developing coronary thrombosis, leading to myocardial infarction. The present cardiac markers are not sufficiently sensitive at an early stage of ACS, thus it is important to investigate the risk factors for an impending acute coronary event.

We conclude that platelet volume parameters mainly PDW and MPV are readily available, relatively inexpensive and useful markers which we detected to be significantly raised in the patients admitted with AMI

as compared to patients admitted with stable CAD. They should be utilized along with other investigational tools to screen patients presenting to the emergency room with chest pain who are suspected to have AMI.

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