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RESEARCH ARTICLE

A study of Platelet Volume Indices (PVI) in patients of coronary artery disease and acute myocardial infarction in tertiary care hospital

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Abstract

SUMMARY: The study was performed to analyse PVI that are useful for identifying large platelets, which are haemostatically more active and risk factor for developing coronary thrombosis and myocardial infarction.

INTRODUCTION: Ischemic heart disease is the leading cause of death worldwide. Platelets have definite role in causing its pathogenesis and its complications. Platelet size reflects its activity. Large platelets are metabolically and enzymatically more active and produce more thromboxane A2.

METHOD AND MATERIALS: In this retrospective study, 200 cases were studied, 100 patients had unstable angina (UA) or acute myocardial infarction (AMI), 70 patients had stable coronary artery disease (stable CAD). The third group comprised 30 healthy control from health check-up with no history of heart disease and normal electrocardiogram. The anticoagulated peripheral blood sample was collected from each patient and analysed in a 3-part automated hematology analyser.

RESULT: All three Platelet indices i.e. Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet to Large Cell Ratio (P-LCR) were increased in patients of UA and AMI. Mean MPV was 11.2 fl, mean PDW was 14.3 fl and mean P-LRC was 28.6% in unstable coronary artery disease. In stable coronary artery disease, mean MPV was 10.7 fl, mean PDW was 13.2 fl and mean P-LRC was 23.0%. In the control group mean MPV was 9.3 fl, mean PDW was 11.3 fl and mean P-LRC was 19.86%.

CONCLUSION: Patients with large platelets can be identified during routine work up. PVI is simple, effortless and cost effective tool for predicting possibility of impending acute events and further patients can be refereed for preventive measures**.**

Introduction

Coronary artery disease (CAD) is new epidemic afflicting Indians in recent years. Both endogenous and exogenous risk factors such as smoking, diabetes mellitus, hypertension, hypercholesterolemia, mental stress, and obesity—acting either singly or in combination—significantly increase the chances of developing coronary atherosclerosis. Platelets have been implicated in the pathogenesis of cardiovascular disorders, including atherosclerosis and its complications, such as acute myocardial infarction (AMI), unstable angina (UA), and sudden cardiac death. Platelet hyper-reactivity and local platelet activation have been suggested to play a causal role in acute coronary events.[(1)] Platelet size has been shown to reflect platelet activity. Large platelets are metabolically and enzymatically more active than

small platelets and produce more thromboxane A2.[2,3]

"Our aim was to study platelet parameters in the spectrum of ischemic artery disease and to attempt a clinicopathological correlation"

Automated cell counters have made the platelet count (PC) and the platelet volume indices (PVI)—mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR)—routinely available in most clinical laboratories. However, there is scope to make better use of the platelet parameters generated. The MPV can reflect changes in either the level of platelet stimulation or the rate of platelet production. Platelet activation is indirectly measured via MPV. Thus, our aim was to study platelet parameters in the spectrum of ischemic artery disease and to attempt a clinicopathological correlation.

Materials and methods

A retrospective hospital based study was carried out on 200 patients over a period of six months.

Three groups were studied. Group A: patients admitted to the intensive care unit with UA and/or AMI (100 patients); group B: patients with stable CAD admitted for coronary angiography or a coronary artery bypass graft procedure for a previous ischemic event (70 patients); and group C: healthy controls from health check-up with no history of heart disease and normal electrocardiogram (30 patients).

We used the histograms which were preserved in our clinical and hematological laboratory after running sample. 2 ml of blood was collected in dipotassium EDTA tubes from all the patients on day 1 and also on day 7 for patients with acute coronary events. The sample was run within two hours of venepuncture using the Sysmex KX 21 automated cell counter in which Internal and external quality controls were strictly followed.

The obtained parameters were evaluated using descriptive statistical analysis. Statistical analyses were performed using the IBM SPSS (Statistical Package for the Social Sciences v15.0) and Microsoft Excel 2007 software. The Student's *t*- test and the one way analysis of variance test were used for comparing the group means. The $\chi 2$ test was used and p values of < 0.05 were taken as significant.

Results

Of the 200 patients enrolled in our study, all 18 parameters were generated by the Sysmex KX 21analyser were statistically analysed. The mean (SD) age of the patients was 51 (SD +/- 10) years with an equal sex predilection (male to female ratio, 1 : 1). This is in accordance with the Asian population at risk for an ischemic heart disease, occurring one decade earlier than in developed countries[4], and equally prevalent among premenopausal women. In our present study, risk factors were evaluated and were evenly distributed. However, significantly more numbers of patients who were diabetics, current smokers, had Hypertriglyceridemia and hypercholesterolemias were present in groups A and B than in group C (table 1).

Table 1: Distribution of risk factors in all the patients

Groups	Group A (n = 100)	Group B (n = 70)	Group C (n = 30)	p Value
Hypertension	22	20	5	NS
Diabetes mellitus	20	10	1	<0.05
Current smokers	20	15	1	<0.05
Hypercholesterolemia	10	05	0	<0.05
Hypertriglyceridemia	10	03	0	<0.05
BMI (obese)	03	02	0	NS
No risk factor	00	00	23	NS
Aspirin	10	10	0	NS
Clopidogrel	05	05	0	NS

BMI- body mass index; NS- not significant.

The white blood cell count was significantly raised in the AMI group compared with the CAD and control groups (table 2).

Table 2: Distribution of hematological (Sysmex) parameters in all the cases

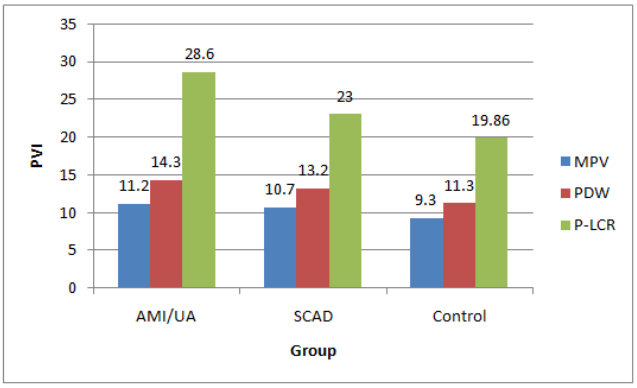
	Group A	Group B	Group C	p Value
Haemoglobin (gm/dl)	12.3(2)	12.1(2.1)	12.5 (1.56)	NS
Haematocrit (%)	35.01 (6.96)	35.14 (7.01)	36.95 (3.24)	NS
WBC ($\times 10^9$/l)	11.2 (4.21)	9.64 (5.05)	6.58 (1.01)	<0.05
PC ($\times 10^9$/l)	220.24 (78.2)	224.2 (74)	274.42 (70.2)	<0.05
PDW (fL)	14.3 (2.20)	13.2 (2)	11.3 (1.44)	<0.001
MPV (fL)	11.2 (1.20)	10.7 (0.96)	9.3 (0.94)	<0.001
P-LCR (%)	28.6 (7)	23.0 (6)	19.86 (5.54)	<0.001

Values are mean (SD), MPV- mean platelet volume; PC- platelet count; PDW- platelet distribution width; P-LCR- platelet large cell ratio; WBC- white blood cell count

No significant difference in PC was seen between groups A and B ($p > 0.05$) or between groups B and C ($p > 0.05$), although the lowest values were seen in group A, followed by group B, and group C. However, a significant difference was seen when the mean PC was compared between the AMI and control groups ($p < 0.05$).

PVI—PDW, MPV, and P-LCR—were significantly raised in group A compared with the group B- stable CAD and group C- control groups (fig 1).

Figure 1: Platelet volume indices in all patients (groups A, B, and C). MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet large cell ratio.



PVI could be measured on day 7 in only 80 of the 100 patients in group A because five patients died before day 7 and 15 patients were discharged. The PC values on day 1 (mean- 220.24 SD- 78.2) and day 7 (mean, 226.2 (SD, 84.2) in group A patients were not significantly different. Similarly, PVI values on day 1 and day 7 were not significantly different. Of the 100 patients, five succumbed to the disease within a week of admission. Mortality among female patients was higher: four women died whereas only one man died. There were no significant differences in the PC and PVI values between the five patients who died and the survivors in group A.

The PC and PVI were independently correlated with: (1) type of infarct/ischemia on electrocardiogram—that is, subendocardial type (62 patients) versus transmural type (38 patients); (2) the site of the infarct (anterior wall, lateral wall, posterior wall, others, and unknown); (3) the severity of the infarct as subtyped using Killips classification—types I–IV; (4) the time before starting treatment (within 24 hours, one to three days, four to seven days); (5) the number of ischemic episodes; and (6) the number of coronaries blocked. No correlations were seen between these parameters. There were no significant differences in PVI and PC values between patients with UA and AMI (table 3).

No correlation was seen between the PVI and haemoglobin value, haematocrit value, or total leucocyte count. No significant effect was noted of antiplatelet drugs, aspirin, or clopidogrel on the PC and PVI results.

The log normality of the platelet distribution curve was preserved in acute coronary events and showed a shift of the whole curve to the right compared with the controls (fig 2). Univariate analysis of the MPV quartiles indicated a value of more than 9.4 fL to be a

significant risk factor for developing a myocardial infarction (MI).

Table 3: Comparison of PVI values in patients with AMI and UA in group A

Type	Total no.	PC (×109/l)	PDW (fL)	MPV (fL)	P-LCR (%)
AMI	70	220.64	14.8	11.4	29.2
UA	30	220.1	14.1	11.0	28.4
p Value	100	NS	NS	NS	NS

AMI, acute myocardial infarction; MPV, mean platelet volume; NS, not significant; PC, platelet count; PDW, platelet distribution width; P-LCR, platelet large cell ratio; PVI, platelet volume indices; UA, unstable angina.

Table 4: Comparison of MPV in AMI and controls in different studies

	AMI		Controls		
Publication	N	MPV (fL)	N	MPV (fL)	p Value
O'Brien *et al* (1973)5	23	8.10	36	7.01	<0.001
Cameron *et al* (1983)6	100	9.07 (SE, 0.08)	200	8.32 (SE, 0.07)	<0.001
Martin *et al* (1983)7	15	7.3	22	6.32	0.05
Martin *et al* (1991)8	126	10.09 (1.43)	1590	9.72 (1.12)	<0.001
Pizulli *et al* (1998)10	108	9.4 (1.23)	97	8.2 (0.95)	<0.001
Vitthal Khode et al (2012)9	39	9.65 (0.9)	65	9.21 (0.6)	0.025
Present study	100	11.2 (1.20)	30	9.30 (0.94)	<0.001

Table 5: Comparison of PDW in AMI and controls in different studies

	AMI/UA		Controls		
Publication	N	PDW (fL)	N	PDW (fL)	p Value
M.M. Khandekar et al (2006)17	94	13.19 (2.34)	30	10.75 (1.42)	<0.001
Vitthal Khode et al (2012)9	39	10.84 (2.2)	65	10.35 (1.3)	0.376
Present study	100	14.3 (2.20)	30	11.3 (1.44)	<0.001

Table 6: Comparison of P-LCR in AMI and controls in different studies

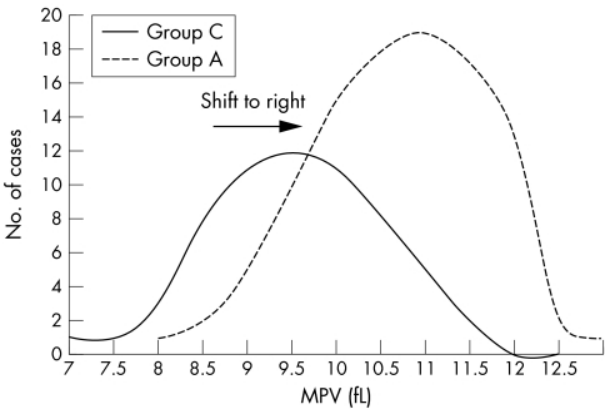
	AMI/UA		Controls		
Publication	N	P-LCR	N	P-LCR	p Value
M.M. Khandekar et al (2006)17	94	29.4 (7.38)	30	20.65 (6.14)	<0.001
Vitthal Khode et al (2012)9	39	21.58 (6)	65	19.93 (4.6)	0.315
Present study	94	28.6 (7)	30	19.86 (5.54)	<0.001

Discussion

We found that PVI (MPV, PDW, and P-LCR) are raised in patients who have suffered an acute coronary event compared with controls and those with stable CAD. This is in agreement with the

results of similar studies by other workers (table 4,5,6).

Fig 2: Normal mean platelet volume curve in patients in groups A and C.



Values are mean (SD) unless otherwise stated. AMI-acute myocardial infarction; MPV- mean platelet volume.

Generalised platelet activation occurs before an acute coronary event. The increase in platelet consumption at the site of the coronary atherosclerotic plaque causes larger platelets to be released from the bone marrow. The fact that the increase persists even after discharge from hospital supports the view that platelet volume is chronically larger in the infarct group[(6,8)] This suggests that PVI, particularly MPV, are indicators of the degree of damage already done and that these markers maintain their strength and predictive value for a long time. However, some workers found no correlation between the time span between MI and measurement of MPV.[(10)] The same group also suggested that MPV does not change during the acute phase reaction, but is determined by other factors. There are studies indicating that platelet size is determined at the level of the progenitor cell. Megakaryocyte ploidy is influenced by interleukin 3 and interleukin [6], which leads to the production of larger platelets that are more reactive.[11,12,13] Using logistic regression analysis of MPV quartiles, we found that a value of > 9.4 fL was a significant risk for developing MI in patients with CAD, whereas a figure of > 11.6 fL was determined by Endler *et al*.[14]

"Our data suggest that the increased MPV, PDW and P-LCR contribute to the prethrombotic state in acute ischemic syndromes and that larger platelets may play a specific role in infarction"

The preservation of log normality of the platelet volume, consistent with the study by Martin *et al*,[7] indicates that the increase in volume is not the result of consumption or production of a platelet subpopulation, because the whole distribution curve was shifted to the right.

Conclusion

- Platelet volume indices (PVI) are a useful means of identifying larger platelets, which are haemostatically more active and are a risk factor for developing coronary thrombosis, leading to myocardial infarction.
- Patients with larger platelets can easily be identified during routine hematological analysis and could possibly benefit from preventive treatment.
- Therefore, PVI are an important, simple, effortless, and cost effective tool that should be used more extensively to predict impending acute events

We found no association between the type and site of infarct and MPV, as has been reported by others.6,8 PC and PVI were not associated with mortality, morbidity, or the severity of MI in our present study, whereas Martin *et al* found that MPV was significantly higher in those patients who died of MI, compared with survivors.[8] Some studies have found higher MPV values in patients with UA than those with MI.15 However, we found no such difference between patients with UA and AMI, as also reported by Senaran *et al*.[16]

The role of PDW specifically in patients with CAD and acute coronary events is yet to be explored. Similarly, the P-LCR is not often quoted in the literature, probably because it is a relatively new PVI parameter.

Our data suggest that the increased MPV contributes to the prethrombotic state in acute ischemic syndromes and that larger platelets may play a specific role in infarction. Because larger platelets are haemostatically more active, the presence of larger platelets is probably a risk factor for developing coronary thrombosis and MI. Patients with larger platelets can easily be identified during routine

hematological analysis because PVI are generated as a byproduct of automated blood counts. Thus, in conclusion, PVI provide an important, simple, effortless, and cost effective tool, which can be useful in predicting an impending acute coronary event.

Abbreviations

AMI - acute myocardial infarction

CAD - coronary artery disease

MI - myocardial infarction

MPV - mean platelet volume

PC - platelet count

PDW - platelet distribution width

P-LCR - platelet large cell ratio

PVI - platelet volume indices

UA - unstable angina

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