

ORIGINAL ARTICLE

Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario

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J Clin Pathol 2006;**59**:146–149. doi: 10.1136/jcp.2004.025387**Aims:** To study platelet volume indices (PVI) in the spectrum of ischaemic heart diseases.**Methods:** A total of 210 cases were studied; 94 patients had unstable angina (UA) or acute myocardial infarction (AMI) diagnosed on the basis of history, characteristic electrocardiographic changes, and increased cardiac enzyme activities. Seventy patients had stable coronary artery disease (stable CAD) or were admitted for a coronary angiography or coronary artery bypass graft procedure. The third group comprised 30 age and sex matched healthy controls with no history of heart disease and a normal electrocardiogram.**Results:** All PVI—mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR)—were significantly raised in patients with AMI and UA (mean MPV, 10.43 (SD, 1.03) fL; mean PDW, 13.19 (SD, 2.34) fL; mean P-LCR, 29.4% (SD, 7.38%)) compared with those with stable CAD (mean MPV, 9.37 (SD, 0.99) fL; mean PDW, 11.35 (SD, 1.95) fL; mean P-LCR, 22.55% (SD, 6.65%)) and the control group (mean MPV, 9.2 (SD, 0.91) fL; mean PDW, 10.75 (SD, 1.42) fL; mean P-LCR, 20.65% (SD, 6.14%)).**Conclusions:** Larger platelets 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 haematological analysis and could possibly benefit from preventive treatment. Thus, PVI are an important, simple, effortless, and cost effective tool that should be used and explored extensively, especially in countries such as India, for predicting the possibility of impending acute events.

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Accepted for publication 7 May 2005

In the new millennium, coronary artery disease (CAD) is looming large as the new epidemic afflicting Indians. Both endogenous and exogenous risk factors such as smoking, diabetes mellitus, hypertension, hypercholesterolaemia, 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 ischaemic 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 ischaemic artery disease and to attempt a clinicopathological correlation.

MATERIALS AND METHODS

A prospective hospital based study was carried out on 210 patients over a period of one year. Institutional ethical committee clearance was obtained. Informed consent was given.

Three groups were studied. Group A: patients admitted to the intensive care unit with UA and/or AMI (94 patients); group B: patients with stable CAD admitted for coronary angiography or a coronary artery bypass graft procedure for a previous ischaemic event (70 patients); and group C: age and sex matched normal healthy controls with a normal electrocardiogram (30 patients).

Blood (2 ml) was collected in dipotassium EDTA tubes from all the patients on day 1 and also on day 7 for patients with acute coronary events by a clean puncture, avoiding bubbles and froth. The sample was run within two hours of venepuncture using the Sysmex K-4500 automated cell counter (TOA Electronics, Kobe, Japan)

Quality control

Internal and external quality controls were strictly followed.

Statistical analysis

Statistical analysis of the data was carried out using the statistical package for social sciences. The Student's *t* test and the one way analysis of variance test were used for comparing the group means. The χ^2 test was used and *p* values of < 0.05 were taken as significant.

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

Table 1 Distribution of risk factors in all the patients

Groups	Group A (n=94)	Group B (n=70)	Group C (n=30)	χ^2	p Value
Hypertension	23 (24.4)	20 (28.5)	7 (23.3)	0.46	NS
Diabetes mellitus	14 (14.8)	10 (14.2)	2 (6.6)	1.4	NS
Current smokers	18 (19.1)	15 (21.4)	5 (16.6)	0.32	NS
Hypercholesterolaemia	20 (21.2)	17 (24.2)	0 (0)	8.6	<0.05
Hypertriglyceridaemia	14 (14.8)	7 (10)	0 (0)	1.47	NS
BMI (obese)	11 (11.7)	13 (18.5)	0 (0)	6.7	<0.05
Manual activity	13 (13.8)	10 (14.2)	4 (13.3)	0.02	NS
Aspirin	17 (18)	20 (28.5)	0 (0)	1.96	NS
Clopidogrel	8 (8.5)	14 (20)	0 (0)	3.62	NS

Figures in parenthesis indicate percentages.
BMI, body mass index; NS, not significant.

RESULTS

Of the 210 patients enrolled in our study, all 18 parameters were generated by the Sysmex analyser in 194 and were statistically analysed. Five samples were clotted and were excluded from the study. In the remaining 11 (nine in group A and two in group B) samples, only the PC value was obtained and PVI were flagged, indicating an abnormality sensed by the machine and the need for manual evaluation of a peripheral blood smear by an expert morphologist. Many giant sized platelets (more than 5 μm in diameter as judged on the blood smear) were noted in these patients.

The mean (SD) age of the patients was 53.9 (11.3) years with an equal sex predilection (male to female ratio, 1 : 1). This is in accordance with the Asian population at risk for an ischaemic 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 obese and had hypercholesterolaemia were present in groups A and B than in group C (table 1).

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

No significant difference in PC was seen between groups A and B (t value, -0.59 ; $p > 0.05$) or between groups B and C (t value, -1.76 ; $p > 0.05$), 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 (t value, 2.10; $p < 0.05$).

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

PVI could be measured on day 7 in only 78 of the 94 patients in group A because six patients died before day 7 and nine patients were discharged. The PC values on day 1 (mean, 236.7 (SD, 93.7) and day 7 (mean, 237.2 (SD, 93.2) in group A patients were not significantly different. Similarly, PVI values on day 1 and day 7 were not significantly different. Of

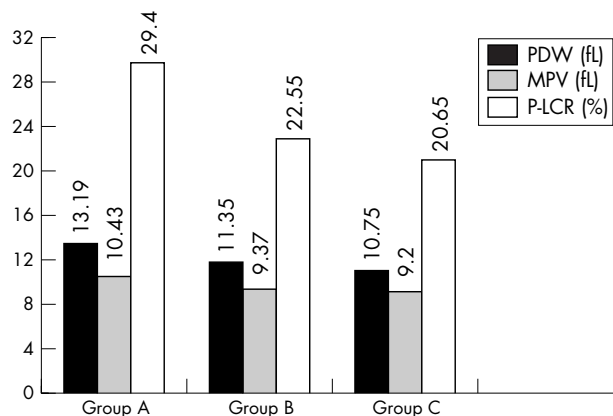


Figure 1 Platelet volume indices in all patients (groups A, B, and C). MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet large cell ratio.

the 94 patients, six succumbed to the disease within a week of admission. Mortality among female patients was higher: five women died whereas only one man died. There were no significant differences in the PC and PVI values between the six patients who died and the survivors in group A.

The PC and PVI were independently correlated with: (1) type of infarct/ischaemia on electrocardiogram—that is, subendocardial type (70 patients) versus transmural type (24 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 Killip's 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 ischaemic 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).

Risk factors such as diabetes mellitus, hypertension, body mass index, physical activity, smoking, hypercholesterolaemia, and hypertriglyceridaemia were not a confounding

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

	Group A	Group B	Group C	F value	p Value
Haemoglobin (g/l)	121.7 (2.68)	122.1 (2.59)	126.6 (1.68)	0.45	NS
Haematocrit	353.8 (7.38)	354.8 (7.42)	372.5 (4.09)	0.87	NS
WBC ($\times 10^9/l$)	10.4 (4.37)	9.52 (5.80)	7.42 (1.49)	4.68	<0.05
PC ($\times 10^9/l$)	232.84 (88.8)	240.79 (79.0)	270.77 (75.2)	3.39	<0.05
PDW (fL)	13.19 (2.34)	11.35 (1.95)	10.75 (1.42)	5.32	<0.001
MPV (fL)	10.43 (1.03)	9.37 (0.99)	9.20 (0.91)	6.63	<0.001
P-LCR (%)	29.4 (7.38)	22.55 (6.65)	20.65 (6.14)	6.09	<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.

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

Type	Total no.	PC ($\times 10^9/l$)	PDW (fL)	MPV (fL)	P-LCR (%)
AMI	77	235.3 (92.6)	13.1 (2.1)	10.4 (1.0)	29.30 (7.4)
UA	17	221.4 (70.4)	13.7 (3.1)	10.5 (1.0)	29.8 (7.2)
t Value		0.58	1.06	0.24	0.27
p Value		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.

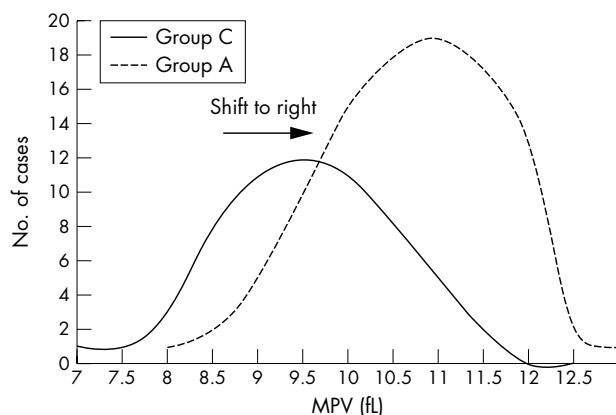


Figure 2 Normal mean platelet volume curve in patients in groups A and C. MPV, mean platelet volume.

factor in the determination of PVI and PC in acute coronary events, and neither were the readings affected by age or sex. 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 9.6 fL to be a significant risk factor for developing a myocardial infarction (MI).

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).

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.¹¹⁻¹³ Using logistic regression analysis of MPV quartiles, we found that a value of > 9.6 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 mean platelet volume contributes to the prethrombotic state in acute ischaemic 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

Take home messages

- 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 haematological analysis and could possibly benefit from preventative treatment
- Therefore, PVI are an important, simple, effortless, and cost effective tool that should be used more extensively to predict impending acute events

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

Publication	AMI		Controls		p Value
	N	MPV (fL)	N	MPV (fL)	
O'Brien <i>et al</i> (1973) ⁵	23	8.10	36	7.01	<0.001
Cameron <i>et al</i> (1983) ⁶	100	9.07 (SE, 0.08)	200	8.32 (SE, 0.07)	<0.001
Martin <i>et al</i> (1983) ⁷	15	7.3	22	6.32	0.05
Martin <i>et al</i> (1991) ⁸	126	10.09 (1.43)	1590	9.72 (1.12)	<0.001
Smyth <i>et al</i> (1993) ⁹	24	8.54 (0.6)	23	8.1 (0.69)	0.04
Pizulli <i>et al</i> (1998) ¹⁰	108	9.4 (1.23)	97	8.2 (0.95)	<0.001
Present study	94	10.43 (1.03)	30	9.20 (0.91)	<0.001

Values are mean (SD) unless otherwise stated.

AMI, acute myocardial infarction; MPV, mean platelet volume.

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.

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 parameter is generated by only a few machines, with the Sysmex analyser being one of them. It 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 ischaemic 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 haematological 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.

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