

Original Article

Study comparing platelet indices between stable angina, acute coronary syndrome with age sex matched normal controls

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Background: Platelet activation is a key factor in the development of coronary artery disease (CAD) and associated acute symptoms. Mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) are all easy and cheap blood tests that show how reactive platelets are. They could also be used as stand-ins for acute coronary syndrome (ACS).

Objectives: To compare platelet indices (MPV, PDW, PCT, and platelet count) among patients with acute coronary syndrome, stable angina, and age- and sex-matched healthy controls, and to evaluate their potential value in predicting ACS.

Materials and Methods: This cross-sectional comparison study was undertaken at Santokba Durlabhji Memorial Hospital cum Medical Research Institute in Jaipur, India, from September 2020 to August 2021. A total of 150 volunteers were recruited and categorized into three groups: acute coronary syndrome (n=50), stable angina (n=50), and healthy controls (n=50). We used an automated hematology analyzer (XN-1000 Sysmex) to assess platelet indices in blood samples that had been treated with EDTA to stop them from clotting. We used one-way ANOVA and Bonferroni post-hoc tests to do the statistical analysis. A p-value of less than 0.05 was considered statistically significant.

Results: The mean age and sex distribution were similar among the three groups ($p>0.05$). The mean platelet volume (MPV) and platelet distribution width (PDW) were significantly elevated in cases (acute coronary syndrome and stable angina) relative to controls (MPV: $p<0.001$; PDW: $p=0.003$). The ACS group had the highest MPV and PDW values, although the difference between ACS and stable angina was not statistically significant. Platelet count was considerably reduced in ACS patients relative to those with stable angina ($p=0.045$). ROC curve study indicated that MPV and PDW provide limited discriminatory power for predicting ACS, however increased sensitivity was noted at lower cut-off values.

Conclusion: MPV and PDW are markedly enhanced in individuals with coronary artery disease, especially in acute coronary syndrome (ACS), indicating heightened platelet activation. While their specificity is constrained, these indices may function as adjunctive, economical screening indicators for patients exhibiting probable ACS and stable angina when analyzed in conjunction with clinical and biochemical metrics.

Keywords: Please provide 3 to 6 keywords which can be used for indexing purposes.

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INTRODUCTION

There has been growing increase in cases of coronary artery disease in epidemic proportion in India. 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. The acute coronary syndromes (ACS) includes ST elevated myocardial infarction (STEMI), Non ST elevated myocardial infarction (NSTEMI) and unstable angina (UA). Platelets not only act as mediators in thrombus formation but have potent inflammatory properties. They induce inflammatory response in nearby adjacent cells like leukocytes and endothelial cells. This bidirectional interaction between platelets and inflammatory cells causes continuing or non resolving inflammation in atherosclerosis^{1,2}. The

increased platelet reactivity causing shorter bleeding time is associated with increased platelet volume. The larger sized platelets with higher volume have more dense granules consequently they are more active enzymatically and metabolically with higher thrombotic potential³. These metabolically active platelets have higher level of procoagulatory surface proteins such as β selectin and glycoprotein III a^{4,5}. The acute coronary syndrome have been shown to be associated with higher mean platelet volume (MPV). MPV been marker of platelet function and is indicative of more reactive platelets which are associated with myocardial damage in ACS. The higher MPV has been associated with unfavourable outcome among survivor of AMI^{6,7}. Therefore larger platelets as measured by hematological analyzers (MPV) may be useful marker in patients with ACS. It could play an important role in the early detection of acute coronary syndrome (ACS) and , could be beneficial in strategies for preventive treatment. The other platelet index – platelet distribution width (PDW) provides information about the range of platelet size in blood sample and is more specific indicator of platelet activation than MPV as it does not increase during platelet swelling.^{8,9,10} Patients with higher plateleterit (PCT) and PDW are at increased risk of ACS.

MATERIAL AND METHODS

A cross sectional study was carried out at Santokha Durlabhji Memorial Hospital cum Medical Research Institute Jaipur, india from 1 september 2020 to 30 august 2021. Sample Size was calculated at 80% study power and alpha error of .05, expecting standard deviation of 10.6 for PLCR as found in reference study. For minimum detectable difference in PLCR of 7 as found in reference study between stable and unstable angina group.46 patients in each of these groups are required as sample size which is further enhanced and rounded off to 50 patients in each of 3 groups as final sample size for present study expecting 10% attrition. Formula used for sample size as follows- $n = (Z\alpha/2 + Z\beta)^2 * 2*\sigma^2/d^2$ Where $Z\alpha/2$ is the critical value of normal distribution at $\alpha/2$ (e.g. for a confidential level of 95%, α is 0.05 and the critical value is 1.96), $Z\beta$ is the critical value of normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84), σ^2 is the population variance, and d is the difference we would like to detect

3 groups were included in the study each consisting of 50 patients. GROUP 1 Age >18 years. Patient with diagnosis of ACS based on ECG or Echocardiography or Positive Trop-T, or h/o typical resting chest pain. 3 Those who consent for participation in study. GROUP 2 Age >18 years. Patients with Diagnosis of stable CAD (angina on exertion), absence of dynamic ECG and Echocardiographic changes, negative Trop-T. Those who consent for participation in study.

Critically ill patients. , Platelet disorders like thrombocytopenia and thrombocytosis, Patients with clotting disorders, Participants who did not give consent for being part of study are excluded from the study5 ml of blood samples were drawn in EDTA vaccutainer from antecubital vein. Samples were runned within 2hrs of vein puncture using XN-19 1000SYSMEX and platelet indices (MPV, PDW, PCT), relevant investigations like ECG, Cardiac Enzymes (Trop-T) were analysed for confirmation of diagnosis. Parameters on automated analyzer: MPV, Platelet distribution width, plateleterit, platelet count. A written informed consent was obtained from the participants before collecting samples.

STATISTICAL ANALYSIS- Quantitative variables will be summarized as mean, standard deviation and will be analysed by using one way ANOVA test and other parametric test to find out the statistical difference in the three groups average values

Nominal and categorical variables will be presumed as proportions and will be analysed using χ^2 test and other non parametric tests.

p value<0.05 will be taken as significant .

SPSS version 20 software will be used for all statistical calculations

RESULTS

Total 150 cases were collected from the department of cardiology for this study between 1 september 2020 to 30 august 2021

Table No. 1: Mean values of age and platelet indices in cases and control

| Parameter | Diagnosis | N | Mean | SD | Min. | Max. | 'p' value* |
|----------------|-----------|-----|--------|-------|------|------|------------|
| Age | Cases | 100 | 57.61 | 11.00 | 35 | 88 | 0.481 |
| | Control | 50 | 58.86 | 8.37 | 45 | 82 | |
| PCT | Cases | 100 | 0.28 | 0.08 | 0.1 | 0.59 | 0.203 |
| | Control | 50 | 0.26 | 0.12 | 0.05 | 0.56 | |
| Platelet Count | Cases | 100 | 246.84 | 84.24 | 84 | 566 | 0.837 |
| | Control | 50 | 244.00 | 68.38 | 150 | 413 | |
| PDW | Cases | 100 | 14.38 | 3.32 | 8.8 | 22.9 | 0.003 |
| | Control | 50 | 12.71 | 2.74 | 8 | 21.5 | |
| MPV | Cases | 100 | 11.50 | 1.34 | 8.7 | 15.1 | <0.001 |
| | Control | 50 | 10.70 | 1.02 | 8.2 | 13.3 | |

1. There is significant difference in PDW between cases and control
2. There is significant difference in MPV between cases and control

Table No.2

| Parameter | Diagnosis | N | Mean | SD | Min. | Max. | 'p' value* | 'p'<0.05 from** |
|----------------|-----------|----|--------|-------|------|------|------------|-----------------|
| Age | ACS | 50 | 57.82 | 10.69 | 38 | 88 | 0.764 | |
| | SA | 50 | 57.40 | 11.41 | 35 | 78 | | |
| | Control | 50 | 58.86 | 8.37 | 45 | 82 | | |
| PCT | ACS | 50 | 0.27 | 0.07 | 0.1 | 0.44 | 0.256 | |
| | SA | 50 | 0.29 | 0.09 | 0.12 | 0.59 | | |
| | Control | 50 | 0.26 | 0.12 | 0.05 | 0.56 | | |
| Platelet Count | ACS | 50 | 227.26 | 73.28 | 101 | 427 | 0.045 | SA |
| | SA | 50 | 266.42 | 90.47 | 84 | 566 | | ACS |
| | Control | 50 | 244.00 | 68.38 | 150 | 413 | | |
| PDW | ACS | 50 | 14.64 | 3.25 | 8.9 | 22.9 | 0.007 | Control |
| | SA | 50 | 14.11 | 3.40 | 8.8 | 22.7 | | |
| | Control | 50 | 12.71 | 2.74 | 8 | 21.5 | | ACS |
| MPV | ACS | 50 | 11.71 | 1.25 | 8.7 | 14.2 | <0.001 | Control |
| | SA | 50 | 11.30 | 1.40 | 8.9 | 15.1 | | Control |
| | Control | 50 | 10.70 | 1.02 | 8.2 | 13.3 | | ACS,SA |

* ANOVA - Analysis of Variance

**Bonferroni t-test

1. Significant difference in platelet count between ACS and stable angina. The platelet count were significantly lower in ACS patient as compared to stable patient.
2. There is significant difference in PDW between ACS and control, stable angina and control.
3. There is significant difference in MPV between ACS and control, stable and control.
4. MPV and PDW was greater in ACS patient compared to stable but the difference was statistically non significant

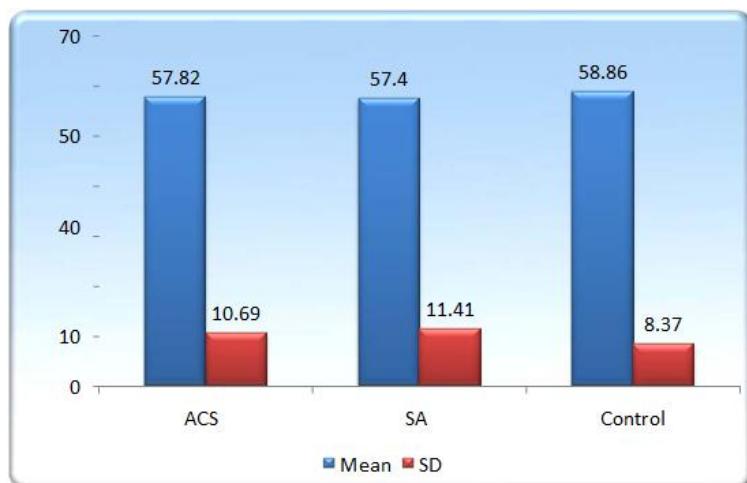


Table No. 3: ROC curve for ACS

| | |
|--------------------------------------|----------------|
| Area under the ROC curve (AUC) | 0.554 |
| Standard Error ^a | 0.0580 |
| 95% Confidence interval ^b | 0.451 to 0.653 |
| z statistic | 0.928 |
| Significance level P (Area=0.5) | 0.3535 |

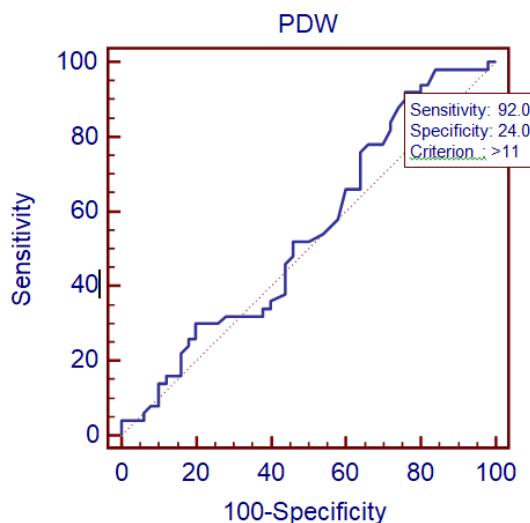
Table No. 4: ROC for PDW

| | |
|--------------------------------------|----------------|
| Area under the ROC curve (AUC) | 0.544 |
| Standard Error ^a | 0.0585 |
| 95% Confidence interval ^b | 0.442 to 0.644 |
| z statistic | 0.759 |
| Significance level P (Area=0.5) | 0.4478 |

Criterion values and coordinates of the ROC curve

| Criterion | Sensitivity | 95% CI | Specificity | 95% CI | +LR | -LR |
|-----------|-------------|-------------|-------------|-------------|------|------|
| >11 * | 92.00 | 80.8 - 97.8 | 24.00 | 13.1 - 38.2 | 1.21 | 0.33 |

Criterion corresponding with highest Youden index



DISCUSSION

Platelet activation plays a central role in the transformation of atherosclerotic cardiovascular disease (CVD) into its potentially major adverse clinical events, such as ischemic stroke and myocardial infarction (MI). Increased platelet activation may also represent the net patho-physiological effects of a number of CVD risk factors, such as smoking and raised cholesterol, thus representing a broad marker of CVD risk. Platelet activation leads to changes in platelet shape (increasingly spherical) with increased platelet swelling leading to an increase in platelet mass and volume. Traditional measures of platelet function/activation, such as the quantification of platelet derived metabolic parameters and the use of platelet aggregometry are technically difficult. Acute coronary syndrome result from acceleration of this chronic process characterized by rupture or fissuring of an unstable atherosclerotic plaque, accompanied by a cascade of platelet reactions resulting into thrombus formation¹¹. Platelets play a crucial role in the pathogenesis of atherosclerotic complications, contributing to thrombus formation or apposition after plaque rupture. After rupture of atherosclerotic plaque in coronary arteries, platelets hyperactivity and local platelets activation have been suggested to play a causal role in prothrombotic events leading to MI. An increased platelet reactivity and shortened bleeding time are associated with increased platelet volume, therefore; platelet size has been considered to reflect platelet level of activity as the large platelets are more active than small platelets and they have a higher thrombotic potential due to high concentration of thromboxane A2.¹¹ We conducted a hospital based cross sectional comparative study with an aim to study the platelet indices in patients with ACS (acute coronary syndrome) and stable angina and to assess whether increase in platelet indices are associated with increased risk of ACS when compared with the stable angina population.

All study participants were similar in terms of age and sex. Mean age of cases was 57.61 ± 11 years while mean age of controls was 58.86 ± 8.37 years ($p > 0.05$) (Table 1, Fig. 1). The age group is younger by a decade in comparison to developed countries. Our finding is in concordance with other studies from Asia where there is increased incidence of cardiovascular disease in younger population.^{12,13} In an another study¹⁴ comprising of ACS and normal healthy controls on MPV the mean age of ACS patient group was 58.7 ± 11.9 years which was similar to our study. ACS group, 36 (72%) were male and 14 (28%) were female. In stable angina group, 32 (64%) were male and 18 (36%) were female, while in control group, 33 (66%) were male and 17 (34%) were female ($p > 0.05$) (Table 3, Fig. 6). Among 50 ACS patients, 14 were diagnosed to have STEMI, 21 as NSTEMI and 15 as unstable angina on the basis of ECG and Troponin levels. As far as smoking history is concerned, there were 32 (64%) smokers in ACS group and 28 (56%) in stable angina group (Table 4, Fig. 7). The history of hypertension was noted in 24 (48%) of ACS patients while in stable angina group a slightly higher 30 (60%) patients were hypertensive (Table 5, Fig. 8). 20 (40%) of patients in ACS group and 18 (36%) in stable angina group were diabetic. (Table 6, Fig. 9) Family history of coronary artery disease was present in 7 (14%) of ACS patients in comparison to 5 (10%) patients of stable angina group (Table 7, Fig 10). The stable angina group had higher number of patients taking antiplatelet medications, 13(26%) in comparison to ACS group where only 2 (4%) patients on antiplatelet drugs (Table 8, Fig. 11). In our study, among 100 cases of ACS and stable angina, mean platelet volume (MPV) ranged from 8.7 fl to 15.1 fl, (mean of 11.5 ± 1.34 fl), while MPV of controls ranged from 8.2 fl to 13.3 fl, (mean of 10.7 ± 1.02 fl). The difference was statistically significant ($p < 0.001$) (Table 1).

CONCLUSION

In our study PDW and MPV showed statistically significant difference between cases and controls with p values 0.003 and < 0.001) respectively. • The MPV and PDW values were higher in ACS group than the stable angina group although the result was not statistically significant. • Based on our study, the cut off value for predicting cardiovascular disease with 94% sensitivity and 26% specificity was 10.1 fl. • Based on our study, 11fl PDW cut off had 92% sensitivity and 25% specificity for predicting cardiovascular disease. • MPV and PDW therefore can be used very carefully as a screening tool for patients of ACS and unstable angina. • The significant difference between MPV and PDW in control, patients with ACS and stable angina could help us in screening patients visiting cardiac OPD for undergoing cardiovascular disease

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