Original Research Article

Evaluation of platelet indices in patients with acute coronary syndrome and chronic stable angina

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ABSTRACT

Background: The objective of the study was to evaluate the levels of platelet indices mean platelet volume (MPV) and platelet distribution width (PDW) in patients with acute coronary syndrome (ACS) and chronic stable angina (CSA) and to study its correlation with the occurrence of disease.

Methods: This was a hospital-based, case-control, prospective observational study which included 333 patients who fulfilled inclusion and exclusion criteria. All the patients were divided into three groups after clinical investigations: i) 100 patients in ACS group, ii) 114 patients in CSA group and iii) 119 patients in control group. MPV and PDW levels were estimated in all the patients along with other routine investigations related to coronary artery disease. All the data were analyzed using independent sample t-test, ANOVA and Pearson correlation at 95% level of significance.

Results: Troponin levels were significantly higher in ACS group compared to CSA and control group (p<0.0001). Mean MPV levels in ACS (15.57±2.11 fL) and CSA (11.27±1.7 fL) groups were significantly higher (p<0.0001) compared with controls (10.48±1.49 fL). A significant elevation in MPV levels was observed in patients with a greater number of diseased vessels. However, no statistically significant correlation was found between PDW and number of diseased vessels (p=0.246).

Conclusions: The study concludes that MPV should be considered as an effective tool in predicting the magnitude of acute events in patients with coronary artery disease. However, larger studies with morphological and functional estimation of platelet indices are required to prove this.

Keywords: Acute coronary syndrome, Chronic stable angina, Mean platelet volume, Platelet distribution width, Platelet indices

INTRODUCTION

According to population based cross-sectional surveys, ischemic heart disease is the first among top five causes of deaths in Indian population with a prevalence of 3-4% in rural areas and 8-10% in urban areas. The disease progression and the development of acute events in patients with coronary artery disease are the leading causes of morbidity and mortality. Platelets play an important role to maintain the integrity of normal homeostasis of human body.¹ Platelets have been implicated in the pathogenesis of cardiovascular disorders, including atherosclerosis and its complications. Platelet hyper-reactivity and local platelet activation have been suggested to play a causal role in acute coronary events.²

Platelet size has been shown to reflect platelet activity. Both the size and number of granules, in the circulating platelets are under independent hormonal control and do not change during the lifespan of the platelet.³,⁵ However, platelets produced during stressful conditions such as
acute coronary syndromes (ACS) are bigger. Literature state that bigger platelets contain denser granules, produce more thromboxane A2, platelet factor-A and β-thromboglobulin, and thus have higher potency and thrombogenicity than the smaller platelets. The platelet volume indices-mean platelet volume (MPV) and platelet distribution width (PDW) are considered as independent risk factors of myocardial infarction and stroke and, when higher values are compared with lower values have worse clinical outcomes and higher mortality rates.\(^6\)\(^9\) Thus, patients with larger platelets can be identified easily by routine hematological analysis and could benefit from preventive treatment, thus warrants the need for this study. MPV is a determinant of platelet function and a newly emerging risk factor of atherothrombosis. An elevated mean MPV is associated with worse outcomes in acute ischemic cardiovascular and cerebrovascular events independent of other clinical parameters. However, there are limited studies comparing platelet activity in patients with stable coronary artery disease, ACS and normal healthy individuals especially in Indian patients. Thus, the present study was designed to evaluate the levels of MPV and PDW in patients with ACS and chronic stable angina (CSA) and to establish its correlation with disease.

**METHODS**

This was a hospital-based, case-control, prospective observational study performed at a tertiary care center in India between January 2016 and August 2017. The study enrolled a total of 333 patients of similar age and sex of which 100 patients had ACS, 114 had CSA and 119 were control patients. The study was approved by the Institutional Ethics Committee and strictly comply with ethical principles of Declaration of Helsinki. The written informed consent was obtained from all the patients or from impartial witness.

The patients diagnosed with ACS and CSA were included in the study. The patients who were diagnosed with immune thrombocytopenia, disseminated intravascular coagulation, myeloproliferative disorders, infectious mononucleosis, pre-eclampsia, hepatitis, hypersplenism, sepsis and critical illness, patients with hereditary platelet disorders (Bernard-Soulier syndrome and Wiskott-Aldrich syndrome) and patients with glomerulonephritis, renal failure, cyanotic congenital heart diseases were excluded from the study.

Upon enrolling, clinical history was received from all the patients. The physical examination including anthropometric data, complete hematogram (including MPV and PDW), electrocardiogram (ECG), echocardiography, treadmill test or stress echocardiogram study [only in chronic stable angina group] and coronary angiography were performed for all the enrolled patients. The control group included healthy patients of similar ages and sexes with no history of heart disease, with normal ECG and echocardiogram.

Estimation of complete haemogram and platelet indices (MPV, PDW) performed using Beckman-coulter LH 780 hematology analyzer machine. ECG’s were taken with Philips page writer 60 ECG machine. Echocardiography was performed using 3.5 MHz probe of IE 33 Philips and Philips affinity-50 echo machine. (Philips medical system, Andover, MA, USA). Coronary angiography was performed using Philips Allura xper FD 10 clarity cath lab machine.

**Statistical analysis**

All the data were analyzed using SPSS version 21 (Chicago, USA). All categorical variables were presented as frequency (percentage) and continuous variables as mean and standard deviation. Inferential statistics was performed using independent sample t-test, chi-square tests, one-way ANOVA with bonferoni correction post-hoc test and Pearson correlation test. \(P<0.05\) was considered as statistically significant.

**RESULTS**

The mean age of patients in control group was 52.5±10.23 years, in ACS group was 54.39±9.48 years and in CSA group was 57.12±8.77 years. Mean duration of diabetes and hypertension were higher in CSA group followed by ACS group and control group (\(p<0.0001\)). Single vessel disease was predominantly reported in ACS group (42%) whereas prevalence of triple vessel disease was more in CSA group (46.5%).

An elevation in the level of systolic as well as diastolic blood pressure was observed in ACS and CSA groups compared to control group (\(p<0.0001\), respectively for both). Troponin levels were higher in ACS group with 1.89±3.69 ng/ml, whereas in CSA and controls it was 0.02±0.01 ng/ml (\(p<0.0001\)). The baseline demographic details and procedural details are depicted in (Table 1).

The mean MPV levels were significantly higher in ACS and CSA group (15.57±2.11 fL and 11.27±1.7 fL, respectively) compared to control group (10.48±1.49 fL) with \(p\)-value<0.0001. Moreover, no statistically significant difference in PDW levels among all three groups was noted (\(p=0.246\)). The inter group correlation for MPV and PDW levels is outlined in (Table 2). MPV showed a statistically significant correlation with number of diseased coronary vessels in patients with ACS and CSA (\(p<0.0001\), \(r^2=0.288\)). However, PDW had no statistically significant correlation with number of diseased coronary vessels (\(p=0.113\), \(r^2=0.087\)). (Figure 1) represents a graph showing MPV levels in comparison to number of vessels affected among the study patients.
| Variables                          | Control     | ACS         | CSA         | P value | HTN: hypertension; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; CAG: coronary angiography |
|-----------------------------------|-------------|-------------|-------------|---------|-------------------------------------------------------------------------------------------------------------------------------------|
| Age, years (mean±SD)              | 52.50±10.23 | 54.39±9.48  | 57.12±8.77  | <0.001  |
| Gender, N (%)                     | 82 (68.9)   | 87 (87)     | 97 (85.1)   | <0.001  |
| Duration of diabetes, years       | 0.91±2.57   | 1.57±2.96   | 2.70±4.14   | <0.0001 |
| Duration of HTN, years            | 1.95±3.30   | 3.19±3.91   | 4.31±6.38   | <0.0001 |
| Duration of smoking, years        | 3.02±5.39   | 10.97±7.42  | 10.93±8.07  | <0.0001 |
| Family history of CAD, N (%)      | 11 (9.2)    | 12 (12)     | 6 (5.3)     | 0.2     |
| SBP, mmHg (mean±SD)               | 122.44±15.02| 136.48±22.03| 135.53±19.24| <0.0001 |
| DBP, mmHg (mean±SD)               | 75.34±8.98  | 84.82±14.88 | 83.25±10.67 | <0.0001 |
| Troponin, ng/ml (mean±SD)         | 0.02±0.1    | 1.89±3.69   | 0.02±0.1    | <0.0001 |
| CAG-number of disease vessel, N (%)| 119 (100)   | --          | --          | --      |
| Mean platelet volume (fL)         | 1.048±1.49  | 15.57±2.11  | 11.27±1.70  | <0.0001 |
| Platelet distribution width (fL)  | 12.08±1.95  | 12.38±2.23  | 12.52±2.19  | 0.246   |

Table 2: The inter group correlation for MPV and PDW levels.

| Dependent variable                        | Group-I | Group-II | P value      | 95% Confidence |
|-------------------------------------------|---------|----------|--------------|----------------|
| Mean platelet volume                       | Control | ACS      | <0.0001      | -5.66 to -4.51 |
|                                           | ACS     | CSA      | <0.0001      | 3.72 to 4.88   |
|                                           | CSA     | Control  | 0.002        | 0.23 to 0.39   |
| Platelet distribution width                | Control | ACS      | 0.886        | -0.99 to 0.39  |
|                                           | ACS     | CSA      | 1.000        | -0.84 to 0.55  |
|                                           | CSA     | Control  | 0.336        | -0.22 to 1.11  |

DISCUSSION

The present study investigated the correlation between MPV, PDW and coronary artery disease in acute and chronic scenarios in comparison with normal controls. The main results of the study are as follows: i) elevation in MPV was observed in ACS and CSA groups in comparison to controls, ii) levels of MPV were higher in ACS group in comparison to CSA group, iii) a positive correlation was observed between increased MPV levels and number of disease coronary vessels in patients with coronary artery disease.

The platelets and associated pro-inflammatory and prothrombotic functions are associated with the development of atherosclerotic plaques and formation of thrombus. Platelets produced in stressful situation such as ACS are larger, which are enzymatically and metabolically more active and have more alpha-granules, have higher capacity for producing thromboxane and have high expression of adhesive glycoproteins. Evidences suggest that causal occlusion of the coronary
artery in unstable angina has been mediated by a platelet-rich thrombus. Several studies have shown increased MPV as one of the risk factors for MI, cerebral ischemia, and transient ischemic attacks. Literature states that people with cardiovascular risk factors reportedly have greater platelet activation that increases the peripheral consumption of platelets leading to the production of larger and more reactive platelets. The existing studies reported elevated MPV levels in ACS patients and were associated with the severity of coronary artery disease. However, no significant elevation in MPV level was found in patients with stable coronary artery disease.\textsuperscript{2,10-14}

A study by Endler et al evaluated platelet indices in 373 cases (188 cases of myocardial infarction and 185 cases of Stable CAD) which reported that patients with highest quintile of increased MPV were at higher risk of myocardial infarction in comparison to patients with lowest quintile.\textsuperscript{15} Similarly, a study by Khandekar et al reported significant elevation in MPV levels in patients with acute myocardial infarction and unstable angina (10.43±1.03 fL) compared with those with stable coronary artery disease (9.37±0.99 fL) and control group (9.2±0.91 fL).\textsuperscript{16} Furthermore, Namak et al reported a correlation of high levels of MPV with the Gensini and Syntax scores, number of diseased vessels (>50%), number of critical lesions (>50% and >70%), and non-critical lesions.\textsuperscript{17} In contrary to our study, Varasteh-Ravan et al reported increased levels of both MPV and PDW in patients with ACS whereas raised MPV levels in ACS are reported in the present study. In the present study a positive correlation was observed between MPV and duration of diabetes, hypertension and smoking.\textsuperscript{18} A proportional correlation was reported between MPV levels and number of disease coronary vessels and occurrence of acute events in patients with coronary artery disease.

Limitations

The small sample size and non-randomized study design are the major limitation of the study. Furthermore, we measured platelet morphological indices rather than its functional indices which play a major role in understanding of platelet activity. The exact role of platelet indices in pathogenesis of CAD is not completely clear, for which further molecular level studies are needed. The variation of platelet indices in other causes of myocardial infarction like type-2 variant is beyond the scope of the study.

CONCLUSION

CAD is a major public health problem with increasing prevalence at an alarming rate. MPV, a morphological index of platelet activity can be used in early diagnosis and for better prognosis after the treatment of CAD. Platelet volume indices 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 in patients with CAD. However, larger studies evaluating both morphological as well as functional indices of platelet activity are required to clear before declaring it as an independent predictor of acute cardiac events.

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