



## A Study of the Diagnostic Importance of Platelet Distribution Width in Acute Coronary Syndrome

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### Abstract

**Objectives:** Routine biomarkers used to diagnose acute coronary syndrome are undetectable in considerable number of patients especially in early stage of ACS. Early stages of ACS involves platelet activation hence change in platelet morphology leading to increase in PDW. Here we aimed to study the diagnostic importance of PDW in acute coronary syndrome.

**Materials and Methods:** A hospital based case-control study was conducted in the period between February 2019 to February 2020. 77 cases and 77 controls satisfying the inclusion and exclusion criteria and having given an informed consent to participate in the study were included in the study. All consecutive patients presenting with the chest pain of < 24 hours duration with ECG changes consistent with ACS with/without raised cardiac biomarkers were taken as cases and age, sex matched non ACS patients were taken as controls. In both groups platelet count and PDW were measured.

**Results:** The mean age of the cases enrolled in the study was 56.81 + 12.86 years and controls enrolled in the study was 56.19 + 12.35 years (p = 0.764). The mean left ventricular ejection fraction (LVEF) was significantly lower in case arm compared to control arm (46.51 + 5.83 Vs 59.32 + 1.70; p < 0.001). In comparison to control group the case arm had lower platelet count (207.81 + 34.29 × 10<sup>7</sup>/L Vs 226.60 + 50.44 × 10<sup>7</sup>/L; p = 0.008) and higher platelet distribution width (17.45 + 2.57 fL Vs 16.58 + 2.44 fL; p = 0.033). The area under the receiver operative curve was used as a predictor of ACS and it showed that the PDW cut-off value of 17.8 fL, the sensitivity and specificity of PDW in diagnosing acute coronary syndrome was found 84.4% and 53.2%, respectively.

**Conclusion:** Our data indicate that both high PDW and low platelet count are early indicators of ACS and it can be used with other cardiac biomarkers for early diagnosis of ACS. It is relatively cheaper, easily available and complementary to other tests used in the patients presenting with chest pain in emergency room.

**Keywords:** Acute Coronary Syndrome; Platelet Count; Platelet Distribution Width; Diagnosis; Marker

### Abbreviations

CHD: Coronary Artery Disease; ACS: Acute Coronary Syndrome; MPV: Mean Platelet Volume; PDW: Platelet Distribution Width;

cTnT: Cardiac Troponin T; ECG: Electrocardiogram; CAG: Coronary Angiography; DM: Diabetes Mellitus; HTN: Hypertension; NSTEMI: NonST-elevation Myocardial Infarction; STEMI: ST Elevation Myo-

cardial Infarction; LVEF: Left Ventricular Ejection Fraction; ROC: Receiver-operator Characteristic

## Introduction

In India, studies have reported increasing CHD prevalence over the last 60 years, from 1% to 9%-10% in urban populations and < 1% to 4% - 6% in rural populations [1]. Acute coronary syndromes (ACS) encompass a spectrum of coronary artery disease, from unstable angina to transmural myocardial infarction caused by atherosclerosis and thrombus formation [2]. For the diagnosis of ACS cardiac troponins and creatine kinase are used routinely. The diagnostic efficiency of cardiac troponins within 2 to 4 hours of the symptom onset is limited. In fact, because of slow-release kinetics from damaged myocardium, cardio specific troponins are often unsuitable for early diagnosis because in 40% - 60% of ACS levels are in nondiagnostic concentrations. Although the troponins enhanced diagnostic sensitivity, they did not resolve the problem of early diagnosis. Therefore, using a multi marker approach may be of benefit for early diagnosis and management of ACS [3,4].

Platelets have a crucial role in the pathogenesis of ACS, where plaque rupture is followed by platelet activation and thrombus formation leading to coronary artery occlusion [5]. The larger platelets are more adhesive and tend to aggregate more than normal platelets [2]. So the variation in size of platelets can be measured by both MPV and PDW. An increased MPV is associated with known cardiovascular risk factors, including diabetes mellitus, hypertension, hypercholesterolemia, and obesity [4]. Some investigations have demonstrated the correlation between elevated MPV and ACS, However, some studies [6,7] have also shown that MPV cannot be considered as either a marker of platelet activation or a cardiovascular risk factor. PDW is relatively simple and more sensitive specific tool than MPV and play an important role in early diagnosis of ACS and early initiation of anti-platelet therapy. It could be used as a screening test of ACS from other noncardiac chest pain, and severity and prognosis of ACS [8].

## Aim of the Study

Here our aim of this study was to investigate whether there is an association between PDW measurement at admission and cTnT elevation in a large sample of consecutive patients admitted to the emergency department with a suspected diagnosis of ACS and to assess the potential diagnostic efficiency of PDW in the diagnostic workup for ACS.

## Materials and Methods

A hospital based case-control study was carried out in the period between February 2019 to February 2020. The project was approved by the Institutional Scientific Advisory Committee as well as the Institutional Ethics Committee. The study protocol was approved by the Clinical Trial Screening and the Ethics Committee of the hospital, and written informed consent was obtained from the patients. All Consecutive patients presenting with the chest pain of < 24 hours duration with ECG changes consistent with ACS with/without raised cardiac biomarkers were taken as cases. Selection of controls was done with the next eligible age and sex matched control fulfilling study criteria were being selected consecutively after each case has been enrolled. A detailed history, complete physical examination including cardio-vascular examination, base line investigations at presentation including electrocardiogram, 2D echocardiography and complete blood count including PDW was done in all cases and controls. Coronary angiography (CAG) was performed via trans-radial or trans-femoral approach in ACS cases after obtaining a detailed written consent. The total study participants were 154 out of which 77 cases and 77 controls matched with age and sex were included in the study. The Inclusion criteria includes the following 1. consecutive patients of ACS presenting within 24 hours of onset of chest pain will be taken as cases 2. Equal number of matched non-ACS patients will be taken as controls. The exclusion criteria includes the following the ACS patients presenting after 24 hours of onset of chest pain and those on anti-platelet, anti-coagulants, anti-inflammatory therapy, peripheral arterial disease, vasculitis, deep vein thrombosis, acute pulmonary thromboembolism, mitral stenosis. prosthetic heart valve, atrial fibrillation/flutter, CKD stage III/IV.

## Statistical analysis

Descriptive analysis was used to describe the socio-demographic characteristics of the study participants in frequency and percentage. Continuous variables were expressed as mean and standard deviation. Percentages were used for categorical variables. Statistical significance was defined as a p-value less than 0.05. Data entry and statistical analysis was done on SSPS version 23.0.

## Results and Observations

The mean age of the cases enrolled in the study was 56.81 + 12.86 years and controls enrolled in the study was 56.19 + 12.35 years with p = 0.764. There was no statistically significant difference in the mean age of the cases and controls (Table 1). In case arm 92.2% patients were male while in the control arm 83.1%

patients were male. However, there was no statistically significant difference in gender population between the two groups (p = 0.086). Diabetes mellitus (DM) was significantly higher in patients in case arm compared to patients in control arm (26% Vs 10.4%; p = 0.012). Except Hypertension (46.8% Vs 40.3%; p = 0.416) and Alcohol consumption (p = 0.083) all other comorbidities (Smoking, Tobacco chewing, Dyslipidemia) were statistically significant (Table 1).

Parameters	Cases (n = 77) Mean + SD	Controls (n = 77) Mean + SD	P-value
Age (Years)	56.81 ± 12.86	56.19 ± 12.35	0.764
Gender (Male)	71 (92.2%)	64 (83.1%)	0.086
DM	20 (26%)	8 (10.4%)	0.012
HTN	36 (46.8%)	31 (40.3%)	0.416
Alcohol (Active+Ex)	32+4 (41.6%+5.2%)	28+0 (36.4%+0%)	0.083
Smoking (Active+Ex)	40+3 (51.9%+3.9%)	24+0 (31.2%+0%)	0.004
Tobacco	50 (64.9%)	30 (39%)	0.001
Dyslipidemia	47 (61%)	26 (33.8%)	0.001

Table 1

In case group 14.3% ACS patients were of non ST-elevation myocardial infarction (NSTEMI) and rest 85.7% were of ST-elevation myocardial infarction (STEMI) while none of the patients in control arm presented with ACS or had past history of CAD. All patients in case arm had ECG changes suggestive of MI (STEMI/NSTEMI) while none of the participants in control arm showed any ischemic changes in ECG.

In case group 13% patients of ACS had all the three cardiac biomarkers (Trop-I, CPK and CPK-MB) within normal range at the hospital presentation. Trop-I was within normal range in 13% patients, CPK in 14.3% patients while CPK-MB in 16.9% patients. On the other hand, all the three cardiac biomarkers (Trop-I, CPK and CPK-MB) were within normal range in the control arm (Figure 2).

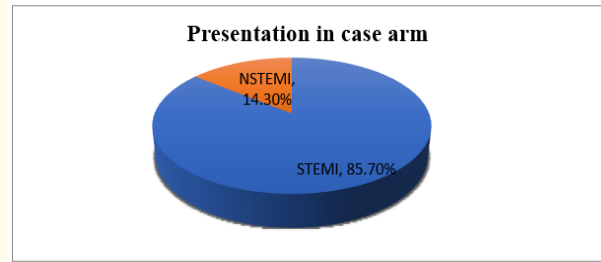


Figure 1: Presentation in case arm.

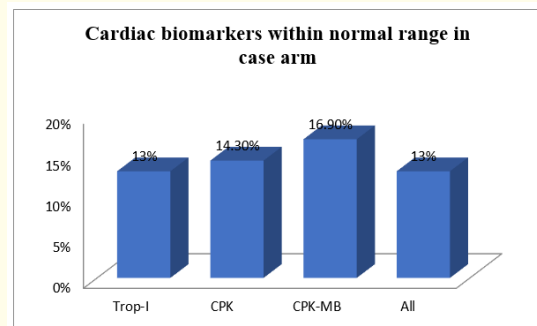


Figure 2: Cardiac biomarkers within normal range in case arm.

Parameters	Cases (n = 77) Mean + SD	Controls (n = 77) Mean + SD	P-value
LVEF (%)	46.51 + 5.83	59.32 ± 1.70	<0.001
PDW (fL)	17.45 + 2.57	16.58 ± 2.44	0.033
Platelet count (×10 <sup>7</sup> /L)	207.81 + 34.29	226.60 ± 50.44	0.008

Table 2: Mean LVEF, PDW and platelet count of the study participants.

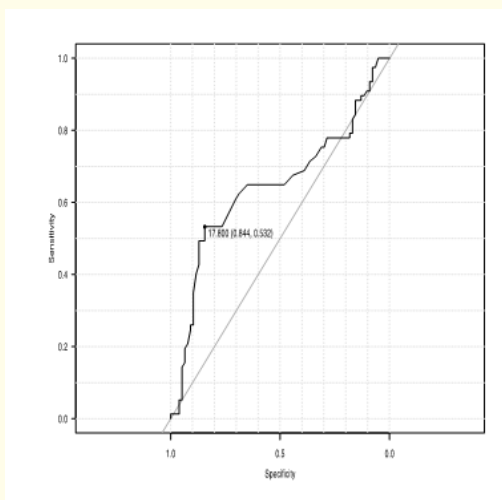
The mean left ventricular ejection fraction (LVEF) was significantly lower in case arm compared to control arm (46.51 + 5.83 Vs 59.32 + 1.70; p < 0.001). In control arm, the LVEF of all participants as well as the mean LVEF of whole control arm was within normal limit whereas in case arm the mean LVEF was below normal range (Table 2). The mean platelet distribution width (PDW) was significantly higher in case arm compared to control arm (17.45 +

2.57 fL Vs 16.58 + 2.44 fL; p = 0.033) (Table 2). The mean platelet count was significantly lower in case arm compared to control arm (207.81 + 34.29 × 10<sup>7</sup>/L Vs 226.60 + 50.44 × 10<sup>7</sup>/L; p = 0.008).

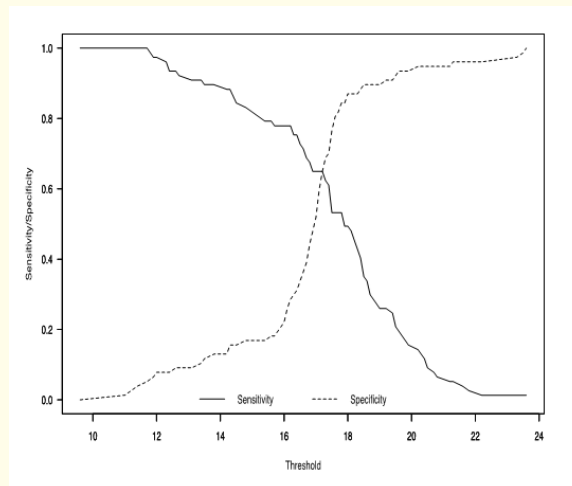
	Cut off value	Sensitivity (%)	Specificity (%)	Area under ROC curve	95% Confidence interval (CI)	
					Lower	Upper
PDW	17.8 fL	84.4%	53.2%	0.643	0.553	0.733
Platelet count	230×10 <sup>7</sup> /L	40.3%	76.6%	0.595	0.506	0.684

**Table 3:** Receiver-operator characteristic (ROC) curve of PDW and platelet count for prediction of acute coronary syndrome.

The area under the ROC curves for the ACS predictors is depicted in table 3. Based on the ROC curves, PDW had the best area under curve compared to platelet counts. Receiver-operator characteristic (ROC) were constructed using PDW value of the patients between two groups, which gave a PDW cut off value of 17.8 fL as the value with a best combination of sensitivity and specificity for acute coronary syndrome. At this PDW cut-off value of 17.8 fL, the sensitivity and specificity of PDW in diagnosing acute coronary syndrome was found 84.4% and 53.2%, respectively (Table 3, Figure 3 and 4). Platelet count cut-off value of 230×10<sup>7</sup>/L showed sensitivity 40.3% and specificity 76.6% in the diagnosis of acute coronary syndrome (Table 3).



**Figure 3:** ROC curve for PDW.



**Figure 4:** Sensitivity-specificity curve of PDW.

**Discussion**

Platelets have been implicated to play an important role in the pathogenesis of atherosclerosis and its complications like ACS. Platelet activation is the preliminary steps of ACS pathogenesis and it also change in shape during activation from discoid to spherical. Platelet indices such as PDW and MPV increases during platelet activation and can easily be measured. PDW directly measures the variability in platelet size, and its high values could suggest larger production of larger reticulated platelets. Elevated platelet indices have been proposed as a risk factor for ACS [9]. Platelet parameters especially PDW could be an important and reliable markers in early detection of ACS when other markers are not available. Because platelet activation is the preliminary steps of ACS and PDW indirectly indicate the activation status of platelets [10,11].

There is no statistically significant difference was detected between the two groups regarding the age or the gender distribution. The mean age of the two groups was similar to many other similar studies [4,8,10]. Similarly, no statistically significant difference was detected between the two groups with regard to hypertension. However hypertension was more prevalent in our study participants compared to similar study conducted by Silpi Pervin., *et al.* [8], Khandekar., *et al.* [12], and Dehgani MR., *et al.* [4].

In our study PDW was statistically significantly (P < 0.033) higher in case arm (17.45 + 2.57 fL) compared to control arm (16.58 + 2.44 fL). Studies by Pervin S., *et al.* [8] Khandekar., *et al.* [12], Patil., *et al.* [13], and Shafaei SH., *et al.* [14], suggested that

there was increase in PDW values in ACS patients compared to the normal population. The mean platelet count was significantly ( $p = 0.008$ ) lower in case arm ( $207.81 + 34.29 \times 10^7/L$ ) compared to control arm ( $226.60 + 50.44 \times 10^7/L$ ). Pervin S., *et al.* [8], Varol E., *et al.* [15], Cemin R., *et al.* [16] and Yilmaz., *et al.* [17] in their studies found that PDW and MPV was significantly higher in patients with ACS groups than controls, along with reverse changes in platelet count.

In our study on admission to the hospital, patients with ACS an increased baseline PDW ( $>17\%$ ) is associated with the severity of CAD. In addition, high levels of PDW may be useful to identify high-risk patients and in determination of appropriate treatment strategies [18].

However, based on the ROC curves, PDW had the best area under curve compared to platelet counts. The ROC gave a PDW cut off value of 17.8 fL as the value with a best combination of sensitivity (84.4%) and specificity (53.2%) for diagnosing acute coronary syndrome. Platelet count cut-off value of  $230 \times 10^7/L$  showed sensitivity 40.3% and specificity 76.6% in the diagnosis of acute coronary syndrome. Our data indicate that both high PDW and low platelet count are early indicators of ACS however higher PDW is better marker with more area under curve and better combination of sensitivity and specificity than low platelet count for early detection of ACS.

Our study has some limitations like it was done in a limited time of span, the sample size was small and prognostic significance of the novel ACS markers was not evaluated.

## Conclusion

ACS is associated with a pre thrombotic state of platelet activation and production of hemostatically more active metamorphic platelets. Because these larger platelets are hemostatically more active leading to coronary thrombus formation and resultant ACS. Patients with larger platelets can easily be identified during routine haematological analysis. In our study we found that patients with acute coronary syndromes had higher PDW and lower platelet count at the time of admission compared to healthy controls. So platelet parameters mainly PDW are readily available, relatively inexpensive and useful markers of ACS and can be utilized with other investigational tools to screen patients presenting to the emergency room with chest pain who are suspected to have ACS.

## Conflict of Interest

None.

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