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A Study on the Correlation between Platelet Indices [Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW)] and STEMI

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ABSTRACT

Introduction: Atherosclerosis and its major complications such as Myocardial Infarction (MI) have been linked to increased activation of platelets. Markers of platelet activity are being studied as risk factors for such complications.

Aim: To study the correlation between platelet volume indices, Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW), and STEMI

Materials and Methods: A case control study using 100 patients, among which 50 had STEMI and the other 50 were apparently normal, was conducted after considering the exclusion and inclusion criteria.

Results: The Mean age of cases was found to be 60.7 ± 11.5 years and of the control group was 60.6 ± 12.1 years. Males constituted 56 % of the healthy control group and 58% of the STEMI group. Female constituted 44% of healthy control and 42% of STEMI group. The MPV was significantly larger in STEMI cases compared to controls (11.4 ± 0.7 fL vs. 10.0 ± 0.8 fL, respectively, $p < 0.001$). The PDW was also significantly higher in cases compared to controls (16.6 ± 3.0 vs 13.0 ± 2.0, respectively, $p < 0.001$). MPV had a larger area under the curve from ROC analysis when compared to PDW.

Keywords: High MPV and PDW values can be used as markers of STEMI and provide an economical means to stratify risk in such patients

INTRODUCTION

Coronary Artery Disease (CAD) is a major cause of mortality worldwide [1] and will be first among the leading causes of disability in coming years [2]. While the death rates have been declining for the past three decades in the West, these rates are rising in India. In the last three decades, the prevalence of CAD has increased from 1.1% to about 7.5% in the urban population and from 2.1% to 3.7% in the rural population [3].

Among the CAD, Acute Myocardial Infarction (MI), which is essentially tissue death (infarction) of the heart muscle, is the commonest cause of mortality. For the purpose of management, the patients are classified into two groups. Patients who will benefit from reperfusion, namely patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram (ECG) and those who do not require reperfusion, called as non- ST-segment elevation acute coronary syndrome (NSTE-ACS).[4]

STEMI usually occurs when coronary blood flow decreases abruptly after a complete

thrombotic occlusion of a coronary artery previously affected by atherosclerosis.[5] Chronic atherosclerotic plaque gets converted to an occluding thrombus in which platelets and the coagulation cascade play a major role in this process. Platelets are heterogeneous blood elements with various sizes and densities. Large platelets are denser, aggregation rate is faster with subendothelial collagen, have higher production of thromboxane A2 and greater expression of glycoprotein Ib and glycoprotein IIb/IIIA receptors [6]. All these features, increase thrombosis, and possibility of STEMI. Large platelets have also been reported in patients with vascular risk factors and been related with myocardial damage in ACS, with a negative outcome of STEMI observed in survivors [7].

Materials and Methods:

The present study was conducted in the department of Medicine, Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. This was a case control study which included 50 patients with STEMI and 50 apparently healthy subjects that presented to the Medicine emergency of Guru Nanak Dev Hospital, Amritsar and fulfilled the inclusion criteria of the study.

The study was conducted after approval from Institutional Ethics Committee, Govt. Medical College, Amritsar. The patients were explained about the procedures to be adopted in the study in their vernacular language and their informed consent was taken prior to enrolment in the study.

Subject Population:

INCLUSION CRITERIA:

 Patients presenting with acute myocardial infarction for the first time, aged 18 years and above of either sex as cases. The diagnosis of STEMI was based on the Fourth Universal Definition of Myocardial Infarction.[5]

 Age and sex matched subjects aged above 18 years without history of

coronary artery diseases.

EXCLUSION CRITERIA:

 Patients having primary platelet disorders, bleeding/clotting disorders, bone marrow disorders.

 Patients with chronic liver diseases.

 Patients with chronic kidney disorders with eGFR 60 mL/min/1.73 m^2 and/or serum creatinine>2.0mg/dl

 Pregnancy and/or blood transfusions within 3 months prior to the study

 Drugs causing thrombocytopenia like penicillin, sulphonamides, quinidine etc.

After applying the inclusion and exclusion criteria, the patients were divided into two groups. Group A included patients with STEMI and group B included patients who did not have STEMI or Ischemic Heart Disease.

All demographical details and clinical variables of the patients were recorded (age, sex, body mass index, diabetes mellitus, hypertension and smoking status). Routine laboratory parameters were also recorded which consisted of Hemoglobin (Hb), Total leucocyte count (TLC), Differential leucocyte count (DLC), Platelets and platelet indices (MPV, PDW) blood urea, serum creatinine, Aspartate Transaminase (AST), Alanine Transaminase (ALT), Total bilirubin, Troponin-T and ECG. Collection of venous blood samples was done in the study group on the day of admission within 24 hours from antecubital vein with all aseptic precautions in plain and EDTA vacutainers for routine baseline blood investigations. Platelet indices, MPV and PDW, were analysed using automated cell counter.

Data analysis:

The data was collected systematically and comparison of demographic, cardiovascular risk factors and laboratory characteristics were done between both the groups and appropriate significance tests were applied including the Chi-squared test and Student's t test. A Receiver Operator Curve Analysis was done at the end to assess the sensitivity and specificity of MPV and PDW values and determine their Areas under the curve. Analysis was done using Microsoft excel 2010 and SPSS (IBM). p value of less than 0.05 was considered statistically significant.

RESULTS

The study participants comprised of 100 patients, who were divided into groups A and B which had patients with and without STEMI respectively. The baseline clinical characteristics are depicted in [Table/Fig-1]. Mean age of Group A was found to be

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60.7 ± 11.5 years and Group B was 60.6 ± 12.1 years. Males constituted 56 % of the healthy control group and 58% of the STEMI group. Females constituted 44% of healthy control group and 42% of STEMI group. No important differences were observed between the two study groups with respect to sex. On comparison of cardiovascular risk factors like Hypertension, Diabetes Mellitus and Dyslipidemia statistical difference was found only for Hypertension and Diabetes Mellitus. [Table/Fig-1].

Table/Fig-1

Parameter	Group A : STEMI (n=50)	Group B : Control (n=50)	p-value
Age (years) mean±SD	60.7 ± 11.5	60.6 ± 12.1	-
Male (%)	29 (58)	28 (56)	0.83
Female (%)	21 (42)	22 (44)	
BMI (kg/m^2) mean±SD	25.51 ± 2.85	24.02 ± 1.65	0.002
Hypertension (%)	33 (66)	17 (32)	0.001
Diabetics (%)	29 (58)	18 (36)	0.028
Dyslipidemia (%)	32 (64)	24 (48)	0.11

Platelet Parameters

Mean platelet count and platelet indices are presented in [Table/Fig-2]. Comparative results showed a lower platelet count in the case group than the control group and it was significant (2.1 ± 0.7 vs 2.7 ± 1.6, respectively, p=0.019). The MPV was significantly larger in STEMI cases compared to controls (11.4 ± 0.7 fL vs. 10.0 ± 0.8 fL, respectively, p < 0.001). The PDW was also significantly higher in cases compared to controls (16.6 ± 3.0 vs 13.0 ± 2.0, respectively, p < 0.001) [Table/Fig-2].

Table/Fig-2

Platelet Parameter	STEMI mean±SD	Control mean±SD	p-value
Platelet count (x10^5/L)	2.1 ± 0.7	2.7 ± 1.6	0.019
Mean platelet volume (fL)	11.4 ± 0.7	10.0 ± 0.8	<0.001
Platelet distribution width (fL)	16.6 ± 3.0	13.0 ± 2.0	<0.001

Sub Group Analysis

We compared the platelet indices in groups with respect to gender as well. Accordingly, there were significant differences in terms of platelet count between both sexes; platelet count was higher in female than male, p = 0.012. However, there were no significant differences in MPV between male and female group in the study population. PDW was higher in males than females in the total population, STEMI cases and controls. [Table/Fig-3].

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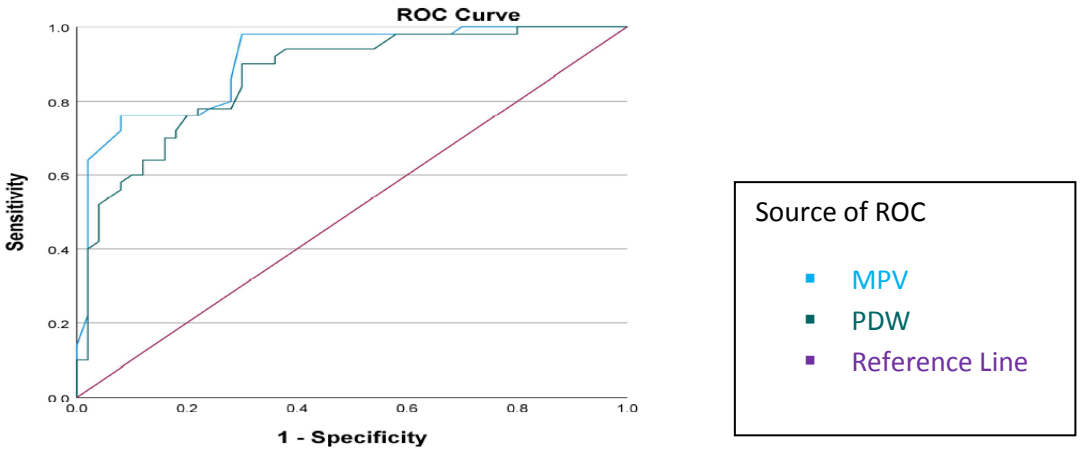
Table/Fig-3			
Parameters	Total (n=100)	STEMI (n=50)	Control (n=50)
Platelet count ($x10^5$/L)			
Male	2.1 ± 0.76	1.97 ± 0.80	2.23 ± 0.70
Female	2.14 ± 1.68	2.20 ± 0.70	3.20 ± 2.20
p Value	0.012	0.258	0.025
Mean platelet volume (fL)			
Male	10.8 ± 0.98	11.5 ± 0.7	10.2 ± 0.7
Female	10.5 ± 1.13	11.3 ± 0.8	9.8 ± 0.9
p Value	0.100	0.248	0.101
Platelet distribution width (fL)			
Male	15.4 ± 3.27	17.4 ± 3.1	13.4 ± 1.9
Female	13.95 ± 2.64	15.5 ± 2.4	12.5 ± 2.0
p Value	0.016	0.021	0.025

Receiver Operator Curve Analysis and Area Under the Curve

Table/Figure 4 and 5 depict the receiver operator curve analysis for MPV and PDW and was used to find the critical points for MPV and PDW to assign the cut off values that would be used to adjudge sensitivity and specificity [Table/Figure 6]. The graph was used to find the area under the curve (AUC) as well. It was observed that for the MPV curve, the point where the sensitivity is 76% and specificity is 92% corresponded to 11.2 fL. On the PDW curve, the point where the sensitivity is 64 % and specificity is 88% corresponded to 15.5 fL. Area under curve for MPV was 0.908 and for PDW was 0.865, suggesting MPV to be a better predictor of STEMI.

Table/Figure 4: RECEIVER OPERATOR CURVE (ROC) ANALYSIS



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Table/Figure 5: AREA UNDER CURVE (AUC) FROM ROC

Variable	Area	Std. Error	Significance	95% Confidence Interval	
				Lower Boundary	Upper Boundary
MPV	0.908	0.029	0.000	0.851	0.965
PDW	0.865	0.036	0.000	0.795	0.936

Table/Fig-6

DISTRIBUTION OF PATIENTS ACCORDING TO THE CUT OFF VALUE OF MPV AS 11.2 FL

MPV	GROUP A (STEMI)	GROUP B (Control)	TOTAL
MPV (≥11.2 fL)	38 (a)	4 (b)	42
MPV (<11.2 fL)	12 (c)	46 (d)	58
Total	50	50	100

- Sensitivity (a/a+c)= 0.76
- Specificity (d/b+d)= 0.92
- Positive Predictive Value (PPV, a/a+b)= 0.90
- Negative Predictive Value (NPV, d/c+d)= 0.79

DISTRIBUTION OF PATIENTS ACCORDING TO THE CUT OFF VALUE OF PDW AS 15.5 FL

PDW	GROUP A (STEMI)	GROUP B (CONTROL)	TOTAL
PDW (≥15.5 fL)	32	6	38
PDW (<15.5 fL)	18	44	62
Total	50	50	100

- Sensitivity (a/a+c)= 0.64
- Specificity (d/b+d)= 0.88
- Positive Predictive Value (PPV, a/a+b)= 0.84
- Negative Predictive Value (NPV, d/c+d)= 0.71

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DISCUSSION

STEMI is a major cause of death globally. Platelets play an important role in the development of atherothrombosis. After atherosclerotic plaque rupture, platelets get activated. Platelets larger in size have a greater mass and are also metabolically and enzymatically more active than smaller platelets [8]. These platelets which are reactive and larger have more granules and adhesion receptors and the net effect is reduced bleeding time indicating increased activation [9]. They have a greater prothrombotic potential, with higher levels of intracellular thromboxane A2 as well as increased levels of procoagulant surface proteins [10].

Platelet activity cannot be ascertained by platelet count alone. Platelet volume indices like MPV and PDW are better indicators of activity as larger platelets have shown to be more reactive. Several studies have demonstrated that an elevated MPV has been associated with increased vascular ischemic events and also have been found to be associated with increased mortality and morbidity and recurrent MI [10]. MPV has been shown to associated with both megakaryocyte ploidy and with the percentage of circulating reticulated platelets [11]. On the other hand, PDW is a marker of the variability of size among the platelets which could suggest increased reactivity of platelets. Among the two, PDW was hypothesized to be better since it didn't increase during mere platelet swelling.[12] However, this has not been proved so far.

The current study examined the relationship between platelet parameters mainly Platelet Count, MPV and PDW and the occurrence of STEMI in patients. We found that patients with STEMI tend to have significantly larger MPV and PDW (which both reflect the platelet volume) than the control group. Lippi G et al. have demonstrated in a large scale study that MPV at admission is higher in STEMI compared to those with chest pain of non cardiac origin [7]. Likewise, similar observations were made by other investigators, where MPV was found to be higher in patients with STEMI compared to healthy controls [13,14]. The results of the present study are comparable with studies by Reddy et al and Agrawal et al., from India which showed MPV was significantly higher in those patients who had MI, compared with healthy group [15,16]. However, these studies did not compare MPV and PDW with each other. In the present study, we demonstrated that MPV is a better predictor of STEMI compared to PDW.

The study has several limitations, such as the follow up of the patients was not possible to examine the prognostic value of our findings and to examine correlation between the high MPV and high PDW and mortality rate.

However, platelet indices are an inexpensive marker and are a part of the routine evaluation. Their assessment can be used for early risk stratification.

CONCLUSION

High Mean Platelet Volume and Platelet Distribution Width seem to be predictors of STEMI. This is a simple and economical method that indicates platelet activation and predicts the risk of STEMI.

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