A Comparative Study of Platelet Indices in Acute Coronary Syndrome

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ABSTRACT

Introduction: Platelet indices are simple and reliable indicators of emerging biomarkers of cardiovascular events and might potentially help in stratifying cardiovascular risk. Studying this correlation may help us in timely interventions. Study aimed to see the platelet indices in patients presenting with acute coronary syndromes and to study the association of platelet indices and the occurrence of acute coronary syndromes

Material and methods: This was a comparative study conducted among three groups each consisting of 25 patients each with STEMI, NSTEMI and Non-Cardiac Chest Pain (NCCP) respectively. The platelet indices were analysed from the venous samples in an auto-analyser. Data were analyzed using SPSS version 16.0. The platelet indices among the three groups were analyzed by chi-square (categorical) and ANOVA (continuous) tests. A *P* value of < 0.05 was considered statistically significant. ROC curves were plotted to assess the predictive efficacy of these platelet indices in predicting acute coronary syndromes.

Results: The platelet indices, the mean platelet volume, platelet distribution width and platelet large cell ratio were significantly higher in STEMI and NSTEMI groups when compared to the NCCP group.

Conclusion: Patients with acute coronary syndromes had higher MPV when compared to NCCP group. Therefore measurement of platelet volume indices may be of help in differentiating the individuals with cardiac and non-cardiac chest pain and hence could benefit from early interventions.

Keywords: Acute Coronary Syndrome, Platelet Indices

INTRODUCTION

Acute coronary syndrome involves a spectrum of coronary artery disease from unstable angina to myocardial infarction. Coronary artery disease is mainly caused by atherosclerosis and its complications. Platelets and their activity play an important role in the initiation of atherosclerotic lesions and thrombus formation.[1,2]

The Global estimate of age-standardized CVD death rate of 272 per 1,00,000 population in India is higher than the global average of 235 per 1,00,000 population. In India, there is increasing CHD prevalence over the last 60 years, from 1% to 9%-10% in urban populations and <1% to 4%-6% in rural populations. Premature mortality in terms of years of life lost because of CVD in India has increased by 59%.[3,4]

Though, Troponin I Troponin T, Creatine Kinase enzymes are most sensitive and specific biomarkers of myocardial damage, platelet indices can be detected earlier and are also easily recordable, routinely available in most clinical laboratories. Hence platelet parameters can be better used as a biomarker for coronary artery disease (CAD) and possibly benefitin timely interventions.[5,6]

It has been an established fact that larger platelets are known to be enzymatically and metabolically more active and have shown to have a major role in the initiation of atherosclerotic lesions and their complications and have higher potential for thrombosis compared to smaller ones.[7] They also act as an indicator of platelet activation, and thus be related to the extent and also clinical presentation of coronary artery disease (CAD).[8] The degree of platelet activation can be assessed by platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW). It is still not clear whether these parameters can be considered risk factors for CAD.[9] Hence the study was undertaken to compare the changes in the platelet parameters among patients presenting with ACS and also assess whether platelet indices can be used as a biomarker in predicting CAD with the objectives to study the platelet indices in patients presenting with acute coronary syndromes and to study association of platelet indices in patients presenting with acute coronary syndrome.

MATERIAL AND METHODS

This is an observational study conducted from 1st January 2015 to 31st December 2015. A total of 75 Patients presenting with chest pain in the casualty/medical OPD, Department of Medicine, S. Nijalingappa medical college and HSK hospital and research centre, Bagalkot were evaluated and divided equally according to clinical manifestations, ECG and enzymatic change into three groups consisting of 25 patients in the control group with NCCP, 25 patients in the STEMI group, 25 patients in the NSTEMI group. Patients with bleeding disorders, blood dyscrasias, preeclampsia, sepsis, with history of recent (within 6 weeks) major operations, trauma, blood transfusion and those receiving drugs which can cause thrombocytopenia and also patients with infections known to cause thrombocytopenia were excluded from the study. Written informed consent was taken from all the patients. The socio-demographic data, clinical history and details about the risk factors of CAD were collected using a semi-structured questionnaire and interview method was administered. Clinical history will include age, sex, history of precipitating factors (vigorous physical exercise, emotional stress or medical or surgical illness), past history of diabetes, hypertension, smoking, previous episodes of chest pain. Clinical examination included vitals, general and systemic examination including detailed examination of CVS. Venous blood samples were drawn at the time of admission before initiation of treatment and processed within 30 minutes of blood collection using an autoanalyser. Investigations included Complete hemogram (including MPV, PDW and PLCR) using an autoanalyser b. Cardiac enzymes (CKMB, Troponin I) c.

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Platelet indices	Mean±SD			ANOVA	
	NCCP	NSTEMI	STEMI	F	*P*-Value
MPV	8.00±1.28	9.73±1.15	10.48±1.42	24.09	0.000*
PDW	11.79±1.70	12.84±1.54	13.92±1.57	10.97	0.000*
PLCR	16.75±4.99	22.74±4.84	25.19±6.15	16.37	0.000*
*indicates a significant statistical difference between the groups with $P<0.05$					

Table-1: Comparison of means of different platelet indices among the three groups NCCP, NSTEMI and STEMI

Other relevant investigations.

STATISTICAL ANALYSIS

Data were entered in excel and analysed with recent available software. Results were presented as mean ± SD and analyzed using SPSS version 16.0. Categorical variables were analyzed by chi-square test and the continuous variables with ANOVA between the groups. The areas under the receiver operating characteristic (ROC) curve for assessing the predictive values of MPV, PDW and PLCR in predicting the occurrence of acute coronary syndromes were constructed by plotting the sensitivities for all individual cut-off values versus the corresponding (1-specificity). A *P* value < 0.05 was considered statistically significant.

RESULTS

In the present study, out of 75 study subjects, 46 (61.3%) were females and 29 (38.7.0%) were males. Majority i.e. 33 (44.0%) study subjects were in the age group of 61- 75 years, followed by 23 (30.7%) were in the age group of 46-60 years. The mean age was 60.37 + 13.87 years with a range from 30 to 93 years.

Platelet indices	Dunnett Post-hoc test	
	Comparison Group	P-Value
MPV	STEMI v/s NCCP	0.000*
	NSTEMI v/s NCCP	0.000*
PDW	STEMI v/s NCCP	0.000*
	NSTEMI v/s NCCP	0.043*
PLCR	STEMI v/s NCCP	0.000*
	NSTEMI v/s NCCP	0.000*
*indicates a significant statistical difference between the groups with P<0.05		

Table-2: Comparison of means of different platelet parameters among the three different groups by applying Dunnett Post-hoc test

The mean age of females and males were 63.79+15.71 years and 58.17+12.92 years respectively. The baseline characteristics viz., age, gender, hypertension, diabetes mellitus, smoking, alcohol, tobacco use and past History of CVD were significantly different among the three groups except for hypercholesterolemia which were significantly higher among the groups with STEMI and NSTEMI. [Table-1]

The means of Mean platelet volume (MPV) was statistically significantly ($P<0.05$) higher in STEMI (10.48±1.42) and NSTEMI groups (9.73±1.15) compared to NCCP group (8.00±1.28)[$F(2,72)=24.09$, $P=0.000$], means of Platelet Distribution width (PDW) was statistically significantly ($P<0.05$) higher in STEMI (13.92±1.57) and NSTEMI groups (12.84±1.54) compared to NCCP group(11.79±1.70) [F(2,72)=10.97, P =0.000]and the means of Platelet Large Cell Ratio (PLCR) was statistically significantly ($P<0.05$) higher in STEMI (25.19±6.15) and NSTEMI groups (22.74±4.84) compared to NCCP group(16.75±4.99) [$F(2,72)=16.37$, $P=0.000$] ($P<0.05$). [Table-2 and Table-3]

Among the various risk factors for acute coronary syndromes smoking, alcohol, use of tobacco, hypertension, random blood sugar, blood urea, serum creatinine were not significantly associated with occurrence of acute coronary syndromes ($P>0.05$). Treatment with antiplatelet drugs also was not associated with occurrence of acute coronary syndromes ($P>0.05$). [Table-4]

The area under the curve for MPV was 0.892 with SE = 0.037 and 95% CI ranging from 0.820 to 0.963 ($P<0.05$); for PLCR was 0.827 with SE=0.046 and 95% CI ranging from 0.736 to 0.918 ($P<0.05$); and for PDW was 0.751 with SE = 0.064 and 95% CI ranging from 0.625 to 0.877 ($P<0.05$). MPV was a good indicator compared to PLCR and PDW to detect patients with acute coronary syndromes.MPV cut off of 9.15 fL predicted

Variables		ACS			χ^2 Value (*P*-Value)
		NCCP	NSTEMI	STEMI	
Smoking	Present	07	06	10	1.63 (0.44)
	Absent	18	19	15	
Alcohol	Present	07	08	10	0.84 (0.65)
	Absent	18	17	15	
Tobacco Use	Present	09	12	09	1.00 (0.60)
	Absent	16	13	16	
HTN	Present	14	14	12	0.42 (0.80)
	Absent	11	11	13	
RBS	Normal	19	14	14	2.85 (0.24)
	Abnormal	06	11	11	
Blood Urea	Normal	25	24	24	1.02 (0.59)
	Abnormal	00	01	01	
Serum Creatinine	Normal	22	18	21	2.28 (0.31)
	Abnormal	03	07	04	

Table-3: Association of various risk factors of acute coronary syndromes and occurrence of acute coronary syndromes

Variables		ACS			χ^2 Value (P-Value)
		NCCP	NSTEMI	STEMI	
Smoking	Present	07	06	10	1.63
	Absent	18	19	15	(0.44)
Alcohol	Present	07	08	10	0.84
	Absent	18	17	15	(0.65)
Tobacco Use	Present	09	12	09	1.00
	Absent	16	13	16	(0.60)
HTN	Present	14	14	12	0.42
	Absent	11	11	13	(0.80)
RBS	Normal	19	14	14	2.85
	Abnormal	06	11	11	(0.24)
Blood Urea	Normal	25	24	24	1.02
	Abnormal	00	01	01	(0.59)
Serum Creatinine	Normal	22	18	21	2.28
	Abnormal	03	07	04	(0.31)

Table-4: Association of various risk factors of acute coronary syndromes and occurrence of acute coronary syndromes

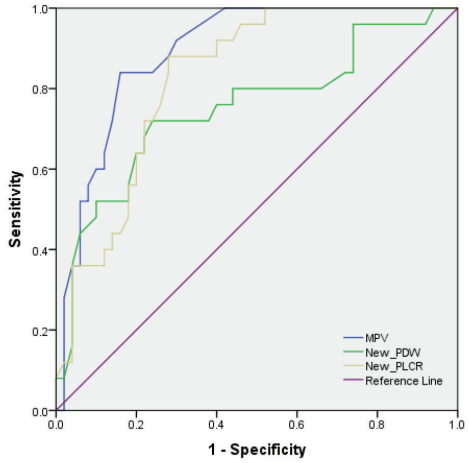

Figure-1: ROC curve for mean platelet volume, platelet distribution width and platelet large cell ratio among patients with acute coronary syndromes

ACS the best with both sensitivity and specificity being 0.84 (84%). [Figure-1]

DISCUSSION

Platelets have been implicated to play an important role in the pathogenesis of atherosclerosis and its complications like IHD. In order to obtain a larger surface, platelets change in shape during activation from discoid to spherical. Platelet indices such as MPV and PDW are easily measured, and they increase during platelet activation. 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 CAD or ACS.[9]

The current study showed higher MPV in STEMI (10.48 ± 1.42) and NSTEMI (9.73 ± 1.15) groups compared to NCCP group which had MPV of 8.0 ± 1.28. As the study was cross sectional, no follow up details are available and the prognostic utility of the values cannot be elucidated. This finding is also corroborated in the studies done by Ranjith M P et al.,[10] done in Jabalpur India, M MKhandekaret al.,[11] done on 210 patients, and also by Pervin S et al.,[12] among 142 patients.

Other Platelet volume indices being PDW and P-LCR are also of clinical importance.

In our study PDW was statistically significantly (P<0.05) higher in STEMI (13.92 ± 1.57) and NSTEMI (12.84 ± 1.54) compared to non-cardiac chest pain group (11.79 ± 1.70).

Studies by M MKhandekaret al.,[11] Pervin S et al.,[12] Turgay C et al.,[13] Shafaei SHet al.,[14] suggested that there was increase in PDW values in unstable angina and MI when compared to the normal population.

Studies by Ranjith M P et al.,[10] M MKhandakaret al.,[11] and Shafaei SH et al.,[14] showed that P-LCR was significantly higher in patients with ACS compared to control population which was similar to our results which showed a statistically significant increase in P-LCR values among (p<0.05) STEMI (25.19 ± 6.15) and NSTEMI (22.74 ± 4.84) groups compared to control group of NCCP (16.75 ± 4.99) which is expected result as P-LCR is another index of platelet volume. But its individual significance in ACS is yet to be established.

In the current study, MPV is a good indicator compared to detect patients with ACS and MPV cut off of 9.15 fL predicted ACS the best with both sensitivity and specificity being 0.84 (84%). Similarly in the study conducted by Pervinet al.,[12] and Khode V et al.,[15] had the similar findings. A study done by Vagdatiet al.,[16] concluded that combined use of MPV and PDW could predict the platelet activation more efficiently.

Diabetes Mellitus is a prothrombotic state associated with accelerated atherosclerosis.We found statistically significant rise in MPV in diabetic patients but there was no significant correlation between PDW and P-LCR and diabetes. Several studies have shown positive correlation between diabetes and MPV, a study by Jindal Set al.,[17] found that MPV was significantly higher in diabetic patients compared to controls. In addition, other platelet indices (PDW and P-LCR) were also higher in diabetic subjects as compared to controls. However study by Eun YM et al,[18] showed no significant correlation between the two. Due to these conflicting results, further studies are required.

Our study showed no statistical difference in platelet-indices between hypertensives and normotensives, but there are few studies by Varolet al.,[19] and Cobbanet al.,[20] which showed contrary results. Karabacak Met al.,[21] showed that MPV was higher in patients with hypertensive emergencies and urgencies. This could be because of the smaller sample size and control

of hypertension in the study population and we found no significant difference in platelet-indices and smoking, which was in concordance with study by Arslan E et al.,[22] but contrary results were found in a study by Kario K et al.[23]
Swaminathan et al.,[24] also showed a significant increase in all the platelet indices in smokers. This difference could be explained by the different types of smoking habits depending on the type and number of cigarettes/ beedi smoked in the study population. Hence further studies are required to conclusively establish the effect of smoking on the platelet indices.

Limitations

The study lacks the generalizability as it was a purposive sampling and the sample size was small and hence needs to be carried out in larger samples. The case control study would have been a better study design as the confounding factors especially dyslipidaemia/ hypercholesterolemia cannot be ruled out in a cross sectional study design. This could not be carried out due to the question of feasibility. Establishing a prognostic significance of the markers needs to be conducted as a separate study.

CONCLUSION

Patients with acute coronary syndromes had higher platelet volume indices at the time of admission compared to NCCP group. Hence measurement of the platelet volume indices especially Mean platelet volume may be of some help in eliciting the pro-thrombotic events, and hence can act as one of the biomarker in detecting and differentiating the occurrence of cardiac or non-cardiac chest pain. Therefore they can benefit from early diagnosis and interventions.

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