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Mean Platelet Volume in Acute Coronary Syndrome

KEYWORDS: Mean Platelet Volume, Acute coronary syndrome, platelet count

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ABSTRACT ***BACKGROUND:*** *Multiple biomarkers are available in risk stratification of acute coronary syndromes. Mean platelet volume is a simple measure of the functional status of platelets. As platelets play a key role in pathogenesis of acute coronary syndrome, We studied the significance of mean platelet volume in acute coronary syndrome.*

METHODS: *This hospital based prospective cross sectional study was conducted in a tertiary hospital in Puducherry from January 2014 to December 2014. We studied 150 patients (81 men: 69 women) defined clinically as acute coronary syndrome (n=50), stable angina (n=50) and control (n= 50). In all the patients the baseline blood samples were collected for routine haematological testing and the mean platelet volume was compared between the groups.*

RESULTS: *There was statistical difference in mean platelet volume between the three groups (p= <0.001). The mean platelet volume in patients with acute coronary syndrome was significantly larger (9.702 ± 0.967fl) than the stable angina (8.482 ± 0.7894fl) (p <0.001) and control group (8.18 ± 0.8123fl) with (p<0.001).*

CONCLUSION: *Acute coronary syndrome might be preceded or associated with increase in platelet volume.*

Introduction:
Acute coronary syndrome has a wide spectrum of presentation from unstable angina to acute myocardial infarction[1]. In developing countries like INDIA, acute coronary syndrome is becoming a leading cause of morbidity and mortality[2] Various risk factors cause coronary heart disease like family history, age, hypertension, cigarette smoking, diabetes mellitus and dyslipidemia. Other risk factors that help in identifying the risk of myocardial infarction are yet to be found out. Prevention and control of the risk factors will alter the incidence and outcome of patients with acute coronary syndrome. Despite the various biomarkers available, the identification of myocardial ischemia is challenging and often there is overestimation of the likelyhood of myocardial ischemia in low risk patients[3].

Only one fifth of the patients with chest pain require emergency care. There is no segregation of these patients in the beginning, resulting in doctors over admitting the patients. This further reduces the quality of care given to the patients who actually require. This calls for the need of biochemical markers which help in the risk stratification of patients with acute coronary syndrome[3].

Platelets play a vital role in thrombus formation and in the pathogenesis of atherosclerosis in patients with myocardial infarction. After rupture of atherosclerotic plaques, platelets get activated and prothrombotic events start predisposing to myocardial infarction. Platelet activation initiates the formation of free arachidonic acid and which is later transformed to Thromboxane A2. Thromboxane A2 causes amplification of the inflammatory response. Thus platelet aggregation and activation play a key role in pathophysiology of coronary heart disease[1].

Platelets are heterogeneous in density, activity and size. Larger platelets are more active and are more adhesive and aggregate more than the platelets of smaller size[4]. Hyperactive and larger platelets play a key role in accelerating the formation of intracoronary thrombus, thereby leading to the occurrence of an acute thrombotic event[5]. Platelets secrete various substances that are crucial mediators of inflammation, thrombosis and atherosclerosis[6] Proteins secreted by activated platelets can adhere to the vessel wall and promote the development of atherosclerosis and thrombosis. Despite this biologic significance, however, the complement of proteins comprising the platelet releasate is largely unknown. Secretogranin III, cyclophilin A, and calumenin were confirmed to localize in platelets and to be released upon activation. Furthermore, while absent in normal vasculature, they were identified in human atherosclerotic lesions. Therefore, these and other proteins released from platelets may contribute to atherosclerosis and to the thrombosis that complicates the disease. Moreover, as soluble extracellular proteins, they may prove suitable as novel therapeutic targets.

Glycoprotein IIIa and P-selectins are expressed by the activated platelets[7] The use of antiplatelet medication to decrease the atherothrombotic process has reinforced the major role of platelets in atherothrombotic process[8].

The platelet physiology and morphology are determined during fragmentation of the precursor cell, megakaryo-

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cytes[9]. Megakaryocyte ploidy correlated closely with platelet volume. Chronic hypoxia has shown to increase the platelet volume[10]. Thrombopoietin, interleukin 3 and cytokines(IL-3, IL-6, IL-11) [11],[12],[13] produces more reactive and larger platelet[14]. Studies have shown that atherosclerosis influences the bone marrow megakaryocytes before platelet production[14],[15].

Mean platelet volume is an indicator of platelet size and mean platelet volume has association with platelet activation[16] Mean platelet volume is a marker for platelet reactivity. Mean platelet volume is useful in prediction of the risk of occurrence of cardiovascular events[17]. Higher mean platelet volume is found in patients with hypertension[18], diabetes[19], obesity[20], hypercholesterolemia[21] and smoking[22] suggesting that there may be a common mechanism by which these factors influence the risk of cardiovascular disease.

There are a wide variety of methods to measure platelet activity and identify the individuals at risk of acute coronary events. There is lack of sufficient data about the optimal method of platelet testing. The optimal cut off for distinguishing increased risk is still uncertain and the clinical utility of the results are not well established[23].

There are many international studies assessing the significance of role of mean platelet volume and acute coronary syndrome. With this regard we investigated the association between MPV in patients admitted with the diagnosis of acute coronary syndrome and to assess the efficiency of MPV in the diagnostic workup for acute coronary syndrome in south Indian scenario.

Materials and methods:
We enrolled 150 adult patients (M:F = 81:69; age mean 56.02± SD 12.35 in ACS group,52.56 ±10.32 in stable angina and 40.04±10.85 in control group)who were consecutively admitted during January to December 2014 to the department of General medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry. In all the patients, baseline blood sampling were done for routine hematological testing and for Mean platelet volume. The blood was collected by venepuncture into a tube containing ethylenediaminetetraacetic acid. The mean platelet volume and platelet count were measured using Mindray BC-5200 automated analyzer. All patients underwent a standard 12 lead ECG which was interpreted by an experienced cardiologist.

Table 1 Demographic Data and Risk Factors in the Study Group

	Patients with ACS	Patients with stable angina	Control group
Age	56.02±12.35	52.56±10.32	40.04±10.85
Females	17	33	19
Platelet count(lakhs/mm^3)	2.427±0.467	2.752±0.754	2.619±0.444
MPV (fl)	9.702±0.9671	8.482±0.789	8.188±0.8123
Hypertension	28(56%)	13(26%)	0
Diabetes mellitus	23(46%)	17(34%)	0
Smoking	16(32%)	12(24%)	10(20%)
Alcohol	15(30%)	10(20%)	17(34%)
Dyslipidemia	8(16%)	3(6%)	4(8%)
Family history	3(6%)	0	0
Previous history of CAD	5(10%)	0	0

Statistical methods:
The statistical analysis was carried out using one way ANOVA followed by post hoc Tamhane's T2 test. P values <0.05 were considered to be statistically significant at 95 % confidence interval.

Results
The baseline characteristics of our study population and the main results of this investigation are shown in the table 1. A total of 50 patients had a diagnosis of ACS based on the presence of the suggestive cardiac symptoms and ischemic ECG changes. Patients diagnosed as ACS(MPV= 9.702±0.9671fl) showed a significantly higher MPV than the stable angina(MPV=8.482 ±0.784 fl) and the control group(8.188±0.812 fl). The platelet count in the ACS group was 2.47±0.467lakhs/mm3, in stable angina group was 2.752±0.754 lakhs/mm3 and in control group was 2.619lakhs/mm3 ±0.584. There was statistically significant difference in the platelet count between ACS and the stable angina groups(p=0.034). The statistically significant difference was noted between ACS and control group and between control and stable angina groups.

DISCUSSION:
Platelets play a vital role in pathogenesis of atherosclerosis[1,16] Platelet size and function are correlated. Activated megakaryocytes produce larger platelets which are more reactive than normal platelets[3]. Hyperactive and larger platelets accelerate the formation and propagation of intracoronary thrombus[24] Hence MPV, as an indicator of platelet size is a reliable index for activation of platelets and may be potentially useful marker for cardiovascular risk stratification[17]. Senaran et al reported that thrombopoietin increases platelet size and platelet counts which in turn contributes to progression of coronary artery disease[5]. In patients with ACS, the higher MPV indicates not only increased risk of ACS but also indicated ischemic complications[16] Boos et al and Kilicli et al in their study concluded that MPV was higher in the myocardial infarction patients when compared with the control and stable angina group[25,26.]

Maden et al reported that MPV may be valuable in planning the need for adjuvant therapy to improve the outcomes in patients undergoing percutaneous coronary intervention[27.]

In various studies, the influence of diabetes28, hypertension[21] and smoking[22] on platelet size was observed. However in our study, there was no influence of smoking, diabetes, and alcohol on MPV.

Based on the results and the methodology employed, we have concluded that:

Mean Platelet volume was found to be increased in ACS group when compared to Stable angina and healthy controls.

Statistical significance was found between ACS and control group. There was no statistical difference between stable angina and control group.

More comprehensive studies are required to further evaluate the beneficial effects of platelet aggregation inhibitors or other drugs on patients with increased MPV.

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Table 2 Comparison of Mean Platelet Volume in various studies

	AMI		Non AMI	
	Number of patients	MPV(fl)	Number of patients	MPV(fl)
Senaran[5]	20	8.2±0.8	37	7.2±0.5
Yilmaz[16]"	111	10.4±0.6	225	9.41±0.7
Hendra[29]	147	10.0±.26	150	9.45±0.98
Avarmakis[30]	86	11.0±1.6	164	99±1.49
Cameron[31]	100	9.24±0.84	1898	8.48±0.71
Khandekar[32]	77	10.4±1.0	117	9.5±0.97
Kilicli-Camur[25]	70	11.75±1.07	130	11.12±0.77
Kishk[33]	70	7.30±0.84	95	6.70±0.97
Martin[34]	15	7.6±0.67	22	6.6±0.38
Trowbridge A[35]	103	7.30±0.84	72	6.56±0.68
Boos[26]	111	8.5±1.2	19	7.7±0.46
Mathur[36]	15	9.8±1.05	15	10.7±0.97
Erne[37]	55	10.9±1.5	526	9.69±1.09
Our study	50	9.70 ± 0.967	50	8.48 ± 0.78

MPV is an economic and simple laboratory measurement with 83% negative predictive value. Hence it may be used along with other cardiac biomarkers in risk stratification of cardiovascular disease. The population studies were small when compared to other studies. The MPV cut off point for predicting the cardiovascular risk is not well defined. Future randomized trials are needed to confirm the clinical usefulness of using MPV in predicting the myocardial infarction or death.

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