MEAN PLATELET VOLUME IN ACUTE CORONARY SYNDROME: A PROSPECTIVE OBSERVATIONAL STUDY
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ABSTRACT: AIM: To study the mean platelet volume in acute coronary syndrome patients and compare it with non acute coronary syndrome patients. MATERIALS AND METHODS: This is a case-control study carried out between November 2012 to October 2013 at the Department of Internal Medicine and the Department of Cardiology, Government Medical College, Jammu. A total of 200 subjects were evaluated after applying proper inclusion and exclusion criterias. These included 100 cases with acute coronary syndromes and 100 age and sex matched controls. Measurement of mean platelet volume was done in both and analysis of other variables like hypertension, diabetes, body mass index, smoking, alcohol, family history, etc was done with respect to mean platelet volume. The results were compiled statistically using student t-test and ANOVA. RESULTS: The mean age of cases was 47.60±7.12 years, while the mean age of controls was 44.34 ± 7.44 years. The mean platelet volume in case cases was 9.33 ± 1.03 fL, while in controls it was 7.05 ± 0.32 fL. When this was statistically compared a highly significant (p=.000) relationship between them was found.
KEYWORDS: Mean Platelet Volume, Acute Coronary Syndrome.

INTRODUCTION: Despite the developments regarding its diagnosis and treatment in recent years, acute coronary syndromes (ACS) keeps its place as one the most significant reason for morbidity and mortality.¹ Acute coronary syndrome is a set of signs and symptoms caused by rupture of an arterial plaque which provokes platelet-rich coronary thrombus formation. The thrombus leads to partial or complete coronary artery occlusion which in turn results in myocardial ischemia and various clinical manifestations, ranging from unstable angina to acute myocardial infarction.² The known major risk factors for coronary heart disease are age, family history, cigarette smoking, hypertension, elevated LDL cholesterol and diabetes mellitus. Apart from that, endothelial dysfunction, lipoprotein (a), homocysteine and C-reactive protein are considered as new risk factors for coronary artery disease.³ Description of risk factors in coronary heart disease has a very important place in the prevention of acute coronary syndromes as well as in the follow-up and treatment of patients with coronary heart disease (Mercan et al., 2010).⁴ Acute coronary syndromes, characterized by the rupture of unstable plaque and the subsequent thrombotic process involving platelets, have been increasing in relative frequency. The central role of platelet activation has long been noticed in this pathophysiology, hence many therapies are directed against it.⁵ Coronary atherosclerosis progression is an active process involving complex interactions between inflammation, thrombosis and endothelial damage/dysfunction. Vascular intimal injury and plaque rupture exposes subepithelial collagen and von Willebrand factor (vWF), leading to prompt platelet-endothelial adhesion at the injured site and subsequent platelet activation.

In addition, there is simultaneous platelet-platelet aggregation and activation of the coagulation cascade, with the formation of a platelet-fibrin plug leading to localized and/or
downstream vascular luminal compromise/obstruction, culminating ultimately in a potential acute coronary syndrome event. Traditionally, platelet function and size correlate because larger platelets, produced from activated megakaryocytes in the bone marrow, are likely to be more reactive than normal platelets. Consequently, larger and hyperactive platelets play a pivotal role in accelerating the formation and propagation of intracoronary thrombus, leading to the occurrence of acute thrombotic events. Given the important role of platelets in both the activation and perpetuation of arterial thrombosis, there has been intense research interest in the utility of platelet function testing as an additional tool in cardiac risk stratification. These observations have led to the hypothesis that increased mean platelet volume, which is an index of platelet size that correlates with platelet activation and is a reliable index of platelet activation, may be a potential useful marker in cardiovascular risk stratification.

Consensus guidelines on a universal definition of myocardial infarction have been issued by the American Heart Association, World Heart Federation, European Society of Cardiology – that recommend cardiac troponin I and cardiac troponin T (cTnT) measurements as the preferred biochemical cardiac biomarkers for diagnosing ACS. However, the diagnostic efficiency of cardiac troponins within 2 to 4 hours of the symptom onset is limited. While atherosclerotic plaque rupture starts the thrombogenic phenomenon in ACS, the activity of circulating platelets plays an important role for the progression of thrombus. Measurement of mean platelet volume is an easy and simple approach to assess platelet function. Mean platelet volume is known to be increased in patients with risk factors for coronary artery disease compared to healthy individuals. Platelets with increased mean platelet volume are more hemostatically active.

This is due to the presence of more active stored mediators in platelets with large volume. As a result, these platelets play a primary role in the process of thrombosis. It is also important in terms of efficacy of fibrinolytic therapy. Increased platelet activation adversely affects thrombolytic process, thereby leading to incomplete reperfusion response to fibrinolytic therapy. The study was conducted in the Postgraduate Department of Internal Medicine and the Department of Cardiology, Government Medical College, Jammu for a period of one year (November 2012 to October 2013). The protocol of the study was approved by the Institutional Ethical Committee.

STUDY DESIGN: The present study was conducted in the Postgraduate Department of Internal Medicine and the Department of Cardiology, Government Medical College, Jammu over a period of one year (November 2012 to October 2013). One hundred patients of acute coronary syndrome were enrolled as cases and 100 subjects without acute coronary syndrome were enrolled as controls. The measurement of mean platelet volume was done along with evaluation for presence or absence of other variables like hypertension, diabetes mellitus, obesity (BMI), smoking, alcohol, family history of CAD, etc. in both the groups.

INCLUSION CRITERIA FOR CASES

- Age between 30 and 70 years.
- Only 1st time diagnosed cases of acute coronary syndrome were enrolled for the study.

INCLUSION CRITERIA FOR CONTROLS

- Age between 30 and 70 years.
- Controls were selected from healthy attendants accompanying various patients.
EXCLUSION CRITERIA FOR CASES AND CONTROLS:
- Age <30 years and age more than >70 years.
- Patients with past history of acute coronary syndrome.
- Acute or chronic liver disease.
- Acute or chronic kidney disease.
- Acute febrile illness.
- Anemic patients.
- Patients on anti-platelet and NSAIDs therapy.
- Hematological disorder i.e. thrombocytopenia, CML, bleeding diathesis, etc.

STUDY PROCEDURE: The enrolled subjects had undergone a 5 ml blood sample collection via antecubital venous access for complete blood count including mean platelet volume estimation. The blood sample was collected within 1 hour of presentation to the hospital in case of acute coronary syndrome patients. Blood sample was analyzed in automatic blood analyzer using anti-coagulant EDTA. The enrolled patients in cases and control groups also underwent renal function tests, liver function tests, lipid profile, X-ray chest PA view, Electrocardiography, Ultrasonography abdomen and cardiac biomarker analysis (For cases only). The data was collected using Microsoft Excel and analysed by using IBM SPSS software for statistical analysis.

RESULTS AND DISCUSSION: The data obtained is shown below in the tabulated form:

| PARAMETER          | ACS (CASES)  | Non-ACS (CONTROLS) |
|--------------------|--------------|-------------------|
| Mean age(years) ± SD | 47.6 ± 7.12  | 44.34 ± 7.44      |
| Male: Female       | 1.94: 1      | 1.70: 1           |
| Abnormal BMI       | 46%          | 32%               |
| Dyslipidemia       | 32%          | 14%               |
| Smoking            | 38%          | 19%               |
| Alcoholism         | 35%          | 15%               |
| Hypertension       | 34%          | 24%               |
| Mean blood sugar ± SD | 124.64 ± 34.32 | 105 ± 18.88 |
| Diabetes mellitus  | 29%          | 22%               |
| Poor Socioeconomic status | 39%   | 42%               |
| MPV(fL) ± SD       | 9.33 (± 1.03) | 7.05 (± 0.33)     |

Table 1

The mean age of cases was 47.60 ± 7.12 years, while the mean age of controls was 44.34 ± 7.44 years. The MPV in cases was 9.33 ± 1.03 fl, while in controls it was 7.05 ± 0.32 fl. When MPV was compared in the two groups, a highly significant (p=.000) relationship between them was found. The cases were further subdivided according to ECG changes and rise in cardiac biomarkers. Myocardial infarction was detected in 31 (31%), stable angina in 35 (35%) and unstable angina in 34 (34%) cases. The subgroup analysis revealed a statistically significant positive association of MPV...
with myocardial infarction (9.06 ± 0.25 fL), unstable angina (10.60 ± 0.53 fL) and stable angina (8.3 ± 0.20 fL).

| Diagnosis                  | MPV (fL) Mean ± SD (Range) | Statistical inference (ANOVA) |
|----------------------------|-----------------------------|-------------------------------|
| Myocardial infarction      | 9.06 ± 0.25 (8.70-9.70)     | F = 347.79; p = .000; Highly significant |
| (n=31)                     |                             |                               |
| Stable angina              | 8.33 ± 0.20 (8-8.80)        |                               |
| (n=35)                     |                             |                               |
| Unstable angina            | 10.60 ± 0.53 (9.50-11.60)   |                               |
| (n=34)                     |                             |                               |

Table 2

Similar results were also reported in studies by Mercan et al. (2010) and Mirzaie et al. (2012). They concluded that unstable angina might be associated with high platelet destruction rate which is not completely compensated for increase in platelet production. It implies that MPV has significant positive association with acute coronary syndrome group. A significant association was not found between MPV and hypertension, diabetes mellitus, obesity (BMI), smoking, alcohol and family history of CAD. Kishk et al. (1985) in their study had similarly reported that mean platelet volume is independent of smoking, area or diameter of infarct, etc. As MPV was increased in patients presenting with acute coronary syndrome as compared to controls, it can be concluded that larger platelets may constitute a higher risk for acute coronary syndrome and ischemic complications.

**CONCLUSION:** MPV is a simpler parameter, easily available in routine CBC analysis in automatic analyzer and is easy to perform. It may serve as an important tool for the assessment of patients with risk factors for CAD without adding any additional economical burden on patients. Also, it can give us some insight about therapeutic management of patients and predicting the possibility of acute coronary events in patients who do not fulfill the criteria of acute coronary syndrome on arrival especially when the patients narrate atypical history and present with non-specific complaints and negative biochemistry. Further studies with larger sample size are required to validate our findings.

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