IS LARGE PLATELET SIZE A RISK FACTOR FOR ACUTE CORONARY SYNDROME: A RETROSPECTIVE CASE-CONTROL STUDY

A BHAYANA*, D JOSHI**

ABSTRACT

Background: Coronary heart disease (CHD) is among the top five causes of morbidity worldwide, and manifests as acute coronary syndrome (ACS). Conventional risk factors for atherosclerosis include smoking, diabetes mellitus, hypertension, hyperlipidemia, and obesity. Platelets are known to play a critical role in conversion of a chronic atherosclerotic plaque into an occluding thrombus, and it is postulated that individuals with a large platelets could be more predisposed to occluding thrombi in coronary vessels. The aim of the current study was to determine if patients with acute coronary syndromes (ACS) have higher mean platelet volume (MPV) as compared to normal healthy individuals.

Methods: A retrospective case-control study was conducted to compared the platelet indices of patients who were admitted with ACS between January-April, 2007 (cases), with age matched individuals admitted for elective surgical procedures (controls). Both cases and controls were identified through electronic hospital records.

Results: A total of 50 cases and 100 controls were included in the study. The mean platelet volume for cases as well as controls was 8.04 fl (OR = 1.00 95% CI (0.74-1.04).

Conclusion: Large platelet size is not a risk factor for acute coronary syndrome.

Introduction

Coronary heart disease (CHD) is among the top five causes of morbidity worldwide, and is increasingly becoming common in India as well. The underlying pathology of CHD is atherosclerosis, which initiates by second decade of life, and progresses chronically to manifest as acute coronary syndromes (ACS) usually in fourth and fifth decades of life. Atherosclerotic process is multi-factorial, and our understanding of its pathogenesis has improved over past few years. Conventional risk factors for atherosclerosis include smoking, diabetes mellitus, hypertension, hyperlipidemia, obesity and stress which either acting singly or in combination increase the chances of developing coronary atherosclerosis. ACS (which include unstable angina, acute myocardial infarction and sudden cardiac death) depict an acceleration of this chronic process characterized by rupture or fissuring of an unstable atherosclerotic plaque, accompanied by a cascade of platelet reactions resulting into thrombus formation.

Platelets are known to play a critical role in conversion of a chronic atherosclerotic plaque into an occluding thrombus. It is unclear if certain platelet characteristics predispose some individuals with atherosclerosis to develop ACS. It is likely that different individuals have platelets of variable size, density, and reactivity. Larger the platelets, they are more likely to be metabolically and enzymatically active. It is known that large

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platelets are denser, aggregate more rapidly with subendothelial collagen, produce more thromboxane A2 and express more glycoprotein Ib and glycoprotein IIb/IIIA receptors. These characteristics may lead to increased thrombosis, and possibly ACS.

Electronic cell counters have made it possible to measure platelet volume indices (PVI), specifically mean platelet volume (MPV), and platelet distribution width (PDW). This is a simple and cost effective method of identifying these larger platelets. The current study was planned to evaluate mean platelet volume as a risk factor in patients with an incident acute coronary syndrome. The specific research question for this study was: Do patients with acute coronary syndromes (ACS) have higher mean platelet volume (MPV) as compared to normal healthy individuals?

Aims and objectives:
The aim of the present study was to measure platelet volume indices specifically mean platelet volume in patients with acute coronary syndromes and to compare the values with normal healthy controls.

Methods:
Setting: The Mahatma Gandhi Institute of Medical Sciences, Sevagram is a rural medical school located in Maharashtra. It is a 648-bed teaching institution with 325,000 out patient visits and about 6,500 indoor admissions to medicine wards each year. Nearly 1-2 cases of acute coronary syndromes are admitted each day in the medicine intensive care unit. Treating doctors order a complete blood count for all patients with ACS as a standard care. Since past eight years, all blood counts are being performed using an electronic cell counter (coulter), in the department of Pathology. This electronic cell counter meets all the quality control requirements and is periodically standardized.

Study design: We did a retrospective case-control study to answer the question of our interest. We compared the platelet indices of patients who were admitted with ACS between January-April 2007 (cases), with age matched individuals admitted for elective surgical procedures (controls).

Inclusion criteria:
Cases - All patients with a discharge/death diagnosis of Acute Coronary syndrome (Acute Myocardial infarction (STEMI / NSTEMI) or Unstable angina) admitted between January and April 2007.

Controls - Patients who were admitted to MGIMS hospital for elective surgical procedures (hernia, hydrocele, cataract extraction). Controls were matched with cases by age (+/- 5 years) and month of admission to the hospital.

Exclusion criteria:
Those cases, 1) Where the electronic cell count was not obtained within 12 hours of hospital admission (as anti-platelet drug therapies can modify platelet therapies), and 2) Where the blood sample either had micro-thrombi or a marked anti-coagulant effect (as reported on peripheral smear), were excluded.

Those controls whose blood samples were reported to have either a micro-thrombi or a marked anti-coagulant effect (as reported on peripheral smear), were also excluded.

Study procedures:
MGIMS hospital has an electronic hospital records system, and records of all discharge diagnosis and electronic cell counts are maintained in an electronic form. The clinical details, and
the electronic cell counts of the same patient are linked using a twelve digit unique identifier, known as a case-record number.

We used hospital information system to obtain a list of CR numbers of all eligible cases and controls. We masked any personal identifiers in the list such as name or address. We also obtained the date and time of admission for these cases from the hospital information system. Then we obtained the electronic cell count data for these eligible patients, using the CR number as a reference. This data is also maintained in an electronic data-base form in the department of pathology. The time interval between hospital admission and cell count, presence of microthrombi or anticoagulation were noted to determine any exclusions. Platelet count and platelet volume indices (MPV and PDW) were noted in both cases and controls. Ethical approval was obtained from the institute’s ethical committee to conduct this study.

*Statistical analysis:* Data was analysed using STATA software.

**Results**

We recruited 50 eligible cases and 100 controls in this study. The clinical and laboratory data of cases and controls is depicted in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n=50)</th>
<th>Controls (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female%</td>
<td>78/22</td>
<td>67/33</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>57.13</td>
<td>55.7</td>
</tr>
<tr>
<td>S.D</td>
<td>9.7</td>
<td>11.0</td>
</tr>
<tr>
<td>Range</td>
<td>31–76</td>
<td>45–87</td>
</tr>
<tr>
<td>Mean Platelet count x 103</td>
<td>290 (108)</td>
<td>279 (124)</td>
</tr>
<tr>
<td>Mean MPV in fl</td>
<td>8.04 (0.94)</td>
<td>8.04 (1.22)</td>
</tr>
<tr>
<td>PDW</td>
<td>17.06 (0.76)</td>
<td>16.81 (1.15)</td>
</tr>
</tbody>
</table>

Mean platelet volume was same for both cases and controls (8.04) and no significant statistical difference was found between mean platelet count and mean PDW of cases and controls. We also computed odds ratio for development of ACS for different platelet derived parameters (Table 2). None of these odds ratio was found to be statistically significant.

**Table 2:** Platelet derived parameters as a risk factor for ACS

<table>
<thead>
<tr>
<th>Variable</th>
<th>O R</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 1 fl rise in MPV</td>
<td>1.00</td>
<td>0.74–1.34</td>
</tr>
<tr>
<td>MPV &gt; 8 fl</td>
<td>1.08</td>
<td>0.51–2.25</td>
</tr>
<tr>
<td>MPV &gt;9 fl</td>
<td>0.71</td>
<td>0.23–1.94</td>
</tr>
<tr>
<td>MPV &gt;10 fl</td>
<td>0.51</td>
<td>0.08–2.07</td>
</tr>
<tr>
<td>Every 1 unit rise in PDW</td>
<td>1.26</td>
<td>0.84–1.88</td>
</tr>
<tr>
<td>Every additional 10^3 platelets in circulation</td>
<td>1.00</td>
<td>0.99–1.00</td>
</tr>
</tbody>
</table>

**Discussion**

One of the principal determining factors in development of acute coronary syndrome is conversion of a stable atherosclerotic plaque into an unstable one. Platelets are known to play a key role in this event and if it is proven that larger platelets are a risk factor for development of ACS, it could have a significant prognostic value.

In an Indian study conducted by Khandekar et al, the authors suggested that all platelet volume indices are significantly raised in patients with acute myocardial infarction and unstable angina patients as compared to those with stable coronary artery disease. The authors had studied platelet volume indices including MPV, platelet distribution width (PDW) and platelet large cell ratio (P-LCR) in a scenario of ischemic heart disease in Indian patients. It has also been suggested by Yilmaz et al that as in
patients with non ST elevation acute coronary syndrome, higher MPV was associated with a higher risk of ischemic complications, it may have a prognostic role as well. Since larger platelets are present in circulation before an acute coronary event,\textsuperscript{7} this could be a risk factor for progression of atheroma into an occluding thrombus. Lakkis et al\textsuperscript{8} also reported increase in reticulated platelets (newly formed larger platelets) in patients with acute myocardial infarction as compared to those with stable angina.

In contrast to the results obtained in these studies, we did not find any significant difference between platelet count and volume indices of cases and controls. Our findings are in concordance with the findings of Damodar et al\textsuperscript{9} who also concluded that raised MPV is not a risk factor for development of acute coronary syndrome.

Though from our findings we concluded that high MPV is not a risk factor for development of ACS, our study has several limitations. Since we conducted a retrospective study, we could not gather reliable information regarding other known risk factors for ACS (obesity, smoking, diabetes mellitus, hypercholesterolemia, hyperlipidemia etc) in controls. Such data was available only for cases so we could not make a comparison. Since MPV has also been reported to be increased in obese individuals, smokers, diabetics and patients with hypercholesterolemia\textsuperscript{6,10} these factors can confound the results. Hence it is important to have data regarding other risk factor variables for both cases and controls and then perform a logistic regression to look for independent predictors.

**Conclusion**

Mean Platelet Volume was not found to be a risk for Acute Coronary syndrome in our study. More research on this subject should be carried out on larger number of subjects before considering mean platelet volume as a risk factor and a marker of progression of disease for ACS.

**References**