Evaluation of platelet count and platelet indices in patients with hyperlipidemia

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Abstract

Background: Larger platelets tend to be metabolically and enzymatically more active than smaller platelets and secrete more prothrombotic factors. Studies have shown that hyperlipidemic patients who have larger platelets are more likely to have an associated disease condition and it is the presence of these conditions that brings the platelet in pre-thrombotic active state as reflected by the changes in its volume indices. The platelet activation is measured indirectly through several platelet indices routinely available without any additional cost in newer fully automated haematology analysers.

Materials and Methods: This is a registered case-control study carried out in the Department of Pathology, Medical College Baroda. A total of 120 subjects were studied including 60 cases (subdivided into two groups - Group A of hyperlipidemia only, Group B of hyperlipidemia with associated morbidities) and 60 controls with normal lipid profile without any associated diseases. The platelet parameters like platelet count and the platelet volume indices (PVI), including mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) were compared. Statistical analysis was done using 2 independent sample t-test and data was expressed as mean ±SD for each parameter.

Results: Mean MPV (8.63±1.09) and PDW (16.88±6.99) were significantly higher for cases than controls (mean MPV: 8.07±0.73 and mean PDW:13.4±2.21); p-value < 0.05. There is no significant difference between the study group and control group with respect to PC and PCT; p-value > 0.05. Also, hyperlipidemic patients having an associated disease had significantly higher MPV and PDW than the patients having hyperlipidemia in isolation. Conclusion: It is the presence of other diseases in hyperlipidemic patients that brings the platelets in pre-thrombotic active state as reflected by the changes in its volume indices. The estimation of these indices can be considered as an early, economical and rapid procedure for identification of complications in hyperlipidemic patients.

Key Words: Hyperlipidemia, Platelet count, Platelet indices.

INTRODUCTION

Finding a platelet function test linked to hyperlipidemia and that is routinely available, could be a first step towards identifying asymptomatic hyperlipidemic patients. Hyperlipidemia is an excess of fatty substances, largely cholesterol and triglycerides in blood. It can be primary (due to some inherited lipoprotein disorder) and secondary (due to any of a variety of metabolic diseases). Studies have shown that hyperlipidemic patients who have larger platelets are more likely to have an associated disease condition and the platelet volume indices may form a basis for the prediction of these diseases in hyperlipidemic patients1,2. The role of hyperlipidemia as a major risk for coronary heart disease, stroke and myocardial infarction has been known since long and several studies have been conducted all over the world linking the role of increased lipids with diabetes, coronary artery disease, hypertension and obesity3,4,5,6,7. Despite this, hyperlipidemia often goes
unnoticed due to absence of any specific symptoms, ignorance of the initial early screening for abnormal lipid profile and lastly but importantly, due to cost factor. Platelets are small anucleate highly complex blood cells, markedly heterogenous in size, density and metabolic, functional and biochemical properties\(^8\) that participate in critical reactions central to hemostasis and thrombosis. Hyperlipidemia increases the cholesterol content in platelets and enhances their reactivity causing platelet activation and thrombotic events. Larger platelets are considered to be metabolically, enzymatically and functionally more active than the smaller platelets\(^8\). These produce more thromboxane B2 than platelets in normal steady state function and are hemostatically more active and hence have more thrombogenic potential\(^9,10\). Thus, platelet activation is indirectly measured via platelet size or mean platelet volume (MPV)\(^9\). Automated cell counters have made the platelet count (PC) and the platelet volume indices (PVI) including mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit routinely available in most clinical laboratories at no additional cost. Studies have shown a constant association of increased MPV with various types of diseases like coronary artery disease, myocardial infarction, cerebral infarction and diabetes mellitus\(^9,11,12\). Given these close associations, hyperlipidemia could be indicated by changes in platelet size. It is the presence of other diseases in hyperlipidemic patients that brings the platelet in pro-thrombotic active state as reflected by the changes in its volume indices\(^1,2\). Therefore the present study deals with testing the platelet volume indices in patients of hyperlipidemia solely as well as in association with closely related disorders. The insight gained from interpretation of platelet count and platelet volume indices might be considerable and may allow for timely diagnosis and treatment of hyperlipidemia and hence prevention of further vascular complications.

**MATERIALS AND METHODS**

The 'Evaluation of platelet count and platelet indices in patients with hyperlipidemia' is a registered case-control study carried out in the Department of Pathology, Medical College Baroda. The study was approved by the local ethical committee. Informed consent was obtained from all the patients. A total of 120 subjects (60 cases and 60 control) were studied. Patients admitted to the wards and visiting OPDs with laboratory confirmed reports of hyperlipidemia comprised the study group. The study group (60 cases) was further subdivided into two groups - Group A (30 cases) of hyperlipidemia only, Group B (30 cases) of hyperlipidemia with associated morbidities (such as hypertension, diabetes mellitus, acute cerebrovascular events, acute coronary events, coronary artery disease with a previous history of ischemic event and not taking anti-platelet drugs) on the basis of clinical history and clinical defining criteria. In our study, the selection of hyperlipidemia cases was done on the basis of laboratory reports of either hypercholesterolemia and/or hypertriglyceridemia and/or high LDL levels as per the third report of the NCEP evidence-based guidelines for cholesterol testing and management:

- Total Cholesterol: \(\geq 240\) mg/dl
- Total Triglyceride: \(\geq 200\) mg/dl
- LDL levels: \(\geq 160\) mg/dl

Control group consisted of 60 age range and gender matched normal subjects attending the hospital OPD - 8 for a general health check up and whose Lipid profile was within normal range on recent laboratory reports. None of the controls had apparent coronary artery disease, diabetes mellitus or hypertension and were not taking any anti-platelet drugs or hypolipidemic drugs. Patients with persistent hyperlipidemia even after treatment were also included based on the study of Fuchs et al.\(^13\). The clotted dipotassium EDTA blood samples were excluded from the study. We also excluded pregnant women and patients with Leukaemia and patients on anti-platelet drugs. 2 ml blood sample was collected in EDTA coated tubes from the antecubital vein by a clean puncture avoiding bubbles and froth. The samples were run within two to six hours of venepuncture using the analyzer to avoid time related artefactual changes\(^14\). These samples were analyzed by the Horiba Pentra XLR Hematology Analyzer for obtaining the platelet parameters. In addition to routine CBC parameters Horiba automated haematology analyzer also gives platelet count and platelet indices which include mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT). The comparisons were made regarding the platelet count and platelet indices in the study group and the control group. The platelet indices of patients with isolated hyperlipidemia were compared to those with associated diseases like atherosclerosis, diabetes and hypertension.

Data analysis was done using statistical tests named mean, standard deviation, independent sample t test. A \(p\) value of \(< 0.05\) was considered to be significant.

**OBSERVATIONS AND RESULTS**

The study and control groups are age and gender matched. There is a male preponderance in the study group with male to female ratio of 2.75 with 73.33% males and 26.67% females (Table-1).
The study and control group subjects fell into the age group between 20 to 70 years. The pediatric patients were not included in the study. Maximum number of patients were in 31-50 years of age (51.67%) followed by 35% in 51-70 years of age, 13.33% in 11-30 years age group (Table-2). The mean age was 44.73±12.50 in study group and 42.3±12.05 in the control group with p-value of 0.28.

Distribution of patients with respect to triglycerides, total cholesterol and LDL is given in Table-3.

Patients having hyperlipidemia were compared against those having normal lipid profile in the control group for PC and PI. Mean MPV (8.63±1.09) and PDW (16.88±6.99) were higher for cases than controls (mean MPV: 8.07±0.73 and mean PDW: 13.4±2.21) as shown in Table-4. By using 2 independent sample t-test, p-value < 0.05, therefore there is significant difference between study group and control group with respect to MPV and PDW. And p-value > 0.05 for PC and PCT, therefore there is no significant difference between the study group and control group with respect to PC and PCT. So, two of the studied PI were found to be significantly higher in the cases than the control group.

Also, comparisons of PC and PI were done separately for hypertriglyceridemic group as shown in Table 5. PI were observed to be higher in hypertriglyceridemic group than the control subjects as shown in Table 5.

By using 2 independent sample t- test, p-value <0.05 for MPV and PDW, therefore there is significant difference between control group and abnormal TG group with respect to MPV and PDW. And p- value >0.05 for PC and PCT, therefore there is no significant difference between control group and abnormal TG group with respect to PC and PCT.

After getting significant difference in platelet indices for hyperlipidemic group against the control group, the statistical tests were applied to comparison of PIs in individual 2 subgroups against that of the control group for PC, MPV, PCT and PDW (Table 6).
There is no significant difference with respect to PC and PCT in group A and group B against the control group. There is significant difference with respect to MPV in group B against the control group, p-value <0.05, whereas in group A, p-value>0.05, so no significant difference is seen in MPV between group A and control group. Mean PDW was seen higher in groups A and B than the control group. There is significant difference with respect to PDW in group B (p-value < 0.05), whereas in group A, p-value >0.05, so no significant difference is seen in PDW between group A and control group.

**DISCUSSION**

Role of hyperlipidemia and platelets in thromboembolic events is well-known and various platelet volume indices have been studied in these conditions. Present study is a humble attempt to study the changes in platelet indices in cases of hyperlipidemia. It was found that two of the platelet indices (PI) — MPV and PDW were significantly higher (p-value <0.05) in the study group than the controls, i.e. hyperlipidemic patients had significantly higher MPV and PDW than the normolipidemic patients. We know that larger platelets are considered to be metabolically, enzymatically and functionally more active than the smaller platelet[15,16]. They contain more dense granules and hence are more potent and thrombogenic and this might be a cause for hyperlipidemia being a pre-thrombotic state. However, with respect to the platelet count and plateletcrit there was no significant difference between the study and control groups. For group A patients (n-30; 50%) having hyperlipidemia without any associated disease, it was found in our study that there was no significant difference (p > 0.05) with respect to the platelet count, MPV, PCT and PDW (p-value —0.2992, 0.3971, 0.3866 and 0.055 respectively) amongst the cases and the controls. This meant that those patients who had only hyperlipidemia without association of atherosclerotic disease, diabetes or hypertension did not have any significant difference in their platelet count and platelet indices from the normolipidemic subjects. A similar study using the same platelet indices in dyslipidemic patients done by Grotto et al. found that MPV, PDW and P-LCR were significantly higher in dyslipidemic patients than in controls (P <0.0001)[17]. This is in discordance with our study if we take into account the results of group A patients having hyperlipidemia only. However, an important point to be considered here is that Grotto et al. didn't mention whether their patients had associated diseases along with hyperlipidemia or not. Some studies were done where only MPV for platelet size was assessed in relation to hyperlipidemia along with other platelet functional parameters[13,18,19,20]. Dogru T et al. found no association between MPV and abnormal lipid profile[20]. However, Pathansali R et al. found an increased MPV in hypercholesterolaemic subjects and observed no changes in platelet count in hypercholesterolaemia[21]. Prisco et al. found a significantly increased number of megathrombocytes in hyperlipoproteinemic patients along with increased thromboxane A2[22]. Ravindran et al. studied platelet count, PDW and plateletcrit in hypercholesterolemic patients and found that there was no significant difference in platelet counts between the healthy controls and the hyperlipidemic patients and an increase in PDW only in patients who had hyperlipidemia associated with CAD, similar to our study. Plateletcrit, the other parameter in their study was found to be reduced in all the patients of hyperlipidemia. This is in discordance with our study Fuchs J et al. found an increased percentage of big platelets in hyperlipidemic patients which persisted even after treatment despite the improvement in lipoprotein profile[13]. So they thought that the relation of big platelets and lipid abnormalities is questionable. We also could not establish the relationship between mere hyperlipidemia and platelet size. However, in contrast to their study, mere hyperlipidemia group of our study didn't have big platelets. (MPV and PDW) (p<0.0001) were significantly higher in group B than the normal controls. This was comparable to the results obtained by many earlier studies done by Pizulli L et al.23], Khandekar MM et al.24, Ranjith MP et al.25. However, in our study; PC was not significantly different from the normal controls. (p-value 0.1806). This was similar to the Pizulli et al. study but in contrast Khandekar et al. and Ranjith MP et al. found a decreased platelet count in AMI patients as compared to the controls. Therefore our study is consistent with the above studies demonstrating that the platelet indices vary between CAD patients and the normal population, and these indices may be of value to detect patient at high risk for future cardiovascular events. Our results were similar to a very recent study done by Jindal S et

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>PC (Mean ± SD)</th>
<th>P-value</th>
<th>MPV (Mean ± SD)</th>
<th>P-value</th>
<th>PCT (Mean ± SD)</th>
<th>P-value</th>
<th>PDW (Mean ± SD)</th>
<th>P-value</th>
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<tr>
<td>Control</td>
<td>60</td>
<td>258.35±62.54</td>
<td></td>
<td>8.07±0.73</td>
<td></td>
<td>0.21±0.05</td>
<td></td>
<td>13.395±2.21</td>
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</tr>
<tr>
<td>Group A</td>
<td>30</td>
<td>277.6±112.52</td>
<td>0.2992</td>
<td>7.94±0.55</td>
<td>0.3971</td>
<td>0.22±0.09</td>
<td>0.3866</td>
<td>15.68±8.58</td>
<td>0.055</td>
</tr>
<tr>
<td>Group B</td>
<td>30</td>
<td>238.07±75.85</td>
<td>0.1806</td>
<td>9.32±1.05</td>
<td>&lt;0.0001</td>
<td>0.22±0.06</td>
<td>0.3902</td>
<td>18.08±4.795</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Conclusions

Our study showed that the platelet indices are significantly raised in hyperlipidemia associated diseases but not in hyperlipidemia present in isolation. Thus it is the presence of other diseases in hyperlipidemic patients that brings the platelet in pre-thrombotic active state as reflected by the changes in its volume indices. Finding a platelet function test linked to hyperlipidemia and that is routinely available, could be a first step towards identifying asymptomatic hyperlipidemic patients. The insight gained from interpretation of platelet count and platelet volume indices might be considerable and may allow for timely diagnosis and treatment of hyperlipidemia and hence prevention of further vascular complications. We recommend further studies to emphasize this hypothesis with larger sample sizes for each category with similar categorical analysis.

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