Role of Mean Platelet Volume in Ischemic Stroke

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Abstract
The present study was done to study the role of Mean platelet volume in the pathogenesis, severity and outcome of ischemic stroke. The present prospective study comprised of 100 patients each of ischemic stroke with equal number of age and sex matched control group. Modified Rankin scale was used to assess the severity of stroke. Mean platelet volume and platelet count were lower and higher in the control group. PDW and PLCR were higher in the study group. 57% stroke patients were independent at the end of first week. Patients with high Mean platelet volume did worse at the end of first week in comparison to the control group (p value = <0.05). Mean platelet volume bears an inverse relationship to the immediate outcome from ischemic stroke independent of stroke subtype.

Key Words
Stroke, Mean Platelet Volume, Ischemic Stroke

Introduction
Platelets are small (1-4 µm in diameter), discoid, non-nucleated structures, arising from the fragmentation of megakaryocytes. Platelets, besides being acute phase reactants, are also influenced by the patient's health and nutritional status (1). Upto 65% of platelets are smooth, disc shaped cells (discocytes), whereas the remaining 10-35% are less clearly defined cells (spherical platelets). A morphological consideration of platelets has important implications for both interpreting the functional expressions of platelets and experimental measurement of platelet size (2). Counter flow centrifugation can be used to separate platelets into fractions by differences in platelet volume. These differences in platelet volume correlate with differences in density, dense body content, enzymatic activity of LDH (lactate dehydrogenase), platelet aggregation to ADP (adenosine diphosphate), and serotonin uptake and release, supporting the relevance of the mean platelet volume (MPV) as a measure of platelet functional capability (3). Platelet size (MPV), a marker (and possibly a determinant) of platelet function is a physiological variable of haemostatic importance (4). Large platelets are metabolically more reactive, produce more prothrombotic factors and aggregate more easily (5,6,7). They also contain more dense granules and release more serotonin and beta thromboglobulin than do small platelets (8). Mean platelet volume, as well as platelet count, are an index of haemostasis and its dysfunction i.e. thrombosis. Changes in MPV play a more important role in haemostasis than platelet count (6). Platelet volume is regulated by various intrinsic and extrinsic factors. The mean lifespan of light platelets is shorter than that of heavy platelets (2). Perturbed megakaryocyte platelet haemostatic axis (MPHA), results in the formation of hyper-functional platelets, which may contribute to the development of vascular disease or an acute thrombotic event such as ischemic stroke or myocardial infarction (9). Increase in platelet volume has been reported as a risk factor for acute myocardial infarction, (10,11,12,13) acute cerebral ischemia, (14,15) transient ischemic attacks, and for death or recurrent vascular events after myocardial infarction (16,17). Moreover, increased platelet size has been reported in patients with vascular risk factors such as diabetes (18), hypercholesterolemia (19), smoking (20), metabolic syndrome (21) and in patients with renal artery stenosis (22). Higher levels of MPV in patients with acute ischemic stroke have been demonstrated than in control subjects (14,15,23). The severity and poor outcome of ischemic stroke patients with increased MPV has been reported in the literature (24,25,26). Stroke patients with high mortality have been found to have low platelet count (24). Again, ischemic stroke patients with higher MPV tend to have poor outcome than their counterparts with low MPV (25). Mean platelet volume has been identified as an independent predictor of the risk of stroke among high risk individuals with a history of prior cerebrovascular
disease (26). Our aim was to study the possible role of platelet morphology in general and mean platelet volume (MPV) in particular in pathogenesis of Ischemic Stroke and role of mean platelet volume, if any, in the severity and outcome of Ischemic stroke.

**Material & Methods**

The present prospective case control study was conducted on 100 consecutive ischemic stroke patients admitted to various medical wards of SMHS hospital (an associated teaching hospital of Govt. Medical College, Srinagar). The diagnosis of stroke was entertained after fulfilling WHO definition of stroke by the patient (27). The ischemic nature of stroke was established by noncontrast cranial computed tomographic scan and the severity of stroke assessed by modified Rankin Scale(m-RS) (28). Patients with an mRS score of 0-2 and 3-6 at the end of first week were classified as independent and dependent/dead respectively. Patients with haemorrhagic stroke, comorbid medical illnesses likely to interfere with platelet function/ morphology and those receiving medication likely to interfere with platelet morphology or function were excluded from the study. Each patient after detailed history and physical examination was subjected to various baseline haematological and biochemical investigations. All patients were subjected to Carotid Doppler, echocardiography, chest x-ray and electrocardiography. Control group comprised of age and sex-matched 100 subjects with no clinical evidence of any active vascular disease, previous cerebrovascular disease, malignancy or infarction and not taking medications known to affect platelet function. Control group included attendants of patients who were enrolled in the study after written consent. After all aseptic precautions 2ml of blood sample was obtained from antecubital vein of the patient within 48 hours of onset of signs and symptoms of ischemic stroke. Samples collected in EDTA vials, kept at room temperature were processed after 6 hours. The printout reports of samples fed to Sysmex KX - 21 were collected and analyzed. Sysmex KX - 21 uses impedance flowmetry for calculating different haematological parameters. The results of all the patients was pooled and various platelet indices obtained ,thereof, were subjected to various requisite statistical analysis.

**Results**

The study sample comprised of 100 cases each of study and control groups. Mean age of the ischemic stroke was 58 years( range 34 to 78 years). Males comprised 59% of the study group. Moreover 73% of cases were from rural areas. The study sample (control as well as study groups) included 23% and 77% cases below and above 45 years of age respectively. There were 59% and 41% males and females respectively in either group. Mean platelet volume and platelet count(x10^9/l) in ischemic stroke patients ranged from 7.8-15.2 (fl)(mean 11.86±0.96fl) and 124-276 ( mean value of 168±29)respectively. Platelet distribution width (fl) and platelet crit ranged from 12.3-23.7 (fl) and 24.7-48.9 (%), with mean values of 17.11±3.4 and 37.4±5.8 respectively. Values of other haematological parameters are also depicted in table 1.

High mean platelet volume and low platelet count was found in the study group which in comparison to the control group was statistically significant. PDW, PLCR were higher in stroke patients than control group(p value=>0.05). These platelet indices in either group were not influenced by age or gender. There was a significant negative correlation between MPV and PC in study group(r=-0.386, p<0.05). This correlation was insignificant in control group(r=-0.08,p>0.05).

**Table 1. Profile of Various Haematological Parameters in Ischemic Stroke Patients**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameter</th>
<th>Range</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MPV (fl)</td>
<td>7.8 – 15.2</td>
<td>11.86 ± 0.96</td>
</tr>
<tr>
<td>2</td>
<td>PC x 10^9/L [ Platelet count ]</td>
<td>124 – 276</td>
<td>168 + 29</td>
</tr>
<tr>
<td>3</td>
<td>PDW (fl)</td>
<td>12.3 – 23.7</td>
<td>17.11 + 3.4</td>
</tr>
<tr>
<td>4</td>
<td>PLCR %</td>
<td>24.7 – 48.9</td>
<td>37.4 + 5.8</td>
</tr>
<tr>
<td>5</td>
<td>Hb g/dl</td>
<td>11.6 – 18.3</td>
<td>14.8 + 1.9</td>
</tr>
<tr>
<td>6</td>
<td>Hct %</td>
<td>31.4 – 61.3</td>
<td>43.7 + 2.8</td>
</tr>
<tr>
<td>7</td>
<td>MCV (fl)</td>
<td>73.3 – 104.8</td>
<td>87.2 + 6.3</td>
</tr>
<tr>
<td>8</td>
<td>RBC count x10^12/L</td>
<td>243 – 984</td>
<td>447 + 44</td>
</tr>
<tr>
<td>9</td>
<td>WBC count x10^9/L</td>
<td>324 – 1283</td>
<td>383 + 47</td>
</tr>
<tr>
<td>10</td>
<td>ESR mm (1 hour)</td>
<td>3 – 65</td>
<td>26.3 ± 3.1</td>
</tr>
</tbody>
</table>

MPV=Mean platelet volume, PDW=Platelet Distribution Width , PLCR=Platelet crit Hb=Haemoglobin , MCV=Mean Corpuscular Volume RBC=Red Blood Cell WBC=White Blood Cell, ESR=Erythrocyte Sedimentation Rate, PC=Platelet count, Hct=Haematocrit
significant difference was observed in MPV in patients with various stroke subtypes. 57% of stroke patients were independent (mRS score=0-2), 39% dependent (mRS score=3-5) and 4% dead (mRS score=6) at the end of one week. MPV had an inverse relationship with outcome at the end of one week and the results were statistically significant. On comparing the MPV-values and mRS-score on admission and at one week, we observed that the patients with high MPV-values did worse as compared to their counterparts with low MPV values (p value=<0.05) (table-2).

### Discussion

The mean age of stroke patients was 58 years which is comparable to the observations made by other authors from Kashmir valley (29). However, it is in contravention to the observations made in similar studies from the developed world (27). This disparity in age may be due to higher life expectancy in the West as compared to the developing world (30). Young strokes (age <45 years) accounted for 23% cases in present study. This observation is not in conformity with data published from India including Kashmir as well as rest of the world (27,31). Nonetheless, there is ample data from India reporting higher prevalence of young strokes in their studies as that of ours, (32,33,34,35). This disparity in occurrence of young strokes may be accounted for by sample bias including methodology used in the present study. Moreover, patients with comorbid illnesses/risk factors such as diabetes mellitus and dyslipidemia were excluded from present study as such risk factors are likely to be encountered more commonly in elderly population (27,30). Males constituted 59% of ischemic stroke patients which is comparable to the data published by Khan et al (29) and in contravention to the observations made by Razdan et al (31) from Kashmir valley. The marginal difference in gender ratio can be attributed to small sample in present study and different methodology used by Razdan et al (31). Preponderance of patients from rural areas in our study is in conformity with other published data (27). This observation is attributed to our demographic profile as 75% of our population resides in rural areas (30). Mean MPV (mean platelet volume), platelet count, platelet distribution width (fl), platelet crit (%), haemoglobin (gm%), haematocrit (%), mean corpuscular volume (fl), red blood cell count (x1012/l), white blood cell count (x109/l), and erythrocyte sedimentation rate (mm1/hour) were to the tune of 11.86±0.96, 168±29, 17.11±3.4, 14.8±1.9, 43.7±2.8, 87.2±6.3, 447±44, 383±47 and 26.3±3.1 respectively. Highest and lowest MPV (mean platelet volume) observed in present series were 15.2 (fl) and 7.8 (fl) respectively. MPV in present series is marginally higher than other published data (23-25). Higher MPV can be accounted for by the use of EDTA during sample collection as use of EDTA is known to increase MPV (36). In addition to this fact, variation in MPV may be attributed to the occurrence of large sized platelets with comparatively low platelet count in apparently healthy Kashmiri population as is the general observation by the haematology department of Govt. S.M.H.S Hospital, Srinagar (personal communication). Mean platelet volume and platelet count in control group were lower and higher respectively, in comparison to the study group. Again, this observation is in conformity with bulk of the published data, (14,15,23,24,25). It is hypothesized that higher MPV may predispose to the occurrence of ischemic strokes which is substantiated by other research workers (14,15). No statistically significant difference was observed in MPV of patients with different stroke sub-types. This observation is in agreement with other research workers (23). Again, age and sex had no influence on MPV and platelet count in our series. This observation is in agreement with other studies (20,24,26,37). There is statistically significant inverse relationship between platelet count and MPV in present study in comparison to the control group. This fact may be attributed to the constant platelet biomass or consumption of platelets during the process of thrombosis (2,15,24). This observation is corroborated by other studies as well (23,24,38). Modified Rankin scale score

### Table 2 Relationship of MPV With Mrs-Score on Admission & at Week

<table>
<thead>
<tr>
<th>MPV (fl)</th>
<th>0 – 2</th>
<th>3 – 6</th>
<th>0 – 2</th>
<th>3 – 6</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.8 – 9.0</td>
<td>10 (16.12)</td>
<td>8 (21.05)</td>
<td>12 (21.05)</td>
<td>6 (13.95)</td>
<td>&lt; 0.05 Significant</td>
</tr>
<tr>
<td>9.1 – 9.8</td>
<td>8 (12.90)</td>
<td>9 (23.68)</td>
<td>9 (15.78)</td>
<td>8 (18.60)</td>
<td></td>
</tr>
<tr>
<td>9.9 – 10.6</td>
<td>16 (25.80)</td>
<td>7 (18.42)</td>
<td>14 (24.57)</td>
<td>9 (20.93)</td>
<td></td>
</tr>
<tr>
<td>10.7 – 11.4</td>
<td>15 (24.19)</td>
<td>6 (15.78)</td>
<td>12 (21.05)</td>
<td>9 (20.93)</td>
<td></td>
</tr>
<tr>
<td>11.5 – 15.2</td>
<td>13 (20.96)</td>
<td>8 (21.05)</td>
<td>10 (17.54)</td>
<td>11 (25.58)</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>62 (100)</td>
<td>38 (100)</td>
<td>57 (100)</td>
<td>43 (100)</td>
<td></td>
</tr>
</tbody>
</table>
(mRS Score) of 0-2, 3-5 and 6 was found in 57%, 39% and 4% cases respectively. Age and sex had no statistically significant impact on mRS score. Patients with higher MPV had worse outcome at the end of one week. This fact is corroborated by other studies as well (24,25,26,37).

Moreover, there was no statistically significant relationship between stroke-subtype and outcome at the end of one week. Again, this observation is substantiated by other workers (39). Thus, mean platelet volume bears an inverse relationship to immediate outcome from ischemic stroke independent of stroke subtype.

References