Role of Platelet to Lymphocyte Ratio (PLR) and its Correlation with NIHSS (National Institute of Health Stroke Scale) for Prediction of Severity in Patients of Acute Ischemic Stroke

Deepti Sharma¹, Nikhil Gandhi²*

Abstract

Background and Objectives: Stroke is the second leading cause of death and third most common cause of disability-adjusted life years in the world. Atherosclerosis plays a key role in the pathogenesis of stroke and inflammation is central in the initiation, progression and complications of atherosclerosis by mediating every stage of atheroma development. High platelet counts may increase thrombocyte activation and aggravate the release of inflammatory mediators. In contrast, lymphocytes exert anti-inflammatory response in atherosclerosis development. The advantage of platelet to lymphocyte ratio (PLR) is that it reflects the condition of both inflammation and thrombosis pathways and is more valuable than either platelet or lymphocyte counts alone. This emerging marker has not been frequently studied with acute ischemic stroke; hence aim of the present study was to find out the role of PLR (Platelet to lymphocyte ratio) in patients of acute ischemic stroke and correlating with NIHSS for predicting the prognosis.

Material and Methods: 100 cases of AIS and equal number of age and gender matched control were enrolled in the study. NIHSS score and PLR (from the CBC test) was calculated both at admission and on day 7 or discharge.

Results: Maximum subjects in our study were in the age range of 61-70 years with males (69%) outnumbering females (31%). Incidence of hypertension, diabetes mellitus, hyperlipidemia, smoking and alcoholism was more in the cases than controls. Mean PLR was higher in the patients of AIS (235.98±93.92) as compared to control group (115.60±27.87) (p=0.0001). Moreover, there was statistically significant, positive correlation between PLR and NIHSS score both at admission and discharge. PLR value increased significantly from the baseline in patients who deteriorated (263.42±108.98 to 346.28±125.35; p=0.016), decreased drastically in patients who improved (242.27±75.14 to 167.19±57.91; p=0.0001) and did not change much in patients who tend to remain static (181.35±105.40 to 183.36±111.61; p=0.955).

Conclusion: Platelet to lymphocyte ratio (PLR) is a simple, cost effective and easily obtainable novel inflammatory marker that may help in predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its increased value in patients of acute ischemic stroke as well as its linear positive correlation with NIHSS score.

Introduction

Stroke or cerebrovascular accident is defined as an abrupt onset of focal neurological deficit that is attributable to vascular cause. It accounts for 80% to 85% of all cerebrovascular disease. Stroke is the second leading cause of death worldwide causing 6.2 million deaths in 2011, and third most common cause of disability-adjusted life years in the world. Atherosclerosis is central in the pathogenesis of stroke. Inflammation plays a key role in the initiation, progression and complications of atherosclerosis by mediating every stage of atheroma development. Thrombosis, platelet activation and inflammation are essential in the pathophysiology of acute ischemic stroke. Platelets represent an important linkage between inflammation, thrombosis, and atherogenesis in acute ischemic stroke. Higher platelet counts may increase thrombocyte activation and aggravate the release of inflammatory mediators, prompting a harmful inflammatory process. Studies have demonstrated relationship between mortality and high platelet in patients with acute coronary syndrome. In contrast, lymphocytes are blood cells responsible for cellular and humoral immunity in the body that have shown to modulate the immunologic response in our body. Lymphocytes modulate the mononuclear cell phenotype and induce tissue inhibitor of metalloproteinase-1 expression that have key role in tissue healing. Experimental models have also revealed that lymphocytes exert anti-inflammatory response in atherosclerosis development. Recently, lymphopenia was associated with the increased risk for developing adverse outcome in terms of morbidity and mortality in cardiovascular diseases particularly MI. Studies have clearly demonstrated a negative correlation between lymphocyte counts and severity of coronary atherosclerosis.

Physiologic stress during acute ischemic stroke leads to high level of cortisol which leads to lower lymphocyte counts. Moreover, acute stressful conditions cause activation of sympathetic nervous system which causes redistribution of lymphocytes.
Malignancies including breast, ovarian, pulmonary embolism and various ischemia, end-stage renal failure, myocardial infarction, critical limb ischemia, and other solid tumors. The advantage of PLR as an inflammatory marker has been correlated with the poor prognosis in various diseases like Myocardial infarction, critical limb ischemia, end-stage renal failure, pulmonary embolism and various malignancies including breast, ovarian, pancreatic, hepatobiliary carcinoma and other solid tumors. The advantage of PLR is that it reflects the condition of both inflammation and thrombosis pathways and is more valuable than either platelet or lymphocyte counts alone. This emerging marker has not been frequently studied with acute ischemic stroke; hence present study was done to find out the role of PLR (Platelet to lymphocyte ratio) in patients of acute ischemic stroke and correlating with NIHSS for predicting the prognosis.

**Objectives**

The main objective of our study was to determine the value of Platelet to lymphocyte ratio (PLR) in patients of acute ischemic stroke and correlate it with NIHSS score to predict the severity of stroke.

**Materials and Methods**

After obtaining approval from institutional ethical committee, a hospital based prospective and observational study was conducted on 100 patients of acute ischemic stroke admitted in Department of Medicine, Govt. Medical College and Associated M.B.S. Hospital, Kota from 2018 to 2020 and compared with 100 equal number of age and gender matched controls.

Table 1: Age and gender distribution of subjects in case and control group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cases (n=100)</th>
<th>Control (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>60.79±13.86</td>
<td>61.33±10.96</td>
</tr>
<tr>
<td>Male (%)</td>
<td>69</td>
<td>63</td>
</tr>
<tr>
<td>Female (%)</td>
<td>31</td>
<td>37</td>
</tr>
</tbody>
</table>

All acute ischemic stroke patients who had symptom onset within 7 days and had given written informed consent to participate were included in our study whereas patients with hemorrhagic Stroke, venous sinus thrombosis, hepatic or renal disease, connective tissue disorders, autoimmune disease, sepsis, malignancy, psychiatric illness, moribund condition and unwillingness to participate in the study were excluded. The diagnosis of acute stroke was made on the basis of temporal profile of clinical syndrome, clinical examination and CT scan / MRI of brain. A detailed history taking, clinical examination, and routine lab investigations were done to identify ischemic stroke risk factors (non modifiable and modifiable).

Severity of stroke was determined with the National Institute of Health Stroke Scale (NIHSS) in all patients at initial presentation and at discharge. Stroke severity was grouped in minor stroke (1-4), moderate stroke (5-15), moderate to severe stroke (16-20) and severe stroke (21-42). For calculating PLR (Platelet to lymphocyte ratio), CBC (Complete Blood Count) test was performed by fully automated five part hematology analyzer [SYSMES] available at our central laboratory. 2 ml of peripheral venous sample with all aseptic precaution was taken just after admission before starting any treatment and another sample just before discharge. The samples were processed immediately. Thus, two CBC test were performed from which Platelet to lymphocyte ratio was obtained by dividing total platelet count by total lymphocyte count. This platelet to lymphocyte ratio was then compared with the reference value calculated from control group of same age and gender and with NIHSS severity score (calculated at the time of admission and discharge).

**Statistical Analysis**

Continuous variables were presented as mean±sd, categorical variables were expressed in frequency and percentages. Demographic, haematological (PLR) and clinical parameters were compared between cases and controls by performing independent t-test. Categorical variables were compared by performing chi-square test. Statistical method used was unpaired Student’s t-test and chi-square test between Platelet to Lymphocyte ratio and severity of ischemic stroke including other variables using Graph pad In Stat Version 3.10. A value of p>0.05 was considered as not significant and p<0.05 as statistically significant. Pearson correlation coefficient was also assessed to study nature and magnitude of correlation between PLR and NIHSS both at admission and discharge.

**Observation and Results**

In our study, cases had mean age of 60.79±13.86 years which was comparable with the mean age of control group i.e. 61.33±10.96 years and both groups had maximum subjects in the range of 61-70 years i.e. 36 and 34 respectively. Males (69%) outnumbered females (31%) with a ratio of 2.2:1. Table 1 depicts the age and gender distribution of subjects in case and control group.

Left hemiparesis was the most common focal neurological deficit observed in 48% of the patients as compared to right hemiparesis (29%). Features of posterior circulatory stroke like vertigo, blurring of vision, incoordination etc. without weakness was present in only 13% of the patients. MCA territory infarction was the dominant CT/MRI finding (65%) followed by PCA (19%) and ACA (16%) territory stroke. Distribution of acute ischemic stroke patients in different NIHSS score shows that maximum cases were present in NIHSS score group 5-15 (moderate stroke) both at the time of admission and discharge i.e. 47 and 41 respectively (Table 2). Mean NIHSS score in AIS patients at admission was 10.80±6.33 as compared to 10.01±7.54 at discharge.

In our study, hypertension was the most common risk factor (64%) followed by smoking (59%), hyperlipidemia (48%), diabetes mellitus (31%) and alcoholism (27%) as shown in (Table 3).

Biochemical and hematological profile of both case and control groups shows that the value of random blood
Table 4: Biochemical and hematological profile of case and control group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Acute Ischemic Stroke group (Mean±SD)</th>
<th>Control Group (Mean±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Sugar (mg/dl) (R)</td>
<td>196.33±92.26</td>
<td>148.97±87.75</td>
<td>0.0001</td>
</tr>
<tr>
<td>B. Urea (mg/dl)</td>
<td>39.57±16.72</td>
<td>30.87±6.51</td>
<td>0.0001</td>
</tr>
<tr>
<td>S. Creatinine (mg/dl)</td>
<td>1.19±0.40</td>
<td>0.984±0.162</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>198.48±62.71</td>
<td>182.10±31.29</td>
<td>0.020</td>
</tr>
<tr>
<td>S. Triglyceride (mg/dl)</td>
<td>145.96±55.04</td>
<td>127.66±35.64</td>
<td>0.006</td>
</tr>
<tr>
<td>Hb (gm/dl), n(%)</td>
<td>12.57±1.69</td>
<td>11.63±1.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>Platelet count (10^3/cu.mm)</td>
<td>266.29±72.29</td>
<td>211.38±44.38</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lymphocyte count (10^3/cu.mm)</td>
<td>1.30±0.54</td>
<td>1.85±0.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>Platelet to Lymphocyte Ratio</td>
<td>235.98±93.92</td>
<td>115.60±27.87</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Fig. 1: Comparison of PLR according to NIHSS score at the time of admission

Fig. 2: Correlation between PLR of patients suffering from AIS with NIHSS at the time of admission

Fig. 3: Comparison of PLR according to NIHSS score at the time of discharge

sugar, urea, creatinine, total cholesterol, triglyceride, hemoglobin, platelet count was significantly higher (p<0.05) in the study group as compared to control group whereas the value of total lymphocyte count was significantly lower in AIS patients than control subjects (Table 4).

When PLR was calculated by dividing absolute platelet count with absolute lymphocyte, it was observed that PLR was significantly higher in patients with acute ischemic stroke (235.98±93.92) as compared to control group (115.60±27.87) with p-value of 0.0001. Moreover, this ratio did not change significantly with gender and presence of risk factors like hypertension, smoking, diabetes and hyperlipidemia (p>0.05).

The value of PLR was higher in patients with MCA infarct (245.34±100.60) followed by ACA (219.91±73.37) and PCA infarct (216.16±82.68). On comparing PLR with patients of different NIHSS score, it was found to be lowest in NIHSS score group 1-4 i.e. 171.23±48.14 which increased to 229.66±98.57 in NIHSS score group 5-15, 296.23±44.09 in NIHSS score group 16-20 and was highest in NIHSS score group of 21-42 amounting to 356.63±43.90 such that a positive, moderately strong and statistically significant correlation was found between PLR and NIHSS score at the time of admission (Figures 1 to 4).

Table 5 shows the distribution of AIS patients according to clinical status in different NIHSS score group assessed on day 7 or at discharge. From this table, we found that out of 100 patients, 56 got improved, 25 got deteriorated and 19 remained static.

Comparison of PLR value according to clinical status in acute ischemic stroke patients showed that PLR value increased drastically in deteriorated patients from 263.42±108.98 at admission to 346.28±125.35 at discharge. On the other hand, PLR value decreased significantly in improved patients from 242.27±75.14 at admission to 167.19±57.91 at discharge whereas value of PLR did not change much in patients who remained static (Table 6).

Discussion

Our study included 100 patients of acute ischemic stroke and 100 age and sex matched control subjects. Although the control subjects were free from acute ischemic stroke, some of them had risk factors for ischemic stroke. Our study had male preponderance with male to female ratio of 2.2:1 which was similar to all other studies done by Aiyar et al, Kay Sin Tan et al and R P Eapen et al etc. The mean age of our study group was 60.79±13.86 years with the maximum cases in the age range of 61 to 70 years. This is in accordance with various other studies done by Grau et al, Aiyar et al and Naik M, Raunyiar, Sharma U.K et al. In our study hypertension was the most common risk factor detected in 64% of the patients followed by smoking (59%), hyperlipidemia (48%), diabetes mellitus (31%) and alcoholism (27%). This is similar to the recent studies by Grau et al, Tallawy et al, Essa et al, El Sayed et al and Benerjee TK et al. Random blood sugar level was higher in the study group (196.33±92.26 mg/dl) as compared to control group (148.97±87.75 mg/dl) with a statistically significant p-value of 0.0001 and was similar to other studies done by Gauri et al, Dalal et al, Nagraja et al, Grindal et al, Bogousslavsky et al, Zunni et al and Alvarez et al. Mean total cholesterol and triglyceride level was also higher in patients of AIS than control and this correlate with the findings of Togha et al and Aabadzhieva et al.
In present study we tried to evaluate the value of PLR in patients of AIS and observed that the mean PLR value in AIS patients was 235.98±93.92 which was significantly higher than the control group (115.60±27.87) with a p value of 0.0001. To the best of our knowledge, this is the first study which has tried to correlate the value of PLR with NIHSS score both at the time of admission as well as discharge. In our study positive, moderately strong and statistically significant correlation was found between PLR and NIHSS score at the time of admission such that the value of PLR increased proportionately with the increasing NIHSS score. (p=0.0001) and (r=0.753). Our study is similar to the studies done by Andres Perez et al.\textsuperscript{18} Pei-Hsun Sung et al\textsuperscript{16} and Xu J-H et al. in which there was a positive correlation between PLR and NIHSS score at the time of admission. In our study, a statistically significant positive correlation between PLR and NIHSS was also observed during the discharge (p=0.0001) and (r=0.8564). In our study out of 100 patients 56 got improved, 25 deteriorated and 19 remained static. It was observed that mean PLR in 56 patients who improved was 242.27±75.14 at admission which decreased to 167.19±57.91 at discharge and this was found to be statistically significant (p= 0.0001). Thus, as the patients in our study improved the value of this ratio also improved (decreased). On the other hand, 25 patients who got deteriorated, their PLR value increased significantly from 263.42±108.98 at admission to 346.28±125.35 at discharge (p=0.016). This highlighted that as the patient got deteriorated the value of PLR also deteriorated i.e. increased. In 19 patients who remained static, their PLR value was nearly similar both at the time of admission and discharge being 181.35±105.40 and 183.36±111.61 respectively and the difference was also not statistically significant (p = 0.955). This shows that the patient who neither gets improved nor gets deteriorated, the value of their PLR also doesn’t change significantly. Our study supports the finding of Ozge Altintas et al,\textsuperscript{17} Andres Perez et al,\textsuperscript{18} Stella Bouziana et al\textsuperscript{19} and Xu J-H et al,\textsuperscript{20} which demonstrated that patients of acute ischemic stroke with higher PLR had poor outcome as compared to patients with lower PLR values.

**Conclusion**

Platelet to lymphocyte ratio (PLR) is a simple, cost effective and easily obtainable novel inflammatory marker that may help in predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its increased value in patients of acute ischemic stroke as well as its linear positive correlation with NIHSS score. This ratio can be obtained even at primary health set ups and may be used for decision making in urgent referral of the patient for better outcome. Though, more studies are needed to validate our results, our study completely support the routine calculation of this ratio that may help in predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its increased value in patients of acute ischemic stroke as well as its linear positive correlation with NIHSS score.

**Limitation of Study**

Despite our best efforts our studies had few limitations

1. The sample size of our study was small involving only single centre patients of acute ischemic stroke.

2. Owing to lack of long term follow up for our patients, we cannot comment whether platelet to lymphocyte ratio is a useful predictor of long term prognostic outcome in patients with AIS or not.

3. Our study was carried out in a tertiary centre where the cases are either serious or referred. Our study may thus be biased towards more serious cases.

**Acknowledgement**

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**References**


