Original Research Article

Neuro vascular injury profile in CVA patients: A study on correlation between hematological indices and severity score in acute ischemic stroke

Sailaja.Y[1], V Ramakrishnan[1], Naveen P[1], C Mutharasu[1,*]

[1]*Dept. of Neurology, Meenakshi Medical College and Research institute, Enathur, Tamil Nadu, India*

A B S T R A C T

Acute ischemic stroke results from sudden loss of blood circulation to an area brain leading to irreversible injury and neurological deficits persisting for more than 24 hours or until death. It accounts for 80-87% of all strokes. In this study, we aim to find the association between various hematological indices such as Mean platelet Volume (MPV), Platelet distribution Width (PDW), Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte ratio (PLR) and National Institute of Health Stroke Scale (NIHSS).

Materials and Methods: It was a prospective study done at Department of Neurology at Meenakshi Medical College Hospital and Research Institute, Kancheepuram, Tamil Nadu in which 100 patients of Acute Ischemic stroke were divided into two groups based on NIHSS score. Proper Exclusion criteria were carried out and the patients' blood samples were taken. Various Hematological indices were measured and statistical analysis was done using SPSS Software.

Results: There is positive correlation between NLR, PLR and NIHSS score. It is statistically significant association. But there is no statistical significance between Platelet indices and NIHSS score.

Conclusion: Being Low cost and easy to measure NLR and PLR, these indices can be used in the prediction of the prognosis in the Acute Ischemic Stroke patients.

1. Introduction

Acute ischemic stroke is not only a severe disabling cerebrovascular event[1] but also has a great impact on patient's life and socioeconomic burden.[2] Although it can be prevented by controlling relevant risk factors,[3] its prevalence and incidence remain rising with aging and atherosclerotic process.[4] It is the commenst cause of mortality after coronary artery disease and the commonest cause of chronic adult disability.[5]

Acute ischemic stroke results from sudden loss of blood circulation to an area of brain leading to irreversible injury and neurological deficits persisting for more than 24 hours or until death. It accounts for 80-87% of all strokes.[6]

Platelets activation and aggregation are critical in the pathogenesis of acute ischemic stroke. There exist parameters to monitor platelets and their changes, namely:

Mean Platelet Volume (MPV), Mean Platelet Count (MPC), Plateletcrit (PCT), and Platelet Distribution Width (PDW).[7] Together, these are called Platelet indices. Studies have shown that these indices are good indicators of thrombotic states.[8]

MPV is a commonly used biomarker of platelet function and activation.[9] Increased MPV has been associated with greater in vitro aggregation in response to ADP and Collagen thereby associated with Myocardial Infraction, Transient Ischemic Attacks and Ischemic Stroke.[10–14] PDW represents variation in platelet size. Larger PDW also indicates prothrombotic status.[15] These indices are cost effective and routinely avaliable.

Since Acute Ischemic stroke is an inflammatory event where the ischemic tissue releases chemokines and cytokines, and recruit peripheral circulating leucocytes.[16] Lymphocytes also infiltrate the ischemic tissues and mediate inflammatory responses.[16] Among the leucocytes,

---

* *Corresponding author.*
E-mail address: drsailajay@gmail.com (C. Mutharasu).

neutrophils were found to be an important mediator and early neutrophilia was found to be associated with larger stroke volumes and poor prognosis. [17]

In recent years, the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have emerged as well accepted biomarkers for the assessment of overall inflammatory status. These are simple and cost effective biomarkers. [18] Elevated levels of NLR and PLR have found to be related to with oxidative stress and increased cytokine production in patients. [19] The NLR has been used as an indicator to reflect the prevalence of intracranial atherosclerosis [20] and is considered to be an independent risk factor for ischemic stroke and a poorer prognosis. [21] The PLR has been used to predict poor prognoses,the rate of insufficient recanalization and the size of infarcted area following stroke. [22]

1.1. Aim of the Study

The aim of our present study is to investigate the relationship between these indices and stroke severity score in acute ischemic stroke.

2. Materials and Methods

The study is conducted in Department of Neurology at Meenakshi Medical College & Hospital, Kancheepuram, Tamil Nadu after getting approval from institutional ethics committee.

2.1. Duration of Study

July 2018 to July 2019

2.2. Sample size

100 Consecutive subjects with ischemic stroke admitted to Department of Neurology

2.3. Type of study

Prospective Study

2.4. Method of collection of Data

After obtaining consent, the patients were subjected to detailed history, clinical examination and investigations as per the proforma. Each patient was assessed and NIHSS score was assigned to them.

2.5. Inclusion Criteria

1. Age more than 18 years
2. All patients with acute ischemic stroke confirmed by history, neurological examination and imaging modalities of both anferior & posterior circulation.
3. Patients who are willing to give written informed consent

2.6. Exclusion Criteria

1. Patients with hemorrhagic stroke and previous attack of ischemic stroke
2. Patients with comorbid medical illness likely to interfere with platelet function or morphology like chronic kidney disease, heart bypass surgery, chronic liver disease, leukemia, active infection without infection and autoimmune diseases.
3. Patients receiving medication likely to interfere with platelet morphology or function like aspirin and other NSAIDs, antihistamines, and some antibiotics.
4. Patients presenting 48hrs after onset of neurological symptoms

For the measurement of indices, blood sample was collected from the antecubital vein uisng 5cc syringe and transfered to an EDTA Test tube and analysed in an Automated cell counter system within 90 min after collection.

2.7. Statistical Analysis

The Data obtained from the hematological investigations was entered in Microsoft Excel and Statistical Package for Social Sciences- SPSS for window ver 18.5 software used for the statistical analysis. The results for each parameter for discrete data and averaged for each parameter were presented in tables.

3. Results

In our study, out of 100 patients, 72 were males and 28 were females. Most of the patients were in 50-70 years age group. Around 62% were in 45-60 years age group, 27% were in 61-70 years age group. 5% were in <45 years age group and 6% were in >70 years age group. (Table 1)

Among the risk factors, order of prevalence is Hypertension > Diabetes Mellitus > Smoking > Alcoholism > Dyslipidaemia. It is depicted in the Table 2.

In our study, these 100 patients are divided into two groups basing on National Institute of Health Stroke Scale (NIHSS) score. The set of patients whose NIHSS score is less than 6 is taken as 'Group 1' and the set of patients whose NIHSS score is more than or equal to 6 is taken as 'Group 2'. Number of patients under 'Group 1' are 56 and those under 'Group 2' are 44.

In our study, the laboratory findings showed that Leukocyte count, Neutrophil, Lymphocyte and Platelet count doesn't shown significant diffreeance between these two groups of patients. (Table 3)

Data Expressed is Means ± standard deviation

In our study, the platelet indices doesn't differ significantly between these two groups of patients.(Table 4)

But Neutrophil-to-Lymphocyte ratio as well as Platelet-to-Lymphocyte ratio is significantly more in Group 2 thereby indicating positive correlation of NLR and PLR

Table 1: Distribution of Patients in different Age Groups

Age Group	Male	Female	%
<45 Years	3	2	5
45-60 Years	46	16	62
61-70 Years	19	8	27
> 70	4	2	6
Total	72	28	100

Table 2: Presenting Risk Factor Distribution in Study Population

Risk Factor	Male (n=72)		Female (n=28)		Total (n=100)	
	Number	%	Number	%	Number	%
Hypertension	62	86	22	79	84	84
Diabetes Mellitus	60	83	20	71	81	81
Dyslipidaemia	28	39	14	50	42	42
Smoking	63	87.5	6	21	69	69
Alcoholism	62	86	0	0	62	62

Table 3: Laboratory Data of Group 1 and Group 2 along with NIHSS score

Variables	Group 1 (n=56)	Group 2 (n=44)	Total (n=100)
Leukocyte count/1000/L	8.60±2.58	8.42±2.34	8.29±2.94
Neutrophil/1000/L	4.78 (3.62–6.94)	5.96 (4.20–7.38)	5.48 (3.64–7.82)
Lymphocyte/1000/L	2.02 (1.47–2.88)	1.61 (1.21–2.72)	1.35 (1.28–2.73)
Platelet count/1000/L	221.42±76.47	207.37±54.50	214.28±66.26
Stroke Severity Score			
Average NIHSS	2.80±1.96	15.04±8.12	8.42±8.78

Data Expressed is Means $\pm$ standard deviation, median (1st quantile to 3rd quantile)

Table 4: Platelet Indices in Group 1 and Group 2

Variable	Group 1	Group 2
Mean Platelet Volume (MPV)	12.56 ±1.18	12.78 ±1.32
Platelet Distribution Width (PDW)	18.39 ± 2.78	18.42 ±2.96

Table 5: NLR and PLR in Group 1 and Group 2

Variables	Group 1	Group 2
Neutrophil-to-Lymhocyte Ratio (NLR)	2.06(1.38–3.81)	3.94(2.14–5.87)
Platelet-to-Lymhocyte Ratio (PLR)	98.7(76.8–126.2)	135.4(96.4–180.9)

with high Stroke Severity Score and poor prognosis.(Table 5)

4. Discussion

The study was conducted to investigate the correlation between various hematological indices in relation to Stroke Severity Score. The study mainly focused on Platelet indices, Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymhocyte Ratio in relation to NIHSS Score.

When assessing the risk factors for stroke in these patients, our study showed that Hypertension is the most prevalant risk factor with a percentage of 84 % which is similar to study conducted by Lok U et al[23] with prevalence percentage of hypertension as 74% and A.Muscari et al[24] with prevalence of 84%.

Diabetes is the second prevalent cause which were in lines with studies conducted by Lok U et al,[23] George J et al[25] and Maydadomac F et al.[26] Dyslipidemia being least prevalant risk factor in our study which is 42% is similar to study by Muscari A et al[24] which is 40.1%.

The laboratory findings showed that the leukocyte,neutrophil,lymohocyte and platelet counts did not differ between these two groups of the patients. There is no significance of these findings since it is almost similar in both groups with NIHSS < 6 and those with

NIHSS > 6.

In our study, there is no significance of MPV in relation to Stroke Score which is consistent with the study conducted by Al-Tameemi et al[27] but studies conducted by Butterworth et al,[28] Ghahremanfard F et al[29] and Shah P et al[30] have shown significant raise in the MPV. There is also no significance of PDW in our study which is consistent with the study conducted by Al-Tameemi et al[27] but study conducted by Shah P et al[30] have shown significant raise in the PDW. Some studies have shown that there is increase in these platelet indices in stroke patients in comparision to healthy patients but these indices are not significant to differentiate the stroke severity score.

Our study showed a positive relationship between NLR, PLR and Stroke Severity Score. There is a significant raise in both NLR and PLR in patients with NIHSS score >6 i.e., Group 2. This is consistent with study conducted by Pei Hsun sung et al[31].

5. Conclusion

Our study has shown significant difference in the values of NLR and PLR in relation to Stroke Severity Score. Therefore, NLR and PLR are strongly related to Stroke Severity Score thereby associated with prognosis of the stroke.

There is no significant difference in MPV and PDW in relation to Stroke Severity Score but these platelet indices can be used as biomarkers in stroke patients since there is significant raise in these indices in stroke patients in relation to healthy people. It is also found that Hypertension is the most predominant risk factor among the ischemic stroke patients.

6. Source of Funding

7. Conflict of Interest

None.

References

1. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet*;371:1612–23.
2. Adams HP, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke:A guideline from the American Heart Association/American Stroke Association Stroke Council, ClinicalCardiology Council, Cardiovascular Radiology and Intervention Council and the Atherosclerotic PeripheralVascular Disease and Quality of Care Outcomes in Research InterdisciplinaryWorking Groups: The AmericanAcademy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke*. 2007;38:1655–1711.
3. D'Agostino RB, Wolf PA, Belanger AJ, Kannel WB. Stroke risk p rofile: adjustment for antihypertensive medication. The Framingham Study. *Stroke*. 1994;25(1):40–3.
4. Ovbiagele B, Nguyen-Huynh MN. Stroke Epidemiology: Advancing Our Understanding of Disease Mechanism and Therapy. *Neurothera-peutics*. 2011;8(3):319–29.
5. Banerjee TK, Das SK. Fifty years of stroke researches in India. *Ann Indian Acad Neurol*. 2016;19(1).
6. D LJ, Carnethon AR, M. Heart disease and stroke statistics 2009 update: a report from the American Heart Association statistics committee and stroke statistics subcommittee. *Circ*. 2009;119:480–6.
7. Giovanetti T, Nascimento A. Platelet Indices: Laboratory and Clinical Applications. *Rev Bras Hematol Hemoter*. 2011;33:164–5.
8. Pizzuli L, Yang A, Martin JF, Luderitz B. Changes in platelet size and count in unstable angina compared to stable angina and non-cardiac chest pain. *Eur Heart J*. 1998;19:80–4.
9. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis*. 1996;7:157–61.
10. Enticknap JB, Gooding PG, Lansley TS, Avis PRD. Platelet size and function in ischaemic heart disease. *J Atherosclerosis Res*. 1969;10(1):41–9.
11. Jagroop IA, Mikhailidis DP. Mean platelet volume is an independent risk factor for myocardial infarction, but not for coronary artery disease. *Br J Haematol*. 2003;120:166–71.
12. Dougherty JH, Levy DE, Weksler BB. Platelet activation in acute cerebral ischemia. *Lancet*. 1997;1:821–4.
13. Toghi H, Suzuki H, Tamura K, Kimura B. Platelet volume, aggregation and ATP release in cerebral thrombosis. *Stroke*. 1991;22:17–21.
14. Smith NM, Pathansali R, Bath PM. Platelets and stroke. *Vasc Med*. 1999;4:165–72.
15. Vagdatli E, Gounari, Lazaridou, Katsibourlia, Tsikopoulou I, Labrianou, et al. Platelet Distribution Width: A Simple, Practical and Specific Marker of Activation of Coagulation. *Hippokratia*. 2010;14:28–32.
16. Kim JY, Park J, Chang JY. Inflammation after ischemic stroke: the role of leukocytes and glial cells. *Exp Neurobiol*. 2016;25:241–51.
17. Buck BH, Liebeskind DS, Saver JL. Early neutrophilia is associated with volume of ischemic tissue in acute stroke. *Stroke*. 2008;39:355–60.
18. Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. *Atherosclerosis*. 2012;225(2):456–60.
19. Kasama T, Miwa Y, Isozaki T, Odai T, Adachi M, Kunkel S, et al. Neutrophil-Derived Cytokines: Potential Therapeutic Targets in Inflammation. *Curr Drug Targets Inflamm Allergy*. 2005;4(3):273–9.
20. Nam KW, Kwon HM, Jeong HY, Park JH, Sh K, Jeong SM, et al. High neutrophil to lymphocyte ratios predict intracranial athero- sclerosis in a healthy population. *Atherosclerosis*. 2018;269:117–21.
21. Goyal N, Tsivgoulis G, Chang JJ, Malhotra K, Pandhi A, Ishfaq MF, et al. Admission Neutrophil-to-Lymphocyte Ratio as a Prognostic Biomarker of Outcomes in Large Vessel Occlusion Strokes. *Stroke*. 2018;49(8):1985–7.
22. Tekesin A, Tunç A. Inflammatory markers are beneficial in the early stages of cerebral venous thrombosis. *Arq Neuropsiquiatr*. 2019;77(2):101–5.
23. Lok U, Gulacti U, Ekmekci B, Bulut T, Celik M. Predictive and prognostic role of mean platelet volume in patients with first-ever acute ischemic stroke. *Neurosci*. 2017;22(2):119–26.
24. Muscari A, Puddu GM, Cenni A, Silvestri MG, Giuzio R, Rosati M, et al. Mean platelet volume (MPV) increase during acute non-lacunar ischemic strokes. *Thromb Res*. 2009;123(4):587–91.
25. George J. A study on risk factors of patients with acute ischemic stroke at a tertiary care hospital. *Int J Med Health Res*. 2017;3(11):99–101.
26. Mayda-Domaç F, Mısırlı H, Yılmaz M. Prognostic Role of Mean Platelet Volume and Platelet Count in Ischemic and Hemorrhagic Stroke. *J Stroke Cerebrovasc Dis*. 2010;19(1):66–72.
27. Al-Tameemi W, Ameen MM. Significance of Platelet Indices in Patients with Acute Ischemic Stroke. *Iraqui J Agricultural Sci*;2012(4):383–9.
28. Butterworth RJ. The relationship between mean platelet volume, stroke subtype and clinical outcome. *Platelets*. 1998;9(6):359–64.

29. Ghahremanfard F, Asghari N, Ghorbani R. The relationship between mean platelet volume and severity of acute ischemic brain stroke. *Neurosci*. 2013;18(2):147–51.

30. Shah P, Mir R, Kamili M. Role of Mean Platelet Volume in Ischemic Stroke. *JK Sci*. 2013;15(3):136–9.

31. Sung PH, Chen KH, Lin HS, Chu CH, Chiang J, Yip HK. The Correlation between Severity of Neurological Impairment and Left Ventricular Function in Patients after Acute Ischemic Stroke. *J Clin Med*. 2019;8(2):190.

Author biography

Sailaja.Y Final Year Neurology Resident

V Ramakrishnan Associate Professor

Naveen P Assistant Professor

C Mutharasu HOD