ORIGINAL RESEARCH PAPER

Volume-8 | Issue-8 | August - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF PLATELET INDICES WITH SEVERITY OF ACUTE ISCHEMIC STROKE

Physiology

Dr. N. Shuba* Associate Professor of Physiology, PSG Institute of Medical Sciences and Research, Coimbatore-641004 *Corresponding Author

Miss. Vidhya K. G CRRI, PSG Institute of Medical Sciences and Research, Coimbatore-641004

ABSTRACT

Background: Stroke serves as the leading cause of death and physical disability. This study was conducted to find the relationship between platelet indices and severity of acute ischemic stroke.

Materials and methods: This was a cross-sectional study conducted among 60 ischemic stroke patients divided into severe and mild stroke based on modified Rankin Score(mRS) with 30 patients in each group and 30 normal individuals. Platelet indices(Platelet count and Mean Platelet Volume) were obtained from CBC report.

Results: There was a significant decrease in platelet count and increase in Mean Platelet Volume(MPV) in stroke patients when compared with normal persons and also in severe stroke patients when compared with mild stroke patients with p values 0.001 and < 0.001 respectively in both comparisons.

Conclusion: Patients with severe stroke had lowest platelet count and the highest MPV in our study.There is a positive association between platelet indices and the severity of acute ischemic stroke. Platelet indices can serve as an important predictor for the prognosis of acute ischemic stroke. It also helps in risk stratification in ischemic stroke patients so that they can be given more vigilant and aggressive care that can lead to decrease in morbidity and mortality.

KEYWORDS

Acute ischemic stroke, Platelet Indices, Platelet count, Mean Platelet volume

INTRODUCTION:

Central nervous system infarction is brain, spinal cord or retinal cell death attributable to ischemia, based on neuropathological, neuroimaging and/or clinical evidence of permanent injury (1). Stroke is the second leading cause of death, after ischemic heart disease accounting for 9% of deaths worldwide (2). Ischemic stroke is an episode of neurological dysfunction caused by cerebral, spinal or retinal infarction (1). As per Global burden of disease data on stroke on 2013, there were about 25.7 million stroke survivors, 6.5 million stroke deaths and 10.3 millions new strokes. Thus stroke is disease of immense public health importance with serious economic and social consequences (3). The two major mechanisms causing stroke are ischemia and haemorrhage. About 85% of all strokes are ischemic in origin (4).About one-fifth of patients with an acute stroke die within one month of the event and at least half of those who survive are left with a physical disability(5).

Cortical strokes which are 60% of ischemic stroke follow in situ cerebral thrombosis or cardiac source in which platelet play an important role. However lacunar stroke comprising 25% of ischemic stroke is due to lipohyalinosis of end arteries, which is unlikely to involve platelets (6). In recent years, there is an increased interest on research documenting the platelet indices (platelet count, mean platelet volume (MPV), platelet distribution width) in association with various ischemic strokes. Increased platelet reactivity is considered to be a relevant pathophysiological factor in approximately 50% of all strokes (7). Large platelets due to greater content in granules are more reactive than ordinary size platelets, produce more prothrombotic factors and show greater aggregation to Adenosine diphosphate (ADP), collagen and secrete more thromboxane A2 (TXA2). Increased platelet size has been described in patients with vascular risk factors such as diabetes, hypercholesterolemia and metabolic syndrome (8).

Platelet indices are calculated during routine blood analysis along with Complete Blood Count but these are generally not considered by clinicians. Mean Platelet Volume and platelet count are inversely associated so that the total platelet mass remains approximately constant (9).Studies have detected increased MPV in different subtypes of stroke both in acute phase and long after disease. Also stroke patients with high mortality have been found to have low platelet count (8). Moreover, studies on association of MPV with severity of ischemic stroke yielded inconsistent results (10).

Our study finds the association between the platelet indices(Platelet count and Mean Platelet Volume) and severity of acute ischemic stroke thus helps to know the diagnostic value of platelet indices in ischemic stroke. It also helps in risk stratification of patients with ischemic stroke, so that such patients can be given more vigilant and aggressive care that can lead to decrease in morbidity and mortality.

MATERIALS AND METHODS:

This was a cross sectional study, conducted among 60 acute ischemic stroke patients admitted in PSG Hospitals, Coimbatore, Tamilnadu and 30 healthy persons. The study was conducted after obtaining clearance from Institutional Human Ethical Committee, of our institution and obtaining written informed consent from the subjects.

Study population: Patients presenting with acute ischemic stroke (without previous history of stroke) in the age group of 40-70 years admitted in Neurology ward are cases. Controls were healthy persons attending Master Health Check up department.

Inclusion criteria:

- Patients with acute ischemic stroke for the first time proven by CT scan
- Patients admitted within 24 hours of onset of symptoms in neurology ward
- Patients of both genders within the age group of 40-70 years
- Known case of diabetes mellitus and hypertension under control

Exclusion criteria:

- Patients with previous history of stroke
- Transient ischemic attack
- Patients with haemorrhagic stroke, cerebral venous sinus thrombosis
- Patients with late admission of stroke (> 24 hours after stroke onset)
- Patients with co-morbidities like chronic renal disease, chronic liver disease, bypass heart surgery.
- Patients who are on drugs which modify platelet morphology like NSAIDS for long time.
- Patients with haematological malignancies and patients showing atypical cells in peripheral smear were excluded.

Sample size: 90 subjects, 60 acute ischemic stroke patients divided into 2 groups (groupI and group II) of 30 patients in each group and 30 healthy subjects(group III)

Calculation of sample size was done by using Open Epi software version 3.01, by using simplified formula for difference in means of

power 80% and confidence interval 95% and substituting mean ± SD values of parameters of platelet count and MPV of stroke patients and controls obtained by study done by Gideon S et al(11).

Sample selection: Every consecutive acute ischemic stroke patients admitted in neurology ward were taken up for the study.

Study procedure:
The demographic information of subjects like name, age, sex and address recorded. History related to stroke symptoms, mode of onset of neurological deficit, hypertension, diabetes mellitus and cardiac diseases got. Special enquiry about smoking, alcohol, use of anticoagulants obtained. Detailed general, systemic and neurological examination was done.

The patients routinely undergo basic investigations on admission for ischemic stroke which includes Complete Blood Count (CBC), Urine routine, Blood sugar, Urea, Serum Creatinine, Serum electrolytes and Lipid profile. Details of these investigations were recorded. The value of platelet indices ie platelet count and MPV were obtained from their CBC report and were taken up for our study.

Control group consists of 30 healthy persons attending Master health check up department. Both cases and controls were selected according to inclusion and exclusion criteria.

Blood for CBC was obtained by venepuncture, of about 2ml of blood sample collected with EDTA and sent to hematology laboratory where CBC is measured by automated hematology analyser Beckman Coulter LH 500.

The severity of stroke was assessed by Modified Rankin Scale (mRS). The modified Rankin Scale(mRS) is a commonly used scale for measuring the degree of disability or dependence in the daily activities in stroke patients. It has become the most widely used clinical outcome measure for stroke clinical trials (12).

The acute ischemic stroke patients were divided into 2 groups based on mRS scale.

Group I: Ischemic stroke patients with mRS score 0 to 2(mild neurological symptoms).

Group II: Ischemic stroke patients with mRS score 3 to 5(moderate or severe disability) 30 patients in group1 and group II were taken for study.

Group III: Controls consisting of 30 healthy individuals.

The platelet indices values (platelet count, MPV) as obtained from CBC report were taken for correlation with severity of stroke (mild and severe) and also between stroke and controls (mild stroke and control; severe stroke and control).

Statistical analysis: Data analysis was done by using SPSS software version 24.Using this software, percentage, mean, standard deviation and p value were calculated by independent t test and one way ANOVA for correlation of platelet indices between mild and severe stroke, mild stroke and controls, severe stroke and controls. p value <0.05 was taken as statistically significant.

RESULTS

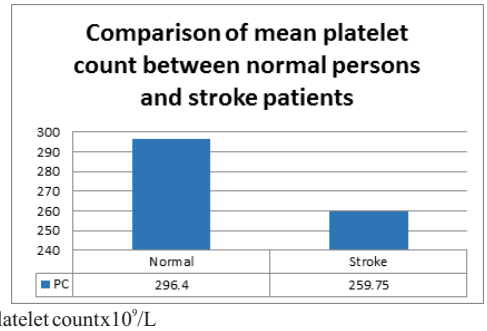
Sixty acute ischemic stroke patients were studied including 32(53%)males and 28(47%) females. The 30 healthy controls comprised of 18(60%) males and 12(40%) females. The mean age of mild stroke patients were 58 and severe stroke patients were 61. The mean age of normal persons were 59. Out of 32 males, 18(56%) had mild stroke(mRSscore 1&2) and 14(44%) had severe stroke(mRSscore 3,4 and 5). Among 28 females, 12(43%) had mild stroke and 16(57%) had severe stroke.

Out of 30 mild stroke patients 7(23%) had mRS score 1 and 23(77%) had mRS score 2.Out of 30 severe stroke patients, 9(30%) had mRS score 3, 18(60%) had mRS score 4 and 3(10%) had mRS score 5 ie gap between mRS and score 5.Majority in mild stroke had mRS score 2(77%), while majority in severe stroke had mRS score 4(60%).

The platelet count and mean platelet volume values were compared between normal and stroke patients. They were also compared between mild and severe stroke patients, normal and mild stroke, and normal and severe stroke patients, statistical analysis was done by SPSS software version 24 using unpaired t test and one way Anova. p values < 0.05 was considered to be statistically significant.

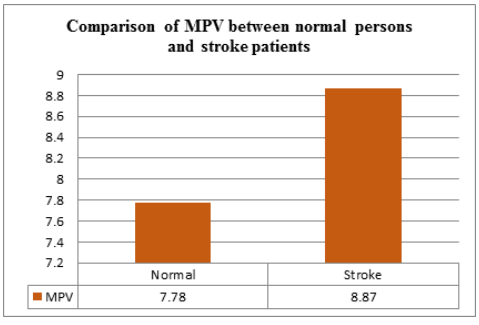
There were 30 normal persons and 60 stroke patients, their platelet count and MPV were analyzed by independent t test. On comparison of platelet count and MPV between normal and stroke patients, the mean ± SD of platelet count in normal persons were 296.40±29.63(x10^9/L) and in stroke patients were 259.75±57.04(x10^9/L). The mean ± SD of MPV in normal persons were 7.78±0.49fl and in stroke patients were 8.87±1.25 fl. There was statistically significant decrease in platelet count and increase in MPV in stroke patients when compared with normal persons with p values 0.001 and < 0.001 respectively as shown in figure 1 and 2.

Figure: 1



PC: Platelet countx10^9/L

Figure: 2



MPV: Mean Platelet Volume in fl

On comparison of platelet count and MPV between mild and severe stroke patients, normal persons and mild stroke patients, normal persons and severe stroke patients, The platelet count of severe stroke patients were statistically significantly lower than mild stroke patients with p value 0.001. MPV of severe stroke patients were statistically significantly higher than mild stroke patients with p value <0.001as shown in Table 1. Mild stroke patients have slightly decreased platelet count and increased MPV when compared with normal persons, but it was not found to be statistically significant as p values were 0.185 and 0.082 respectively as shown in Table 2. The platelet count of severe stroke patients was statistically significantly lower than normal persons with p value< 0.001. MPV of severe stroke patients were statistically significantly higher than normal persons with p value< 0.001 as shown in Table 3. The mean ± SD values of the parameters are given in Tables 1,2,3.

Table: 1 Comparison of platelet count and MPV between mild and severe stroke

Parameter	Group	Mean± SD	p Value
Platelet count(x10^9/L)	Mild stroke	282.133±64.757	0.001**
	Severe Stroke	234.667±36.260	
Mean Platelet Volume(fl)	Mild stroke	8.183±1.099	<0.001**
	Severe stroke	9.547±1.007	

N=30 in both mild and severe stroke, values represent the mean±SD, p<0.05 significant,

** highly significant

Table: 2 Comparison of platelet count and MPV between normal persons and mild stroke

Parameter	Group	Mean± SD	p Value
Platelet count($x10^9$/L)	Normal persons	296.400±29.630	0.185(NS)
	Mild Stroke	282.133±64.757	
Mean Platelet Volume(fl)	Normal persons	7.78±0.490	0.082(NS)
	Mild Stroke	8.183±1.099	

N=30 in both normal persons and mild stroke, values represent the mean±SD, p<0.05 significant, NS Not significant

Table: 3 Comparison of platelet count and MPV between normal persons and severe stroke

Parameter	Group	Mean± SD	p Value
Platelet count($x10^9$/L)	Normal persons	296.400±29.63	<0.001**
	Severe Stroke	234.667±36.260	
Mean Platelet Volume(fl)	Normal persons	7.78±0.49	<0.001**
	Severe stroke	9.547±1.007	

N=30 in both normal persons and severe stroke, values represent the mean±SD, p<0.05 significant, **Highly significant

Since the analysis involved comparison among mild stroke, severe stroke and normal persons, we also did analysis by one way ANOVA followed by posthoc test to compare means. It showed both platelet count (p<0.001) and MPV(p<0.001) values had statistically significant difference among three groups.

DISCUSSION:

Stroke is a common medical emergency and is the second most common cause of death. It is the most common cause of severe physical disability. Many of the patients are left with variable degree of permanent neurological impairment. Mean Platelet Volume (MPV) is a measurement of the average size of platelets found in blood and is typically included in routine blood tests. MPV is a marker of platelet function and is a positively associated with indicators of platelet activity (13). Elevated mean platelet volume is associated with a shortened bleeding time. Larger platelets are enzymatically and metabolically more active and have a higher potential thrombotic ability as compared with smaller platelets. The release of large and more reactive platelets may contribute to the thrombophilic state associated with ischemic events (6). MPV is arousing increasing interest as a new independent cardiovascular risk factor. We have taken up this study to find association between platelet indices and severity of stroke.

We used modified Rankin Scale(mRS) to assess the severity of stroke. The Rankin Scale (RS) was developed in 1957 to assess the extent of disability after a serious illness such as stroke and the functional status of patients. The original scale was 0-5, later modified (mRS) to a 7-point scale. The mRS scores from 0 to 2 are classified as independent; patients scoring 3 to 5 are categorised as experiencing moderate to severe disability. On the mRS, death is rated 6.The mRS has moderate to excellent inter-rater reliability (14).Furthermore, the mRS has good validity ratings and is considered by many authors to be more powerful than the Barthel Index (BI) as a primary endpoint in clinical trials of stroke therapy (15,12).

Muralidharan et al did a study in 50 ischemic stroke patients, compared MPV at the time of admission and after 8 months and used mRS to assess the functional outcome of stroke in 3 groups with mRSscore 0-2,3-4 and 5-6 (16). Elsayed AM et al studied Mean platelet volume and mean platelet volume/platelet count ratio as a risk stratification tool in the assessment of severity of acute ischemic stroke (8). The Severity of ischemic stroke was assessed by the Modified Rankin scale, considering mRSscore≤2 as mild stroke and ≥3 as severe stroke. We also used mRS score to assess the severity of ischemic stroke.

Stroke rates were greater among individuals with higher measures of MPV both overall and for ischemic stroke alone (p=0.01) there was no evidence of an association of MPV with the rates of either intracerebral hemorrhage or stroke of other causes as per Erasmo D et al (17). They got mean±SD of platelet count in stroke patients as 213.61±65.65 and in controls as 299.52±60.61. Their MPV in cases were 11.26±1.29 and in controls were 8.93±0.93. We got similar results in our study with platelet count in cases as 259.75±57.04 and in controls as 296.40±29.63: and MPV in cases were 8.87±1.25 and in controls were 7.78±0.49.

Acute ischemic stroke patients with highest quintile of MPV had a significantly higher risk of suffering a severe stroke, with modified Rankin Scale of 3 to 6, compared with patients within the lowest quintile (odds ratio=2.6; 95% confidence interval,1.6 to 4.1;p<0.001). This association remained significant after adjustment for possible confounding factors (odds ratio=2.2; 95% confidence interval,1.2 to 4.0; p=0.013). Our results were consistent with the study by Greisenegger et al(18), but we did not do adjustment for confounding variables in analysis.

A study by Mayda-Domac F et al conducted study on 692 patients with either ischemic or hemorrhagic stroke and compared them with 208 control subjects with similar risk factors, but without the evidence of vascular events. The association of MPV and Platelet count with cause, localisation and size of the infarct or haemorrhage was examined. Prognosis was determined by Glasgow Outcome Scale. They found out that mean platelet volume is independent risk factor for ischemic stroke(P=0.007, OR= 0.866;P= 0.000,95% confidence interval).Ischemic group MPV (P=0.013,OR=1.02,95%CI) was in correlation with worse outcome(P= 0.001,OR=1.004,95% CI) (19).We also got positive association of MPV with severity of acute ischemic stroke.

The association between increased MPV, larger infarct volume on CT scan with worse clinical outcome was found in 81 ischemic stroke patients (7). Higher mean platelet volume was independently associated with larger infarct volume (estimate 0.259.95% CI 0.004-0.513,P=0.046), greater risk of death/dependence 7 days post stroke (relative risk=1.077,95% CI 1.005-1.115,P=0.036) and greater risk of death/dependence 3 months post-stroke (RR=1.077,95% CI 1.001-1.158, P=0.048).

Neki et al studied association of MPV with ischemic stroke in 50 patients. Clinical severity was assessed with mRSscore. MPV in cases were 8.92±1.03fl when compared with controls 7.67±1.38 fl (p=0.000).They studied the relation between MPV and severity of stroke based on mRS, which was not significant(p=0.191) showing MPV is not associated with severity of stroke (20). We studied the association of Platelet count and MPV with severity of ischemic stroke and found mean MPV in mild stroke was 8.18±1.09, severe stroke 9.54±1.01 and in normal persons were 7.78±0.49. The findings regarding significantly increase in MPV between cases and controls are similar to study done by Neki et al. But we also got significantly lower platelet count and higher MPV in severe stroke than mild stroke and also in severe stroke and normal persons (P<0.001), showing the association with severity of ischemic stroke inconsistent with the study.

A study by Ntaios G et al showed that there were no significant difference in the frequency of minor strokes (p=0.46) and good functional outcome (p=0.06) across MPV quartiles. MPV was not associated with stroke severity or outcome in univariate analysis. There was no significant difference in MPV between stroke subtypes according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification (10). The results of this study are contradictory to our results.

Most of the studies have seen only relationship of MPV with ischemic stroke. We have found the association of both platelet count and MPV with ischemic stroke and also found association of them with severity of stroke in a tertiary care hospital.

Decreased platelet count and increased MPV is associated with severity of acute ischemic stroke in our study. These findings corroborate those of Greisenegger S et al (18). Their study showed that mean platelet volume was elevated in 57% of patients having mild stroke while mean platelet volume was found to be elevated in 67% of patients having severe stroke. Most of the studies report positive correlation between MPV and stroke outcome. Measurement of MPV is easy to establish and therefore might serve as a valuable predictor of a worse outcome in patients with acute ischemic stroke.

The limitation of our study is small sample size and the results cannot be generalized. The follow up study to assess platelet indices after improvement was not done in our study. The analysis did not involve adjustment for confounding variables like diabetes, hypertension, atherosclerosis etc involved in stroke. The study can be improvised by analysing large sample size and proper follow up of patients over period of time to assess platelet indices.

CONCLUSIONS:

Patients with severe stroke had lowest platelet count and the highest MPV in our study.There is a positive association between platelet indices and severity of acute ischemic stroke. Platelet indices (especially MPV) that are done routinely may be helpful in predicting the prognosis of acute ischemic stroke. Hence platelet indices can act as an additional tool to identify people at high risk and such people can be targeted for aggressive acute management and improved secondary stroke prevention measures.

Funding Source: ICMR STS Project 2017
Conflict of Interest: None declared

REFERENCES:

1) Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44;2064-2089.
2) Rodrigo R, Fernández-Gajardo R, Gutiérrez R, Matamala JM, Carrasco R, Miranda-Merchak A, Feuerhake W. Oxidative stress and pathophysiology of ischemic stroke: novel therapeutic opportunities. CNS Neurol Disord Drug Targets .2013 Aug;12(5):698-714.
3) Moran A., Forouzanfar M., Sampson U., Chugh S., Feigin V., Mensah G. The epidemiology of cardiovascular diseases in sub-Saharan Africa: the Global Burden of Diseases, Injuries and Risk Factors 2010 Study. Progress in Cardiovascular Diseases. 2013;56(3):234–239.
4) Feign VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990-2010:findings from the Global Burden of Disease Study 2010.The Lancet 2014; 383(9913):245-54.
5) Steffi Hillmann, SilkeWiedmann, Rucker V. Stroke unit care in germany: the german stroke registers study group (ADSR). BMCNeurology 2017; 17:49.
6) Nicholas M Smitha, Rohan Pathansalia, Philip MW Batha. Platelets and stroke. Vascular Medicine 1999; 4: 165–172.
7) Pikija S, Cvetko D, Hajduk M, Trkulja V. Higher mean platelet volume determined shortly after the symptom onset in acute ischemic stroke patients is associated with a larger infarct volume on CT brain scans and with worse clinical outcome. Clin Neurol Neurosurg 2009;111(7):568-73.
8) Amira M, Elsayed , Ghada A, Mohamed. Mean platelet volume and mean platelet volume/platelet count ratio as a risk stratification tool in the assessment of severity of acute ischemic stroke. Alexandria journal of medicine. 2017;53(1):67-70.
9) David J Kuter. The Physiology of Platelet production.Stem cells 1996; 14 Suppl 1: 88-101.
10) Ntaios G, Gurer O, Faouzi M, et al. Mean Platelet Volume in the early phase of acute ischemic stroke is not associated with severity or functional outcome.Cerebrovasc Dis 2010;29(5):484-9.
11) Gideon S, Igbida F, Mgbeoma E. Changes in Haematological Parameters in Stroke Patients in Port Harcourt, Nigeria. International Journal of Science and Research 2016;5(3): 912-915.
12) Wilson JL, Hareendran A, Grant M, et al. Improving the Assessment of Outcomes in Stroke: Use of a Structured Interview to Assign Grades on the Modified Rankin Scale. Stroke 2002;33 (9): 2243–2246.
13) Philip Bath, Charles Algert, Neil Chapman, Bruce Neal, The PROGRESS Collaborative Group. Association of Mean Platelet Volume With Risk of Stroke Among 3134 Individuals With History of Cerebrovascular Disease. Stroke 2004; 35(3):622-26.
14) Lai SM, Duncan PW. Stroke recovery profile and the Modified Rankin assessment. Neuroepidemiology 2001;20: 26-30.
15) Young FB, Lees KR, Weir CJ; Glycine Antagonist in Neuroprotection International Trial Steering Committee and Investigators Strengthening acute stroke trials through optimal use of disability end points. Stroke 2003;34: 2676-2680.
16) Muralidharan K, Murugesan S, Kumar P, et al. A study of mean platelet volume levels in patients with ischemic stroke. J.Evid. based med. Healthc 2016; 3(71): 3874-77.
17) Erasmo E,.Aliberti G, Celi F S Platelet count, mean platelet volume and their relation to prognosis in cerebral infarction.. Journal of internal medicine 1990; 227(1):11-14.
18) Greisenegger S, Endler G, Hsieh K, Tentschert S, Manhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worst outcome in patients with acute ischaemic cerebrovascular events? Stroke 2004; 35(7):1688-91
19) Mayda – Domaç F, Misirli H, Yilmaz M. Prognostic role of mean platelet volume and platelet count ischemic and hemorrhagic stroke. J Stroke Cerebrovasc Dis. 2010; 19 (1): 66-72.
20) Neki NS, Minda N ,Jain A. A study on association of mean platelet volume and ischaemic stroke. Asian Pac . J.Health Sci.,2016;3(4):212-219.