ORIGINAL RESEARCH

A study of platelet indices in patients with acute ischemic stroke

[1]Dr. K N Sree Sai Gayathri, [2]Dr. Mariyam Mohammed, [3]Dr. Sirisha Peddi, [4]Dr. P Swetha

[1]Associate Professor, Department of General Medicine, Government Medical College, Vikarabad, Telangana, India
[2]Final year resident as DM, Department of Medical Gastroenterology, Gandhi Medical College and Hospital, Secunderabad, Telangana, India
[3]Associate Professor, Department of General Medicine, Gandhi Medical College and Hospital, Secunderabad, Telangana, India
[4]Associate Professor, Department of General Medicine, Government Medical College, Nagarkurnool, India

Corresponding author
Dr. P Swetha
Associate Professor, Department of General Medicine, Government Medical College, Nagarkurnool, India

Received: 25 March, 2024 Accepted: 02 April, 2024

ABSTRACT

Introduction: Ischemic strokesuggested that platelet count was significantly lower in patients with ischemic stroke compared to healthy controls. Since platelets play principal roles in the patho physiology of the diseases, it is important to monitor platelets and their changes in various disease processes. Platelet indices are biomarkers of platelet activation. **Aims**: The aim of this investigation is to study the platelet indices such as MPV, PDW, PCT and PLCR in patients with Acute Ischemic stroke. The objective is to assess if any correlation exists between the studied platelet indices and Acute ischemic stroke. **Materials and methods:** One hundred consecutive patients with first ever acute ischemic stroke were recruited in this study. Non-contrast CT head was done to easily identify and differentiate acute ischemic stroke from haemorrhagic stroke. 5 ml venous peripheral blood collected in Ethylene diamine tetra acetic acid (EDTA) anti- coagulated tubes at the time of admission and processed within 2 hours of collection. The platelet indices were analyzed in whole blood using a blood cell counter. The severity of acute ischemic stroke patients was assessed using National Institute of Health Stroke Scale. **Results:** The mean age of total sample is 54.51 years with mean age of 54.54 years for males and 54.48 years for females. All the platelet indices studied were found to be increased with increase in severity of stroke and this increase was statistically significant for all platelet indices. Pearsons correlation showed that there is positive and high correlation between the mean values of platelet indices and NIHSS scores, and it is statistically significant. **Conclusion:** present study has shown that, higher the value of platelet indices, that severe is the acute ischemic stroke. Therefore, platelet indices can be used as positive predictor for acute ischemic stroke, as all the indices are well correlated with the severity of stroke.

Keywords: Mean Platelet Volume, Platelet large cell ratio, National Institute of Health Stroke Scale,Modified Rankin's score.

INTRODUCTION

Stroke is a sudden loss of neurologic function resulting from focal disturbance of cerebral blood flow due to ischemia or haemorrhage.According to Global Burden of Disease 2010 study (GBD 2010), stroke is second leading cause of death globally and third leading cause of premature death.It is in 1960s, Denny Brown, Russell and Hollenhorst first suspected a potential relationship between platelet activation and cerebral ischemia.They reported platelet containing thrombi in cerebral and retinal arteries in patients during or before focal cerebral ischemia. [1] Stroke is a major global public health problem. A global systematic review of population- based stroke studies documented that incidence of stroke in low- and middle- income countries (LMIC) has been doubled i.e., from 56 to 117/100, 000 persons from the period of 1970's to 2008. It also reported a decreased incidence of stroke in high income countries (HIC) which is approximately 42 percent, when compared to double increase in incidence in LMICs.Evidence from literature suggested that reliable mortality and morbidity estimates for stroke in India are very limited.They concluded that there is a paucity of epidemiological studies on stroke in India, as most of them so far on urban population, rather than rural settings which constitutes up to 80 percent of population. MPV is the most common used measure of platelets size and it is a marker of platelets function. At times of decreased platelet production,

young platelets become bigger and more active, that leads to increase in levels of MPV. Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation.Bath and co- workers in their study followed 3134 patients with cerebrovascular disease and found that risk for stroke was greater among individuals with high measured MPV.MPC refers to measure of mean refractive index of the platelets by modified two- angle light scatter and it is useful in determining changes in the status of platelet activation. PCT is the volume occupied by platelets in the blood as a percentage and calculated according to the formula PCT = platelet count × MPV / 10,000. The normal range for PCT is 0.22–0.24%.PDW is an indicator of volume variability in platelets size and it measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology.PLCR is an indicator of circulating larger platelets, used to monitor platelet activity. The normal percentage range of PLCR is 15-35%. [2,3] Studies have shown strong association between increased MPV and ischemic stroke. It was also proved that raised MPV is a common finding in recurrent stroke. Shah and co- workers studied role of MPV in the pathogenesis, severity and outcome of ischemic stroke. They found inverse relation of MPV to immediate outcome irrespective of stroke subtype.Evidence from literature indicated the lack studies with respect to platelet indices and cerebrovascular accidents. Some studies reported increased MPV associated with stroke subtypes, while other studies showed association between MPV and stroke recurrence. Owing to such differences, with presence of very few studies which looked into the association between platelet size and ischemic stroke, the present study is designed to study the platelet indices in patients with acute ischemic stroke.

MATERIALSANDMETHODS

Prospective study done in Patients with acute ischemic stroke presenting to the Gandhi hospital, Secunderabad are taken for the study from December 2017 to May 2019

Inclusion Criteria: Patients who are above 18years of age, who presented to the hospital within 48 hours of onset of the stroke symptoms, who had diagnosis of ischemic stroke made according to the evidence from computerised tomography (CT) scan.

Exclusion Criteria: Patients presenting to hospital after 48 hours of onset of symptoms, with intracranial haemorrhage or haemorrhagic stroke or hematomas, with recurrent cerebro vascular ischemic stroke, diagnosed cases of hereditary disorders of large platelets,druginducedthrombocytopenia, ischemic stroke with sepsis, ischemic stroke with co existing malignancy. All participants gave informed consent to participate in the study, and we obtained ethical approval from the ethical committee of Gandhi medical college and Hospital, Secunderabad. A detail history, general and systemic examination was done for all the subjects. Patient with history and clinical feature suggestive of acute stroke within onset of 48 hours, non-contrast CT head had been done. It easily identifies and differentiate acute ischemic stroke from haemorrhagic stroke. At the time of admission blood sample was collected from all the patients for laboratory investigations. 3ml venous peripheral blood collected in Ethylene Diamine tetra acetic acid (EDTA) anti- coagulated tubes at the time of admission and processed within 2 hours of collection. The platelet indices were analyzed in whole blood using a blood cell counter (Abbott Cell Dyn 3500 CS). Under physiological conditions, the number of platelets in the blood is maintained in an equilibrium state by regeneration and elimination. A simultaneous reduction of platelet count and PCT indicates that platelets have been excessively consumed.

Severity of acute ischemic stroke: National Institute of health stroke scale (NIHSS): The acute ischemic stroke patients were assessed using NIHSS score. The NIH stroke scale is a common diagnostic method for quickly assessing the severity of stroke experienced by the patient. It objectively quantifies the impairment caused by a stroke. The NIH stroke scale is composed of 11 items, each of which scores a specific ability between a 0 and 4.

Table-1: National Institute of Health Stroke scale

Category	Score/ Description
1a. Level of Consciousness (Alert, Drowsy etc.)	0= Alert1= Drowsy 2= Stuporous 3= Coma
1b. LOC Questions (Month, age)	0= Answers both correctly 1= Answers one correctly 2= Incorrect
1c. LOC Commands (Open/ close eyes, make fist/ let go)	0= Obeys both correctly 1= Obeys one correctly 2= Incorrect
2. Best gaze (Eyes open- Patient follows examiners finger/ face)	0= Normal 1= Partial gaze palsy 2= Forced deviation
3. Visual fields (Introduce visual stimulus/ threat to patient's visual field quadrants)	0= No visual loss1= Partial Hemianopia2= Complete Hemianopia 3= Bilateral Hemianopia (Blind)
4. Facial Paresis (Show teeth, raise eyebrows and	0= Normal 1= Minor2= Partial3= Complete

squeeze eyes shut)	
5a. Motor arm Left 5b. Motor arm Right (Elevate arm to 90^0 if patient is sitting, 45^0 if supine)	0= No drift1= Drift2= Can't resist gravity3= No effort against gravity4= No movement5= Untestable(Joint fusion or limb amp)
6a. Motor leg Left 6b. Motor leg Right (Elevate leg to 30^0 if patient is supine)	0= No drift1= Drift2= Can't resist gravity 1. 3= No effort against gravity4= No movement5= Untestable(Joint fusion or limb amp)
7. Limbataxia (Finger- nose, heel down shin)	0= No ataxi1= Present in one limb 2= Present in two limbs
8. Sensory (Pin prick to face, arm, trunk and leg- compare side to side)	0= Normal1= Partial loss 2= Severe loss
9. Bestlanguage (Name item, describe a picture and read sentences)	0= No aphasia1= Mild to moderate aphasia 2= Severe aphasia3= Mute
10. Dysarthria(Evaluate speech clarity bypatient repeating listed words)	0= Normal articulation1= Mild to moderate slurring ofWords2= Near to unintelligible orWorse X= Intubated or other physicalbarrier
11.Extinction and Inattention (Use information from prior testing to identify neglect or double simultaneous stimuli testing)	0= No neglect1= Partial neglect2= Complete neglect
patient repeating listed words)	Words2= Near to unintelligible orWorse X= Intubated or other physicalbarrier
11.Extinction and Inattention (Use information from prior testing to identify neglect or double simultaneous stimuli testing)	0= No neglect1= Partial neglect2= Complete neglect

The clinical severity of stroke was assessed on day of admission using NIHSS. The patients were rated based on their ability to answer questions and perform activities. Stroke severity was grouped as follows:

1. Minorstroke:Score1-4
2. Moderatestroke:Score5-15
3. Moderatetoseverestroke:Score16-20 4. Severe stroke: Score 21- 42

Statistical analysis

All data were first analyzed for normality of distribution using the Kolmogorov– Smirnov test of normality.Descriptive statistical methods were used to calculate means and standard deviation (SD). Categorical variables were expressed in terms of frequency and percentage. Platelet indices of the groups (based on stoke severity using NIHSS) were compared using one-way ANOVA for continuous variable; the chi-squared test was used to compare the categorical parameters. Comparisons between normally distributed continuous variables were made using ANOVA with post-hoc analysis of least significant difference. Pearson's correlation coefficients were calculated to evaluate the relationships between MPV and admission clinical variables (NIHSS).Statistical significance was set at *P*-value <0.05 for all analyses. The statistical analyses were performed with the IBM SPSS Statistics for Windows version 20.0 (IBM Corp., Armonk, N.Y., USA).
Modified Rankin's score was seen at 90 days after presentation and disability was assessed accordingly.

RESULTS:

Table-2: Baseline characteristics and clinical data according to severity of acute ischemic stroke

Characteristics		NIHSS Scale				p- value
		Minor	Moderate	Moderate to severe	Severe	
Gender	Male (%)	8 (14.8)	21 (38.9)	14 (25.9)	11 (20.4)	0.802 (NS)
	Female (%)	10 (21.7)	15 (32.6)	11 (23.9)	10 (21.7)	
Mean age (SD)		50.4 (4.7)	56.4 (7.9)	55.7 (4.9)	53.1 (5.7)	0.008 (S)
Mean MPV (SD)		9.53 (0.5)	11.15 (1.2)	13.35 (1.5)	15.62 (2.4)	0.000 (S)
Mean PDW (SD)		10.32 (0.6)	12.57 (1.8)	15.26 (1.5)	17.84 (2.6)	0.000 (S)

Mean PCT (SD)	0.16 (0.06)	0.32 (0.11)	0.48 (0.11)	0.53 (0.21)	0.000 (S)
Mean PLCR (SD)	25.8 (2.6)	31.96 (7.7)	37.52 (4.1)	40.36 (5.1)	0.000 (S)

Table-3: Correlation between Platelet indices and NIHSS scores of Ischemic strokes

Age groups	Pearson's correlation	p-value
MPV Vs NIHSS	0.786	0.000 (S)
PDW Vs NIHSS	0.794	0.000 (S)
PCT Vs NIHSS	0.671	0.000 (S)
PLCR Vs NIHSS	0.663	0.000 (S)

It was also observed that there is a statistically significant difference between different NIHSS scores and mean age of the patients (p=0.008; significant). And also, whether if there is any significant difference between platelet indices and NIHSS scores was tested. It was showed that there is a statistically significant difference between different NIHSS scores and mean values of various platelet indices (p<0.05).

Table-4: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the MPV values in patients according NIHSS scale

NIHSS Scale	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
Minor stroke	18	9.533	0.5901	0.1391	8.5	10.6	
Moderate stroke	36	11.156	1.2006	0.2001	9.8	13.7	
Moderate to severe stroke	25	13.352	1.5559	0.3112	10.7	16.0	**0.000 (S)**
Severe stroke	21	15.624	2.4491	0.5344	10.0	19.2	
Total	100	12.351	2.6184	.0.2618	8.5	19.2	

Table-5: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
Minor Vs Moderate stroke	-1.622	0.003 (S)
Minor Vs Moderate to severe stoke	-3.818	0.000 (S)
Minor Vs Severe stroke	-6.091	0.000 (S)
Moderate Vs Moderate to severe stoke	-2.196	0.000 (S)
Moderate Vs Severe stoke	-4.468	0.000 (S)
Moderate to severe Vs Severe stoke	-2.271	0.000 (S)

It can be seen that there is statistically significant difference for all multiple comparisons (p=0.000). The mean difference between minor and moderate stroke scores was -1.622 (p=0.003), between minor and moderate to severe was -3.818 (p=0.000), between minor to severe was -6.091 (p=0.000), between moderate and moderate to severe was -2.196 (p=0.000), between moderate and severe was -4.468 (p=0.000) and between moderate to severe and severe was -2.271 (p=0.000) respectively.

Table-6: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PDW values in patients according NIHSS scale

NIHSS Scale	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
Minor stroke	18	10.322	0.6726	0.1585	9.3	11.6	
Moderate stroke	36	12.576	1.8955	0.3159	10.8	19.4	
Moderate to severe stroke	25	15.260	1.5135	0.3027	11.5	17.3	**0.000 (S)**
Severe stroke	21	17.848	2.6178	0.5712	11.2	21.9	
Total	100	13.949	3.1658	.0.3166	9.3	21.9	

Table-7: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
Minor Vs Moderate stroke	-2.254	0.000 (S)
Minor Vs Moderate to severe stoke	-4.937	0.000 (S)
Minor Vs Severe stroke	-7.525	0.000 (S)
Moderate Vs Moderate to severe stoke	-2.683	0.000 (S)
Moderate Vs Severe stoke	-5.271	0.000 (S)
Moderate to severe Vs Severe stoke	-2.587	0.000 (S)

It can be seen that there is statistically significant difference for all multiple comparisons (p=0.000). The mean difference between minor and moderate stroke scores was -2.254 (p=0.000), between minor and moderate to severe was -4.937 (p=0.000), between minor to severe was -7.525 (p=0.000), between moderate and moderate to severe was -2.683 (p=0.000), between moderate and severe was -5.271 (p=0.000) and between moderate to severe and severe was -2.587 (p=0.000) respectively.

Table-8: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PCT values in patients according NIHSS scale.

NIHSS Scale	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
Minor stroke	18	0.1656	0.0614	0.0144	0.07	0.31	
Moderate stroke	36	0.3297	0.1143	0.0190	0.23	0.65	
Moderate to severe stroke	25	0.4884	0.1186	0.0237	0.17	0.65	**0.000 (S)**
Severe stroke	21	0.5343	0.2183	0.0476	0.06	0.80	
Total	100	0.3828	0.1886	0.0188	0.06	0.80	

Table-9: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
Minor Vs Moderate stroke	-0.164	0.000 (S)
Minor Vs Moderate to severe stoke	-0.322	0.000 (S)
Minor Vs Severe stroke	-0.368	0.000 (S)
Moderate Vs Moderate to severe stoke	-0.158	0.000 (S)
Moderate Vs Severe stoke	-0.204	0.000 (S)
Moderate to severe Vs Severe stoke	-0.045	0.673(NS)

It can be seen that there is statistically significant difference for all multiple comparisons (p=0.000) except moderate to severe and severe NIHSS scores(p=0.673). The mean difference between minor and moderate stroke scores was -0.164 (p=0.000), between minor and moderate to severe was -0.322 (p=0.000), between minor to severe was -0.368 (p=0.000), between moderate and moderate to severe was - 0.158 (p=0.000), between moderate and severe was -0.204 (p=0.000) and between moderate to severe and severe was -0.045 (p=0.673) respectively.

Table-10: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PLCR values in patients according NIHSS scale

NIHSS Scale	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
Minor stroke	18	25.800	2.6027	0.6135	21.1	31.2	
Moderate stroke	36	31.967	7.7524	1.2921	24.8	54.8	
Moderate to severe stroke	25	37.520	4.1332	0.8266	29.7	44.1	**0.000 (S)**
Severe stroke	21	40.367	5.0101	1.0933	24.8	44.2	
Total	100	34.009	7.5551	0.7555	21.1	54.8	

Table-10: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
Minor Vs Moderate stroke	-6.166	0.002 (S)
Minor Vs Moderate to severe stoke	-11.720	0.000 (S)
Minor Vs Severe stroke	-14.566	0.000 (S)
Moderate Vs Moderate to severe stoke	-5.553	0.002 (S)
Moderate Vs Severe stoke	-8.40	0.000 (S)
Moderate to severe Vs Severe stoke	-2.846	0.338 (NS)

It can be seen that there is statistically significant difference for all multiple comparisons (p=0.000) except moderate to severe and severe NIHSS scores (p=0.338). The mean difference between minor and moderate stroke scores was -6.166 (p=0.002), between minor and moderate to severe was -11.720 (p=0.000), between minor to severe was -14.566 (p=0.000), between moderate and moderate to severe was -5.553 (p=0.002), between moderate and severe was -8.4 (p=0.000) and between moderate to severe and severe was -2.846 (p=0.338) respectively.

Table-11: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the MPV values in patients according mRs score

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
No symptoms	2	9.100	.1414	.1000	9.0	9.2	0.000 (S)
No significant disability	6	9.283	.6494	.2651	8.5	10.2	
Slight disability	17	10.153	.6587	.1598	8.9	11.3	
Moderate disability	18	11.739	1.5324	.3612	9.9	15.1	
Moderately severe disability	23	12.283	2.3847	.4973	9.8	17.7	
Severe disability	24	14.129	2.0577	.4200	10.8	18.2	
Dead	10	15.570	2.6073	.8245	10.9	19.2	
Total	100	12.351	2.6184	.2618	8.5	19.2	

Table-12: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
No symptoms vs No significant disability	-0.183	1.000 (NS)
No symptoms vs slight disability	-1.052	0.989 (NS)
No symptoms vs moderate disability	-2.683	0.504 (NS)
No symptoms vs moderately severe disability	-3.182	0.264 (NS)
No symptoms vs severe disability	-5.029	0.009 (S)
No symptoms vs dead	-6.47	0.001 (S)
No significant vs slight disability	-0.869	1.000 (NS)
No significant vs moderate disability	-2.455	0.960 (NS)
No significant vs moderately severe disability	-2.999	0.014 (S)
No significant vs severe disability	-4.845	0.000 (S)
No significant disability vs dead	-6.286	0.000 (S)
Slight vs moderate disability	-1.585	0.179 (NS)
Slight vs moderately severe disability	-2.129	0.012 (S)
Slight vs severe disability	-3.976	0.000 (S)
Slight disability vs dead	-5.417	0.000 (S)
Moderate vs moderately severe disability	-0.543	0.970 (NS)
Moderate vs severe disability	-2.39	0.002 (S)
Moderate disability vs dead	-3.831	0.000 (S)
Moderately severe vs severe disability	-1.846	0.020 (S)
Moderately severe vs dead	-3.287	0.000 (S)
Severe disability vs dead	-1.44	0.407 (NS)

It can be seen that there is statistically significant difference for multiple comparisons between no symptoms and severe disability (-5.029; p=0.009), between no symptoms and dead (-6.47; p=0.001), between no significant disability and moderately severe (-2.999; p=0.014), between no significant and severe disability (-4.845; p=0.000), between no significant disability and dead (-6.286; p=0.000),slight vs moderately severe disability (-2.129; p=0.012), slight vs severe disability (-3.976; p=0.000), slight disability vs dead (-5.417; p=0.000), moderate vs severe disability (- 2.39; p=0.002), moderate disability vs dead (-3.831; p=0.000), moderately severe vs severe disability (-1.846; p= 0.020), moderately severe vs dead (-3.287; p=0.000) respectively.

Table-13: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PDW values in patients according mRs score

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
No symptoms	2	10.000	.1414	.1000	9.9	10.1	0.000 (S)
No significant disability	6	10.400	.3899	.1592	9.9	11.1	
Slight disability	17	11.071	1.2707	.3082	9.3	13.4	
Moderate disability	18	12.703	2.0613	.4859	10.9	19.4	
Moderately severe disability	23	14.257	2.7474	.5729	11.3	20.0	
Severe disability	24	16.412	2.1906	.4471	11.2	20.3	

Dead	10	17.380	2.9028	.9179	11.5	21.9	
Total	100	13.949	3.1658	.3166	9.3	21.9	

Table-14: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
No symptoms vs No significant disability	-0.4	1.000 (NS)
No symptoms vs slight disability	-1.07	0.995 (NS)
No symptoms vs moderate disability	-2.702	0.653 (NS)
No symptoms vs moderately severe disability	-4.256	0.131 (NS)
No symptoms vs severe disability	-6.412	0.003 (S)
No symptoms vs dead	-7.38	0.001 (S)
No significant vs slight disability	-0.67	1.000 (NS)
No significant vs moderate disability	-2.303	0.296 (NS)
No significant vs moderately severe disability	-3.856	0.004 (S)
No significant vs severe disability	-6.012	0.000 (S)
No significant disability vs dead	-6.98	0.000 (S)
Slight vs moderate disability	-1.632	0.310 (NS)
Slight vs moderately severe disability	-3.185	0.000 (S)
Slight vs severe disability	-5.341	0.000 (S)
Slight disability vs dead	-6.31	0.000 (S)
Moderate vs moderately severe disability	-1.553	0.284 (NS)
Moderate vs severe disability	-3.709	0.000 (NS)
Moderate disability vs dead	-4.677	0.000 (S)
Moderately severe vs severe disability	-2.156	0.019 (S)
Moderately severe vs dead	-3.123	0.006 (S)
Severe disability vs dead	-0.967	0.905 (NS)

It can be seen that there is statistically significant difference for multiple comparisons between no symptoms and severe disability (-6.412; p=0.003), between no symptoms and dead (-7.38; p=0.001), between no significant disability and moderately severe (-3.856; p=0.004), between no significant and severe disability (-6.012; p=0.000), between no significant disability and dead (-6.98; p=0.000),slight vs moderately severe disability (-3.185; p=0.000), slight vs severe disability (-5.341; p=0.000), slight disability vs dead (-6.31; p=0.000), moderate vs severe disability (- 3.709; p=0.000), moderate disability vs dead (-4.677; p=0.000), moderately severe vs severe disability (-2.156; p= 0.019), moderately severe vs dead (-3.123; p=0.006) respectively.

Table-15: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PCT values in patients according mRs score

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
No symptoms	2	.0900	.02828	.02000	.07	.11	0.000 (S)
No significant disability	6	.1750	.04680	.01910	.09	.22	
Slight disability	17	.2335	.09578	.02323	.09	.40	
Moderate disability	18	.3072	.07873	.01856	.23	.51	
Moderately severe disability	23	.4600	.16871	.03518	.23	.71	
Severe disability	24	.4933	.17244	.03520	.06	.80	
Dead	10	.5130	.22081	.06983	.06	.71	
Total	100	.3828	.18869	.01887	.06	.80	

Table-16: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
No symptoms vs No significant disability	-0.08	0.992 (NS)
No symptoms vs slight disability	-0.14	0.848 (NS)
No symptoms vs moderate disability	-0.217	0.434 (NS)
No symptoms vs moderately severe disability	-0.370	0.016 (S)

No symptoms vs severe disability	-0.403	0.006 (S)
No symptoms vs dead	-0.423	0.006 (S)
No significant vs slight disability	-0.058	0.980 (NS)
No significant vs moderate disability	-0.132	0.481 (NS)
No significant vs moderately severe disability	-0.285	0.001 (S)
No significant vs severe disability	-0.318	0.000 (S)
No significant disability vs dead	-0.338	0.000 (S)
Slight vs moderate disability	-0.073	0.755 (NS)
Slight vs moderately severe disability	-0.226	0.000 (S)
Slight vs severe disability	-0.259	0.000 (S)
Slight disability vs dead	-0.279	0.000 (S)
Moderate vs moderately severe disability	-0.152	0.022 (S)
Moderate vs severe disability	-0.186	0.002 (S)
Moderate disability vs dead	-0.205	0.011 (S)
Moderately severe vs severe disability	-0.033	0.987 (NS)
Moderately severe vs dead	-0.053	0.963 (NS)
Severe disability vs dead	-0.019	1.000 (NS)

It can be seen that there is statistically significant difference for multiple comparisons between no symptoms and moderately severe disability (-0.37; p=0.016), no symptoms and severe disability (-0.403; p=0.006), between no symptoms and dead (-0.423; p=0.006), between no significant disability and moderately severe (-0.285; p=0.001), between no significant and severe disability (-0.318; p=0.000), between no significant disability and dead (-0.338; p=0.000),slight vs moderately severe disability (- 0.226; p=0.000), slight vs severe disability (-0.259; p=0.000), slight disability vs dead (- 0.279; p=0.000), moderate vs moderately severe disability (-0.152; p=0.022), moderate vs severe disability (-0.186; p=0.002), moderate disability vs dead (-0.205; p=0.011) respectively.

Table-17: ONE-WAY ANOVA showing mean, standard deviation, the minimum and maximum values and the significance (p) of the PLCR values in patients according mRs score

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	p- value
No symptoms	2	25.650	.2121	.1500	25.5	25.8	0.000 (S)
No significant disability	6	25.850	3.3369	1.3623	21.1	31.2	
Slight disability	17	27.159	3.3871	.8215	22.8	34.4	
Moderate disability	18	33.750	9.0150	2.1249	24.8	54.8	
Moderately severe disability	23	33.930	6.9582	1.4509	24.8	54.8	
Severe disability	24	39.138	4.1351	.8441	28.0	44.2	
Dead	10	40.560	4.3826	1.3859	31.4	44.2	
Total	100	34.009	7.5551	.7555	21.1	54.8	

Table-18: Post- hoc test/ test of multiple comparisons

Multiple comparisons	Mean Difference	Summary
No symptoms vs No significant disability	-0.200	1.000 (NS)
No symptoms vs slight disability	-1.508	1.000 (NS)
No symptoms vs moderate disability	-8.10	0.526 (NS)
No symptoms vs moderately severe disability	-8.280	0.486 (NS)
No symptoms vs severe disability	-13.48	0.040 (S)
No symptoms vs dead	-14.91	0.026 (S)
No significant vs slight disability	-1.308	0.980 (NS)
No significant vs moderate disability	-7.90	0.079 (NS)
No significant vs moderately severe disability	-8.808	0.055 (NS)
No significant vs severe disability	-13.28	0.000 (S)
No significant disability vs dead	-14.71	0.000 (S)
Slight vs moderate disability	-6.591	0.023 (S)
Slight vs moderately severe disability	-6.771	0.010 (S)

Slight vs severe disability	-11.978	0.000 (S)
Slight disability vs dead	-13.401	0.000 (S)
Moderate vs moderately severe disability	-0.180	1.000 (NS)
Moderate vs severe disability	-5.387	0.064 (NS)
Moderate disability vs dead	-6.81	0.064 (NS)
Moderately severe vs severe disability	-5.207	0.049 (S)
Moderately severe vs dead	-6.629	0.058 (NS)
Severe disability vs dead	-1.422	0.995 (NS)

Multiple comparisons, shows which groups differed from each other. It can be seen that there is statistically significant difference for multiple comparisons between no symptoms and severe disability (-13.48; p=0.040), between no symptoms and dead (-14.91; p=0.026), between no significant and severe disability (- 13.28; p=0.000), between no significant disability and dead (-14.71; p=0.000),slight vs moderatedisability (-6.59; P=0.023), slight vs moderately severe disability (-6.771; p=0.010), slight vs severe disability (-11.978; p=0.000), slight disability vs dead (- 13.401; p=0.000), moderately severe vs severe disability (-5.207; p=0.049) respectively.

DISCUSSION

Stroke is a major global health problem, and according to Global Burden of diseases (GBD), it was the second leading cause of death worldwide with 26% increase in global stroke deaths from 1990 to 2010. According to global systematic review of population- based stroke studies by Feigin et al.[4], the incidence rate of stroke in low- and middle- income countries has increased from 56/ 100, 000 persons (1970- 79) to 117/ 100, 000 persons (2000- 08). And, they also reported a decrease in stroke incidence in high- income countries with approximately 42% decrease.India has been experiencing significant demographic, economic and epidemiological transition during past two decades. Stroke is one of the leading causes of death and disability in India.The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334- 424/ 100,000 in urban areas, with incidence rate of 119- 145/100,000. Reliable mortality and morbidity estimates for stroke in India are very limited. Kannan et al., [5]with an intention to understand the true magnitude of problem (stroke) conducted a systematic review of epidemiological studies of stroke in India with an objective to investigate the incidence and prevalence of stroke in India.Their results showed that the crude stroke prevalence in different parts of India ranged from 44.29 to 559/100,000 persons during last two decades. And, the cumulative incidence ranged from 105 to 152/100,000 persons. These estimates were found to be higher than those of high-income countries.They believed that there is paucity of epidemiological studies on stroke in India which emphasized the need for a focused, coordinated effort at the state and national level to study the extent of stroke in India. Accumulated evidence from literature suggested that megakaryocytic changes with resultant platelet changes can result in development of fresh platelet- rich thrombi, suggesting that platelet adhesion and aggregation, as well as fibrin deposition, are pathogenic factors in Ischemic heart disease.According to the recent studies, larger platelets are enzymatically and metabolically more active and have higher thrombolytic ability. It was demonstrated that increased platelet size was seen in patients with diabetes mellitus and obesity. This has suggested that there is a positive association between platelet size and ischemic cardiac events. Platelet indices are biomarkers of platelet activation. They allow extensive clinical investigations focusing on the diagnostic and prognostic values in a variety of settings without bringing extra costs.Platelet parameters include platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet- large cell ratio (P-LCR) etc. Among these platelet indices, PCT, MPV and PDW are related to platelets morphology and proliferation kinetics and are determined together in automatic CBC profiles.The prothrombotic stage of platelet can be detected early with ease using the newer hematologicalanalyzers through these platelet parameters. Measurement of these indices will provide a valid instrument for measuring disease severity and also provides an insight into the potential etiology that resulted in changes. Platelet volume heterogeneity occurs during its production and increases MPV and PDW comparatively, suggesting the production of them in bone marrow and their rapid release into the circulation.A simultaneous reduction of PC and PCT indicates that platelets have been excessively consumed. [6] In the present study, one-hundred patients with first- ever ischemic stroke were chosen randomly for the known risk factors, with an aim to study platelet indices in those patients and to assess if any correlation exists between platelet indices and acute ischemic stroke. It was observed that there was male preponderance (54%) when compared to females (46%), which is similar to the study of Vyawahare and Dhonge.[7]In the present study, platelet indices were studied in view of traditional risk factor for ischemic stroke. We also analysed the variation in platelet indices with increase in severity of ischemic stroke, which was analysed NIH stroke scale. Our results showed that there is an increase in MPV values with increase in NIHSS scores. The

mean (SD) of MPV in minor stroke group was 9.53 (0.5), in moderate group 11.15 (1.2), in moderate to severe group 13.35 (1.5) and in severe stroke group it was 15.62 (2.4). These findings were found to be similar to the results of Vyawahare and Dhonge[7] where constant increase in MPV values was seen with increase in NIHSS scores. On the contrary to the results of present study, Ntaios et al.,[8] demonstrated that MPV is not associated with the severity of the ischemic stroke. They suggested that platelet size during the short period before stroke does not influence stroke severity. The conclusions on the associations between the MPV and severity as well as outcome were found to be inconsistent. This may be due to several reasons such as employing different cell countries in studies to assess MPV, which further leading to different methods that incorporate for the measurement of platelet parameters. Secondly, the time of measurement of MPV varied between the studies, ranging from admission to 48 hours after stroke onset. Similar to our findings, results of Greisenegger et al.[9], study showed that increased MPV was associated with a worse outcome in patients suffering an acute ischemic cerebrovascular event. Patients within the highest quintile of MPV had a the lowest quintile.One might argue that increased MPV and higher platelet reactivity simply reflect a marker for a more severe stroke event and a more pronounced acute-phase reaction. In our study, we included only patients whose MPV was determined on admission. Given the average life span of a platelet of 8 days, it is unlikely that the platelet size at the time of measurement was affected by the acute vascular event. Our results suggest that patients who then suffered a severe stroke already had an increased MPV, reflecting higher platelet reactivity, before the stroke occurred.It is therefore reasonable to speculate that a proinflammatory state before the cerebrovascular event may confer a higher MPV and a prothrombotic condition. In another study by Ghahremanfard et al.[9], where they assessed the role of MPV for predicting severer and extensive acute ischemic stroke from its mild status. It was showed from their results measuring MPV within the first 24 hours of brain stroke appearance was strongly related to the severity of the disease. They also observed that increased MPV was associated with a poorer outcome. And, also patients with higher MPV range had more than 4- fold risk of suffering a severe stroke compared with patients within the lower range of MPV.was correlated with PDW, it showed a positive and statistically significant correlation, which Mayda DF et al.[10], mentioned that platelet size is determined at the level of the progenitor cell and is not changed as given to the circulation, therefore it is reasonable to speculate that a proinflammatory state confers a higher MPV and a prothrombotic condition before the ischemic stroke.Our study is different from previous studies that suggested that platelet changes occur as a result of acute ischemic stroke.This study probably may failed to reveal time- dependant changes in MPV that occur with both EDTA and citrate anticoagulants. As blood cell counts are stable in EDTA at room temperature, we used blood sample anti-coagulated with EDTA within 2 hours. It is mentioned in literature that EDTA anticoagulation increases MPV only 3% to 4% after 60 to 120 minutes. It is also showed that the increase of platelet size amounts to less than 0.5fL when the analysis is performed within 2 hours after venepuncture. Our results also showed that there is an increase in PDW values with increase in NIHSS scores. The mean (SD) of MPV in minor stroke group was 10.32 (0.6), in moderate group 12.57 (1.8), in moderate to severe group 15.26 (1.5) and in severe stroke group it was 17.84 (2.6). These findings were similar to that findings from the study of Vyawahare and Dhonge[7] with high PDW values from minor stroke (12.73 + 4.5) to severe stroke (22.26 + 7.2). According to literature, PDW reported to vary markedly, with reference intervals ranging from 8.3 to 56.6%.Similar findings were reported in study by Shah PA et al.[11], in which PDW was found to be higher in stroke than controls.The range of PDW in ischemic stroke patients was found to be 12.3 to 23.7fL. It is indicated that platelet volume heterogeneity occurs during its production and increases MPV and PDW comparatively, suggesting that bone marrow produces platelets and rapidly releases them into the circulation.When severity score of stroke is that with increase in NIHSS score, the mean PDW increased. This finding was similar to that of Vyawahare and Dhonge.[7] Our results also showed that there is an increase in PCT values with increase in NIHSS scores. The mean (SD) of PCT in minor stroke group was 0.16 (0.06), in moderate group 0.32 (0.11), in moderate to severe group 0.48 (0.11) and in severe stroke group it was 0.53 (0.21). It is indicated that a simultaneous reduction of platelet count and PCT shows that platelets have been excessively consumed. In a study by Mohamed et al.[12], it was found that the PCT were significantly higher in patients with unfavorable outcome. In their study, the mean (SD) PCT was 0.26 (0.11), with mean value of 0.25 in favorable outcome patients and 0.28 in unfavorable outcome patients, indicating that there is association between PCT and ischemic stroke functional outcome.[13] PCT is considered an important platelet index, reflecting the total platelet mass. But it is not a frequently used biomarker, and its importance been underestimated. Even though limited information is available in literature, evidence has suggested that PCT is associated with inflammatory as well as vascular diseases. The results of Tewatia et al.[14], showed an increase in PCT values compared to healthy controls, but not statistically significant.They believed that PCT along with other platelet parameters could be useful in potential stroke events and might serve as a prognostic tool to predict patients with possibility of impeding acute cardiac or ischemic stroke events. With respect to P-LCR values, our

results showed an increase in P-LCR values with NIHSS scores respectively. The mean (SD) of P-LCR in minor stroke group was 25.8 (2.6), in moderate group 31.96 (7.7), in moderate to severe group 37.52 (4.1) and in severe stroke group it was 40.36 (5.1). These results were similar to that of Vyawahare and Dhonge[7] in terms of increase in mean P-LCR with stroke severity. But nostatistically significant difference was observed. In another study Tewatia et al.[14], it was observed that P-LCR in the cases is 34.14+ 6.35 % with the range being 14.5 – 51% while in controls the mean was 28.31+ 5.88 % with a range from 12.40-52.0% and this difference is not statistically significant.They also revealed that the risk of a thrombotic event in the high P-LCR group was 1.89 times higher when compared to the controls. Elevated P-LCR levels had the highest risk with odds ratio of 1.89 regarding the risk of ischemic event.

CONCLUSION

In present study, the comparison of severity of NIHSS score with platelet indices such as MPV, PDW, PCT and P- LCR showed increase in respective mean values and found to be statistically significant. All the platelet indices positive correlation with NIHSS scores and also statistically significant. Hence the present study has shown that, higher the value of platelet indices, that severe is the acute ischemic stroke. It is therefore reasonable to speculate that a proinflammatory state before the cerebrovascular event may confer a higher platelet index value and a prothrombotic condition. Platelet indices is cost effective investigation and can be obtained in most health care centers. The present study is corroborating with other observations that platelet indices are higher in acute ischemic stroke and increase in platelet indices are associated with severity of stroke. The primary goal of these biomarkers in ischemic stroke patients should be early identification of high-risk individuals who can be targeted for aggressive acute management and improved secondary preventive measures. Hence, evaluation of these parameters in stroke patients can predict the possibility of an impending thrombotic event. Further research is required into the role of platelet indices in stroke pathology, outcome, and most importantly, in individuals at risk for stroke. We also recommend to investigate the role of the indices as a predictive factor in the severity of the ischemic stroke. And also, future predictive modelling should try to introduce follow-up NIHSS scores and also analysis of platelet parameters at multiple time points of the treatment.

Larger sample size studies are required using this simple, relatively inexpensive markers of platelet activation.

REFERENCES

1. Leslie M. Cell biology. Beyond clotting: the powers of platelets. Science. 2010;328(5978):562-4.
2. Holinstat M. Normal platelet function. Cancer Metastasis Rev. 2017;36(2):195-8.
3. Broos K, Feys HB, De Meyer SF, Vanhoorelbeke K, Deckmyn H. Platelets at work in primary hemostasis. Blood reviews. 2011;25(4):155-67.
4. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. The Lancet Neurology. 2009;8(4):355-69.
5. Kamalakannan S, Gudlavalleti ASV, Gudlavalleti VSM, Goenka S, Kuper H. Incidence & prevalence of stroke in India: A systematic review. Indian J Med Res. 2017;146(2):175-85.
6. Ranjith MP, Divya R, Mehta VK, Krishnan MG, KamalRaj R, Kavishwar A. Significance of platelet volume indices and platelet count in ischaemic heart disease. Journal of clinical pathology. 2009;62(9):830-3.
7. Vyawahare M, Dhonge O. Correlation of platelet indices with severity and clinical outcome in patients with acute ischemic stroke. IJBAR [Internet]. 2018;9(10):338- 44.
8. Ntaios G, Gurer O, Faouzi M, Aubert C, Michel P. Mean platelet volume in the early phase of acute ischemic stroke is not associated with severity or functional outcome. Cerebrovascular diseases (Basel, Switzerland). 2010;29(5):484-9.
9. Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events? Stroke. 2004;35(7):1688-91.
10. Mayda-Domac F, Misirli H, Yilmaz M. Prognostic role of mean platelet volume and platelet count in ischemic and hemorrhagic stroke. Journal of stroke and cerebrovascular diseases: the official journal of National Stroke Association. 2010;19(1):66-72.
11. .Shah P, Mir R, Kamili M. Role of Mean Platelet volume in Ischemic stroke. JK science. 2013;15(3):136- 9.
12. Mohamed A-AB, Elnady HM, Alhewaig HK, Moslem Hefny H, Khodery A. The mean platelet volume and plateletcrit as predictors of short-term outcome of acute ischemic stroke. Egypt J NeurolPsychiatrNeurosurg. 2019;55(1):4.
13. Wu Z, Zeng M, Li C. Time-dependence of NIHSS in predicting functional outcome of patients with acute ischemic stroke treated with intravenous thrombolysis. 2019;95(1122):181-6.
14. Tevatia MS, Nair KS, Somasundaram V. Evaluation of platelet parameters in patients of ischemic heart disease and ischemic stroke. Global J Res Anal. 2019;8(9):47-9.