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Research Article

ASSOCIATION AND CORRELATION OF MEAN PLATELET VOLUME AND PLATELET COUNT IN ACUTE ISCHEMIC STROKE

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ABSTRACT

Objectives: The objectives of this study were to study the correlation and significance of platelet count (PC) and mean platelet volume (MPV) on the clinical severity of stroke and the interrelation of MPV and PC in acute ischemic stroke (AIS) patients.

Methods: We studied MPV and PC of 52 AIS patients consecutively admitted in Neurology department at Geetanjali Medical University, India. Platelet variables were measured and compared with control of similar age, sex, and without vascular events.

Results: Thirty (57.69%) patients had significantly higher MPV in AIS group (12.45fL compared with normal range of 6–11 fL in control, $p<0.001$). No significant differences were found between male and females, but the total mean was elevated. The mean of PC was 1.76×10^5 cells/cumm (normal range) and there was no correlation between the change in PC and AIS in both sexes. Repeated measurements of MPV and PC were also recorded on follow-up which showed no significant changes from the acute phase; however, MPV remained elevated. The comparison of MPV in patients with mRS score 2 versus 4, 2 versus 5, 3 versus 4 and 5 and 4 versus 5 were found to be statistically significant ($p<0.05$).

Conclusion: Increased MPV has an independent association with AIS and its severity and the mean MPV range did not change after acute treatment. It may be possible that these changes precede the vascular event, and further studies are warranted to unravel the underlying mechanism.

Keywords: Mean platelet volume, Platelet count, Acute ischemic stroke.

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INTRODUCTION

Stroke is a major cause of death and disability in Asia [1]. Stroke is the second leading cause of death worldwide as studied by the Global Burden of Diseases. It is the third leading cause of death in men, (after ischemic heart disease and lung cancer), whereas a leading cause of mortality in women [2]. AIS accounts for about 85% of cases, primary intracerebral hemorrhage (ICH) for 10%, and subarachnoid hemorrhage (SAH) for the remaining 5% [3].

The mechanism of stroke undergoes a disease course that impedes oxygen and nutrient-rich bloodstream to the brain tissues and leads to focal neurologic syndromes. The interruption of oxygen and glucose supply, essential for the production of high-energy phosphate compounds, and the existence of mediators of ischemic cellular injury are the secondary mechanisms leading to stroke [4,5]. Stroke is also associated with residual physical, cognitive, and behavioral impairments, recurrence, and increased risk of other types of vascular events [6].

The mechanism underlying AIS is atherothrombotic pathogenesis. The equilibrium between platelet activation, fibrin construction, and fibrinolysis plays a pivotal role in atherothrombotic process. These events are of prime importance in the progression and prognosis of stroke. Platelets play the leading role in the formation of cerebral atherothrombotic – ischemic processes, adhesion and aggregation [6,7]. Platelet size is found to be elevated in individuals with vascular diseases such as hypertension and diabetes mellitus [8].

Circulating platelets are heterogeneous in their size, density, and reactivity. The platelet volume indices are also thought to be directly associated with inflammatory responses. These indices include platelet count (PC), mean platelet volume (MPV), and platelet distribution width (PDW). The important role of platelets in the pathogenesis and prognosis of the atherothrombosis and ischemic stroke has been observed [9,10]. MPV is regarded as a marker of platelet turnover [11]. It is noted that increased MPV acts as an indicator of increased platelet activation and is directly related to the severity of stroke; the larger the MPV, the worse the outcome. Elevated MPV simultaneously with the elevated PC enhances the risk of thrombosis [12]. Modification of platelet function has been documented in patients with both ischemic and hemorrhagic strokes [13]. It has been shown that PC and MPV are independent predictors for poor outcome in ICH [14]. The previous studies have documented above-average levels of MPV with vascular events such as acute myocardial infarction, acute cerebral ischemia, and transient ischemic attack [15].

METHODS

A prospective observational study was planned after the approval from the Institutional Research Ethical Board. A well-informed, written consent was taken by all the patients in the study. The study was conducted at Geetanjali Medical College and Hospital, Udaipur, India between time period January 2019 and June 2020.

Inclusion criteria

All admitted acute ischemic stroke patients above 18 years of age and patients with informed consent were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

Patients with history of head trauma, previous intracranial surgical procedures, hemorrhagic stroke, and history of previous stroke.

Patients with the history of previous vascular events, malignancies, autoimmune diseases, HIV-AIDS-positive status, and patients on antiplatelet drugs.

Patients with known bone marrow,hematological diseases, Vit.B12 deficiency, and hyperhomocysteinemia that may lead to morphological changes in platelets and its counts.

This study was conducted on 52 AIS patients admitted in ICU, Neurology and Medicine Wards of Geetanjali Medical College and Hospital, Udaipur. Patients fulfilling the criteria were enrolled into the study after obtaining an informed consent. Each patient was assessed and a modified Rankin's Scale (mRS) [16,17] was assigned to them. A blood sample was collected from antecubital vein using a 5cc syringe and transferred to an EDTA vacutainers. The samples were taken to laboratory within 2 h of collection and analyzed using the automated analyzer ABX Pentra. The MPV and PC were assessed on admission. MPV and PC were assessed after giving anti-platelet treatment at the time of discharge as any change of their values in comparison to admission. mRS score was used to assess clinical severity [16,17].

Score description

0: No symptoms at all
1: No significant disability despite symptoms; able to carry out all usual duties and activities.
2: Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3: Moderate disability; requiring some help, but able to walk without assistance.
4: Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5: Severe disability; bedridden, incontinent, and requiring constant nursing care and attention.
6: Dead

Reference range

Mean platelet volume = 6–11 fL [18].

Platelet counts = 1.5–4.5 × 105 cells/cumm [19].

Patient was assessed for the following parameters:

- Detailed clinical history.
- Demographic data and history of illness in past
- General examination with detailed neurological examination
- CT Head/MRI Brain with Angiography
- MPV and PC were assessed in first 12 h of admission and on discharge.
- Other relevant investigation as needed for a stroke patient was performed.

Statistical analysis

Data were analyzed using SPSS. The quantitative data were analyzed using Independent Student's t test, Pearson's correlation test, and ANOVA test. $p<0.05$ was considered as statistical significant.

RESULTS

In our study out of 52 patients, 32 (61.54%) were male and 20 (38.46%) were female and mean age was 61.51±14.22 years with range from 31 to 85 year of age. Mean of MPV on admission in male was 12.36 fL and 12.59 fL in female, total mean of MPV was 12.45 fL. On discharge, MPV was 11.79 fL and 12.11 fL, respectively, in male and female, while total mean of MPV was 11.91 fL, which is more than upper limit of normal range of MPV (6–11 fL). There was no significant difference between male and females, but total mean was elevated. Although the total MPV at discharge was observed in decreasing trend as compared to on admission, it was not statistically significant. Mean of PC on admission in male was 1.70×10^5 cells/cumm and 1.85×10^5 cells/cumm in female, total mean was 1.76×10^5 cells/cumm. On discharge, it was 1.75×10^5 cells/cumm and 1.71×10^5 cells/cumm in male and female, respectively. The values were well within the normal limits and at discharge did not change significantly as compared to admission and difference between male and females was also non-significant (Figs. 1 and 2).

Out of 52 patients, on admission, 24 (46.15%) patients had a mRS score of three and 15 (28.85%) patients had a score of four and 8 (15.38%) patients had a score of five (bed ridden), rest were ≤ 2. No death in our study was reported. Maximum patients 20 (38.46%) with mRS score-2 on discharge were observed, followed by 14 (26.92%) patients had score-3, 7 (13.46%) patients had score-1, and 5 (9.62%) cases of score-4 and 5 each (Table 1).

The clinical severity of stroke was assessed and graded according to mRS with scores varying from 0 having no significant disability to six implying deaths. The mean of MPV of patients in each score from 0 to 6 was compared. The patients who had a score of 6, that is, death had significantly elevated mean platelet volumes compared to lower scores such as 0, 1, and 2. As baseline MPV increased mRS score on discharge also increased. There was strong positive correlation between mRS score on discharge and MPV on admission ($p<0.05$). This indicates poorer outcome with higher MPV values (Table 1 and Fig. 1).

The severity of stroke on clinical basis at presentation was higher in patients with higher MPV values. As MPV increased grading of mRS

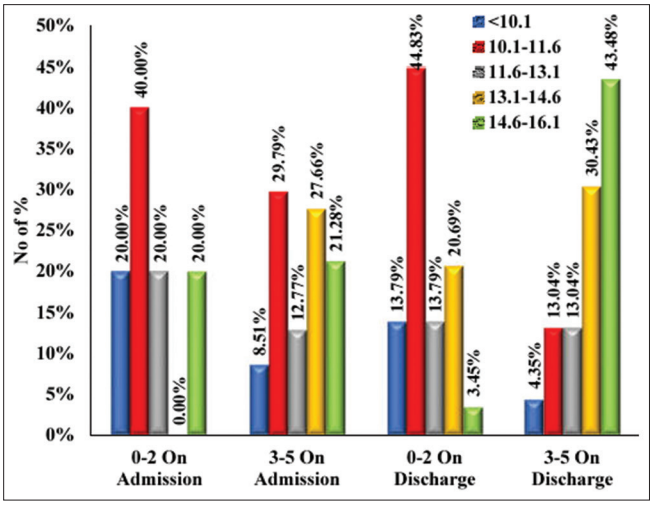

Fig. 1: Relationship of MPV with mRS score on admission

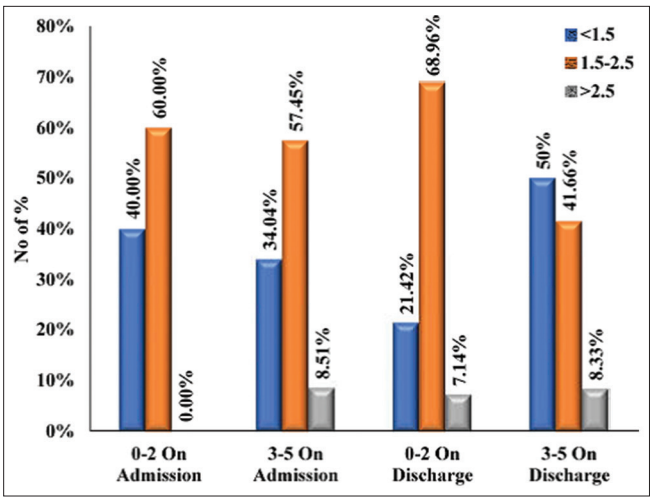

Fig. 2: Platelet count and mRS on admission

score also increased. When MPV in patients with score 2 versus 4 and 2 versus 5 was compared, the difference in MPV was found to be statistically significant ($p<0.05$). Similarly, when MPV in patients with score 3 versus 4 and 5 and 4 versus 5 was compared, the difference in MPV was found to be statistically significant ($p<0.05$) (Table 2).

When compared mRS on admission versus discharge in range of 0–2 which indicates good prognosis and range of 3–5 indicates poor prognosis, the MPV increases improvement in patients, while mRS score decreases. As MPV goes higher above its normal range, the recovery rate was declined. There was inverse relation between levels of MPV and mRS on discharge. We observed that high MPV – values did worse as compared to their counterparts with low MPV values ($p<0.001$, HS) (Table 3).

DISCUSSION

The platelets play an important role in the pathogenesis of vascular diseases, where MPV and PC are key factors of hemostatic importance. It is well known that elevated MPV is an indicator of increased platelet activation and may be directly related to the severity of stroke. Elevated MPV and PC are the leading risk factors for thrombosis [20].

In our study, the mean age was 61.51±14.22 years with youngest patient of 30 years and oldest patient was of 85 years of age. Similar to our findings in study by Shah *et al*. [21], mean age of the ischemic stroke was 58 years (range 34–78 years). Whereas O'Malley *et al*. [15] study had a mean age of 79 years; range, 65–93 years, it is in contravention to the observations made in similar studies from the developed world [22]. In our study, nine patients (27%) were having age below 45 years, which were cases of stroke in young patients. In study done by Shah *et al*. [21] had 23% patients having cases of stroke in young.

In our study, out of 52 patients, 32 (61.54%) were male and 20 (38.46%) were female. Similar to ours in a study by Shah *et al*. [21], there were 59% and 41% males and females, respectively. There was a clear male preponderance in the cases of stroke recruited in our study. Similar patterns were seen in all the other studies compared except for O'Malley *et al*. [15] and Pikija *et al*. [23], where a female preponderance was seen.

The clinical severity of the patients was assessed using mRS ranging from 0 to 6. Twenty-four (46.15%) of patients had a mRS score of 3 and 15 (28.85%) patients had a score of 4 and 8 (15.38%) patients had a score of five (bed ridden). No death in our study was reported. In a study of Poornima *et al*. [24], 26% of patients had a score of 2 and 18% had a score of 3. About 19% had no symptoms. About 8% of patients did not survive. In a study by Shah *et al*. [21], mRS was classified in a group of 0–2 and 3–6 having 62% and 38% patients, respectively.

In our study, out of 52 patients, 30 patients had higher MPV more than its normal range (6–11 fL) which is 57.69%. Mean platelet volume in male cases was 12.36 fL and 12.59 fL in female cases. Total mean of MPV was 12.45 fL. There was no significant difference between male and females, but the total mean was elevated. In a study by Poornima *et al*. [24], overall mean MPV was 12.28 fL which was similar to our results, and in male cases, it was 12.27fL and 12.25fL in female cases. In another studies by Shah *et al*. [21], the mean MPV was 11.86 fL; similar to our study, it was above the normal range. Similar findings were observed by O'Malley [15], who reported mean MPV as 11.30 fL. Highest and lowest MPV observed in present study were 14.9fL and 7.6 fL, respectively, which is nearly same as study done by Shah *et al*. [21], which was 15.2 fL and 7.8 fL, respectively.

Our findings suggest that mean platelet volume is increased before stroke occurs, the increase in volume seen within the first 12 h of admission suggests that the increase was present before stroke, as the life span of the platelet is about eight days. More than 90%, of the platelet population whose distribution was measured after stroke were circulating before the vascular occlusion occurred. Platelet size is determined at the level of the progenitor cell (i.e., the megakaryocyte), and recent studies reported that cytokines such as interleukin-3 and interleukin-6 influence megakaryocyte ploidy and can lead to the production of more reactive, larger platelets [25]. As platelet volume is determined by the megakaryocyte, the evidence of change in platelet volume in stroke as presented in our study indicates that stroke may be preceded by changes in megakaryocytes [11,25].

The mean platelet volume is of most hemostatic importance as it signifies the activation of megakaryocytes, as heralded by an increase in MPV, a

Table 1: mRS (on admission and discharge) with baseline MPV

mRS	On admission (%)	On discharge (%)	MPV		p value
			Mean	SD	
0	0 (0)	1 (1.92)	10.90	-	<0.05
1	0 (0)	7 (13.46)	11.10	2.72	
2	5 (9.62)	20 (38.46)	11.75	1.59	
3	24 (46.15)	14 (26.92)	12.95	1.59	
4	15 (28.85)	5 (9.62)	14.44	0.86	
5	8 (15.38)	5 (9.62)	14.10	0.79	
6	0 (0)	0 (0)	-	-	
Total	52 (100)	52 (100)	12.45	1.84	

Table 2: Comparison of MPV and mRS (p value)

Comparison of MPV in different mRS	p value	Significance
2 versus 4	<0.05	S
2 versus 5	<0.001	HS
3 versus 4	<0.05	S
3 versus 5	<0.05	S
4 versus 5	<0.05	S

Table 3: Relationship of MPV with mRS score on admission and discharge

MPV	mRS								
	On Admission				On Discharge				% of patients recovered
	0–2		3–5		0–2		3–5		
	No.	%	No.	%	No.	%	No.	%	
<10.1	1	20.00	4	8.51	4	13.79	1	4.35	75
10.1–11.6	2	40.00	14	29.79	13	44.83	3	13.04	78
11.6–13.1	1	20.00	6	12.77	4	13.79	3	13.04	50
13.1–14.6	0	0.00	13	27.66	6	20.69	7	30.43	46
14.6–16.1	1	20.00	10	21.28	1	3.45	10	43.48	0
Total	5	100	47	100	29	100	23	100	-

$p<0.001$ (HS) when compared on discharge

feature of ischemic stroke [15]. The observations in our study suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis and large platelets may promote the thrombotic event in a susceptible individual. The increase in MPV may have contributed to the development of the stroke rather than simply being a consequence of the acute event itself. Our results suggest that there is an independent association between MPV and stroke and elevated MPV may assess as a risk factor for acute ischemic stroke.

In our study, the mean of platelet count was 1.76 × 10^5 cells/cu mm; in male cases, it was 1.70 × 10^5 cells/cu mm and 1.85 × 10^5 cells/cu mm in female cases. The values were well within the normal limits and difference between male and females was not significant. There is indirect evidence that the changes in MPV and platelet count are likely to have preceded the vascular event and are unlikely to be due to platelet consumption at the infarct site. It has been suggested that MPV and platelet count are under independent hormonal control, so there is no correlation found between any change in platelet count and acute ischemic stroke in our study. It is unlikely that platelet consumption due to localized thrombosis would affect peripheral venous estimations of platelet count. These findings were in concordance with Shah *et al*. [21], who reported 1.68 × 105 cells/cu mm and Poornima *et al*. [24] reported platelet count of 1.84 × 10^5 cells/cu mm that of O'Malley [15] was 2.55 × 105 cells/cu mm. The mean values were well within the normal and had no significance. The age and sex had no influence on MPV and platelet count in our study. This observation is in agreement with other studies [21,25].

We observed that the total mean platelet volume at discharge was 11.91 fL; in male, it was 11.79 fL and 12.11 fL in female cases, which is more than upper limit of normal range of MPV (6–11 fL). There was no significant difference between male and female, but total mean values remained elevated as seen at admission. This remained statistically non-significant. The total mean of platelet count at discharge was 1.74 × 10^5 cells/cu mm; in male cases, it was 1.75 × 10^5 cells/cu mm and 1.71 × 10^5 cells/cu mm in female cases. The value was well within the normal limits and difference between male and female was not significant. Mean of platelet count at discharge did not change significantly as compared to admission. Similar findings were shown in the study by Poornima *et al*. [24] which had 12.30 fL MPV as compared to 12.28 fL which was statistically non-significant.

We observed in our study that the severity of stroke on clinical basis at presentation was higher in patients with higher MPV values. As MPV increased grading of MRS score also increased. When MPV in patients with score 2 versus 4 and 2 versus 5 was compared, the difference in MPV was found to be statistically significant ($p<0.05$). Similarly, when MPV in patients with score 3 versus 4 and 5 and 4 versus 5 was compared, the difference in MPV was found to be statistically significant ($p<0.05$). In a study by Poornima *et al*. [24], the mean of mean platelet volumes of patients in each score from 0 to 6 was compared. The patients who had higher score had significantly elevated mean platelet volumes compared to lower scores such as 0, 1, and 2. This implies that patients who have a higher mean platelet volume on day 1 have high risk of adverse outcomes compared to patients having low mean platelet volume. In summary, we can conclude that there is an independent association between MPV and stroke which can be directly related to the role of larger platelets in the genesis of cerebral thrombosis. This study finds and supports the statistical significant correlation between MPV and clinical severity of stroke at the time of presentation.

AUTHORS' CONTRIBUTIONS

Conceptualization, V.K.M., Y.P.; Data acquisition, V.K.M, R.K. and A.J.; Formal analysis, A.J. and K.K.V.; Supervision, V.K.M., Y.P., R.K.; Validation, K.K.V., A.J.; Writing – original draft, V.K.M., K.K.V, and Y.P.; Writing – review and editing, R.K., A.J., Y.P., and V.K.M. All authors have read and agreed to the published version of the manuscript.

INFORMED CONSENT STATEMENT

All participants were informed about subject of the study and prior consent was signed.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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