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Document heading **doi: 10.21276/apjhs.2016.3.4.34** **Case report**

A Study of Association of Mean Platelet Volume and Ischaemic Stroke

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ABSTRACT

Background: Cerebrovascular diseases include some of the most common and devastating disorders. Mean platelet volume (MPV) is a physiological variable of haemostatic importance. Large platelets are more reactive, produce more prothrombotic factors and aggregate more easily.Thus, the detection of large platelets in patients with cerebrovascular diseases would lend support to the idea that platelet volume influences thrombotic large vessel occlusion leading to ischaemic stroke. Here the aim of our study is to correlate the size of pletelet with ischaemic stroke.**Subjects and method:** This was a case control study carried out in Department of Medicine in Guru Nanak Dev Hospital attached to Govt. Medical college. The study was carried out among 50 patients diagnosed with an acute ischemic stroke and presenting with in 48 hours of onset. Clinical severity was assessed using Modified Rankin's scale. Mean Platelet Volume was measured using an automated analyzer. Fifty age and sex matched controls were also recruited and their Mean Platelet Volumes assessed and association was calculated. **Results**: MPV has got a statistically significant correlation with ischemic stroke with a p value of 0.000 (highly significant) with an average MPV in cases being 8.92±1.03fl compared to controls in which average being 7.67±1.38fl. The range of MPV in cases was 7.40 to 12.80. The range of MPV in control was 4.90 to 10.10. The association of MPV with severity of stroke was determined by comparing the modified Rankin's score with corresponding mean values of MPV in each group. MPV – EDTA showed a p value of 0.191 which was statistically insignificant.**Conclusion:** MPV was significantly higher in patients of ischemic stroke which suggest a association of MPV with ischemic stroke. Further there was no significant association between severity of ischemic stroke and MPV.

Key words: Mean Platelet Volume; Ischemic stroke ; Modified Rankin's scale.

Introduction

Cerebrovascular diseases are one of the common causes of morbidity and mortility. They cause~200,000 deaths each year in the United States and are a major cause of disability. The incidence of cerebrovascular diseases increases with age and the number of strokes is projected to increase as the elderly population grows, with a doubling in stroke deaths in the United States by 2030[1].It ranked as the sixth leading cause of disability-adjusted years (DALY; one DALY is one of the lost year of healthy life) in 1990and is projected to rank fourth by the year 2020[2].Most cerebrovascular diseases manifest by the abrupt onset of a focal neurologic deficit, as if the patient was" struck by the hand of God. Stroke is associated with increased long term mortality, residual physical, cognitive, and behavioral impairments, recurrence, and increased risk of other types of vascular events. Platelets play a crucial role in the pathogenesis of atherosclerotic complications, contributing to thrombus formation. Platelet size (mean platelet volume, MPV) is a marker and possibly determinant of platelet function, large platelets being potentially more reactive˙For example, large platelets contain more dense granules, undergo greater in vitro aggregation in response to agonists such as ADP and collagen, and release more serotonin and b- thromboglobulin (b-TG).˙Though there have been quite a few studies which have demonstrated an association between myocardial infarction and platelet size, very few studies has looked

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at the association between platelet size and ischemic stroke. There are no documented studies in India comparing the association of mean Platelet volume with ischemic stroke; hence an attempt has been made to study the association if any between mean platelet volume and stroke in an Indian population.

Material and method

This was a case control study carried out in Department of Medicine in Guru Nanak Dev Hospital attached to Govt. Medical college, Amritsar a tertiary care centre.The study was carried out among 50 patients diagnosed with an acute ischemic stroke and presenting to the medicine emergency and wards in the hospital within 48 hours of onset of symptoms and satisfying the inclusion and exclusion criteria. Clinical severity was assessed using Modified Rankin's scale. Mean Platelet Volume was measured using an automated analyzer available in Central lab of GNDH, Amritsar. Fifty age and sex matched controls were also recruited and their Mean Platelet Volumes assessed.

Definition of stroke (in this study):
Focal neurological deficit lasting more than 24hrs with no evidence of a non–vascular cause.

Inclusion criteria:

1. Gender: Males/Females
2. Age Range: 18 years and above
3. Socioeconomic group: All groups eligible

Exclusion criteria:

1. Thrombocytopenia.
2. Known cases of hereditary disorders of large platelets.
3. Medications that can reduce the platelet count: hydroxyurea, antineoplastic agents, and inhibitors of the platelet integrin αIIbβ3.
4. Haemorrhagic stroke.
5. Patients unable to communicate because of severe stroke, aphasia or dementia without a valid surrogate respondent. (A valid surrogate respondent is considered a spouse or first degree relative that is living in the same home or is self-identified as aware of the participant's previous medical history and current therapies)
6. Patients presenting 48hrs after the onset of neurological symptoms.
7. Peripheral smear showing platelet aggregates.

CONTROLS:

Controls were selected from age and sex matched individuals who had no history of stroke or thrombocytopenia in the past.

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 affair 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

STATISTICAL METHODS

Sample size:

50 cases admitted in Guru Nanak Dev Hospital, Amritsar who gave informed consent and who met the inclusion criteria were recruited. 50 age and sex matched controls were also recruited from the hospital.

Data analysis:

The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Statistical Methods**:**

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student 't' test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups . A Multivariate logistic regression analysis has been carried out to find the risk factors associated with stroke[3,4]

1. Analysis of Variance: F test for K Population means[5]
Objective: To test the hypothesis that K samples from K Populations with the same mean.
Limitations: It is assumed that populations are normally distributed and have equal variance. It is also assumed that samples are independent of each other.

Method: Let the j^{th} sample contain nj elements (j = 1, 2…K). Then the total number of elements is N

$$x.j = \sum \frac{xij}{nj}$$

$$S_1^2 = \frac{\sum \sum_{i-1}^{n1}(x1 - \bar{x}.j)^2}{N-K} \qquad S_2^2 = \frac{\sum_{i-1}^{n1} nj.(\bar{x}.j - \bar{x}..)^2}{K-1}$$

$F = S_2^2 / S_1^2$ which follows F distribution (K-1, N-K)

2. **Student t test (Two tailed, independent)**[6]

$$t = \frac{\bar{x}_1 - \bar{x}_2) - (\mu_1 - \mu_2)}{\sqrt{s^2 \left(\frac{1}{n1} - \frac{1}{n2}\right)}}$$

Where, $s^2 = \frac{(n1-1)\sum_{i=1}^{n1}(x1 - \bar{x1})^2 + (n2-1)\sum_{i-1}^{n2}(x2 - \bar{x2})^2}{n1+n2-2}$

3. Significant figures
+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P □□0.05)
** Strongly significant (P value: P □□0.01)

Results

Table 1: stroke- clinical severity score

Modified Ranking's score	No. (N=50)	%age
Score 1: No significant disability	12	24.00
Score 2: Slight disability	13	26.00
Score 3: Moderate disability	10	20.00
Score 4: Moderately severe disability	8	16.00
Score 5: Severe disability	7	14.00
Total	**50**	**100.00**

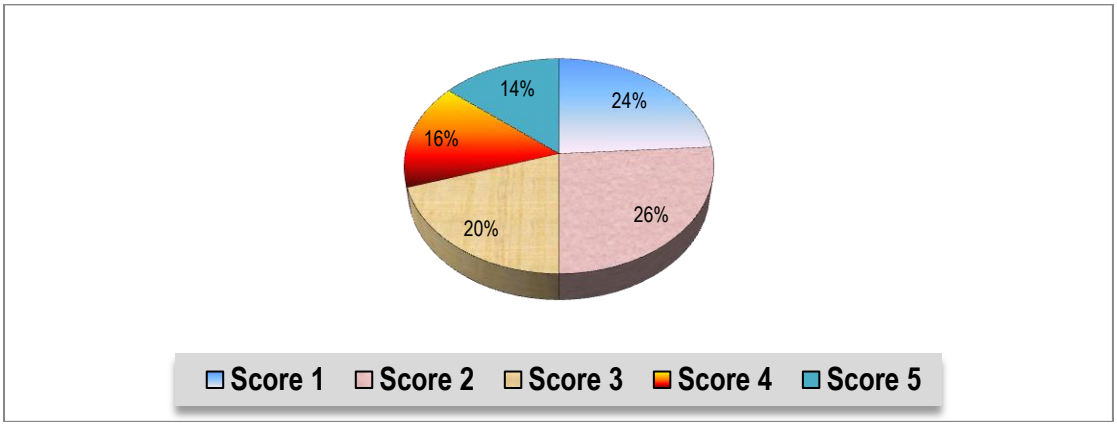

Table 1 shows 12 (24%) were found with no significant disability, 13 (26%) patients had slight disability followed by 10 (20%) patients with moderate disability, 8 (16%) patients with moderately severe disability and 7 (14%) with severe disability.

Table 2: Comparison of mpv in cases and controls

MPV (fL)	Cases		Control		Significance	
	Mean	S.D.	Mean	S.D.	't' value	'p' value
MPV (EDTA)	8.92	1.03	7.67	1.38	4.80	0.000
Range	7.40-12.80		4.90-10.10			(HS)

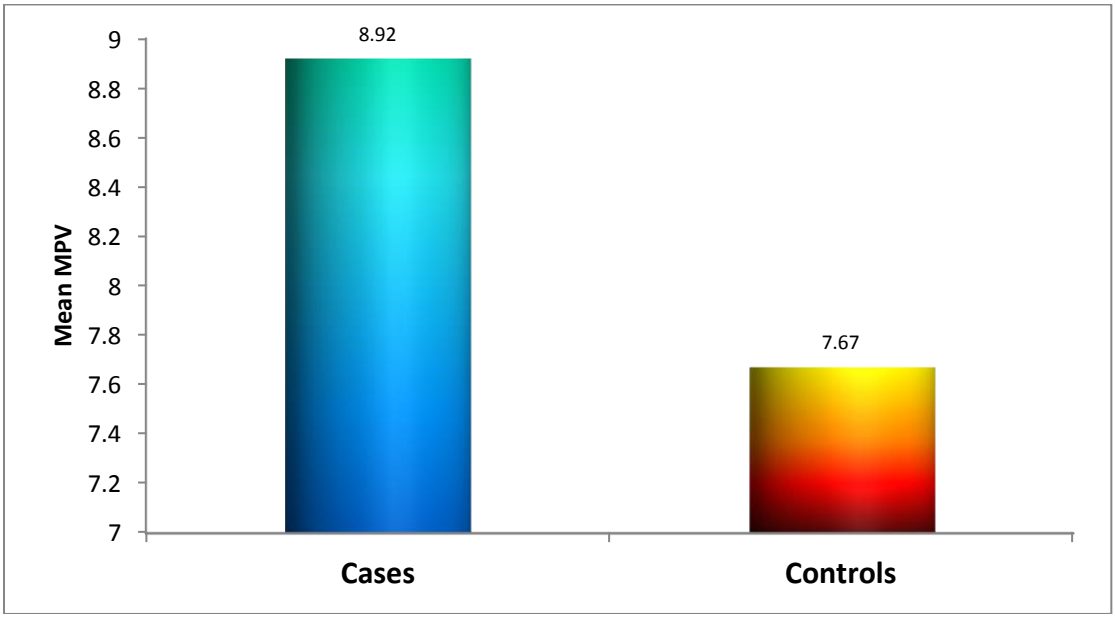

Table 2 shows that MPV has got a statistically significant correlation with Ischemic stroke with a P value of 0.000 with an average MPV in cases being 8.92±1.03 compared to controls who average 7.67±1.38.

Table 3: Stroke- clinical severity score and mpv

Modified Rankin's score	Number (N=50)	MPV (Mean ± SD)
Score 1: No significant disability	12	9.00 ± 1.60
Score 2: Slight disability	13	8.83 ± 1.03
Score 3: Moderate disability	10	8.96 ± 0.71
Score 4: Moderately severe disability	8	8.97 ± 0.48
Score 5: Severe disability	7	8.82 ± 0.89
Significance	P value	0.191 (NS)

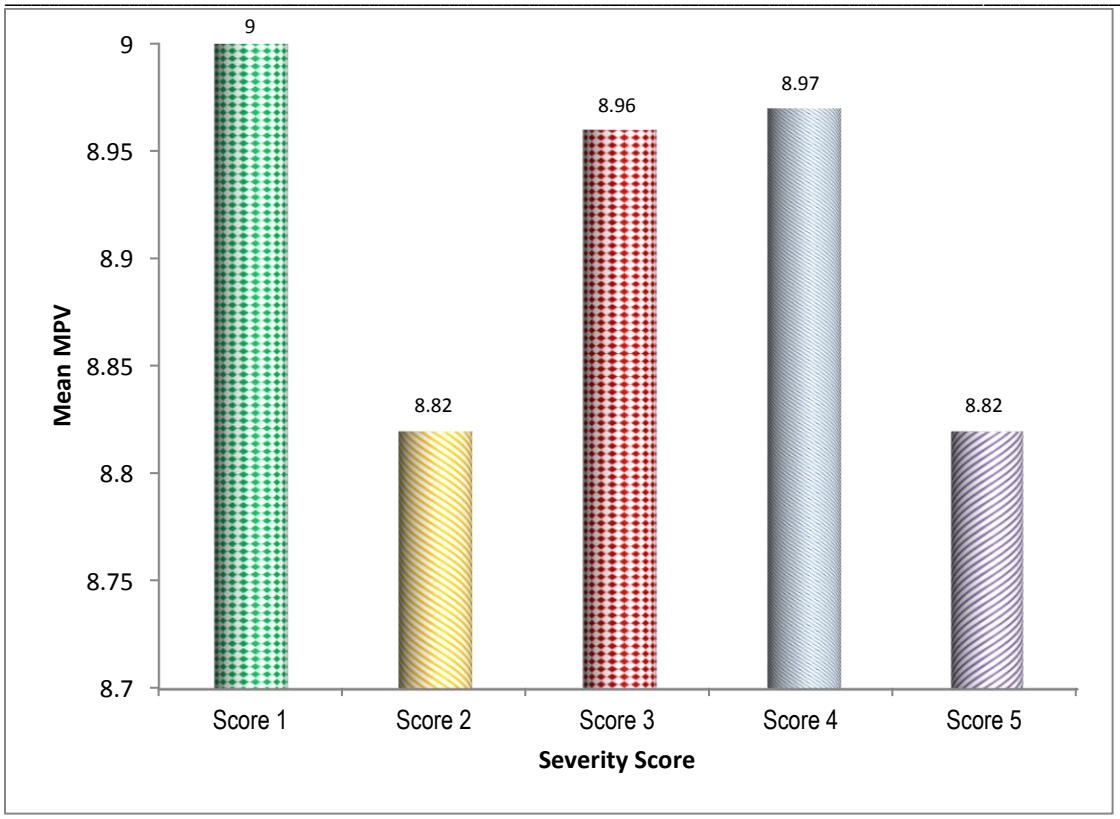

Table3. shows relation between MPV and severity of stroke (on the basis of Modified Ranking's score) with a p value of 0.191 which is not significant. This shows MPV is not associated with severity of stroke.

Table 4: Association of mpv quintiles and stroke severity

MPV Quintiles	Stroke severity score		P value
	Score 0-2	Score 3-6	
7.00 - 8.00	10 (40%)	3 (12%)	0.10 (NS)
8.01 - 9.00	6 (24%)	11 (44%)	
9.01 - 10.00	5 (20%)	10 (40%)	
10.01 - 11.00	1 (4%)	1 (4%)	
11.01 - 12.00	2 (8%)	0	
12.01 - 13.00	1 (4%)	0	
Total	25 (100%)	25 (100%)	

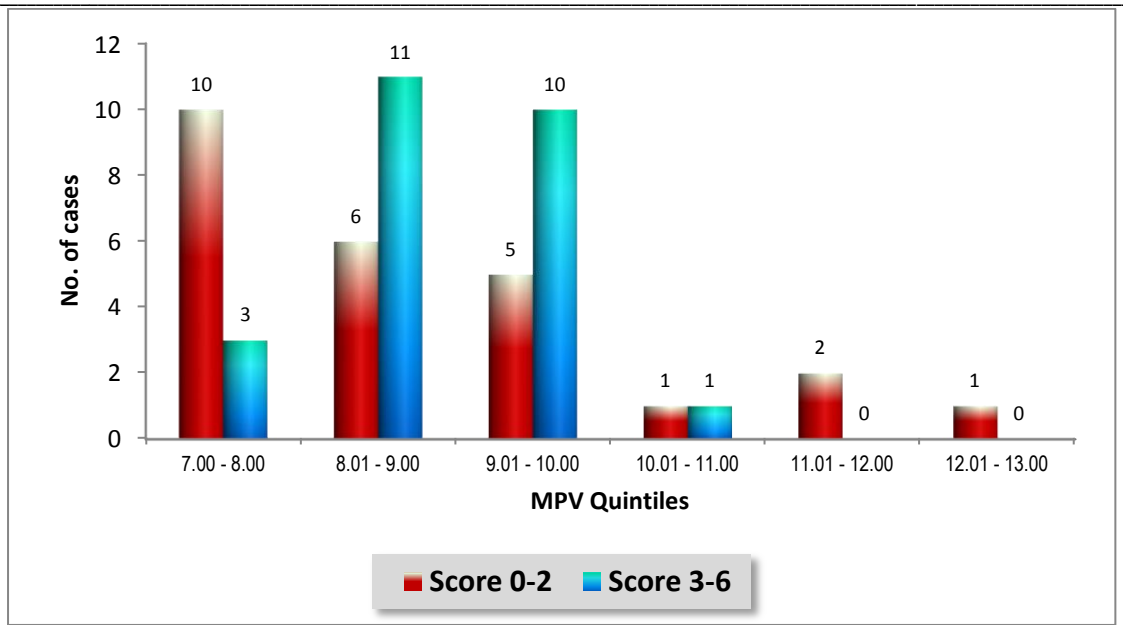

Table 4 shows MPV was arranged into quintiles and compared with the stroke severity score which was further subdivided into two groups. Group 1 with a score of 0-2 being less severe and group 2 with a score of 3-6 being more severe. The p value obtained is 0.10 in EDTA anticoagulated samples and has no statistical significance.

Discussion

The study was a case control study carried out at Guru Nanak Dev Hospital, attached to Govt. Medical college, Amritsar a tertiary care centre. 200 patients of strokes admitted to the medical and neurology wards were screened to get 50 cases. 150 cases of stroke were excluded due to various reasons and as they are not matchuing inclusion criteria of study.The mean age for the cases was 58.30±11.93 when compared to 57.78±13.64 for the controls. Both were significant as p value was 0.05 for cases and 0.04 for control. The maximum number of cases in this study was in the age group between 51-60 which was followed by age group of 61-70. The average age in males was 54.96±13.18 when compared to 57.71±13.07 in controls. The average age in females was 63.06±9.23 when compared to 63.01±9.78 in controls. Females were older. 50% of the cases and controls recruited were males and 50% were females.

RISK FACTORS FOR STROKE

Out of the many risk factors for stroke hypertension was the most prevalent in this study group with a percentage of 52 among cases and 34 among controls. Diabetes mellitus came second with percentage of 28 among cases and 24 among controls. Similar trend was seen in the other studies as mentioned below with hypertension being most prevalent risk factor (84.7% in Muscari et al and 82.7% in Pikija et al)[7,8].When compared to the other western studies the representation of previous strokes as a risk factor was only 8%. Bath et al had 72% of previous strokes since this study was a sub study which looked at the benefits of ACE inhibitors (perindopril) in preventing recurrent stroke[2].Diabetes mellitus had a representation of 28% of the cases which was higher when compared to the other studies. MPV has been compared with the various risk factors for stroke. Multiple logistic regression done of the baseline risk factors showed that hypertension was the most common risk factor involved in stroke with a p value of <0.001and adjusted OR of 10.12. MPV was higher in patients with stroke and diabetes mellitus with a suggestive significance (0.022) when compared to controls. Other risk factors compared were age, hypertension, dibetes mellitus, and smoking and alcohol consumption.

DRUG HISTORY

16% of the stroke patients recruited where on aspirin either because of previous strokes or history of ischemic heart diseases. This was a cause for concern since doubts were raised if concurrent usage of aspirin would influence the mean platelet volume studied. However there have been previous studies with aspirin and MPV and it showed no interference in vitro and in vivo. The other drugs used were predominantly

antihypertensive with 55% of the hypertensives on calcium antagonist followed by β blockers and diuretic and there is no such correlation of platlet size and these drug also[9].

MEAN PLATELET VOLUME AND STROKE

Platelet parameters assessed was mean platelet volume (MPV). MPV has got a statistically significant correlation with ischemic stroke with a p value of 0.000 (highly significant) with an average MPV in cases being 8.92±1.03fl compared to controls in which average being 7.67±1.38fl. The range of MPV in cases was 7.40 to 12.80. The range of MPV in control was 4.90 to 10.10. This pattern has been seen in all the other case control studies which included O'Malley et al, Butterworth et al and Tohji et al[10-12].

STROKE SEVERITY AND MPV

The clinical severity of stroke at presentation was determined by the modified Rankin's scale and severe disability was seen with 14% of the cases. 24% of the cases had no significant disability. Others included 26% with slight disability, 20% with moderate disability and 16% with moderately severe disability. There were no deaths recorded. The association of MPV with severity of stroke was determined by comparing the modified Rankin's score with corresponding mean values of MPV in each group. MPV showed a p value of 0.191 which was statistically insignificant. O'Malley conducted similar studies and divided the outcomes as independent (Rankin's grade 0 to 2), dependent (Rankin's grade 3 to 5) and dead (Rankin's grade 6)[10]. However no statistical significance with MPV was obtained[1]. Butterworth et al studied patients who were dead or dependent at 3 months, using the Lindley score, and they had a significantly higher platelet volume, and a tendency to a lower platelet count, as compared with those who fared well.[12].However statistical significance was not found.

ASSOCIATION OF MPV QUINTILES AND STROKE SEVERITY

MPV was arranged into quintiles though the sample size was too small for such a study and was compared with the stroke severity score which was further subdivided into two groups. Group 1 with a score of 0-2 being less severe and group 2 with a score of 3-6 being more severe. The p value obtained is 0.10 in EDTA anticoagulated samples and has no statistical significance. Similar study was conducted by Griesenegger et al and an increased MPV was associated with a worse outcome in patients suffering an acute ischemic cerebrovascular event[13]. Patients within the highest quintile of MPV had a 2-fold risk of suffering a severe stroke compared with patients within the lowest quintile. The association of high MPV with severe stroke remained significant after adjustment for confounding factors. The p value was 0.002 in this particular study.

Conclusion

1. This study has shown an elevation of MPV in acute phase of ischemic stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, it can be stated that an increase in MPV is independently associated with stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required into the role of platelet volume in stroke pathology, outcome and most importantly, in individuals at risk for stroke.
2. This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume.
3. There was no stastistical significance found between MPV quintiles and severity of stroke(based on Modified Rankin's score) though the sample sizes were small.

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