

## Platelet size in stroke: A study in a tertiary hospital

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### Abstract

**Introduction:** Stroke is one of the leading causes of death and disability in India. Various risk factors like smoking, diabetes mellitus, hypertension, hyperlipidemia, obesity and stress are associated with atherosclerosis. Platelets are known to play a critical role in conversion of a chronic atherosclerotic plaque into an occluding thrombus. Various studies have postulated that large platelets or raised mean platelet volume (MPV) are more vulnerable for development of occluding thrombus. The present hospital-based case control study was undertaken to evaluate the importance of platelet volume indices specifically increased MPV in patients with stroke and to compare those values with the normal healthy controls.

**Materials and Method:** We studied 157 cases of stroke patients admitted in our hospital over a period of two years. Platelet variables of stroke patients were measured in an automated analyzer immediately after hospital admission and preferably within 2 hours. Group matching was done for the control subjects and the controls were matched for age, sex and other demographic characteristics.

**Results:** There was no significant difference in mean platelet volume between patients with stroke and the control subjects (p value >0.05, Student's t test).

**Conclusion:** Raised MPV or large platelets are not a risk factor for stroke.

**Keywords:** Large platelets, Mean platelet volume, Stroke

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### Introduction

Stroke is one of the leading causes of death and disability in India. Stroke prevalence among the elderly in rural India was 1.1% and urban India was 1.9%.<sup>(1)</sup> The underlying pathology of stroke is atherosclerosis, which initiates by second decade of life, and progresses chronically to manifest as cerebro-vascular accidents in the later part of life. The process of atherosclerotic is multi-factorial, and our understanding of its pathogenesis has improved over past few years.<sup>(2)</sup> The major risk factors responsible for the development of atherosclerosis are hypertension, smoking, diabetes mellitus, hyperlipidemia, obesity and stress.

Platelets are known to play a critical role in conversion of a chronic atherosclerotic plaque into an occluding thrombus.<sup>(3)</sup> It is likely that different individuals have platelets of variable size, density, and reactivity.<sup>(4)</sup> Larger the platelets, they are more likely to be metabolically and enzymatically active. Mean platelet volume (MPV) is the most commonly used measure of platelet size.<sup>(5)</sup> Though, various studies have shown that an increase in MPV is independently associated with acute stroke,<sup>(6)</sup> and an elevated MPV has been associated with worse outcome in acute ischaemic cerebro-vascular events<sup>(7)</sup> but the platelet volume that have been measured have shown inconsistent results that may be related to the highly selected patient populations or to the different methods of measuring MPV. Electronic cell counters have made it possible to measure platelet volume indices (PVI),

specifically mean platelet volume (MPV), and platelet distribution width (PDW). This is a simple and cost effective method of identifying these larger platelets. The present hospital-based case control study was planned to evaluate whether a higher mean platelet volume (MPV) is a risk factor in patients with stroke as compared to normal healthy individuals.

### Materials and Method

A hospital based case-control study was conducted at Sikkim Manipal Institute of Medical Sciences, Sikkim during the period from Jan, 2013– Jan, 2015. A total of 157 cases with acute stroke and 157 control subjects were studied over the period. Patients were studied immediately after hospital admission or preferably within 2 hours. Group matching was done for the control subjects and the controls were matched for age, sex and other demographic characteristics; they had no past or present history of any vascular disease, malignancy and were not taking any medications known to affect platelet function. The criteria of exclusion were those cases where the electronic cell count was not obtained even after 6 hours of hospital admission (as anti-platelet drug therapies can modify platelet variables) and where the blood sample either had micro-thrombi or a marked anti-coagulant effect (as reported on peripheral smear).

A detailed Performa was filled up for each and every case and their matched controls enrolled for the study which comprised of a standard questionnaire. A

written consent was taken before the sample was drawn. 2ml of peripheral blood was withdrawn from the ante-cubital vein into the potassium salt of ethylene diamine-tetra acetic acid (K2EDTA) and was stored at room temperature. MPV and platelet count were measured immediately after hospital admission or preferably within 2 hours using auto-analyzer Ac.T5 diff CP, Beckman Coulter, Inc. that uses aperture – impedance technology to size platelets. The normal reference range for MPV and platelets were 6.0-10.0 femtolitre (fl) and 150 – 400 X 10<sup>3</sup>/μL respectively. The peripheral smears were prepared and stained by Leishman stain for confirmation of large platelets consistent with increased MPV. The study was approved by the institutional ethical committee (attached at the end).

**Results**

Out of the total 157 patients analyzed, stroke was seen to be more common in males (63.7%) as compared to females (36.3%) (Table 1). The majority of the cases were seen in the 60 to 80 years of age group (Table 2). The study showed a high mean platelet volume (>10 fL) in both the cases and the control subjects but there was no significant differences between both the groups (p value >0.05, Student’s t test) (Table 3-5). The peripheral blood smears were also examined simultaneously which confirmed the presence of large platelets. (Fig. 1a, 1b) However, platelet count was reduced in patients with stroke (176X10<sup>9</sup>/L) as compared with control subjects (204X10<sup>9</sup>/L).

**Table 1: Distribution of study subjects and controls as per sex**

Study population	Sex			
	Male	%	Female	%
Cases	100	63.7	57	36.3
Controls	73	46.4	84	53.5

**Table 2: Distribution of study subjects and controls as per age**

Age Distribution	Study population			
	Cases	%	Controls	%
31-40	11	7.0	18	11.5
41-50	21	13.4	25	15.9
51-60	30	19.1	32	20.4
61-70	34	21.7	26	16.6
71-80	33	21.0	33	21
91-100	4	2.5	2	1.3

**Table 3: Distribution of cases as per their level of MPV**

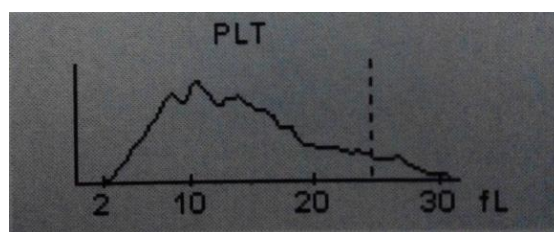
MPV	Cases	
	Male	Female
High	62	39
Normal	38	18

**Table 4: Distribution of controls as per their level of MPV**

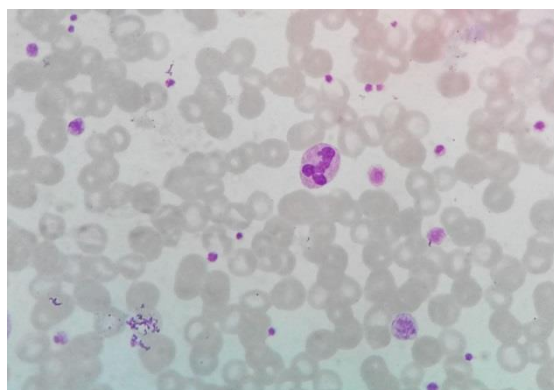
MPV	Controls	
	Male	Female
High	40	58
Normal	33	26

**Table 5: Association of level of MPV with occurrence of stroke**

MPV	Study population		P value
	Stroke (cases)	Normal (controls)	
High	101	98	0.8148
Normal	56	59	



**Fig. 1a: Graphic representation from automated analyzer showing presence of large platelets**



**Fig. 1b: Peripheral blood smears showing the presence of large platelets (40x)**

**Discussion**

Platelets are known to play a key role in the conversion of a stable atherosclerotic plaque into an unstable one, and if it is proven that larger platelets are a risk factor for development of stroke, it could have a significant prognostic value. The studies have reported increase in platelet volume in acute cerebral ischemia<sup>(8,9)</sup> and transient ischemic attack.<sup>(10)</sup> A cross-sectional study found that increase in mean platelet volume is associated with worse outcome in patients with ischaemic stroke (Greisenegger S et al, 2014) RJ Butterworth et al also noted an increase in MPV in patients with ischaemic stroke and increased MPV is associated with poor outcome.<sup>(11)</sup> Another study concluded that there was an elevation of MPV and reduction of platelet count in patients with acute stroke

(O'Malley T et al, 1995).<sup>(6)</sup> However, the results of mean platelet volume (MPV) that have been measured in patients of stroke are matter of intense debate and can be attributed to the various methods used for the measurement of MPV. Mean platelet volume (MPV) and platelet distribution width (PDW) are calculations that are best performed by automated blood analyzers.

In contrast to the results obtained in these studies, we did not find any significant difference between platelet volume indices of cases and controls. Our results matched with the study of Cho SY et al 2013, who also did not find any significant association of raised mean platelet volume with occurrence of stroke.<sup>(12)</sup> The patients with stroke had high MPV values but there was no significant difference when compared with the control subjects.

The finding of our study concluded that high MPV is not a risk factor for development of stroke, but our study had several limitations. We had conducted a retrospective study, so reliable data regarding other known major risk factors for stroke (hypertension, smoking, diabetes mellitus, hypercholesterolemia, hyperlipidemia etc) could not be gathered for the control population. There are reports of high MPV value in obese individuals, smokers, diabetics and patients with hypercholesterolemia so these factors can confound the results. Hence, it is important to have data regarding other risk factor variables for both case and control and then perform a logistic regression to look for independent predictors. The results of our study debate the association of raised MPV and the occurrence of stroke.

Moreover, a study by Naina H V et al 2002, have mentioned giant platelets are being inherited in the population depending upon the geographical variation.<sup>(13)</sup> Though, no studies on platelet size have been undertaken in Sikkim, our results also emphasize the inheritance of large platelets in this part of the country.

## Conclusion

We would like to conclude that high MPV or large platelets were not found to be a risk factor for stroke in our study. However, further research should be carried out on a large number of subjects.

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