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A Study of Platelet Indices in Patients of Acute Ischemic Stroke: A Prospective Study

*Priyanka Meena[1],Manika Khare[2],Ashish Airun[3],Manohar[4],Anudeep Saxena[5]
[1](Department of pathology, SMS Medical College Jaipur,India)
[2](Department of pathology, JNUIMSRC Jaipur, India)
[3](Department of Pathology, JNUIMSRC, Jaipur, India)
[4](department of Medicine, SMS medical college jaipur, India)
[5](department of Critical Care Jaipur, India)
Correspondence to: *Manika Khare*

Abstract
Introduction: *Cerebro-vascular diseases include some of the most common and devastating disorders after coronary heart disease (CHD) and cancer of all types. In normal individuals the platelet count is inversely proportional to MPV; platelet mass (the product of MPV and platelet count) is a near constant. There are evidence that platelet function is accentuated in acute ischaemic stroke. There have been only few studies which have demonstrated an association between platelet size and ischemic stroke. Among them, there have been discrepancy regarding the sample size, methodology used and the final result. So we have done the study to establish the correlation between MPV and stroke.*
Aims And Objectives: *To determine the difference in platelet indices MPC (mean platelet count) & MPV (mean platelet volume) among acute ischemic stroke patient's in age & sex matched healthy subjects.*
Materials And Methods: *The study was a hospital based cross sectional study, data was collected from Dec1st2013 to July 31st 2014 at SMS Medical College and Hospital Jaipur. The study was carried out among fifty patients diagnosed with an acute ischemic stroke and presenting to the hospital within forty eight hours of onset of symptoms. Fifty age and sex matched controls were also recruited.*
The samples were then taken to the Advanced Hematology Lab department of pathology (SMS medical college) between 2hrs of collection and to measure the platelet count and mean platelet volume (MPV).
Results: *Comparison of different hematological parameters was also performed between the cases and the controls, which showed significant in Mean RBC, Mean HB , mean MPV and mean platelet count among the two groups.*
Conclusion: *In conclusion, this study has shown an elevation of MPV and reduction of platelet count in acute stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, an increase in MPV is independently associated with stroke.*

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I. Introduction

Cerebro-vascular diseases include some of the most common and devastating disorders after coronary heart disease (CHD) and cancer of all types.[1] However unlike the caucasians, Asians have a lower rate of CHD and a higher prevalence of stroke.[2] Among the Asians, the number who died from stroke was more than three times that for CHD. In one report, the age standardized, gender-specific stroke mortality rate was 44 to 102.6/100,000 for Asian males, compared with only 19.3 for Australian white males.[3] In normal individuals the platelet count is inversely proportional to MPV; platelet mass (the product of MPV and platelet count) is a near constant. Although platelets are incapable of de novo protein synthesis they are very active metabolically and respond rapidly to vascular injury or trauma by undergoing a series of reactions (adhesion, release of granule contents, shape change and aggregation), which ultimately result in the formation of a platelet–fibrin plug. Thus there is evidence that platelet function is accentuated in acute ischaemic stroke.[4]

Though there have been quite a few studies which have demonstrated an association between myocardial infarction and platelet size, very few studies has looked at the association between platelet size and ischemic stroke. Among them, there have been discrepancy regarding the sample size, methodology used and the final result. So we have done the study to establish the correlation between MPV and stroke.

II. Aims And Objectives

To determine the difference in platelet indices MPC (mean platelet count) & MPV (mean platelet volume) among acute ischemic stroke patient's in age & sex matched healthy subjects.

III. Materials And Methods

The study was a hospital based cross sectional study, data was collected from Dec1st2013 to July 31st 2014 at SMS Medical College and Hospital Jaipur. SMS Medical College& Hospital is a tertiary care referral centre. The study was carried out among fifty patients diagnosed with an acute ischemic stroke (Focal neurological deficit lasting more than 24hrs with no evidence of a non – vascular cause) and presenting to the hospital within forty eight hours of onset of symptoms. Fifty age and sex matched controls were also recruited.Patients above the age of 18 years and from both the gender were included in the study. Patients who had hemorrhagic stoke and those who have received anti platelet therapy were excluded from the study. Controls were primarily hospital based. Each control was matched for sex and age (+/- 10 years). There was at least one control for each case recruited. All stroke patients admitted to the hospital were screened during the time period described above. A blood sample was collected from the antecubital vein using a 5cc disposable syringe and transferred to EDTA vacationers. The samples were then taken to the Advanced Hematology Lab department of pathology (SMS medical college) between 2hrs of collection and analyzed using the SYSMEX-4000iXT automated analyzer using electrical impedance to measure the platelet count and mean platelet volume (MPV).

IV. Statistical Analysis

All data were entered on MS excel sheet and the data were analyzed in PRIMER and SPSS version 20 Statistical software. The difference between the two groups was compared using independent student 't' test. The p-value <0.05 was considered as statistically significant.

V. Results

The mean age of the study group was 54.85 ±11.85 yrs (range 31 to 76 yrs) with male predominance. The distribution of the cases according to the presence of risk factors with mean MPV was done which showed that only diabetes mellitus and MI showed significantly high MPV values. (Table 1) Comparison of different hematological parameters was also performed between the cases and the controls, which showed significant in Mean RBC, Mean HB , mean MPV and mean platelet count among the two groups. Significantly Lower Mean RBC and platelet count while higher Hb and MPV were observed in cases as compared to controls. (table 2)
When MPV and total platelet count were compared in patients a inverse correlation was seen in the the MPV values and mean platelet count (r= - p < 0.01) by using Pearson's correlation coefficient . The r2= 0.282 ,it means 28 % of the total variation in MPV was explained by the linear relation with mean platelet count .(table 3, graph 1)

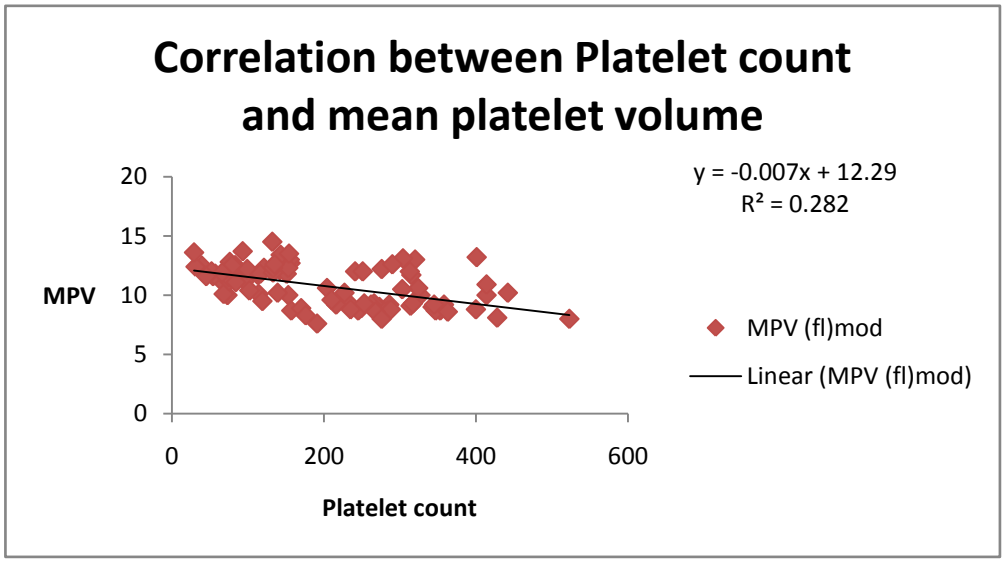
A logistic regression analysis was done to predict stroke for 50 pts of Acute ischemic stroke using age, sex, MI, smoking ,Hypertension ,alcohol, MI,TLC,MPV as predictors. A test of full model was statistically significant indicating that the predictors as asset reliably distinguish between outcome happening or not. (Chi square 54.320 ,df 7, p<0.001) Also the Hosmer and Lemshow test shows a good fit by high p value and low Chi square value. (Chi square 10.002 ,df 8, p=0.265). NegelKerke R^2 of 0.59 indicates fair relationship between predictors and grouping. Prediction success overall was 81% . The Wald criteria demonstrated that **only MPV (p>.001 HS) made a significant contribution to prediction. Other predictors were not significant predictors. (table 4)**

	MPV (fl)						
Risk factors	Cases			Controls			
	N	Mean	Std. Deviation	N	Mean	Std. Deviation	P Value LS
Hypertension	32	11.87	1.01	15	11.42	1.33	0.205 NS
Diabetes Mellitus	14	12.05	1.58	13	9.62	1.42	<0.001 HS
MI/IHD/Angina	10	11.96	0.91	2	9.60	0.85	0.007 HS
smoking	7	11.83	0.46	5	11.54	1.10	0.7 NS
Alcohol	5	11.74	0.79	3	10.30	1.65	0.138 NS

Table 1 Distribution of the cases according to presence of risk factors with mean MPV (fl)

Table 2. Comparison of Mean values of different hematological parameters

N=100	Mean	Std. Deviation	R	R Square	Equation	P Value LS
Mean Platelet volume	11.27	1.54				
mean platelet count	196.99	116.84	-0.53	.282	y = -0.007x + 12.29	<0.001S



Correlation Between Mean Platelet volume and mean platelet count
Table 3.

Graph 1. Correlation between platelet count and MPV

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	MPV	1.230	.251	24.082	1	.000	3.420	2.093	5.588
	TLC	.064	.129	.247	1	.619	1.066	.828	1.374
	MI	1.487	1.096	1.842	1	.175	4.424	.517	37.890
	Smoking	-1.111	.895	1.542	1	.214	.329	.057	1.902
	Alcohol	.949	1.090	.758	1	.384	2.583	.305	21.863
	Age	-.015	.028	.276	1	.600	.985	.932	1.041
	Sex(1)	-.320	.727	.194	1	.660	.726	.175	3.018
	HTN	-.378	.666	.323	1	.570	.685	.186	2.528
	Constant	-12.726	3.043	17.485	1	.000	.000		
a. Variable(s) entered on step 1: MPV, TLC, MI, Smoking, Alcohol, Age, Sex, HTN.									

Table 4 different factors which can affect the prediction of the stroke.

VI. Discussion

Thus the mean age in our study was much lower (55.92±11.33) compared to the other studies. There was a clear male preponderance in the cases of stroke recruited in this study. Similar patterns were seen in all the other studies compared except for O'Malley et[5]al and Pikija et al where a female preponderance was seen.[6] Out of many risk factors (eg. HTN, DM, IHD/MI/Angina, Smoking, Alcolol) for stroke, hypertension was the most prevalent in this study group with a 64% among cases and 30% among controls (Odd ratio 4.14). Similar trend was seen in the other studies done by A. Muscari et al (84.7%) [7] and Pikija et al (82.7%) [6]with hypertension being the most prevalent risk factor. Voko Z et al reported that Hypertension and isolated systolic hypertension are strong risk factors for stroke in the elderly.[8] Platelet parameters assessed were MPV, Platelet mass, and platelet count. The main parameter studied was MPV and platelet count. MPV shows a difference in cases and controls 11.88 (9.5 to 14.5) and 9.72(7.6 to 13.2) the difference is statistically significant

MPV has been compared with the various risk factors for stroke. MPV was higher in patients with stroke and diabetes mellitus with a suggestive significance ($p<0.001$) when compared to controls.(Mean MPV of cases-12.05fl & controls 9.62fl)

Thus our study found **Significantly higher mean MPV in cases** with history of diabetes mellitus and MI. No significant difference was observed in cases with history of hypertension ,smoking and alcohol. Philip Bath et al(1998) in a sub study of the PROGRESS trial followed 3134 individuals for an average of 3.9 years and assessed the association of MPV with the risk of stroke and found significantly raised MPV in such patients.[9] Similarly in 2009 Mayda-Domac F et al investigated the possibility of mean platelet volume & platelet count being an independent risk factor of ischemic & hemorrhagic stroke along with effect on prognosis and found significant association.[10] In January 2013 Farabnaz G et al reported that MPV is associated with ischemic stroke severity and has a high value for discriminating sever from mild ischemic stroke.[11]

The only study with a lower MPV in cases compared to controls is Tohji et al. This study did not specify the time after venipuncture at which samples were analysed or temperature at which it was stored.[12] In the current study the platelet count is showing a slightly lower trend in the cases with an average of 96.52(29 to 156) when compared to the controls in which the average was 297.46 (157 to 523). This trend is however statistically significant. This pattern has been seen in all the other case control studies which included O'Malley et al [5], Butterworth [13]et al and Tohji et al.[12] It has been suggested that MPV and platelet count are under independent hormonal control, although control of platelet production remains obscure. Some have suggested a role for interleukin-6, interleukin-3, thrombopoietin, and colony stimulating factors.[6] It is, however, generally accepted that platelet volume and count are determined at thrombopoiesis-8 and as in ischemic heart disease, these findings may implicate primary changes occurring at the bone marrow (megakaryocyte) level.[14] Moreover, an increase in megakaryocyte size and ploidy (DNA content) coincides with an increase in MPV. This direct association suggests the possibility that activation of megakaryocytes, as heralded by an increase in MPV, is a feature of ischemic stroke

In conclusion, this study has shown an elevation of MPV and reduction of platelet count in acute stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, 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

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