



ORIGINAL RESEARCH PAPER

Medicine

STUDY OF ASSOCIATION OF PLATELET INDICES WITH ACUTE ISCHEMIC STROKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS – A HOSPITAL BASED STUDY

KEY WORDS: Platelet Indices , Ischemic Stroke

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ABSTRACT

INTRODUCTION- High MPV acts as a risk factor for vascular complications of Diabetes Mellitus. Increased MPV in diabetic patients might have a role in genesis or worsening of acute ischemic stroke.

OBJECTIVE-

- To study the Association between platelet indices and acute ischemic stroke
- To study the Association between platelet indices and severity of acute ischemic stroke in Diabetes patients
- To study Association between platelet indices and outcome of acute ischemic stroke in Diabetes patients.

METHODS-

- prospective observational study
- Inclusion- all patients with acute ischemic stroke
- NIHSS assessed at admission
- Platelet indices
- MRS score assessed on 7th day
- Exclusion- haemorrhage in CT scan , patients < 18 years of age.
- Sample size = 100

RESULTS-

- Diabetic patients with ischemic stroke had higher PDW , MPV & PCT
- No significant association was found between platelet indices and severity of stroke
- Higher value of MPV, PDW & PCT were associated with poor outcome.

INTRODUCTION

Acute ischemic stroke results from sudden loss of blood circulation to an area of cerebral hemisphere leading to irreversible brain injury and neurological deficits persisting for more than 24 hours or until death. The prevalence of stroke in India was estimated as 203 per 100,000 population above 20 years, amounting to a total of about 1 million cases¹. The most important risk factors are

- hypertension
- heart diseases, atrial fibrillation
- diabetes mellitus
- cigarette smoking and
- hyperlipidemia²

Platelet size is also found to be elevated in individuals with hypertension and diabetes mellitus³, both conditions that predispose to the development of vascular disease⁴. Since stroke is a huge public health problem, other risk factors and possible preventive measures need to be identified. It is in this context that this study has its significance. Platelets 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 stroke⁵. Mean platelet volume (MPV) is a commonly used biomarker of platelet function and activation^{3,5}. Particularly, the patients with DM show increased platelet activity. The factors that contribute to this are not clearly elucidated; however, metabolic abnormalities such as insulin resistance, hyperglycemia, hyperlipidemia, and conditions such as oxidative stress, endothelial dysfunction and inflammation have been presumed⁶. Studies also have stated that high MPV acts as a risk factor for several vascular complications of DM, which include thromboembolism, myocardial infarction and stroke⁷. Platelet distribution width (PDW) represents variation in platelet size. Larger PDW also indicates pro-thrombotic status⁸. Furthermore, an increase in MPV and PDW is associ-

ated independently with stroke and increased levels of MPV and PDW have been found in acute ischemic stroke patients than in normal subjects. The patients with highest quintile of MPV had a >2 fold risk of severe stroke than those with lower quintiles⁹. These findings postulate that, the increase of MPV, specifically in diabetic patients might have a critical role for genesis or worsening of acute ischemic stroke. This prompted us to describe association between platelet indices and acute ischemic cerebrovascular events, which may serve as a valuable indicator for outcome of the event.

AIMS AND OBJECTIVES :

1. To study if there is any association between platelet indices and acute ischemic stroke in patients with type 2 diabetes mellitus
2. To study the association between platelet indices and severity of acute ischemic stroke in patients with type 2 diabetes mellitus
3. To study the association between platelet indices and outcome of acute ischemic stroke in patients with type 2 diabetes mellitus.

PLATELET INDICES

NORMAL VALUES FOR MPV -

measuring MPV in normal subjects suggest an approximately normal range of 4.5 variation in MPV is 8.5 fl with a mean of 6.5 fl small (CV = 2.1%) compared with platelet count. (CV = 6.1)

PLATELET DISTRIBUTION WIDTH (PDW)

Reflects the status of platelet activity.

PLATELET CRIT (PCT)

Plateletcrit is derived from the formula: Pct. (%) = MPV (fL) × Plt (x10³/ L) ÷ 1000.

PLATELET LARGE CELL RATIO (PLCR) Platelet large cell ratio is defined as the percentage of platelets that exceed the normal value of platelet volume of 12 fL in the total platelet

count.

METHODOLOGY

This prospective observational hospital based study was conducted at the Department of General Medicine of Jhalawar Medical College, Jhalawar. The only inclusion criteria was the diagnosis of Acute Ischemic Stroke (with or without prior history of DM) based on history, physical examination and computed tomography (CT) scan that was performed within 24 hours of symptom onset.

Each patient was assessed and an NIHSS score assigned to them. A Blood sample was collected and transferred to an EDTA vial. The samples were then taken to the laboratory between 2hrs and 4hrs of collection and analyzed using the SYSMEX automated analyzer using electrical impedance to measure the platelet indices. After the analysis the same sample was taken to the central laboratory and a peripheral smear was done to look for platelet aggregates. If platelet aggregates were found then such cases were excluded from the study. On the 7 th day after admission MRS score was calculated for each patient to determine the outcome.

EXCLUSION CRITERIA WERE:

1. Age <18 years
2. CT features of cerebral hemorrhage
3. Patients who had anemia with hemoglobin levels <12 gm.% in men and 10 gm.% in women

4. Diagnosed cases of immune thrombocytopenic purpura, autoimmune disorders, valvular heart diseases, acute post streptococcal glomerulonephritis, renal failure, deep vein thrombosis, congenital cyanotic heart disease, coronary artery disease and peripheral vascular disease.
5. Patient on anti-platelet medications, medications for dyslipidemia, immunosuppressants.

Sample size was a total of 100 ischemic stroke patients.

RESULTS

- The minimum and maximum age of stroke patients included in this study was 45 and 102 years respectively with mean age of 71.12 and standard deviation of 10.874.
- Out of 100 patients 78 were male and 22 were female.
- Diabetics had mean NIHSS score of 17.9 at presentation, with standard deviation of 1.052 NIHSS score of nonwhile mean diabetics was 15.05 with standard deviation of 6.029. The analysis was done using Independent sample t test and P value obtained was <0.05. significant
- Mean MRS score of diabetic group was 3.97 with standard deviation of 1.243 while that of nondiabetic group was 3.06, with standard deviation of 0.926. P value obtained was significant at the 0.001 level. Using Fischer Exact test, significant association was observed between the outcome of stroke and diabetes status of the study population with P value significant at the 0.001 level.

TABLE 1: COMPARISON OF MEANS OF PLATELET INDICES BETWEEN DIABETICS AND NON DIABETICS

	DIABETIC			NON DIABETIC			P Value
	N	Mean ± Std. Deviation	Std. Error Mean	N	Mean ± Std. Deviation	Std. Error Mean	
PLT	34	198.97 ± 45.664	7.831	66	208.32 ± 48.852	6.013	0.360
PDW	34	14.600 ± 1.4439	.2476	66	9.559 ± 1.5355	.1890	.000* (significant)
MPV	34	10.2868 ± 1.29948	.22286	66	8.0470 ± 1.43416	.17653	.000* (significant)
PLCR	34	27.82353 ± 6.271729	1.075593	66	28.03939 ± 6.382497	.785631	0.872
PCT	34	.1994 ± .01938	.00332	66	.1650 ± .02591	.00319	.000* (significant)

*significance is at the 0.001 level

TABLE 2: ASSOCIATION OF MEANS OF PLATELET INDICES WITH SEVERITY OF STROKE

Mean ± Std. Deviation	MINOR STROKE	MODERATE STROKE	MODERATELY SEVERE STROKE	SEVERE STROKE	P Value
PLT	207.50 ± 57.216	205.37 ± 56.897	203.51 ± 42.652	208.89 ± 48.832	0.981
PDW	10.075 ± 3.7607	11.396 ± 2.7198	10.908 ± 2.5472	12.389 ± 3.4105	0.221
MPV	7.3625 ± 2.62849	8.6937 ± 1.84731	8.7533 ± 1.54042	9.4583 ± 1.83783	0.144
PLCR	32.425 ± 1.3622	27.796 ± 6.5688	27.700 ± 6.3870	27.983 ± 6.3978	0.557
PCT	0.1500 ± 0.02160	0.1719 ± 0.03329	0.1757 ± 0.02744	0.1928 ± 0.01965	0.058

TABLE 3: ASSOCIATION OF MEANS OF PLATELET INDICES WITH OUTCOME/ DISABILITY OF STROKE

Mean ± Sd	No Significant Disability	Slight Disability	Moderate Disability	Moderately Severe Disability	Severe Disability	Death	P Value
PLT	162.67±37.233	238.30±30.714	210.98±50.792	200.27±38.233	195.29±53.410	173.67±22.121	0.026
PDW	12.967±2.8388	9.040±1.6721	9.664±1.4895	13.086±2.6192	13.850±2.7632	14.133±2.5007	0.000
MPV	10.1433±2.01493	7.3410±0.60874	8.0593±1.16827	9.7050±1.80670	9.9036±1.88765	10.5833±1.00828	0.000
PLCR	33.4167±2.48951	27.0900±7.33613	27.7222±6.13166	28.4955±6.01138	25.7000±6.61316	30.3333±9.12213	0.212
PCT	.1617±.02563	.1750±.02121	.1696±.03082	.1900±.02690	.1850±.02710	.1833±.00577	0.060

Using one way ANOVA test, significant association was found between PDW, MPV, PCT and outcome of stroke, with P value < 0.05. Higher values of MPV, PDW and PCT were associated with poor outcome and residual disability.

DISCUSSION

• SEVERITY AND OUTCOME OF STROKE

Diabetic stroke was more severe than non diabetics. In our study, most of the diabetics had moderate to severe stroke (41.2%) followed by severe stroke (29.4%). Among nondiabetics, most had moderate to severe stroke (56.1%) followed by moderate stroke (27.3%). The percentage of diabetics with severe stroke was much more than the nondiabetics.

Study conducted by Patil et al revealed identical results, with most of the diabetics having moderate to severe stroke (52%) followed by severe stroke (36%). Among nondiabetics, most had moderate to severe stroke (68.52%) followed by moderate stroke (16.67%)

- On the seventh days of admission, outcome was assessed by MRS score and means MRS score of the two study groups were compared. Mean MRS score of diabetic group was 3.97 with standard deviation of 1.243 while that of nondiabetic group was 3.06, with standard deviation of 0.926. P value obtained was significant at the 0.001 level. Similar results were given by Patil et al . Conclusively, diabetic people who had stroke had higher MRS score and

hence poorer outcome and more chances of residual disability than non-diabetics. Majority of non-diabetic patients had “moderate disability” (63.6%) followed by “slight disability” (13.6%) whereas majority of diabetic patients had “moderately-severe disability” (47.1%) followed by “severe disability” (26.5%). More diabetics (5.9%) died due to stroke and its complications than non-diabetics (1.5%). Majority of diabetics (80.5%) had MRS score more than 3 while most of the non-diabetics (81.8%) had MRS score less than 3.

- **PLATELET PARAMETERS AND STROKE** Minimum and maximum platelet counts among all the stroke patients were 90 and 354 ($\times 10^9/L$) respectively with mean of 205.14 ± 47.768 . Minimum and maximum MPV observed in our study was 5.10 and 11.97 with mean of 8.8085 ± 1.74655 . The strength of association of MPV with ischemic stroke was such that each 1fL rise in MPV was associated with 12 % increased relative risk of stroke. Similar pattern of raised MPV in ischemic stroke has been seen in most of the case control studies which included O'Malley et al, Butterworth et al, Bath et al, Pikija et al, A. Muscari et al and Tohji et al¹⁰. This direct association suggests the possibility that activation of megakaryocytes, as heralded by an increase in MPV, is a feature of ischemic stroke.

- **COMPARISON OF PLATELET INDICES BETWEEN DIABETICS And non DIABETICS**

The mean platelet count (PLT) of diabetics was 198.97 ± 45.664 while that of non diabetics 208.32 ± 48.852 . Thus, non-diabetics had higher platelet counts than diabetics but the results were not statistically significant with P value of 0.360. Mean platelet distribution width (PDW) of diabetics was 14.600 ± 1.4439 while that of nondiabetics was 9.559 ± 1.5355 . Thus, diabetics had higher PDW than non results were statistically significant at the 0.001 level. Mean of diabetics and the mean platelet values (MPV) of diabetics was 10.2868 ± 1.29948 while that of non-diabetics was 8.0470 ± 1.43416 . Thus, diabetics had higher MPV than non diabetics and the results were statistically significant at the 0.001 level. The platelet mass or platelet large cell ratio (PLCR) is almost a constant. There was a little difference in PLCR values of the two groups and the results were not statistically significant, with p value of 0.872. Mean platelet mass was 27.82353 ± 6.271729 while that of nonlet large cell ratio (P diabetics was 28.03939 ± 6.382497 . Mean plateletcrit (PCT) of diabetics was 0.1994 ± 0.01938 while that of non 0.02591 . Thus, diabetics had higher PCT than non- (LCR) of diabetics diabetics was $0.1650 \pm$ diabetics and the results were statistically significant at the 0.001 level. From the above analysis we conclude that there is a trend of higher PDW, MPV, and PCT among diabetics with ischemic stroke as compared to nondiabetics and these associations were significant statistically.

- **ASSOCIATION OF PLATELET INDICES WITH SEVERITY OF STROKE AND ITS OUTCOME**

No significant association was found between platelet indices and the severity of stroke, with P value > 0.05 for each comparison. However, significant association was found between PDW, MPV, PCT and outcome of stroke, with P value < 0.05. Higher values of MPV, PDW and PCT were associated with poor outcome and residual disability. These findings are in concurrence with those of Patil et al who concluded that patients with high MPV (> 11.01 fL) had 1.5 times greater vascular mortality than those with low MPV (< 8.7 fL).

CONCLUSION

Patients having Diabetes Mellitus who presented with acute ischemic stroke had increased platelet indices with worse outcome. Hence, platelet indices can be used in patients with diabetes mellitus to assess the outcome of acute ischemic stroke. A large scale study with large sample size will be helpful. This study holds prognostic value in such patients.

FINANCIAL SUPPORT

Nil.

NO CONFLICTS OF INTEREST

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