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Mean Platelet Volume and Plateletcrit as Predictors of Outcome of Acute Ischaemic Stroke

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Abstract:

Background: Platelet morphology plays a key role in occurrence and may determine prognosis in acute ischemic stroke.**Aims and objectives:** To assess the relation of mean platelet volume and plateletcrit with outcome in acute ischemic stroke.**Material and methods:**The study was conducted in 100 patients with acute ischaemic stroke in a tertiary care hospital.***Study Design*:** This was a prospective, observational and non interventional study conducted on cohort of patients with Acute ischemic stroke in tertiary care teaching hospital, over period of 6 months. The Institutional Ethical committee approval was taken. All enrolled patient underwent platelet indices platelet count, mean platelet volume and plateletcrit (PC, MPV, PCrt) , haemoglobin, Serum creatinine, fasting Lipid profile, Blood sugar level, HbA1c, modified Rankin Scale (mRS) and Brain imaging study (CT scan or MRI).***Statistical Analysis*:** Data was analysed for mean, percentage, standard deviation and chi square test for quantitative data. Appropriate statistical tests were applied using SPSS software version 21 (trial version) for analysis and 'p' value <0.05 was considered statistically significant. **Results:**Total 57 (57%) were males and 43 (43%) female fulfilling enrolment criteria were included in present study. The mean of platelet count in present cohort was 248.4 (SD±93.64), mean of mean platelet volume was 8.247 (SD±1.41) and the mean of plateletcrit was 0.20 (SD±0.08). The mean of modified Rankin Scale in present cohort was 3.11 (SD±1.22). The MPV had positive correlation with age (0.23), triglycerides (0.08), glycosylated haemoglobin (0.26) and modified Rankin scale (0.64). Platelet count had positive (0.13) correlation with total cholesterol, low density lipoprotein (0.10), high density lipoprotein (0.22) and glycosylated haemoglobin (0.26).Plateletcrit had positive (0.14) correlation with total cholesterol, low density lipoprotein (0.10), high density lipoprotein (0.19), glycosylated haemoglobin (0.39) and Modified Rankin scale (0.25). **Conclusion:** Acute ischemic stroke was significantly associated with raised MPV level, which is likely to be severe with high Modified Rankin scale score. Raised MPV level can be used as surrogate marker in patient with AIS along with other risk factors.
Keywords: ischaemic stroke, mean platelet volume, plateletcrit, modified rankin scale, lipids, diabetes mellitus

Introduction:

Platelets play a fundamental role in atherosclerosis and endorse the thrombotic event that is seen in acute ischemic stroke (AIS). This is particularly accredited to platelet sizeand raised platelet activity leading to increased platelet activation which furthers causes a pro coagulant effect leading to thrombus formation. Changes of mean platelet volume (MPV) could be a marker or a forecaster of AIS due to atherothrombosis. Significant increased MPV in patients with deep vein thrombosis and isolated elevated PC in patients with pulmonary embolism have been documented.Some groups reported that patients with AIS had significantly increased MPV or PC compared with controls. Modification of platelet function and consequently a

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hypercoagulable state has been suggested in patients with AIS.[1]Taking these erratic findings into consideration, we undertook this study to investigate the association between MPV, PC, and AIS.This study is designed to investigate role of platelets by measuring mean platelet volume (MPV) and plateletcrit as markers to predict the outcome in patients of acute ischemic stroke.

Material and methods:

Aim and Objectives: To assess the relation of mean platelet volume and plateletcrit with outcome in acute ischemic stroke.Study Design: This was a prospective, observational and non interventional study conducted on cohort of patients with Acute ischemic stroke in tertiary care teaching hospital. This study was conducted over period of 6 months.Study sample: The study was conducted in 100 patients presenting with acute ischaemic stroke in a tertiary care hospital.Study setting: This study was conducted in KIMS Hospital, over period of six months (July 2020 to December 2020). The Institutional Ethical committee approval was taken (*protocol number: 427/2019-2020*). The Informed and written consent were taken from patients before enrolment for study. A total 100 patients were included in this study satisfying the Inclusion criteria. Inclusion criteria were patients with the diagnosis of acute ischemic stroke. The patient with Hemorrhagic stroke and ACS were excluded from this study. All enrolled patient underwent platelet indices (platelet count [PC], mean platelet volume [MPV] and plateletcrit [Pcrt]) , haemoglobin, Serum creatinine, fasting Lipid profile, Blood sugar level, resting 12 lead ECG, CK-MB, HbA1c and Brain imaging study (CT scan or MRI). We aim to study association between platelet indices like MPV and plateletcrit and outcome of acute ischemic stroke assessed on admission and at discharge by modified Rankin scale (mRS). Statistical Analysis: Data Collected was entered in *Microsoft Excel*. Data was analysed for mean, percentage, standard deviation and chi square test for quantitative data by using Microsoft *excel* spread sheet. Appropriate statistical tests were applied using SPSS software version 21 (trial version) for analysis and 'p' value <0.05 was considered statistically significant.

Result:

Total 57 (57%) were males and 43 (43%) female fulfilling enrolment criteria were included in present study. The mean of age in present cohort was 62.51 (SD±12.72).The mean of cholesterol in present cohort was 156.04 (SD±42.07), mean of triglycerides was 120.43 (SD±76.26), mean of LDL was 83.65 (SD±36.29), and mean of HDLwas 46.5 (SD±12.18). The mean of haemoglobin in present cohort was 12.35 (SD±2.51). The mean of glycosylated haemoglobin(HbA_1c) in present cohort was 6.57 (SD±1.60). The mean of platelet count in present cohort was 248.4 (SD±93.644), mean of mean platelet volume was 8.247 (SD±1.417) and the mean of platelet-crit was 0.20 (SD±0.08). The mean of modified Rankin Scale (mRS) in present cohort was 3.11 (SD±1.22). MPV in patients with HbA1c ≤ 6 was significantly high (10.86 ± 0.79 fL) compared to HbA1c > 6 patients (8.47 ± 0.96 fL; p<0.02). **[Table1]**

Table 1: The mean and standard deviation of numerical variables of patients with AIS

Variable	MEAN	SD (±)
Age	62.51	12.72
Total cholesterol (T-CHO)	156.04	42.07
Trigelycerides(TRG)	120.43	76.26
Low density lipoprotein (LDL)	83.65	36.29
High density lipoprotein (HDL)	46.5	12.18
Glycosylated Haemoglobin (HbA1c)	6.57	1.60
Haemoglobin	12.35	2.51
Platelet count	248.42	93.64
Mean platelet volume	8.24	1.41
Plateletcrit	0.20	0.08
Modified Rankin scale (mRS)	3.11	1.22

The MPV had positive correlation with age (0.23), triglycerides (0.08), glycosylated haemoglobin (0.26)and modified Rankin scale (0.64). MPV had negative correlation with total cholesterol(-0.01), low density

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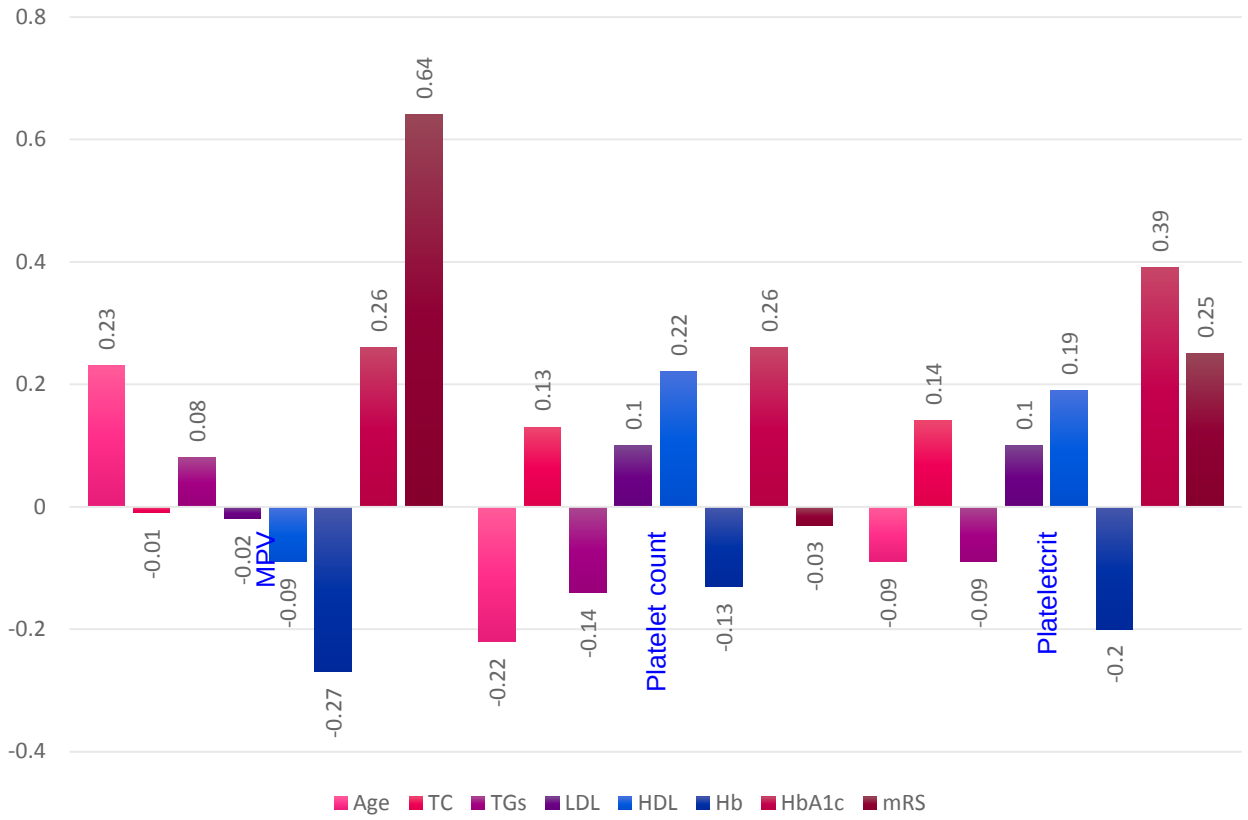
lipoprotein (-0.02), high density lipoprotein(-0.09) and haemoglobin(-0.27).Plateletcount had positive correlation with total cholesterol (0.13), low density lipoprotein (0.10), high density lipoprotein (0.22) and glycosylated haemoglobin (0.26). Platelet count had negative (-0.22) correlation with age, triglycerides (-0.14),haemoglobin (-0.13) andModified Rankin scale (-0.03).Plateletcrithad positive correlation with total cholesterol(0.14), low density lipoprotein (0.10), high density lipoprotein (0.19),glycosylated haemoglobin (0.39) and Modified Rankin scale (0.25). Plateletcrit had negative correlation with age(-0.09),triglycerides (-0.09) and haemoglobin (-0.20).**[Graph 1]**

Graph 1: The correlation platelet indices with various parameters of stroke



The mean of platelet indices were high in patient with duration of stay > 7 days compared to ≤7 days (‘p’ < 0.05). **[Table 2 and Graph 2]**

Table 2: Relation of platelet indices with outcome and duration of stay of patient with AIS

Duration of stay	≤7 days	>7 days
Mean platelet value	8.16 (1.36)	8.67(1.27)
Platelet count	217.12 (76.57)	245.76 (95.28)
Plateletcrit	0.17 (0.06)	0.21(0.08)

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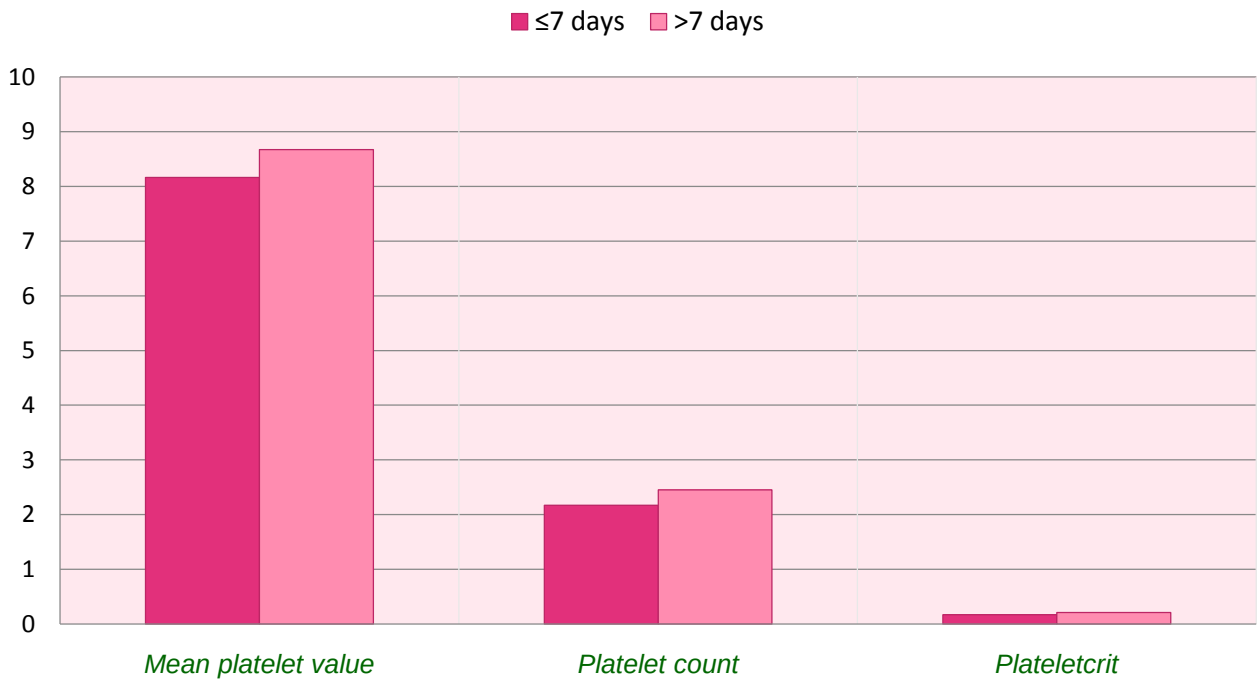
Graph 2: Platetet indices in patient with AIS



Discussion:

Mean platelet volume (MPV) is regarded as a marker of platelet turnover, thus releasing more chemokines promoting further platelet aggregation and activation. Elevated MPV simultaneously with the elevated PC increases the risk of thrombosis. In the present study, MPV revealed positive correlation with age, triglycerides, HbA_1c and modified Rankin scale. Platelet count had positive correlation with total cholesterol, LDL, HDL and HbA_1c. Plateletcrit had positive correlation with total cholesterol, LDL, HDL, HbA_1c and Modified Rankin scale. Acute ischemic stroke in was significantly associated with raised MPV level, which is likely to be severe AIS. The mean of platet indices were high in patient with duration of hospital stay > 7 days. MPV is an easily obtainable blood parameter, which defines platelet reactivity and proves to be a good predictor of severity and outcome of stroke. We compared our observations with various studies. Similar to present study Ayas ZÖ et al(2018)quoted that the MPV values increased after stroke ($p<0.0001$). There was a positive correlation between age and MPV values during acute stroke ($p<0.05$).[2]Bath P et al(2004) quoted that the MPV was positively associated with the risk of stroke. They stated that the MPV is an independent predictor of the risk of stroke. Similar to present study.[3]Sadeghi F et al (2020)quoted that the Ischemic stroke patients had higher MPV.[1] Arikanoglu A et al(2013) quoted that the MPV and CRP were statistically significantly higher ($p < 0.05$) in ischemic stroke patients who died and may be an indication of the roles these markers play in the mortality of stroke patients.[4]Tamer D et al(2013)quoted, that the statistically significant Mean Platelet Volume increased in the stroke patients.[5]Dogan NO et al(2013) quoted, that the weak positive correlation was identified between the National Institute of Health Stroke Scores and mean platelet volume levels ($r=0.207$; $p <0.001$). A significant relationship was identified between mean platelet volume levels and previous stroke ($p <0.005$).[6]Zheng M et al (2020)reported that the MPV level and CHA_2DS_2-VASc scores of the stroke group were higher than those of the control group ('p'< 0.001). The $CHA_2D_2S_2$-VASc combined with MPV can improve predictive value with higher sensitivity and it could be a powerful tool for stratifying patients in terms of ischaemic stroke risk.[7]Greisenegger S et al (2004) quoted, with acute ischemic stroke. Patients within the highest quintile of MPV had a significantly higher risk of suffering a severe stroke, defined as modified Rankin Scale score of 3 to 6 ($P<0.001$). An elevated MPV is associated with a worse outcome for acute ischemic cerebrovascular events.[8]Elsayed AM et al(2017)quoted, that the ischemic stroke patients had significantly higher MPV and MPV/PC ratio compared to the control group ($p= 0.001$ and $p= 0.017$) respectively. The MPV value was higher and more significant ($p= 0.011$) in patients group with high Rankin scale in comparison with those with lower scores. MPV and MPV/PC ratio could be considered meaningful

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laboratory markers for the risk of acute ischemic stroke.[9]Mohamed AA et al(2019)quoted, that MPV was significantly higher in the patient with AIS ($P < 0.001$). MPV was an independent predictor of poor short-term outcome of acute stroke after controlling for confounders like diabetes mellitus.[10]O'malley T et al(1995)quoted, thatthe MPV was higher in acute stroke (P<.001).[11]Lim HH et al (2019)quoted, that themean platelet volume (MPV) showed statistically significant results in both at admission and after 3 months. MPV could be used as a relatively good tool for predicting severity at the time of admission and after 3 months, these findings are similar to the present study.[12]Ghahremanfard F et Al (2013) quoted that,in the multivariate logistic regression model, the effect of MPV in ischemic stroke remained statistically significant (p=0.012).The MPV is associated with ischemic stroke severity and has a high value for discriminating severe from mild ischemic AIS. Similarly in present study the mean of platelet indices were high in patient with duration of hospital stay > 7 days.[13]Patil P et al (2018)(n= 79) quoted that the MPV in patients with DM was significantly high compared to nondiabetic patients (p<0.001). The mean MRM scores were significantly high in diabetics than that of nondiabetics (p<0.001), these findings are comparable with present study.[14]Aslan S et al (2019) quoted that, high plateletcrit levels were demonstrated to be statistically higher in patients with MACCE (in the MACCE (+) group vs. in the MACCE (–) group, $p < 0.001$). Plateletcrit has an independently predictive value for long-term mortality and MACCE, and it can be used as a marker to predict the long-term adverse outcomes in patients with carotid stenosis.[15]**[Table 3]**

Table 3: Comparison of various studies with relation of platelet indices with AIS with present study

Author; Study year	**(n)**	**Type of study**	**Result**	**Conclusion**
Sadeghi F et al [1]	3615	Meta analysis	The MPV was significantly higher [SMD = 0.52, P < .001] compared with controls	MPV was significantly higher in ischemic stroke.
Ayas ZÖ et al (2018)[2]	67	Cross-sectional	MPV values increased after stroke compared with the values before stroke (p<0.0001)	There was a positive correlation between age and MPV values (r=0.270; p<0.05).
Bath P et al (2004)[3]	3134	Randomized, double-blind trial	MPV was positively associated with the risk of stroke, with an 11% increased relative risk of stroke per femtoliter MPV.	MPV is an independent predictor of AIS. The measurement of MPV may be useful prognostic for AIS.
Tamer D et al (2013)[4]	797	Case control	The median value in stroke patients was 9.0 fL, while in control it was 8.80 L.	MPV increased in the stroke patients. (Z=-2.80; p<0.05).
Arikanoglu A et al (2013)[5]	63	Case control	A significant difference (p = 0.027) was observed between the MPV of the stroke patients (8.6 fL) and the control (7.93 fl).	MPV and CRP in ischemic stroke patients are higher in the ischemic stroke patients who died.
Dogan NO et al (2013)[6]	242	Prospective cross-sectional	MPV results were significantly higher in patients with cortical infarction (p <0.001). A statistically significant increase was also noted in hospitalised patients (p <0.036).	The measurement of mean platelet volume levels may provide useful diagnostic and prognostic information of patients with AIS.
Zheng M et al (2020)[7]	370	Case-control	The MPV level and CHA_2DS_2-VASc scores of the stroke group were higher than those of the control group (all p < 0.001).	MPV could be a new predictor of ischaemic stroke risk in patients with AF.
Greisenegger S et al (2004)[8]	776	Cross-sectional	Patients within the highest quintile of MPV had a significantly higher risk of suffering a severe stroke, defined as modified Rankin Scale score of 3 to 6.	An elevated MPV is associated with a worse outcome for AIS independent of other clinical parameters.
ElsayedAM et al	70	Cross-sectional	The ischemic stroke patients had significantly higher MPV and	MPV could be considered laboratory marker for the risk of

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Author; Study year	(n)	Type of study	Result	Conclusion
(2017)[9]			MPV/PC ratio compared to the control group (p= 0.001 and p= 0.017) respectively.	AIS. The MPV value was higher and significantin patients with high Rankin scale.
Mohamed AA et al (2019)[10]	157	Observational prospective	MPV was significantly higher in the unfavourable group than in the favourable one (P < 0. 001).	MPV and PCT were significantly correlated with poor outcome.
O'malley T et al (1995)[11]	58	Observational prospective	MPV was higher in acute stroke (11.3 compared with 10.1 fL in control subjects; P<.001, Student's t test).	An increase in MPV and a reduction in platelet count are features of acute phases of cerebral ischemia.
Lim HH et al (2019)[12]	104	Cross-sectional	Mean platelet volume (MPV) showed statistically significant with AIS.	MPV could be used as a relatively good tool for predicting severity at the time of admission of AIS.
Ghahremanfard F et Al (2013)[13]	100	Cross-sectional	The MPV value was higher and more significant in those with mRS: 3 or more than those with mRS 0-2 (p<0.001).	The MPV has a high value for discriminating severe from mild ischemic stroke.
Patil P et al (2018)[14]	79	Cross-sectional	MPV in patients with DM was significantly high (10.16 fL) compared to nondiabetic patients (8.25 fL; p<0.001).	Acute ischemic stroke in diabetic patients is significantly associated with raised MPV level.
Aslan S et al (2019)[15]	230	Cross-sectional	High plateletcrit levels were demonstrated to be statistically higher in patients with MACCE (0.247 in the MACCE (+) group vs. 0.213 in the MACCE (–), p < 0.001).	Plateletcrit has an independently predictive value for long-term mortality and MACCE in patients with carotid stenosis

Conclusion:

To conclude we observed that, the MPV had positive correlation with age, triglycerides, glycosylated haemoglobin and modified Rankin scale. Platelet count had positive correlation with total cholesterol, LDL, HDL and HbA_1c. Plateletcrit had positive correlation with total cholesterol, LDL, HDL, HbA_1c and Modified Rankin scale. Acute ischemic stroke in was significantly associated with raised MPV level, which is likely to be severe AIS. The mean of platelet indices were high in patient with duration of stay > 7 days compared to ≤7 days. MPV is an easily obtainable blood parameter, which defines platelet reactivity and proves to be a good predictor of severity and outcome of stroke. The measurement of MPV may add useful prognostic information for clinicians managing patients with AIS. It is possible that platelet indices changes precede the vascular event, and further studies are warranted to find weather it's a cause or the effect.

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