ORIGINAL ARTICLE

Frequency of Elevated Mean Platelet Volume in Patients with Different Severities of Acute Ischemic Stroke

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ASBTRACT

Objective: *Determine the frequency of elevated mean platelet volume in patients with different severities of acute ischemic stroke who presented in Lahore general hospital Lahore.*

Study Design: *Cross sectional survey.*

Duration: *Study duration was 1year.*

Sample Size: *130 patients of acute ischemic stroke.*

Sample Technique: *Non-probability purposive sampling.*

Methodology: *Consecutive 130 patients of acute ischemic stroke presented to emergency department or admitted through OPD within 24 hours of onset of symptoms and fulfilling the inclusion criteria were selected. Patients were divided in two groups based on mRS scoring. MPV was measured by automated hematology analyser Sysmex KX-21. The severity of stroke was assessed by Modified Rankin Score (mRS) between 24 to 72 hours of onset of symptoms.Patients with acute ischemic stroke proved by CT brain presenting within 24 hours of symptom onset and Age 40 and above and both genders were include. Patients with hematological malignancies were excluded from study.*

Data Collection: *130 patients admitted patients (through emergency and outdoor), Lahore General Hospital, Lahore fulfilling the inclusion criteria were selected for study.The severity of stroke was assessed by modified Rankin Scoring (mRS). The patients were divided in to two groups based on mRS scoring. Mean platelet volume and mRS score were recorded. Major risk factors like hypertension, diabetes mellitus, smoking history and hypercholesterolemia if present were also recorded. The demographic information of these cases like name, age, sex and address recorded. The collected information was entered into SPSS version 11.0. Quantitative variables like age, mean platelet volume were analyzed as mean and standard deviation. Frequencies of elevated MPV in both groups were described. Gender and severity of stroke (mild, moderate to severe) were analysed as frequency and percentage. Elevated MPV was also analysed as frequency and percentage in both groups*

Results *Among the enrolled 130 patients 80 (61.5%) were males and 50 (38.5%) were females (Table 1, Graph 1) with age ranging from 41 – 74 years with a mean age of 56.85 ± 10.15 years. 45 (35%) patients had modified Rankin scale (mRS) between 0 to 2 while 85 (65%) patients had mRS between 3 to 6. Overall mean platelet volume was found to be elevated in 85 patients. Among them 62 (73%) patients had mRS of 3 – 6 (group 2) while 23 patients had mRS of 0 – 2 (group 1). Among the 45 (23%) patients who had normal mean platelet volume, 22 belonged to group 1 (mRS 0 – 2) while 23 were in group 2 (mRS 3 – 6).*

Conclusion: *MPV, with an easy way of measurement, may be anearly and important predictor for the prognosis of ischemic stroke.*

Key Words: *Stroke, Modified Rankin Score, Mean Platelet volume.*

Abbreviations: *mRS: Modified Rankin scale. CBF: Cerebral blood flow. DALYs: Disability-adjusted life years. MPV: Mean Platelet Volume.*

INTRODUCTION

Stroke is a common medical emergency with an annual incidence of between 180 and 300 per 100,000.[1] In Pakistan ischemic stroke is more common, nearly 80% of the stroke cases.[2] The brain receives its blood supply from the internal carotid arteries (anterior circulation) and vertebrobasilar system. The four arteries lie within the sub-arachnoid space. In general, branches derived from the vertebral arteries supply the caudal half of the brain, including the brainstem, midbrain, and most of the thalamus, while branches of the internal carotid arteries supply basal ganglia, frontal and parietal lobes, the lateral portions of the temporal lobes, and most of the internal capsule.[3] The average of cerebral blood flow (CBF) in young adults is 50 – 65 ml / 100 grams of brain / min. For the entire brain, this amounts to a total of 750 – 900 ml / min, or 15% of the cardiac output.

Stroke is rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause other than of vascular origin[1.] It is the leading cause of adult disability in the United States and Europe and it is the second leading cause of death worldwide.[1] In Western countries, about 80% of strokes are caused by focal cerebral ischemia due to arterial occlusion, and the remaining 20% are caused by hemorrhages.[4,5]

Stroke accounts for about 10% of all deaths in most industrialized countries and most of these deaths are among persons over the age of 65. About one – fifth of patients with an acute stroke die within one month of the event, and at least half of those who survive are left with a physical disability.[1]

Mortality in the first month after stroke has been reported to range from 2.5% in patients with multiple lacunar infarcts to 78% in patients with space – occupying hemispheric infarction.[20] Stroke causes over 5.5 million deaths annually and two third of these occur in the developing world. Among the stroke subtypes, ischemic stroke is more common, nearly 80% of all strokes are of this variety in developing countries.[2] In the last decade, according to the American Heart Association the mortality rate from stroke has declined by 12%, but the total number of strokes may again be rising.[6] Cerebrovascular disease was also the fifth leading cause of lost productivity, as measured by disability – adjusted life years (DALYs). DALYs include years of productivity lost to either death or varying degrees of disability. In 1990, cerebrovascular disease caused 38.5 million DALYs throughout the world.[21] Modifiable risk factors for stroke include hypertension, cardiac diseases (particularly atrial fibrillation), diabetes, hyperlipidaemia, smoking and transient ischemic attack.[2] In last few years MPV is arousing increasing interest as a new independent cardiovascular risk factor.[7] High mean platelet volume has been shown to be associated with coronary atherosclerosis, acute coronary syndrome and myocardial infarction.[7,8] A considerable body of experimental evidence documents a role of increased platelet reactivity in the development of various ischemic stroke types and it is considered to be a relevant pathophysiological factor in approximately 50% of all strokes[9]. In the last decade, according to the American Heart Association the mortality rate from stroke has declined by 12%, but the total number of strokes may again be rising.[6]

The rationale of the study is to help attending physicians to know about the possible risks of increased platelet volume on stroke severityand such patients can be given more vigilant and aggressive care that can inturn lead to reduction in morbidity/mortality.

METHODOLOGY

It was a cross sectional study with non probability purposive sampling technique conducted in Lahore general hospital Lahore from July 2014 to July 2015. All consecutive 130 patients of acute ischemic stroke who fulfilled the inclusion criteria were included in the study. All Patients with acute ischemic stroke proved by CT brain presenting within 24 hours of symptom onset and age 40 and above and both genders were included in the study.

Patients with hematological malignancies assessed on blood count and blood smear and patients with abnormally high numbers on blood counts and patients showing atypical cells on blood smear were excluded from study.

The severity of stroke was assessed by modified Rankin Scoring (mRS). The patients were divided in to two groups based on mRS scoring. Patients in group 1 had mRS score 0 to2 (no or only mild neurological symptoms) and patients in group 2 had mRS score 3 to 6 (moderate or severe disability / death). 3 cc of venous blood for mean platelet volume was collected in CBC vacuum tube and was sent to Hematology Laboratory, where MPV was measured by automated hematology analyser Sysmex KX-21. Mean platelet volume and mRS score were recorded. Major risk factors like hypertension, diabetes mellitus, smoking history and

hypercholesterolemia if present were also recorded. Confounding variables like age of patients, sex, and history of smoking, diabetes, hypertension, hypercholesterolemia and any heart disease were controlled through matching of patients. The demographic information of these cases like name, age, sex and address recorded. Informed consent was taken before including patients in the study.The collected information was entered into SPSS version 11.0. Quantitative variables like age, mean platelet volume were analyzed as mean and standard deviation. Frequency of elevated MPV in both groups was described. Gender and severity of stroke (mild, moderate to severe) were analyzed as frequency and percentage. Elevated MPV were also analyzed as frequency and percentage in both groups.

RESULTS

Among the enrolled 130 patients 80 (61.5%) were males and 50 (38.5%) were females with age ranging from 41 – 7 years with a mean age of 56.85 ± 10.15 years. Among the different age groups 32 (25%) were in between 40 – 50 years, 78 (60%) were in between 51 – 60 years and 20 (15%) were in between 61 – 70 years of age.

Among 130 patients, 45 (35%) patients had modified Rankin scale (mRS) between 0 to 2 while 85 (65%) patients had mRS between 3 to 6. Patients having modified Rankin scale (mRS) 0 to 2 were included in group 1(mild stroke) while patients having modified Rankin scale (mRS) 3 to 6 were included in group 2 (moderate / severe stroke).

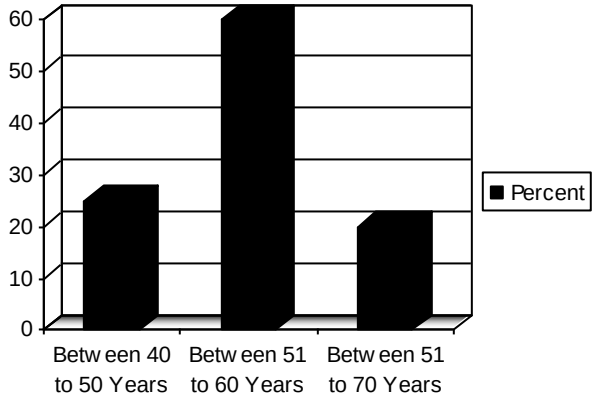

Fig. 1:

Table 1: *Distribution of cases based on severity of stroke.*

mRS	Number	Percentage
0 – 2 (Group – 1)	45	35.0
3 – 6 (Group – 2)	85	65.0
Total	130	100.0

Table 2: *Frequency of normal and elevated MPV in group 1.*

Gender	Mean Platelet volume		Total
	Normal	Elevated	
Male	12 (54.5%)	12 (52%)	24
Female	10 (46.5%)	11 (48%)	21
Total	22	23	45

Table 3: *Frequency of normal and elevated MPV in group 2.*

Gender	Mean Platelet volume		Total
	Normal	Elevated	
Male	14 (60.8%)	42 (67.7%)	56
Female	9 (39.2%)	20 (32.3%)	29
Total	23	62	85

Table 4: *Overall frequency of normal and elevated MPV in both groups.*

mRS	Mean Platelet volume		Total
	Normal	Elevated	
0 – 2	22 (49%)	23 (51%)	45
3 – 6	23(27%)	62 (73%)	85
Total	45	85	130

In Group 1, out of total 45 patients, 24 (53.4%) were males and 21 (46.6%) were females. Mean platelet volume was found to be elevated in 23 patients (51%) where as remaining 22 (49%) patients had mean platelet volume with in normal range. Among the 23 patients who had elevated mean platelet volume, 12 (52%) were male while 11 (48%) were females (Table 5).

Group 2 included 85 patients who had modified

Table 5: *Distribution of cases by neurologic impairment.*

mRS	Male	Female	Total
1	10	8	18 (13.8%)
2	14	13	27 (20.7%)
3	16	7	23 (17.7%)
4	31	17	48 (37%)
5	9	5	14 (10.7%)
Total	80	50	130 (100%)

Rankin scoring (mRS) 3 to 6. Out of these 56 (65.8%) were males and 29 (34.2%) were females. Mean platelet volume was found to be elevated in 62 (73%) patients while it was with in normal limits in 23 (27%) patients. Among 62 patients who had elevated mean platelet volume, 42 (67.7%) were males and 20 (32.3%) were females. Among 23 patients who had normal mean platelet volume, 14 (60.8%) were males while 9 (39.3%) were females.

Out of total 130 patients, 85 (65%) patients had elevated mean platelet volume. Out of them 54 (63.5%) were males while females patients were 31 (36.5%). Mean platelet volume was not raised in 45 (35%) patients. Among them, 26 (57.8%) were males and 19 (42.2%) were females.

Overall mean platelet volume was found to be elevated in 85 patients. Among them 62 (73%) patients had mRS of 3 – 6 (group 2) while 23 patients had mRS of 0 – 2 (group 1). Among the 45 (23%) patients who had normal mean platelet volume, 22 belonged to group 1 (mRS 0 – 2) while 23 were in group 2 (mRS 3 – 6).

Patients had spectrum of neurological deficit ranging from no significant disability to severe disability resulting in immobility and limitation to bed. As mentioned previously, modified Rankin scale (mRS) was used to describe the disability of patient. Among all the patients, 18 (13.8%) patients had no significant disability despite symptoms and were able to carry out all usual activities and hence had modified Rankin scale (mRS) of 1. Patients falling under this category included 10 (55.5%) males and 8 (44.4%) females. 27 (20.7%) patients had slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance and hence had modified Rankin scale (mRS) of 2. This group included 14 (51.8%) males and 13 (48.1%) females. Patients having moderate disability; requiring some help, but able to walk without assistance (modified Rankin scale (mRS) of 3) constituted 17.7% (23 patients) of proportion. Among them male patients were 16 (69.5%) and female patients were 7 (30.4). Patients who had moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance (modified Rankin scale (mRS) of 4) were 48 (37%), 31 (64.5%) males and 17 (35.4%) females fell into this category. Patients who had severe disability; bedridden, incontinent and required constant nursing care and attention were included in modified Rankin scale (mRS) of 5, 14 (10.7%) patients had neurological dysfunction to this extent and patients included 9 (64.2%) males and 5 (35.7%) females.

DISCUSSION

Stroke is the third most common cause of death in the developed world after cancer and ischemic heart disease, and is the most common cause of severe physical disability.[1] Many of the patients are left with variable degree of permanent neurological impairment. Stroke causes over 5.5 million deaths annually and two third of these occur in the developing world. Among the stroke subtypes, ischemic stroke is more common, nearly 80% of all strokes are of this variety in developing countries.[2]

Epidemiological investigations of the manner in which strokes arise and evolve have begun to identify highly vulnerable persons and the factors which predispose. Estimates of the risk associated with identified stroke precursors, singly and in combination, have been ascertained.[10]

Mean Platelet Volume (MPV) is a measurement of the average size of platelets found in blood and is typically included in routine blood tests.[11] MPV is a marker of platelets' function and is positively associated with indicators of platelet activity, including aggregation and release of thromboxane A_2, platelet factor 4 and B thromboglobulin.[12] Elevated mean platelet volume (MPV) is associated with a shortened bleeding time.[7] Large platelets contain more dense granules and produce large amounts of thromboxane A_2.[13] Larger platelets are enzymatically and metabolically more active and have a higher potential thrombotic ability as compared with smaller platelets.[14] The release of large and more reactive platelets may contribute to the thrombophilic state associated with ischemic events.[15]

In last few years MPV is arousing increasing interest as a new independent cardiovascular risk factor.[7]

High mean platelet volume has been shown to be associated with coronary atherosclerosis, acute coronary syndrome and myocardial infarction.[7,8] A considerable body of experimental evidence documents a role of increased platelet reactivity in the development of various ischemic stroke types and it is considered to be a relevant pathophysiological factor in approximately 50% of all strokes.[9]

A study conducted by Greisenegger, Endler and their colleagues to observe the affect of elevated MPV on outcome of acute ischemic stroke showed that 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, compared with patients within the lowest quintile (odds ratio = 2.6; 95% confidence interval, 1.6 to 4.1; P < 0.001). This association remained significant after adjustment for possible confounding factors (odds ratio = 2.2; 95% confidence interval, 1.2 to 4.0; P = 0.013).[16]

In 2008, Slaven Pikija, Danijel Cvetko, Martina Hajduk, Vladimir Trkulja conducted a study on 81 consecutive patients of acute ischemic stroke patients in attempt to find an association between elevated mean platelet volume with larger infarct volume on CT brain scans and with worse clinical outcome. They showed that higher mean platelet volume was independently associated with larger infarct volume [estimate 0.259, 95% confidence interval (CI) 0.004 –0.513, *P* = 0.046], greater risk of death/dependence 7 days post-stroke [relativerisk (RR) = 1.077, 95% CI 1.005 – 1.115, *P* = 0.036], and greater risk of death / dependence 3 months post-stroke (RR = 1.077, 95% CI 1.001 – 1.158, *P* = 0.048)[9].

In 2010, Mayda-Domaç F, Misirli H, Yilmaz M. conducted study on 692 patients with either ischemic or hemorrhagic stroke and compared them with 208 control subjects withsimilar risk factors, but without evidence of vascular events. The association of MPV and PC with cause, localization, and size of the infarct or hemorrhage was examined. Prognosis was determined by Glasgow Outcome Scale. They found out that mean platelet volumeis independent risk factor for ischemic stroke (P 5.007, odds ratio [OR] 5 0.866; P 5.000, 95%confidence interval). Ischemic group MPV (P 5 .013, OR 5 1.02, 95% CI) was in correlation with worse outcome (P 5.001, OR 5 1.004, 95% CI).[17]

Up till now, we do not have any local study in Pakistan that is attempted to find any association of elevated mean platelet volume with stroke severity/ prognosis. Our study was designed to determine and categorize the severity of acute ischemic stroke presenting in a tertiary care hospital and to determine frequency of elevated mean platelet volume in patients with different severities of acute ischemic stroke.

My study was conducted at Lahore General Hospital, Lahore over a period of 6 months. 130 patients of acute ischemic stroke fulfilling the inclusion criteria were included in the study. There were 80 (61.5%) males and 50 (38.5%) females in our study with male to female ratio of 1.6:1. There was male predominance in our study which is similar to studies done by George Ntaios and his colleagues[19] (Male 57.7%, Female 42.3%) and Greisenegger S. and his colleagues[16] (Male 55%, Female 45%). However studies done by Slaven Pikija and his colleagues[9] (Males 39.5%, Females 60.5%) and Mayda – Domaç F and colleagues[17] (Males 49%, Females 51%) reported female predominance in patients presenting with acute ischemic stroke. Mean age in our study was 56.85 ± 10.15 years which is less than studies done by Mayda-Domaç F and colleagues[17] (65.16 ± 12.6), George Ntaios and his colleagues (73 ± 15.8).[18.]

The results of my study showed that the majority i.e. 65% of patients had moderate to severe (mRS 3 to 6) acute ischemic stroke while 45% patients had mild (mRS 0 to 2) acute ischemic stroke. These findings are similar to those of Slaven Pikija, Danijel Cvetko, Martina Hajduk, Vladimir Trkulja.[9] Their study also showed that patients presenting with moderate to severe stroke (66.7%) outnumbered the patients presenting with mild stroke. Similarly study by George Ntaios and his colleagues also had majority (57%) of patients presenting with severe stroke.[19] However study by Greisenegger, Endler and their colleagues[16] showed that majority (57.6) of patients had mild stroke (mRS 0 to 2).

Mean platelet volume was found to be elevated in 51% of patients having mild stroke (mRS 0 to 2) where as it was elevated in 73% patients having moderate to severe stroke (mRS 3 to 6). These findings show that higher MPV was associated with higher risk of dependence/death i.e. mRS score 3 to 6 (P = 0.039). These findings again corroborate those of Greisenegger S and his colleagues. Their study showed that mean platelet volume was elevated in 57% of patients having mild stroke while mean platelet volume was found to be elevated in 67% of patients having moderate / severe stroke.[16]

Majority of currently available studies report positive correlation between MPV and stroke outcome.[9,16,17]

We described a relation between MPV and clinical

severity of acute ischemic cerebrovascular events. Measurementof MPV is easy to establish and therefore might serve as a valuablepredictor of a worse outcome in patients with acute ischemic cerebrovascular events.

CONCLUSION

In conclusion, our study agrees with the clinical importance of MPV in ischemic stroke. Platelet volume indices that are done routinely may be helpful in predicting the outcome of acute ischemic stroke. Our data support the view that MPV is a determinant of stroke severity / outcome. MPV, with an easy way of measurement, may be anearly and important predictor for the prognosis of ischemicstroke. Thus the study of MPV might act as additional tool to identify people at high risk and such patients can be given more vigilant and aggressive care that can in-turn lead to reduction in morbidity/mortality.

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