STUDY OF CLINICAL PROFILE, RISK FACTORS AND PLATELET INDICES IN SPONTANEOUS INTRACEREBRAL BLEED

Neurology

Dr. Priyanka Ranga

Dr. Abha Dua*   *Corresponding Author

ABSTRACT

INTRODUCTION: Stroke is a devastating medical disease that imposes the greatest burden of disability-adjusted life years (DALYs) of all neurological disorders. Patients with spontaneous intracerebral hemorrhage have subtle platelet dysfunction associated with ICH progression and larger ICH size. In our study clinical profile, risk factors and platelet indices were studied in patients of ICH. Platelet indices which includes platelet count, mean platelet volume, plateletcrit and platelet distribution width were compared in case group and control groups and correlated with severity of stroke.

Material and method: 50 cases and 50 controls were included in our study group after applying all inclusion and exclusion criteria. Platelet indices (platelet count, MPV, PDW, PCT) were studied in both cases and controls groups. Clinical profiling, risk factors analysis and severity of ICH assessed by NIHSS score were done in cases group.

RESULTS: It was found that among all risk factors in cases group, most common risk factors were hypertension, smoking, DM and dyslipidemia (62%, 62%, 54% & 4% respectively) with male preponderance in cases and control groups. Mean Platelet count in cases & controls were 260120±70954 SD & 218020±60845.64 SD respectively with significant statistically (p<0.0002). Mean platelet volume in cases (11.36±0.97 SD) & in controls (9.27±0.78 SD). PDW in cases (15.42±2.79 SD) & in controls (12.74±1.45SD). In both the parameters, difference was found to be statistically significant (p<0.0001). The difference between mean PCT of cases (0.3±0.08 SD) & of controls (0.29±0.05 SD) was not statistically significant (p>0.05).

CONCLUSION: To conclude, in our study that ICH patients having significant higher values of MPV, PDW in cases as compare to controls groups and reason postulated to increase in MPV and PDW in cases due to acute inflammation response in ICH patients and ongoing chronic illness. With highest risk factors found in ICH cases were hypertension, smoking, and majority were males.

KEYWORDS

INTRODUCTION:

Stroke is 5th leading cause of death in world that imposes the greatest burden of disablily-adjusted life years (DALYs) of all neurological disorders. This increase is estimated to be increase in 71·7% of DALYs lost due to stroke in patients younger than 75 years old[1] In India the estimated adjusted prevalence rate of Stroke range from 84-262/100,000 in rural to 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 all documented in a recent population based studies.[2]

ICH which is 20% of all stroke patient having subtle platelet dysfunction associated with progression and larger size in ICH.[3] Besides common risk factors of ICH such as age and hypertension, the intensity of anticoagulation, previous ischemic stroke, and the presence of cerebral vasculopathies are associated with a greater risk of ICH.[4]

Fewer studies have been done regarding platelet dysfunction in ICH patients. This study is designed to determine platelet function in terms of platelet indices in cases of spontaneous intracerebral bleed and its correlation with severity of stroke.

MATERIAL AND METHODS:

The hospital based case-control study was conducted in 50 cases of ICH patients which were NCCT head proven and 50 controls who admitted in department of medicine of VMMC and SAFDARJUNG HOSPITAL, NEW DELHI.

NCCT head was carried out for all suspected cases of stroke by Siemens Somatom Emotion 6®.Then severity of stroke assessed by NIHSS SCORE. A proper history, informed consent either from patient or relatives taken.

Blood sample collection: 5 ml venous peripheral blood collected in EDTA anti-coagulated tubes at the time of admission and processed within 2 hours of collection by using Sysmex XT 2000 I hematology automated analyser.

RESULTS:

This study was conducted in department of medicine and department of hematology to study clinical profile, risk factors and platelet indices in spontaneous ICH patients which was diagnosed by NCCT head. 50 cases of ICH and 50 controls were included after fulfilling the inclusion and exclusion criteria and giving consent.

Age of cases and controls group were above 40 years with maximum in age group of 51-60 years. The mean age of cases was 55.86 ±7.1 years, while in controls it was 54.44 ±9.63 years.(table 1)

TABLE 1.

Age distribution in cases and controls

AGE GROUP	CASES	CONTROL
1)=40	1 (2.00%)	2 (4.00%)
2)41-50	12 (24.00%)	18 (36.00%)
3)51-60	22 (44.00%)	20 (40.00%)
4)61-70	15 (30.00%)	7 (14.00%)
5)>70	0 (0.00%)	3 (6.00%)
Total	50 (100.00%)	50 (100.00%)

Mean age in cases and controls

AGE	Case	Control	P value
Mean ± Stdev	55.86 ± 7.1	54.44 ± 9.63	0.138

In cases, males were 35 (70%) and females were 15(30%), while in controls males were 27 (54%) and females were 23(46%) shown in table 2.

TABLE 2.

SEX	CASES	CONTROLS
FEMALE	15 (30.00%)	23 (46.00%)
MALE	35 (70.00%)	27 (54.00%)
TOTAL	50 (100.00%)	50 (100.00%)

When risk factors were assessed in cases found that hypertension, smoking and DM were commonest risk factors which was 31(62%), 31(62%), 27(54%) respectively. Table 3

TABLE 3:

RISK FACTORS	FREQUENCY	PERCENTAGE
HYPERTENSION	31	62.00%
DIABETES	27	54.00%
SMOKING	31	62.00%

Platelet indices individually were studied in cases and controls groups

which found that platelet count, MPV and PDW were significantly higher in cases group as compared to controls. Platelet count in cases and controls were 260120 ±70954.61 and 210820±60845.64 respectively which was stastically significant p value 0.0002 but within normal range. table 4.

TBALE 4. Platelet count in cases and controls.

PLATELET COUNT	CASES	CONTROLS	p value
Mean ± Stdev	260120 ± 70954.61	210820 ± 60845.64	0.0002

MPV in cases was higher (11.39±0.97) then in controls (9.27 ± 0.78) with p value <0.0001.table 5.

TABLE 5.MPV in cases and controls.

MPV	CASES	CONTROL	p value
Mean ± Stdev	11.36 ± 0.97	9.27 ± 0.78	<.0001

PDW in cases was 15.42±2.79 and in control groups was 12.74±1.45 (p value <0.0001) table6.

TABLE 6.PDW in cases and controls

PDW	CASES	CONTROLS	p value
Mean ± Stdev	15.42 ± 2.79	12.74 ± 1.45	<.0001

PCT in cases was 0.3±0.08 and in control group was 0.29±0.05 which found to be statistically non-significant with p value >0.05.

Platelet indices were also assessed according to risk factors found to be non-significant.

DISCUSSION :
Stroke, which remains the third leading cause of death after heart disease and cancer in developed countries. Intracerebral hemorrhage remains a grave medical emergency with high morbidity and mortality. Outcome in ICH (Intracerebral hemorrhage) patients still remains poor with no specific treatment.[5]

The present study was undertaken to study the risk factors, clinical profile and to compare the platelet indices in the ICH patients and control groups and to find out correlation, if any, between platelet indices and stroke severity which was assessed by NIHSS score.

Majority of patients belonged to age group of 51-60 years both in cases and controls. According to Rajiv B Pandya et al[6] study maximum number of cases 38 (76%) out of 50 were between the age group 45 to 74 years and age ranged from 35 to 74 years.

A.K.Thacker[7] et at reported, out of 50 cases of ICH (78%) were in age group of 41-70 years and age ranged from 16-85 years, in our study age ranged from 40 to 79 years in which 22 (44%) were in age group of 51-60 years.

Number of males and females were 35(70%) and 15(30%) in cases respectively and 27(54%) and 23(46%) in controls respectively with p value >0.05.This result was in concordance with study done by Rajiv B Pandya et al[6] who stated that ICH was most common in males. Jamil et al where he showed age and sex were not associated with the outcome of ICH (Intracerebral hemorrhage) patients.

Mean age group in cases were 55.86± 7.1 years (15 females and 35 males) and in control group were 54.44 ±9.63 (23 females and 27 males) with p value 0.138.

our results showed similar correlation with study done by F.Mayda-Domac[8] et al who stated mean age for hemorrhagic stroke was 62.2±13.1yrs (123males and 85 females), control groups included 208 subjects with a mean age of 63.2±10.7 yrs (123 males and 85 females) with p value 0.97.

In this study, hypertension in 31(62%) and smoking 31(62%) and DM 27(54%) and de-arranged lipid profile 4%(cholesterol >200) were commonest risk factors in ICH patients.

Rajiv B Pandya et al[6] and Nilsson et[8] all reported hypertension as a commonest risk factor in ICH. Smoking was second most common risk factor as 62% cases in our study which showed similar results as studied by Craig S anderson[7] who reported history of smoking in

29% (15 cases) of patients and ex-smoking in 19% (10 cases) of patients out of 60% (30 cases) cases of ICH.

The prevalence of diabetes in our study in ICH cases were quite high 24/50 while some studied Juvela et at[9] reported diabetes mellitus in only 14 out of 156 patients with ICH (9%) showed lower prevalence of DM. The higher percentage of prevalence of diabetes mellitus in our study could be due to higher prevalence of diabetes mellitus in general Indian population. One study done by Ferhat et al[10] also showed 20 patients out of 54 patients were diabetes.

Platelet count in cases (260120±70954) and in controls (218020±60845.64)(p<0.0002). Although there is significant difference when statistically compared with control group, platelet count in cases in range of 260120±70954, which was normal in range as per our laboratory values.

F.Mayda Domac et al[8] stated platelet count in hemorrhagic group (247.1±76.9) and in controls (269±70)with p value =0.01 but there was no significant correlation found between volume and localization of hemorrhage and platelet count (p >0.05). Ziai WC et al[11] reported that platelet dysfunction was common among patients with ICH.

Platelet count was assessed with all risk factors with included in our study, Platelet count in hypertensive group was 267709.68 ± 70527.15, in diabetes group 250666.67 ± 79847.93 which was statistically non-significant with p value >0.05

This result in our study was in consonance with the findings by Akinsegum A et al[12] ,platelet count for the diabetics was 235.29±76.81*109/L and controls, 211.32±66.44*109/L. There was a statistically significant difference in platelet counts of diabetics and healthy controls p =0.038. This difference was not significant when subjected to statistical testing. (p=0.593). The discordant result in this study may be accounted for by the fact that the majority of diabetics utilized for this study had been on treatment and in particular antiplatelet medications like clopidogrel varying durations.

Platelet count in smokers 256967.74±69971.65 and according to gender distribution in our study was in males and females 257714.29±65980.64 and 265733.33±83666.4 respectively none of was found to be statistically significant p value >0.05.

Our result was accordance to the study done by Shenwai et al, [13] who reported statistically significant increase in the platelet aggragbility (P< 0.01 & Z >2) and change in the platelet count was statistically insignificant. Number of patients were 70 [smokers (n=35) & non-smokers (n=35)] between the age group 26-40 yrs.

Mean platelet volume (MPV) in cases (11.36±0.97) was found to be higher than in controls (9.27±0.78) (p<0.0001). Similar results accordance to our study found by Adalet et al and Smith et al.

Adalet et al[14] observed that MPV in ICH (8.33 ± 1.27) and in control group (7.76 ± 1.14) (p=0.018). This increased of MPV in ICH patients may point to a disorder in the platelet function.

Smith et al[15] found a non-significant increase in p-selectin levels and slightly elevation of MPV after hemorrhagic stroke and suggested that these findings have reflected pre-existing ischemic vascular disease or other vascular risk factors. Platelet aggregation was found to be decreased in patients with acute hemorrhagic stroke.

Bath et al[16] reported that a higher measurements of MPV was primarily associated with ischemic stroke but there was no association between MPV and hemorrhagic stroke.

MPV when compared with risk factors which discussed in our study. In hypertensive patients MPV was 11.46±1.1 which found to be statistically non-significant when compared with non-hypertensive group.

Ozgur Surgit et al[17] showed that MPV were higher in patients with resistant hypertension than in controlled hypertensive and non-hypertensives with p value <0.001(n= 279 patients) Similar results were obtained by Coban E et al.[18]

In diabetes, MPV was 11.34±1.21 and in non-diabetes group, it was

11.38±0.62 which found to be statistically non-significant with p value >0.05.

Zuberi et al[19] compared MPV in patients with diabetes (105), patients with impaired fasting glucose and in non-diabetes (106). Comparison of MPV for the three showed statistically significant intergroup and intragroup difference, with MPV being higher in diabetes. Mean MPV was significantly higher in the diabetic group compared to the controls (9.94 ± 1.07 fl versus 9.36 ± 0.96 fl; p=.00003). High MPV in diabetics may indicate platelet hyperactivity, which may contribute to the vascular complications of type II DM

Kodiatte TA et[20] al also showed that MPV was higher in diabetes (300 patients) versus controls 8.29 ± 0.74 fl versus 7.47 ± 0.73 fl respectively and this association was found to be statistically significant with *p*= 0.001

However, Akinsegum A et al[12] did not find any significant association between MPV and diabetes(200 DM patients). MPV for the diabetics was 8.69±0.67 fl and in controls, 8.91±0.80 fl. in a study conducted in Lagos, Nigeria.

In smokers, MPV was 11.18±0.89, but found to be statistically non-significant with p value >0.05.

In the study conducted by Butkiewicz et al [21], smoking (27% patients smoker) was not found to have any statistically effect on MPV.

In males MPV was 11.28±0.9 and in females 11.53±1.15 with p value >0.05. Amira et al [22] did not find significant difference in MPV according to gender.

F.Mayda-Domac et at[8] also reported no association between MPV and platelet count in hemorrhagic stroke with p>0.05. Ferhat et al[20] reported that MPV have prognostic impact on ischemic stroke but did not have any prognostic impact on hemorrhagic stroke.

PDW in cases (15.42±2.79) and in controls (12.74±1.45) (p<0.0001). PDW was assessed with all risk factors with included in our study, PDW in hypertensive group was 15.68±3.17, in diabetes group 15.72±3.41 and in smoker 14.91±2.47. In males PDW was 15.27±2.6 and in females 15.78±3.26, but none of them found to be statistically significant with p value >0.05. Ferhat et al[11] didn't observe any prognostic relationship between number of platelets and PDW in hemorrhagic stroke. Toghi et al,[24] in their study, reported a decrease in PDW in acute and sub-acute phase of lacunar stroke. The significance of platelet indices associated with spontaneous intracerebral hemorrhage had not been studied extensively.

PCT in cases (0.3±0.08) and in controls (0.29±0.05) and the difference was found not be statistically significant (p>0.05).PCT was assessed with all risk factors with included in our study, PCT in hypertensive group was 0.3±0.08 vs in non-hypertensive group was 0.28±0.09, diabetes group vs non-diabetes 0.29±0.1 vs 0.31±0.07, in smoker vs non-smokers 0.29±0.09 vs 0.3±0.08 and in males 0.29±0.08, in females 0.3±0.1 with non-significant p value >0.05.

PCT is a measure of the total platelet mass and may come across to be more clinically useful than being just an additional value to the laboratory test.

According to Akpinar et al,[25] PCT reported to be in higher levels in patients with coronary artery disease, slow coronary flow. Among the platelet indices, only PCT was an independent predictor of slow coronary flow on the basis of a multivariate logistic regression analysis of all parameters (platelet count, MPV, PDW and PCT).

To the best of our knowledge, no studies have be done regarding association of PCT and intracerebral hemorrhage patients.

In another study done by J.Du et al[26] showed that neither MPV nor platelet count has significant association with prognosis of hemorrhagic stroke. The association of MPV and platelet count with occurance and prognosis of stroke have not been fully clarified.

F.Mayda-Domac[8] didn't observe an association between MPV and hemorrhagic stroke, there was a negative and significant correlation between platelet count and hemorrhagic stroke (p=0.001),but no

association found with MPV (p>0.05). MPV and platelet count were not statistically significant related to etiological subgroups, localization and size of the infarct and hemorrhage (p>0.05). Hemorrhagic group platelet counts (p=0.001, OR-1.004,95%CI) and ischemic group MPV (p=0.13,OR=1.02,95%CI) were in correlation with worse outcome.

Although the effects of dysfunction or number of platelets in the pathophysiology of hemorrhagic stroke are not fully understood, platelets do play an important role in pathophysiology of stroke. The relationship between MPV and severity and prognosis of stroke still controversial. There are several studies indicating the prognostic impact of MPV, while other studies report no relationship between MPV and prognosis of stroke.

REFERENCES:

1. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishanamurthi R, Chugh S, et al."Global burden of stroke and risk factors in 188 countries during 1990-2013: A Systematic Analysis for Global Burden of Disease Study 2013". Lancet. 2016; 15:892-893.
2. Pandian JD, Sudhan P.Stroke Epidemiology and Stroke Care Services in India. J Stroke. 2013; 15: 128-134.
3. Ziai WC, Torbey MT, Kickler TS, Oh S, Bhardwaj A, Wityk RJ. J Stroke Cerebrovascular Disease. 2003; 12: 201-6.
4. Veltkamp R, Rizos T, Horstmann S, Veltkamp R, Rizos T, et al,editors. Pletelet count and function in spontaneous intracerebral hemorrhage. 2013; 39:963-71.
5. Celikbilek A, Goksel B K, Zararsi z G, Benli S. Spontaneous intra-cerebral hemorrhage: A retrospective study of risk factors and outcome in a Turkish population .J Neurosci Rural Pract. 2013; 4(3): 271–277.
6. Nileshkumar M , Pandya R, V Vaghani, Mehul R Marwadi, Gheewala GK. National Journal of Medical Reasearch. A Study On Clinical Profile, Risk Factors in Hypertensive intracerebral Heamorrhage. 2013; 3:381-4.
7. Thacker AK, Radhakrishna K: Clinical and computed tomography analysis of intracerebral hemorrhage. JAP.I 1991;39(4):317-319.
8. Mayda-Domaç F, Misirli H, Yilmaz M. Prognostic role of mean platelet volume and platelet count in ischemic and hemorrhagic stroke. J Stroke Cerebrovasc Dis.2010;19(1):66-72.
9. Juvela S, Hillbom M : Risk factors for spontaneous intracerebral hemorrhage. Stroke. 1995; 26: 1558-1564.
10. Ferhat I, Ozugar D, Gluen M. Prognostic Relationship Between Complete Blood Count Parameters and Transient Ischemic Attack, Ischemic Stroke and Hemorrhagic Stroke. Turk Geriatri Dergisi. 2014;17(1):23-28.
11. Bath P, Algert C, Chapman N. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke. 2004 ;35 :622-626.
12. Smith NM, Pathensali R, Bath PMW. Platelet and stroke. Vasc Med. 1999;4:165-172.
13. Ziai WC, Torbey MT, Kickler TS, Oh S, Bhardwaj A, Witkey RJ. Journal of Stroke . Platelet count and function in spontaneous intracerebral hemorrhage. 2003; 12:201-206.
14. Akinsegun A, Olusola DA, Sarah JO, Olajumoke O, Adewami A, Majeed O, et al.mean platelet volume and platelet counts in type 2 diabetes mellitus on treatment and non-daibetes mellitus controls in Lagos,Nigeria. Pan afr Med J.2014;18:42.
15. Shenwai M R, Aundhakar N.V. Study of effect of cigratte smoking on platelet count and platelet aggregability in young male smokers. IJBMS.2017;7:235.
16. Adalet A, Cevik M V, Vzar E, Acar A. The increase in mean platelet volume in patients of intracerebral hemorrhage.Turk J Neurol.2012;18(2):54-56.
17. Surgit O, Pusuroglu H, Erturk M, Akgul O. Assessment of mean platelet volume in patients with resistant hypertension, controlled hypertension and normotensives. Eurasian J Med.2015;47(2):79-84.
18. Coban E, Yazicioglu G, Berkant AA, Akcit F. The mean platelet volume in patients with essential and white coat hypertension. Platelet. 2005;16:435-438.
19. Zuberi BF, Akhtar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non diabetes subjects. Singapore Med J.2008;49:114.
20. Kodiatte TA, Manikyam UK, Rao SB, Reddy M, Lingaish HK. Mean platelet volume in type 2 diabetes mellitus. J Lab Physicians.2012;4:5-9.
21. Butkiewicz AM, Kemona-Chetwik I, Dymicka-Piekarsaka V, Matowiska-Karna J, Kemona H, Radziwon P. Does smoking affect thrombocytosis and platelet activation in women and men. Adv Med Sci.2006;51:111-120.
22. Amira M, Ghada A M.Mean platelet volume and mean platelet volume/platelet count ratio as a risk stratification tool in the assessment of severity of acute ischemic stroke. Alexandria Journal of Medicine.2017;53:67-70.
23. Toghi H, Suzuki H, Tamura K, Kimura B. Platelet volume, aggregation and adenosine triphosphate release in cerebral throm-bosis. Stroke. 1991; 22(1):17-21.
24. Du J,Wang Q, Quan H. Association of mean platelet volume and platelet count with the development and prognosis of ischemic and hemorrhagic stroke. International Journal Of Laboratory Hematology.2016;38(3):233-239.
25. Akpinar I, Sayin MR, Gursoy YC, Aktop Z, Karabag T, Kucuk E, et al. Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. J Cardiol. 2014;63:112-118.