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To Observe the Mean Platelet Volume and Mean Platelet Volume / Platelet Count Ratio in the Patients of Acute Ischemic Stroke

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Abstract: ***Purpose: To observe mean platelet volume & mean platelet volume/platelet count ratio in the patients with Acute Ischemic Stroke. Methods: This is a cross sectional, single centre study, where in data about 94 patients with acute ischemic stroke diagnosed with the help of imaging NCCT head or MRI Brain admitted within 7 days of stroke, examination was done, NIHSS and modified Rankin scale was evaluated, MPV and Platelet count of the cases was recorded. Statistical significance was defined as p value <0.05. Results: Majority of the patients were >71 years of age (46.81%) and were males (69.58%).93.62 % patients had acute ischemic stroke of thrombotic type, 50.00% had right sided weakness and 44.68% had history of hypertension while 26% had history of diabetes mellitus. For assessment of disability of stroke by modified Rankin scale majority had a score of 4 (30.85%) and 52.13% had moderately severe stroke (NIHSS 11 - 20). Both MPV and MPV/PC ratio was found to be significantly higher in patients with thrombotic stroke and MPV/PC ratio was even found to be significantly associated with both modified Rankin scale and NIHSS score (p <0.05). Conclusion: MPV and MPV/PC ratio can be used as a marker for predictability of acute ischemic stroke and elevated MPV/PC ratio was found to be positively associated with modified Rankin scale and NIHSS and hence can be a marker for predicting disability and severity of stroke. Certain associations were found but further studies are needed on a larger sample size to explore more on these findings.***

Keywords: National institute of health stroke scale (NIHSS), Mean Platelet volume (MPV), Mean platelet volume/Platelet count (MPV/PC)

1. Introduction

Stroke is the most prevalent neurological condition globally and the most frequent neurological condition overall. Stroke, additionally referred to as Cerebrovascular Accident (CVA), is a term that was coined in 1599 and comes from the Greek words meaning ‘struck down’ [1]. Stroke is characterized by quickly evolving clinical indicators of focal (or global) disruption of cerebral function, with no evident cause other than vascular origin, and symptoms that persist 24hours or more or result in death. [2].

87percent of strokes are ischemic, though they can also be caused by haemorrhage. The primary causes of ischemic stroke are thromboembolism & atherothrombosis. Crucial elements of thrombosis platelets are vital to the disease and can be triggered by inflammation, platelet rupture, and other factors [3].

MPV (Mean platelet volume) has been widely used laboratory marker that indicates platelet function along with activation. MPV is positively associated with platelet reactivity as it measures the average size of platelets. Large platelets contain more granules, which make them more reactive, generate more prothrombotic factors, display greater accumulation to ADP (adenosine diphosphate), collagen or else adrenaline, as well as release more thromboxane A2 (TxA2). Patients suffering from acute myocardial infarction (MI) & stroke have been found to have greater MPV values than control people. Furthermore, it has been demonstrated that MPV can predict stroke in patients who have experienced prior cerebrovascular episodes, even if those events occurred 3.9 years prior. Furthermore, an elevated MPV/platelet count (MPV/PC) ratio is linked to hepatocellular carcinoma, anaemia, and MI, and it is a risk factor for a number of illnesses. A greater MPV may result in a worse outcome, and it is also linked to the severity and prognosis of stroke. In accordance with reports, a novel marker called the MPV/PC ratio can be utilized for predicting 90day outcome of LAA stroke. [4 - 7].

Studies have demonstrated that increased MPV & MPV/PC ratio have been connected to a prothrombotic state and an elevated danger of several cardiovascular events, that include MI, deep vein thrombosis, & atherosclerosis. Given role of platelets in the pathophysiology of AIS, exploring the association among MPV & MPV/PC ratio and AIS may offer valuable insights into stroke pathogenesis and potential prognostic implications.

The goal of this investigation is to observe Mean platelet volume along with MPV/PC ratio in patients of AIS (acute

ischemic stroke) in the Himalayan belt region and also to assess severity of AIS using Rankin scale & functional disability using NIHSS (National Institutes of Health Stroke Scale).

2. Materials and Methods

This cross - sectional, observational investigation had been executed in the HIMS (Himalayan Institute of Medical Sciences), Swami Ram Nagar, Dehradun, Uttarakhand, India, over 12month period following acquisition of the patient's written informed consent as well as institutional ethics committee approval. A total of ninety - four newly diagnosed, hospitalized within 7days of onset of stroke above 18years of age with CVA were included in research. AIS diagnosis had been made on the basis of NCCT/MRI brain. Other types of stroke, such as haemorrhagic, along with conditions like pregnancy, myocardial infarction, peripheral vascular disease, any trauma or malignancy, had been excluded from the research.

Demographic data that include sex, socioeconomic status, residence & age had been collected. Detailed history of all enrolled patients was taken. A detailed clinical examination was accomplished. NIHSS, along with modified Rankin scale, was calculated to assess for functional disability and severity of stroke. Cases were subjected to relevant investigations, including complete hemogram with Platelet count & mean platelet volume. Imaging studies in form of NCCT head or MRI brain were done.

Data was analysed by SPSS® Version 22 software. Fischer's exact test, as well as the chi square test, have been employed to compare qualitative data and find correlations between various factors. When comparing regularly distributed qualitative data, the Student's T test was employed. For statistical significance, $P<0.05$ was utilized.

3. Results

The demographic characteristics of patients were suggestive that majority of individuals were in the age group >71 years, comprising 46.81% of the sample size, with male patients (69.58%) more than female patients (59.57%). On assessing for the cause of stroke majority were of thrombotic type (93.62%), and embolic stroke with atrial fibrillation was 6.38%. (Table 1, 2, 3)

Table 1: Demographic Characteristics by Age Group

Age Group (Years)	Number (N=94)	Percentage (%)
18 - 30	1	1.06
31 - 40	5	5.32
41 - 50	6	6.38
51 - 60	16	17.02
61 - 70	22	23.40
>71 years	44	46.81
Total	94	100

Table 2: Demographic Characteristics by Gender

Gender	Total (N=94)	Percentage (%)
Male	56	69.58
Female	38	59.57

Table 3: Types of Strokes

Type of Stroke	Number of Patients (n=94)	Percentage (%)
Thrombotic Stroke	88	93.62
Embolic Stroke with Atrial Fibrillation (AF)	6	6.38
Total	94	100

On clinical examination, among stroke patients, weakness occurred predominantly on the left side in 44 individuals (46.81%) on the right side in 50 individuals (50.00%). Regarding past medical history, 42 individuals (44.68%) had a history of hypertension, while 27 individuals (28.72%) had diabetes mellitus. Stroke was reported in 1 case (1.06%), and 6 individuals (6.38%) had experienced Transient Ischemic Attacks (TIA). (Table 4)

Table 4: Clinical Characteristics of Study Participants

Clinical Characteristics	Total Sample (N=94)	Percentage (%)
Site of weakness		
Left	44	44.00
Right	50	50.00
Past History of		
Hypertension	42	44.68
Diabetes mellitus	27	28.72
Stroke	1	1.06
Transient Ischemic Attack (TIA)	6	6.38

When assessing for functional disability of stroke by modified ranking scale, majority of patients (30.85%) had a score of 4 followed by score of 3 (27.66%) score of 5 (22.34%) with approx.14% of patients had slight disability, and 3% of patients exhibited no disability. (Table 5)

Table 5: Modified Rankin Scale for Functional Disability

Ranking Score	Number of Patients (N=94)	Percentage (%)
0 (No symptoms)	0	0.00
1 (No significant disability)	3	3.19
2 (Slight disability)	13	13.83
3 (Moderate disability)	26	27.66
4 (Moderately severe disability)	29	30.85
5 (Severe disability)	21	22.34
6 (Death)	2	2.12

The severity of stroke was assessed by using NIHSS, where 2.12% of participants have mild strokes (NIHSS 0 - 4), 31.91% have moderate strokes (NIHSS 5 - 10), 52.13% have moderately severe strokes (NIHSS 11 - 20), and 13.82% experience severe strokes (NIHSS >20). (Table 6)

Table 6: NIHSS Grading for Severity of Stroke

NIHSS Score	Number of Patients (N=94)	Percentage (%)
0 - 4	2	2.12
5 - 10	30	31.91
11 - 20	49	52.13
21 - 42	13	13.82

For assessment of MPV in different types of ischemic stroke, it was found that mean MPV was significantly greater in individuals with thrombotic lesions in comparison with patients with embolic stroke with AF ($p<0.05$). Patients with thrombotic stroke exhibit a mean MPV of 10.68 ± 1.66

femtoliters (fl), while those with embolic strokes and atrial fibrillation (AF) have a slightly lower mean MPV of 9.03 ± 1.74 fl. (Table 7)

Table 7: Comparison of MPV in Patients on type of stroke

	MPV (Mean ± SD)	p value
Thrombotic stroke	10.68 ± 1.66	<0.05
Embolic stroke with AF	9.03 ± 1.74	

The mean MPV/PC had been substantially greater in patients with thrombotic stroke in comparison with embolic stroke (p <0.05). Individuals with thrombotic stroke exhibit mean MPV/PC ratio of 0.0078±0.0026, while those with embolic strokes and atrial fibrillation (AF) had mean MPV/PC ratio of 0.0056±0.0003. (Table 8)

Table 8: Comparison of MPV/PC Ratio in Patients

	MPV/PC Ratio (Mean ± SD)	p value
Thrombotic stroke	0.0078 ± 0.0026	<0.05
Embolic stroke with AF	0.0056 ± 0.0003	

On assessing the relationship between NIHSS and MPV/PC ratio, it had been discovered to be significantly associated, The MPV/PC ratios for NIHSS score ranges were as follows: 0.0061 ± 0.0002 for scores 0 - 4, 0.0068 ± 0.0037 for scores 5 - 10, 0.0064 ± 0.0054 for scores 11 - 20, and 0.0066 ± 0.0013 for scores >20, no significant relationship was found between NIHSS and MPV. (Table 9)

Table 9: Relationship between NIHSS Score and MPV/PC Ratio

NIHSS Score Range	Mean MPV/PC Ratio	p value
0 - 4	0.0061 ± 0.0002	<0.05
5 - 10	0.0068 ± 0.0037	
11 - 20	0.0064 ± 0.0054	
>20	0.0066 ± 0.0013	

Similarly, on assessing the relationship between modified Rankin scale and MPV/PC ratio, it had been discovered to be significantly associated, MPV/PC ratios for different Rankin Scores were as follows: 0.0069 ± 0.0023 for Score 0, 0.0061 ± 0.0010 for Score 1, 0.0065 ± 0.0046 for Score 2, 0.0067 ± 0.0009 for Score 3, 0.0060 ± 0.0087 for Score 4, 0.0063 ± 0.0012 for Score 5, and 0.0066 ± 0.0094 for Score 6, no significant relationship was found between modified ranking scale and MPV. (Table 10)

Table 10: Relationship between Rankin Score and MPV/PC Ratio

Rankin Score	Mean MPV/PC Ratio	p value
0	0.0069 ± 0.0023	<0.05
1	0.0061 ± 0.0010	
2	0.0065 ± 0.0046	
3	0.0067 ± 0.0009	
4	0.0060 ± 0.0087	
5	0.0063 ± 0.0012	
6	0.0066 ± 0.0094	

4. Discussion

The rationale for studying the MPV & MPV/PC ratio in patients with AIS lies in potential of these haematological parameters to serve as valuable indicators of platelet activation and overall thrombotic status. One of the leading causes of morbidity as well as mortality globally is AIS, often credited to the occlusion of cerebral blood vessels by thrombi. Platelets show a crucial part in the initiation and propagation of thrombosis, and alterations in their size and function may reflect the underlying pathological processes.

The MPV, representing the average size of circulating platelets, is considered a marker of platelet activity. Raised MPV has been linked with enhanced platelet reactivity and is acknowledged as potential risk factor for cardiovascular events. Additionally, MPV/PC ratio reflects both platelet size and concentration, offering a comprehensive perspective on platelet dynamics. Investigating these parameters in the context of AIS may provide insights into the extent of platelet activation and the thrombotic burden in affected individuals.

It was once believed that platelet volume was connected to platelet age, but this has since been disproven. It is now thought that platelet volume is determined during thrombopoeisis. Given the fact that platelets have a lifespan of around 8 - 10days, that samples had been collected within 48hours of onset of stroke, The elevated MPV seen in ischemic stroke patients likely present prior to the incidence of stroke. This contributes to a prothrombotic state and a higher risk of stroke. There are a few possible reasons for thrombomegaly prior to stroke, such as platelet consumption, marrow stimulation, and congenital thrombomegaly. Ischaemic stroke bears similarity to myocardial infarction in that platelets may change before the acute thrombotic event. This means that the elevation of MPV may increase the risk of ischaemic stroke. [8 - 11]

The size of platelets is influenced by cytokines like interleukin - 3 or interleukin - 6 at the level of the progenitor cell (megakaryocyte). Recent studies have suggested that these cytokines can cause an increase in megakaryocyte ploidy, which results in the production of bigger and more reactive platelets. As a result, it is reasonable to assume that a proinflammatory state prior to a cerebrovascular event may lead to a greater MPV and a prothrombotic condition. [12 - 14]

AIS is associated with higher MPV & MPV/PC ratios than healthy people. Both during the acute phase of AIS and later, as the patient's illness worsens, a greater MPV/PC ratio has been identified. [15] Rising infarct size is linked to even higher MPV & MPV/PC ratio values. Measurements of MPV & MPV/PC ratio are easy, quick, and very economical laboratory indicators for risk assessment and cerebrovascular stroke early detection. Therefore, the MPV/PC ratio can be utilized as a clinically useful metric for early diagnosis and as a direct indicator of the connection among infarct volume as well as clinical severity of AIS. It has also been demonstrated that stroke patients with low platelet counts die at a higher rate. These findings suggest that MPV/PC may have a role in genesis or else deterioration of stroke outcomes.

The importance of utilizing MPV and MPV/PC ratios in CVA individuals for early identification of clinical severity of stroke was highlighted by our research, which revealed that these ratios are greater in stroke patients with a higher CVA score (≥3) on the Rankin scale than in stroke patients with a

lower CVA score (0–2). This suggests that the blood may release more reactive platelets in reaction to mediators released by peripheral ischemia regions.

Findings from our present study illustrate a significant correlation between the NIHSS score range MPV & the MPV/PC ratio among individuals with AIS. NIHSS, an extensively employed clinical instrument for finding the severity of strokes, categorizes patients into distinctive score ranges predicated on the extent of neurological impairment. Our investigation delved into this relationship, unveiling a discernible pattern in the MPV, MPV/PC ratio across varying NIHSS score categories. It was found that as the stroke's severity increased, which was evaluated by NIHSS, MPV also increased and a significant association was found between the two. It was also worth noting that as the score increased, the ratio also increased, indicating the severity of stroke and its relation with higher MPV/PC ratio. This exploration of the association between NIHSS score ranges and MPV, MPV/PC ratio emphasizes complex relationship among platelet characteristics & the AIS severity. These findings not only provide valuable insights into the haematological markers associated with stroke severity but also pave the way for further research. Such research could hold the potential to inform risk stratification strategies and guide targeted therapeutic interventions in the clinical management of patients facing acute ischemic strokes. Importantly, our study's results diverged from those reported by Mayda - Domaç F et al., [16] emphasizing the need for further exploration and the consideration of potential variables that may contribute to such discrepancies in the literature but our results align with a study conducted by Lok U et al., [17] reinforcing the consistency and relevance of these observed patterns across different cohorts and settings.

Understanding relationship among MPV, MPV/PC ratio, along AIS could have clinical implications. It may aid in risk stratification, prognosis assessment, and the development of targeted therapeutic strategies aimed at modulating platelet function. Therefore, this study seeks to contribute to the growing body of knowledge concerning haematological biomarkers in acute ischemic stroke, ultimately advancing our ability to identify and manage individuals at heightened risk of thrombotic events.

5. Limitations

1) The exclusion criteria of the study did not have any conditions affecting the platelet count such as infections like Viral hepatitis, Malaria, any Autoimmune disease, Chronic liver disease or Idiopathic thrombocytopenia. However, during data collection, no such history was found in my subjects. [18]
2) Variation in platelet size due to time dependent platelet swelling in vitro utilizing EDTA as an anticoagulant.
3) It was not possible to evaluate the variability of platelet size during stroke evolutions since serial MPV measurements were not performed at various stages of stroke.
4) Comparison of haematological parameters in patients of acute ischemic stroke was done against their established and previously reported values in literature for which a descriptive cross sectional study design was chosen however, comparing against age and gender matched controls in the same population could have yielded better picture. [19]

6. Conclusion

The study provides a comprehensive analysis of demographics, stroke types, clinical characteristics, and platelet indices in stroke patients. While certain associations were identified, further research may be needed to explore these relationships in larger populations and diverse settings.

Statements and Declarations

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Competing Interests
The authors have no relevant financial or non - financial interests to disclose**.**

Author contributions
SK, MM and AB contributed to the study conception and design. VM and AB carried out the clinical assessment. All authors analyzed and interpreted the data. AB drafted the initial manuscript. SK, MM and AB revised the manuscript for its intellectual content. All authors read and approved the final manuscript.

Data availability
Data are available from the corresponding author on reasonable request.

Ethics approval
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics committee of Swami Rama Himalayan University, Dehradun, India. (SRHU/HIMS/ETHICS/2024/39 dated 02/03/2024)

Consent to Participate
Informed consent was obtained from all individual participants included in the study.

Consent to publish
The authors affirm that human research participants provided informed consent for publication of their data.

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