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Corresponding Author: Dr Nayanjyoti Bez Email: nayanj_bez@yahoo.co.in

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ISCHAEMIC STROKE AND ITS CORRELATION WITH CAROTID INTIMA MEDIA THICKNESS

Mridu Paban Rajkhowa¹, Nayanjyoti Bez², Abdul Barik Ahmed³, Balmiki Datta⁴, Subrata Roy⁵

¹Post-PG Specialist, Harmen Sub Divisional Civil Hospital, Assam, India.

²Assistant Professor, Department of General Medicine, Fakhruddin Ali Ahmed Medical College & Hospital, Barpeta, Assam, India.

³Associate Professor, Department of General Medicine, Pragjyotishpur Medical College & Hospital, Guwahati, India.

⁴Professor and Head of Department Department of Pathology Fakhruddin Ali Ahmed Medical College & Hospital, Barpeta, Assam, India.

⁵Postgraduate Trainee, Department of General Medicine, Fakhruddin Ali Ahmed Medical College & Hospital, Barpeta, Assam, India.

ABSTRACT

Background: Ischaemic stroke, primarily caused by atherosclerosis and thrombosis, is a major health concern. Platelet activation plays a crucial role in stroke pathogenesis, and the large platelets, being nascent are postulated to be more thrombogenic. Thus, Platelet-Large Cell Ratio (P-LCR) may help in risk stratification in ischaemic stroke. Objective: This study examines the prevalence of elevated P-LCR in ischaemic stroke patients and its correlation with Carotid Intima Media Thickness (CIMT), a marker of atherosclerosis and the traditional risk factors of ischaemic stroke. Materials and Methods: A cross-sectional study of 70 patients with Ischaemic stroke was conducted. P-LCR was measured using an automated hematology analyzer, and CIMT was assessed via B-mode ultrasound. Statistical analysis included were Pearson's correlation and the Chi-square tests. Result: Elevated P-LCR was observed in 70% of patients. A significant positive correlation (r = 0.4432, p < 0.05) was found between P-LCR and CIMT. P-LCR was also found to be significantly associated with hypertension, smoking, and alcoholism. Conclusion: Elevated P-LCR is common in ischaemic stroke and correlates with CIMT, suggesting a role in atherosclerosis progression. Its association with varrious traditional stroke risk factors highlights its potential as a marker for stroke risk assessment.

INTRODUCTION

Stroke is sudden loss of neurologic function resulting from focal disturbance of cerebral blood flow due to ischemia or hemorrhage.

World Health Organization(WHO) put forward the definition stroke proposed in 1970 as, "Stroke is rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer, or leading to death, with no apparent cause other than of vascular origin".^[1] In global scenario, stroke finds its place as the second leading cause of death, which approximately results in 5.5 million fatalities annually, making it a significant public health concern that necessitates continued research and efforts to improve prevention, diagnosis, and treatment strategies.^[2] The impact of stroke extends beyond its high mortality rate, as it also leaves a significant

proportion of survivors with long-term disabilities,

with approximately 50% experiencing chronic impairments that significantly affect their quality of life and independence.^[3] In addition to its direct impact, stroke also increases the risk of developing other conditions such as seizures, experiencing falls, and suffering from depression. Furthermore, stroke is also a common cause of long-term functional impairments, with a significant proportion of survivors needing rehabilitaional care for at least three months period and up to 30% experiencing permanent disability.

In developing and middle-income countries like India, stroke is rapidly becoming a primary disease for premature death and disability, driven by a combination of change in demographic scenario and an increasing prevalence of crucial modifiable risk factors such as hypertension, diabetes, and smoking. This trend disproportionately affects the poor, who are not only more vulnerable for getting exposed to these risk factors but also face significant barriers in accessing affordable healthcare. The consequences of stroke are devastating, with the majority of survivors left to live with debilitating disabilities that require ongoing rehabilitation and long-term care. The economic burden of stroke falls heavily on families, who must bear the costs of care, often leading to financial hardship and even impoverishment. This perpetuates a cycle of poverty and health inequity, underscoring the need for urgent action to address the growing stroke epidemic in these regions.^[4,5]

Among the two major variants of stroke namely Ischemic and haemorrhagic stroke, the predominant one, ischemic stroke, which results when perfusion to the brain is obstructed, usually on account of a thrombosis or embolism, leading to neuronal death and resulting neurological deficits.^[6] Identifying individuals at high risk for ischemic stroke is essential for timely prevention and improved outcomes. Atherosclerosis and platelet activation are two critical underlying pathophysiological processes that contribute to the development of ischemic stroke.^[7,8]

Platelets, small blood cells without a nucleus are the key components in blood clotting, also can be attributed as an important factor in the development of ischemic stroke.^[9] In development of atherosclerosis, platelets can contribute to blood clot formation and vessel blockage, leading to ischemic events.^[10] Certain platelet indices, such as mean platelet volume (MPV) and platelet distribution width (PDW), have been explored as potential biomarkers of platelet activation and predictors of ischemic stroke risk.^[11]

In Complete Blood Count, along with other routine blood parameters platelet indices are commonly evaluated and usually ignored in common practice. Emerging evidence suggests that platelet indices may allow extensive clinical investigations focusing on the diagnostic and prognostic values in a variety of settings without bringing extra costs.^[12]

The platelet-large cell ratio (P-LCR), defined as the percentage of platelets in blood larger than 12 femtoliters (fL), is a novel platelet index that may reflect platelet activation and reactivity.[13] The Platelet Large Cell Ratio (P-LCR) is a valuable parameter obtained from routine hemogram tests, which measures the proportion of larger platelets that are more significantly associated with ischemic events. Specifically, P-LCR is calculated as the ratio of platelets with a volume exceeding 12 femtoliters (fL), indicating a larger and younger platelet population. These larger platelets contain more intracellular granules, rendering them more thrombogenic and potentially contributing to an increased risk of blood clot formation. As a result, P-LCR serves as a useful indicator for assessing thrombotic risk and may aid in the identification of individuals prone to cardiovascular events.^[14] Elevated P-LCR has been associated with various cardiovascular disorders, including coronary artery disease and peripheral artery disease.^[15] Elevated P-

LCR levels, are associated with increased circulating levels of cholesterol and triglycerides in the serum. This suggests that high P-LCR levels may serve as a marker for dyslipidemia, which is a prominent risk factor for various cardiovascular disorders. The correlation between P-LCR and serum lipid levels highlights the potential utility of P-LCR as a emerging tool for identifying individuals with dyslipidemia and potentially stratifying cardiovascular risk.^[16]

The P-LCR is calculated as the percentage of large platelets that have a volume more than 12fl and expressed as P-LCR = P-LCC/PLT (where P-LCC = Platelet Large cell count and PLT = Platelet count).

Carotid intima-media thickness(CIMT), is an ultrasound measurement of the carotid artery wall's inner layer thickness, has proven to be a dependable indicator of subclinical atherosclerosis and a predictor of future cardiovascular events, including ischemic stroke.^[17] The carotid arteries, responsible for supplying blood to the brain, are prone to atherosclerotic plaque buildup, and an increased CIMT is linked to a heightened risk of ischemic stroke.^[18] It has also been shown that CIMT was correlated to various cardiovascular risk factors such as age, obesity, high blood pressure etc.

In this study if a significant association between P-LCR and ischemic stroke is established and a correlation between P-LCR and CIMT is demonstrated, P-LCR could serve as a readily available and cost-effective marker for identifying individuals at high risk for ischemic stroke. Moreover, P-LCR may aid in stratifying stroke severity and predicting functional outcomes, facilitating personalized treatment strategies and resource allocation.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional study was conducted at Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH), Barpeta, from July 2023 to June 2024. It aimed to examine the relationship between platelet-large cell ratio (P-LCR) and ischemic stroke, as well as its correlation with carotid intima-media thickness (CIMT). 70 no.s of patients diagnosed with ischemic stroke admitted to the medicine ward or attending the OPD at FAAMCH were included in this study.

Inclusion and Exclusion Criteria

Inclusion

- 1. Patients of age more than or equal to18 years with clinical signs of focal neurological deficits.
- 2. NCCT Brain or MRI Brain confirming ischemic stroke.

Exclusion

- 1. Patients refusing consent.
- 2. Patients with haemorrhagic stroke.
- 3. Those with AES(Acute Encephalitis Syndrome) , head injury, intracranial malignancy,

metabolic encephalopathy, or other neurological conditions.

- 4. Patients with platelet disorders (e.g., thrombocytopenia, ITP etc.).
- 5. Patients with sepsis.

Data Collection and Investigations

Informed consent was obtained. Stroke diagnosis was based on history, clinical examination, and imaging. Data were collected using a structured proforma, including history of hypertension, diabetes, smoking, alcoholism, and coronary artery disease.

Investigations

- 1. CBC (including P-LCR levels).
- 2. Carotid artery Doppler (B-mode USG) to assess CIMT.
- 3. Routine tests: Renal/liver function, lipid profile, blood sugar, HbA1c.

Data Analysis

Data were analyzed using statistical methods. Descriptive statistics (mean, SD, percentages) summarized patient characteristics. Associations between P-LCR and stroke risk factors were assessed using chi-square tests (p<0.05 considered significant), and the correlation of P-LCR with CIMT was evaluated using Pearson's correlation coefficient.

Ethical Considerations

The study was approved by FAAMCH's Institutional Ethics Committee. Informed consent was obtained, ensuring confidentiality per the Declaration of Helsinki.

Operational definitions

Hypertension: "Hypertension is defined as a systolic blood pressure (SBP) of \geq 140 mmHg and/or a diastolic blood pressure (DBP) of \geq 90 mmHg" [American Heart Association (AHA). (2017)] or had a history of diagnosis of hypertension in the past or usage of anti-hypertensive medications.

Diabetes mellitus:"Diabetes is defined as a fasting plasma glucose (FPG) level of \geq 126 mg/dL (7.0 mmol/L) or a 2-hour plasma glucose level of \geq 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT), or a random plasma glucose level of \geq 200 mg/dL (11.1 mmol/L) in a patient with symptoms of hyperglycemia, or a hemoglobin A1c (HbA1c) level of \geq 6.5%." [American Diabetes Association (ADA). (2022)] or had a history of

diabetes diagnosis and using anti-diabetic medications.

Smoking: "Smoking is defined as the self-reported use of at least 100 cigarettes or other tobacco products (e.g., cigars, pipes, hookahs) in a person's lifetime, with current smoking status determined by asking, 'Do you currently smoke cigarettes or other tobacco products every day, some days, or not at all?" [Centers for Disease Control and Prevention (CDC). (2022).]

Dyslipidemia: "Dyslipidemia is defined as a fasting lipid profile showing one or more of the following: 1. Total cholesterol $\geq 200 \text{ mg/dL}$

2. Low-density lipoprotein (LDL) cholesterol \geq 130 mg/dL

3. Triglycerides $\geq 150 \text{ mg/dL}$

4. High-density lipoprotein (HDL) cholesterol <40 mg/dL for men or <50 mg/dL for women"

[National Cholesterol Education Program (NCEP) (Adult Treatment Panel III). (2002)]

Alcoholism: "Consuming ≥ 4 drinks/day (women) or ≥ 5 drinks/day (men) for ≥ 2 weeks, or experiencing ≥ 2 DSM-5 AUD criteria within a 12-month period." [National Institute on Alcohol Abuse and Alcoholism (NIAAA) and DSM-5 criteria]

Coronary artery disease: "CAD is defined as the presence of \geq 50% stenosis in one or more coronary arteries, or a history of myocardial infarction, coronary revascularization, or angina pectoris."[American Heart Association (AHA) and the American College of Cardiology (ACC)]

P-LCR level: According to the Practical Hematology Textbook 11th edition by Dacie and Lewis (pg:47) "all derived platelet parameters are highly specific to the individual technologies with different analyzers having different normal ranges." The automated analyzer of the laboratory of dept. of pathology (FAAMCH), has the normal range of P-LCR 11-45%. So, here P-LCR level >45% is taken as 'elevated'.

CIMT level: According to 2018 guidelines for the management of arterial hypertension by the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) a carotid intima media thickness > 0.9 mm is considered abnormal. Here, intima media thickness of either right or left common carotid artery(CCA) more than 0.9 mm is considered abnormal.

RESULTS

Risk factors	Yes		No		
	Frequency	%	Frequency	%	
Diabetes mellitus	36	51.43%	34	48.57%	
Hypertension	51	72.86%	19	27.14%	
Smoking	30	42.86%	40	57.14%	
Alcoholism	30	42.86%	40	57.14%	
Dyslipidemia	22	31.43%	48	68.57%	
Coronary artery disease	25	35.71%	45	64.29%	

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The table shows, out of total 70 participants, 51(72.86%) participants have hypertension which is the most prevalent risk factor, 36 (51.43%) participants have diabetes mellitus, 30(42.86%) participants have smoking and alcoholism as risk

factors, 25(35.71%) have coronary artery disease, 22 no. of participants (31.43%) have dyslipidemia.

Table 2: Distribution of the participants as per P-LCR level							
Platelet Large Cell Ratio	Frequency	Percent					
≤45%	21	30%					
>45%	49	70%					
Total	70	100					

Prevalence of elevated platelet large cell ratio (i.e. P-LCR>45%) level in patients of ischemic stroke in the study has been found to be 70% i.e. among the 49 individuals.

Table 3: Distribution of the participants according to carotid intima media thickness							
CIMT Group	Frequency	Percent					
CIMT ≤0.9	33	47.10%					
CIMT >0.9	37	52.90%					
Total	70	100					

In this study, CIMT has been found to be more than 0.9 mm in 37 patients i.e. 52.9% of the total participants, whereas 33 no of patients i.e. 47.1% have CIMT value below 0.9 mm.

Table 4: A	ssociation of P-LCR level	with age				
Age	P-LCR I	Level	Total		đf	D Voluo
Group	≤45%	>45%	Totai	χ2	ui	<i>r</i> - value
31-40 Yrs	3(4.29%)	2(2.86%)	5(7.14%)			
41-50 Yrs	1(1.43%)	5(7.14%)	6(8.57%)			
51-60 Yrs	5(7.14%)	14(20%)	19(27.14%)			
61-70 Yrs	5(7.14%)	10(14.29%)	15(21.43%)	8.34	6	0.214 ^{NS}
71-80 Yrs	6(8.57%)	7(10%)	13(18.57%)			
> 80 Yrs	1(1.43%)	11(15.72%)	12(17.15%)			
Total	21(30%)	49(70%)	70(100%)	1		
NSNT C CC	D 0.05					

^{NS}Not Significant P>0.05

For the 31-40 age group, 4.29% have P-LCR \leq 45%, while 2.86% have >45%. In the 41-50 age group, 1.43% have P-LCR \leq 45%, with 7.14% having >45%. The 51-60 age group shows 7.14% with P-LCR \leq 45% and 20% with >45%. Among those aged 61-70, 7.14% have P-LCR \leq 45%, and 14.29% have

>45%. In the 71-80 age group, 8.57% fall within the \leq 45% category, and 10% exceed 45%. For individuals over 80, 1.43% have P-LCR \leq 45%, while 15.72% have >45%. Here, as P=0.214, χ 2 (6) = 8.34; P-LCR Level in the participants is not significantly associated with age.

Table 5: Association of P-LCR level with gender								
Condon	P-LCR Level		Tatal		36	D Value		
Gender	<u>≤</u> 45%	>45%	Totai	χ^2	ul	<i>P</i> -value		
Female	11(15.71%)	8(11.43%)	19(27.14%)	0.66	1	0.002**		
Male	10(14.29%)	41(58.57%)	51(72.86%)	9.00	1	0.002**		
Total	21(30%)	49(70%)	70(100%)					

**Highly Significant P<0.01

Among females, 15.71% have P-LCR \leq 45% and 11.43% have >45%, accounting for 27.14% of the total population. In contrast, males have 14.29% with P-LCR \leq 45% and a much higher 58.57% with

>45%, making up 72.86% of the total. Here, as $\chi^2(1)=9.66$, P=0.002; P-LCR Level is significantly associated with gender.

Table 6: Association of P-LCR level with hypertension								
P-LCR Level		Tatal		46	D Value			
<u>≤</u> 45%	>45%	Total	χ2	u	r-value			
15(21.43%)	4(5.71%)	19(27.14%)	20.75	1	-0.001***			
6(8.57%)	45(64.29%)	51(72.86%)	29.75	1	<0.001***			
21(30%)	49(70%)	70(100%)						
	n of P-LCR level w P-LCF ≤45% 15(21.43%) 6(8.57%) 21(30%)	n of P-LCR level with hypertension P-LCR Level ≤45% >45% 15(21.43%) 4(5.71%) 6(8.57%) 45(64.29%) 21(30%) 49(70%)	n of P-LCR level with hypertension P-LCR Level Total ≤45% >45% 15(21.43%) 4(5.71%) 19(27.14%) 6(8.57%) 45(64.29%) 51(72.86%) 21(30%) 49(70%) 70(100%)	A of P-LCR level with hypertension γ2 P-LCR Level Total χ2 ≤45% >45% 19(27.14%) 15(21.43%) 4(5.71%) 19(27.14%) 6(8.57%) 45(64.29%) 51(72.86%) 21(30%) 49(70%) 70(100%)	A of P-LCR level with hypertension P-LCR Level Total χ2 df ≤45% >45% 19(27.14%) 29.75 1 15(21.43%) 45(64.29%) 51(72.86%) 29.75 1 21(30%) 49(70%) 70(100%) 2 1			

***Very Highly Significant P<0.001

Among those without hypertension, 21.43% have P-LCR \leq 45%, and 5.71% have P-LCR >45%, totaling

27.14% of the study population. In contrast, individuals with hypertension show 8.57% with P-

LCR \leq 45% and a much higher 64.29% with P-LCR >45%, comprising 72.86% of the total. The P-value is less than 0.001, signifying a strong, statistically

significant association between elevated P-LCR levels and the presence of hypertension.

Table 7: Association of P-LCR level with diabetes mellitus								
Diabetes	P-LCR Level		Total		46	B Value		
Mellitus	<u>≤</u> 45%	>45%	Total	χ2	ai	<i>r</i> -value		
No	12(17.14%)	22(31.43%)	34(48.57%)	0.88	1	0.348 ^{NS}		
Yes	9(12.86%)	27(38.57%)	36(51.43%)					
Total	21(30%)	49(70%)	70(100%)					

NSNot Significant P>0.05

The total sample is divided into those without diabetes (48.57%) and those with diabetes (51.43%). Among diabetic participants, 38.57% have P-LCR levels above 45%, while 12.86% have levels at or

below 45%. The chi-square value (χ^2) is 0.88, and the p-value is 0.348, suggesting no significant association between P-LCR levels and the presence of Diabetes Mellitus (P>0.05).

Table 8: Association of P-LCR level with smoking									
Smoking	P-LCR Level		T-4-1		36	D 37-1			
	<u>≤</u> 45%	>45%	Totai	χ2	ai	<i>P</i> -value			
No	18(25.71%)	22(31.43%)	40(57.14%)						
Yes	3(4.29%)	27(38.57%)	30(42.86%)	10.00	1	0.002**			
Total	21(30%)	49(70%)	70(100%)						

**Highly Significant P<0.01

Among non-smokers, 25.71% have P-LCR \leq 45% and 31.43% have P-LCR >45%. For smokers, 4.29% have P-LCR \leq 45% and 38.57% have P-LCR

>45%. Smoking is significantly associated with P-LCR Level as $\chi^2(1)=10, P=0.002$.

Table 9: Associat	tion of P-LCR level	with alcoholism				
Alcoholism	P-LCR Level		T-4-1		16	D 37-1
	<u>≤</u> 45%	>45%	Totai	χ2	ui	r - value
No	18(25.71%)	22(31.43%)	40(57.14%)			
Yes	3(4.29%)	27(38.57%)	30(42.86%)	10	1	0.002**
Total	21(30%)	49(70%)	70(100%)			
**IT 11 C' 'C' D	0.01					

**Highly Significant P<0.01

Among non-alcoholics, 25.71% have P-LCR \leq 45% and 31.43% have P-LCR >45%. Among alcoholics, 4.29% have P-LCR \leq 45% and 38.57% have P-LCR

>45%. From this table, Alcoholism is significantly associated with P-LCR Level, $\chi^2(1)=10$, P=0.002.

Table 10: Association of P-LCR Level with Dyslipidemia								
Dyslipidemia	P-LCR Level		Tatal		36	D Value		
	≤45%	>45%	Totai	χ2	ui	<i>P</i> -value		
No	17(24.29%)	31(44.29%)	48(68.57%)	2.12	1	0.144NS		
Yes	4(5.71%)	18(25.71%)	22(31.43%)	2.15	1	0.144		
Total	21(30%)	49(70%)	70(100%)					
SNot Significant D: 0.05								

^sNot Significant P>0.05

Among individuals without dyslipidemia, 24.29% have P-LCR \leq 45% and 44.29% have P-LCR >45%. For those with dyslipidemia, 5.71% have P-LCR \leq 45%, while 25.71% have P-LCR >45.The chi-

Table 11: Association of P-LCR Level with Coronary Artery Disease									
P-Value									
	s								

^{NS}Not Significant P>0.05

The data shows that 64.29% of participants do not have CAD, while 35.71% do. Among those with CAD, 25.71% have P-LCR levels above 45%, and 10% have P-LCR levels at or below 45%. The statistical analysis, with a chi-square value (χ^2) of 0.07 and a p-value of 0.785, indicates no significant association between P-LCR levels and CAD (P > 0.05).

Table 12: Association of P-LCR Level with Glasgow Comma Scale									
Glasgow Comma Scale	PLATELET LARGE CELL RATIO			χ2	df	P-Value			
	RANGE		Total						
	≤45%	>45%							
≤ 8	1(1.4%)	3(4.3%)	4(5.7%)						
9-12	6(8.60%)	13(18.60%)	19(27.10%)	0.71	2	0.965 ^{NS}			
>12	14(20.00%)	33(47.10%)	47(67.10%)						
Total	21(30.00%)	49(70.00%)	70(100.00%)						

^{NS}Not Significant P>0.05

For GCS ≤ 8 , 1.4% have P-LCR $\leq 45\%$ and 4.3% have P-LCR >45%. For GCS scores of 9-12, 8.6% have P-LCR $\leq 45\%$ and 18.6% have P-LCR >45%.

Among those with GCS >12, 20% have P-LCR \leq 45% and 47.10% have P-LCR >45%.

Statistical Inference: Glasgow Comma Scale is insignificantly associated with P-LCR Level, $\chi 2(2)=0.071$, P=0.965.

Table 13: Association of P-LCR Level with NIHSS Score							
NIHSS Score	P-LCR		Tatal		46	D Malaa	
	≤45%	>45%	Total	χ2	aı	<i>P</i> -value	
Mild (1-5)	5(7.14%)	13(18.57%)	18(25.71%)	- 1.67	3	0.645 ^{NS}	
Mild to Moderately Severe (5-14)	14(20.00%)	32(45.71%)	46(65.71%)				
Severe (15-24)	2(2.86%)	2(2.86%)	4(5.71%)				
Very Severe (>25)	0(0.00%)	2(2.86%)	2(2.86%)				
Total	21(30.00%)	49(70.00%)	70				

NIHSS (National Institutes of Health Stroke Scale) scores has been categorized into four severity levels: Mild (1-5), Mild to Moderately Severe (5-14), Severe (15-24), and Very Severe (>25) [Brott et al,1989]. For Mild cases, 7.14% have P-LCR \leq 45% and 18.57% have >45%. In the Mild to Moderately Severe category, 20% have P-LCR \leq 45% and

45.71% have >45%. For Severe cases, both \leq 45% and >45% categories have 2.86% each, while in the Very Severe group, 0% have P-LCR \leq 45% and 2.86% have >45%.From this, statistical inference can be drawn as P-LCR is not significantly associated with NIHSS score, $\chi^2(3,70)=$ 1.67. P=0.645.

Table 14: Association of P-LCR level with carotid intima media thickness						
D I CD I aval	CI	MT	Total	χ2		
r-LCK Level	CIMT ≤0.9	CIMT >0.9				

	-		'L'atal			D Value	
P-LCK Level	CIMT ≤0.9	CIMT >0.9	Total	χ2	ai	<i>r</i> -value	
≤45%	15(21.4%)	6(8.6%)	21(30%)	7 10	1	0.000**	
>45%	18(25.7%)	31(44.3%)	49(70%)	7.10	1	0.008***	
Total	33(47.1%)	37(52.9%)	70(100%)				

In the group of participant with P-LCR level \leq 45%, 21.4% have CIMT value \leq 0.9 mm and 8.6% have CIMT >0.9 mm ;whereas the group having P-LCR level <45% 25.7% have CIMT value \leq 0.9 mm and 44.3% have CIMT >0.9 mm.

Statistical Inference: The P-LCR Level (average 48.33 \pm 6.21) is significantly associated with Carotid Intima Media Thickness (0.93 \pm 0.17), χ 2 (1) =7.10, *P*=0.008.





Figure 1: Scatter diagrams showing correlation between P-LCR and CIMT

The Pearson correlation coefficient (r) between P-LCR and CIMT is calculated by using Pearson formula and it came out to be r=0.4432, which implies a moderately positive correlation between the two variables.

DISCUSSION

This study is a cross sectional study conducted on 70 no. of patients presented with acute ischemic stroke. In 70 patients 51 were male and 19 were females. The mean age of participant studied studied was 65.17 years. The maximum number of cases in this study were in the age group 51 to 60 years. The mean age in males was 49.10 years, the mean age in female was 60.08 years.

In our study, maximum number of participants i.e. 27.14% of the total study group belongs to the age group 51 to 60 years. The mean age of the study group was 65.17 ± 14.40 years (36-93Yrs). It is consistent with the study done by Alawneh KZ et al,^[19] for ischaemic stroke demographics, where the mean age was 67.8 years. Maximum participants belong to the age group of 51 to 60 years which is consistent with the study done by Rajkumar I et al.where maximum belongs to 50 to 59 years (34.1%).^[20]

In our study, 72.86% of the participants were men and 27.14% were women. The male preponderance is consistent with most of the studies done with ischaemic stroke. Among those, one of the study done by Rajkumar I et al. on ischaemic stroke found that 79.5% of the participants were male.^[20]

In our study out of 70 participants,72.86% participants has hypertension which is the most prevalent risk factor. In a study done in ischaemic stroke patients by Lok U et al. hypertension was the most prevalent risk factor with 74% prevalence.^[21] Other risk factors found in our study are diabetes mellitus found in 51.43% participants. 42.86% participants are smokers, 42.86% participants are alcoholics, 35.71% have coronary artery disease and 31.43% participants have dyslipidemia. In another study done by Alawneh KZ et al for risk factors evaluation of ischaemic stroke, it was found that hypertension was the most frequently identified risk factor among the cases, accounting for 50.56%. This

was followed by diabetes mellitus at 19.88%, hyperlipidemia at 15.34%, and coronary artery disease at 6.25%, among others.^[22]

In our study, it is found that P-LCR level is not significantly associated with age. It is inconsistent with a large population study done by Yong M. et al to see age and gender variation of platelet indices where they found that all platelet indices including P-LCR display increasing trend with aging. The same study also found significant association of P-LCR with sex which is consistent with our study.^[23]

Hypertension is found to be significantly associated with P-LCR Level with a p value of <0.001 in our study. It is consistent with a study done by Elkhalifa H et al where individuals with hypertension is found to be with higher P-LCR values with other platelet volume indices.^[24] In another study done by Maluf et al. it was found that hypertensive individuals had higher P-LCR levels (p value≤ 0.045).^[25]

In our study diabetes mellitus is not significantly associated with P-LCR Level which is inconsistent with the studies done by Bhattacharjee P et al and Nageli Rahul et al.; where statistical significance has been established with diabetes and P-LCR levels.^[26,27]

Smoking is significantly associated with P-LCR Level in our study (p=0.002) which is consistent with a study done by Anandhalakshmi S. et al. on impact of cigarette smoking on platelet parameters where it was shown that P-LCR value has significant association with intensity of cigarette smoking ^[28].

Alcoholism has also been found to be significantly associated with P-LCR Level, which is consistent with a study done by Huang J et al. where it has been shown that among the workers who drink alcohol P-LCR was significantly elevated than non alcoholics in benzene exposed group.^[29]

Dyslipidemia is not significantly associated with P-LCR Level in our study.It is inconsistent with the study done by Singh A. et al. where they found significant association of P-LCR with dyslipidemia.^[30]

In our study prevalence of coronary artery disease is not significantly associated with P-LCR level which is similar to a study done by De Luca G et al where also P-LCR was not found to be associated with prevalence of CAD.^[31]

The P-LCR Level (average 48.33 ± 6.21) is significantly associated with Carotid Intima Media Thickness (0.93±0.17) in our study with a p value of 0.008. In scatter plot, CIMT and P-LCR displayed a moderately positive correlation with Pearson correlation coefficient (r) of 0.4432.It is consistent with a study Waghale RM et al. where it was stated that 'P-LCR had moderate positive relationship with CIMT which was statistically significant'.^[32]

CONCLUSION

Studies pertaining to the platelet volume indices recently have shown these parameters to have emerging prospects in clinical applications. Easy availability and low cost make platelet indices very handy and convenient for being diagnostic and prognostic markers of various conditions as well as risk assessment tools for cardiovascular diseases.

In spite of promising utility, platelet indices are not being extensively studied. Mean Platelet volume (MPV) is the sole platelet volume index which had been studied to some extent while others along with Platelet large cell ratio has a lot of ground yet to be covered.

In our study, high prevalence of elevated P-LCR levels in ischemic stroke patient and significant association with traditional risk factors of stroke like male sex, hypertension, smoking, alcoholism along with moderately positive linear correlation with carotid intima media thickness reiterate the likelihood of P-LCR to be a cardiovascular risk assessment tool if studied extensively in the future.

Limitations

The sample size was relatively small and duration of the study was short. Moreover, no control group was taken and the study was done as a cross sectional study. This study was done in a hospital setting but to calculate prevalence of a parameter more accurately the study should be a community based one. Modified Rankin scale has not been used in this study to measure the level of disability in ischemic stroke.

Further studies are needed to establish platelet large cell ratio as a marker for cardiovascular risk assessment.

REFERENCES

- Warlow CP. Epidemiology of stroke. Lancet. 1998 Oct;352Suppl 3:SIII1- 4. doi: 10.1016/s0140-6736(98)90086-1. PMID: 9803954.epidemiology and quality of life. Stroke Res Treat. 2018; 3:3238165.
- Lopez A. D., Mathers C. D., Ezzati M., Jamison D. T., Murray C. J. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. The Lancet. 2006;367(9524):1747–1757. doi:10.1016/S0140-6736(06)68770-9.
- Caplan L. R. Caplan's Stroke: A Clinical Approach. 3rd. Woburn, England: 2000.
- Bonita R, Beaglehole R. Stroke prevention in poor countries. Time for action. Stroke.2007;38:2871–2872.
- Pandian JD, Srikanth V, Read SJ, Thrift AG. Poverty and stroke in India.A time to act. Stroke.2007;38:3063–3069.
- Campbell BCV, De Silva DA, Macleod MR, Coutts SB, Schwamm LH, Davis SM, et al.Ischaemic stroke. Nat Rev Dis Primers. 2019 Oct 10;5(1):70
- Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, et al. Atherosclerosis. Nat Rev Dis Primers. 2019 Aug 16;5(1):56.
- Stegner D, Klaus V, Nieswandt B. Platelets as Modulators of Cerebral Ischemia/Reperfusion Injury. Front Immunol. 2019 Nov 29;10:2505.
- Mezger M, Nording H, Sauter R, Graf T, Heim C, von Bubnoff N, et al. Platelets and Immune Responses During Thromboinflammation. Front Immunol. 2019 Jul 31;10:1731.

- Pujara K, Chaudhary N. Platelet indices as a predictive tool for the diagnosis and prognosis of ischemic stroke: an updated review. Int J Neurosci. 2021 Jun;131(6):595-603.
- Sadeghi F, Kovács S, Zsóri KS, Csiki Z, Bereczky Z, Shemirani AH. Platelet count and mean volume in acute stroke: a systematic review and meta-analysis. Platelets. 2020 Mar;31(2):231 236.
- Yasemin UB, Murat P, Huysa K, et al. The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review. BiochemMed . 2016;26:178– 193.
- Shao W, Li Y, Chen F, Xiao X, Fu Q, Xie J, et al. Plateletlarge cell ratio: A potential biomarker for peripheral artery disease. ClinChimActa. 2021 Feb;513:17-21.
- Osselaer JC, Jamart J, Scheiff JM. Platelet distribution width for differential diagnosis of thrombocytosis. Clin Chem. 1997;43:1072–6.
- Chen F, Xiao X, Lin Y, Chen S, Xie J, Qin W, et al. Plateletlarge cell ratio as a prognostic marker for coronary artery disease: A systematic review and meta-analysis. ClinChimActa. 2020 Nov;510:726-732.
- Grotto HZ, Noronha JF. Platelet larger cell ratio (P-LCR) in patients with dyslipidemia. Clin Lab Haematol.2004;26(5):347-9. doi: 10.1111/j.1365-2257.2004.00634.
- Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. JACC Cardiovasc Imaging. 2014 Oct;7(10):1025-38.
- Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, et al. Mannheim carotid intima-media thickness and plaque consensus (2004-2006-2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, Cerebrovasc Dis. 2012;34(4):290-6.
- Alawneh KZ, Qawasmeh MA, Raffee LA, Al-Mistarehi A-H. Ischemic Stroke demographics, Clinical Features and Scales and Their Correlations: an Exploratory Study From Jordan. Future Science OA. 2022 Aug.
- Rajakumar I, Vidya TA, Ramachandran K, Hussain A, Aarthi J, Poovitha M, et al. Platelet indices as prognostic markers of ischemic stroke and their correlation with lipid profile. Clinical Neurology and N hneurosurgery . 2024 Feb.
- Lok U, Gulacti U, Ekmekci B, Bulut T, Celik M. Predictive and prognostic role of mean platelet volume in patients with first-ever acute ischemic stroke. Neurosciences . 2017 Apr.
- 22. Alawneh KZ, Al Qawasmeh M, Raffee LA, Abuzayed B, Bani Hani DA, Abdalla KM, et al. A snapshot of Ischemic stroke risk factors, sub-types, and its epidemiology: Cohort study. Annals of Medicine and Surgery . 2020 Nov.
- Yong M. Large Population Study for Age- and Gender-Related Variations of Platelet Indices in Southwest China Healthy Adults. Hematology & Company, Transfusion International Journal. 2015 Dec 29
- Elkhalifa H, Mustafa R, Elkhalifa R. A18882 Platelet volume indices in Hypertensive Sudanese patients. Journal of Hypertension. 2018 Oct.
- 25. Maluf, Chams B., Barreto, Sandhi M., dos Reis, Rodrigo C.P. and Vidigal, Pedro G. "Platelet volume is associated with the Framingham risk score for cardiovascular disease in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)" Clinical Chemistry and Laboratory Medicine (CCLM), vol. 54, no. 5, 2016, pp. 879-887
- Bhattacharjee P, Datta A, Debbarma R.K., Das S.K.."Platelet indices in diabetics and influence of glycemic control – a hospital based study in North-East India" Int J Med Res Rev 2016;4(12):2186-2192.doi:10.17511/jimrr. 2016.i12.18.
- 27. Nagelli Rahul,D Pavan Kumar, Sanjay H Kalbande."A study on role of platelet indices - platelet large cell ratio (P- LCR), mean platelet volume [MPV], platelet distribution width [PDW] and high-sensitivity C- reactive protein (hs CRP) as predictive markers for complications in Type 2 diabetes mellitus" Journal of Cardiovascular Disease Research, ISSN:0975 -3583,0976-2833, VOL14, ISSUE 02, 2023
- 28. Anandhalakshmi S,Kalaivani A,Shivasekar G, Saravanan A. Evaluation of the impact of cigarette smoking on

plateletparameters.NatlJPhysiolPharmPharmacol2015;5:426-430.

- 29. Huang J, Zhao M, Wang P, Li X, Ma L, Zhang J, et al. Effects of Low Concentrations of Benzene Exposure on Levels of Platelet-Associated Antibodies and Platelet Parameters. Journal of Occupational & amp; Environmental Medicine. 2014 Oct.
- Singh A, singh A, Kushwaha R, Yadav G, Tripathi T, Chaudhary SC, et al. Hyperlipidemia and Platelet Parameters: Two Sides of the Same Coin. Cureus. 2022 Jun 12.
- 31. De Luca G, Santagostino M, Secco GG, Cassetti E, Giuliani L, Coppo L, Schaffer A, Fundaliotis A, Iorio S, Venegoni L, Bellomo G, Marino P. Platelet-large cell ratio and the extent of coronary artery disease: results from a large prospective study. J Thromb Thrombolysis. 2010 Nov;30(4):426-33. doi: 10.1007/s11239-010-0456-6. PMID: 20978881.
- 32. Waghale RM, Khot RS, Joshi PP. Platelet volume indices: markers of carotid atherosclerosis in type 2 diabetes mellitus? Clinical Diabetology . 2020 May 14.