

Platelet To Lymphocyte Ratio In Acute Ischemic Stroke

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ABSTRACT

Background: Stroke is the the second largest cause of mortality worldwide. Thrombosis, platelet activation and inflammation are essential in the pathophysiology of ischemic stroke. Lymphocytes exert an anti-inflammatory response in development of atherosclerosis. In comparison to platelets or lymphocyte counts alone, the platelet to lymphocyte ratio (PLR) is an unique marker that assesses the state of thrombosis and inflammatory pathways.

Objectives: To estimate PLR in patients with acute ischemic stroke and to assess the association between PLR and severity of acute ischemic stroke using NIHSS on admission.

Methodology: 243 patients admitted in Government Medical College, Kottayam diagnosed as acute ischemic stroke who fulfilled the inclusion criteria were selected after obtaining informed consent. Patients were subjected to complete blood count and CT brain. NIHSS (National Institute of Health Stroke Scale) score and PLR was calculated in each patient at the time of admission. Relationship between stroke severity and Platelet to lymphocyte ratio was then assessed.

Results: In our study, the mean PLR among the patients with acute ischemic stroke was found to be 132 ± 57.59 . The mean PLR in patients with NIHSS score group as mild was 82.09 ± 13.96 , those with moderate score group was 103.62 ± 23.73 , those with moderate -severe score group was 135 ± 29.23 , and those with severe score group was 221.9 ± 50.28 . The mean PLR significantly increased with increasing NIHSS score .

Conclusion: The mean PLR in patients with acute ischemic stroke in this study was 132 ± 57.59 . There was statistically significant association between PLR and NIHSS severity. Higher PLR ratios were associated with more severity of stroke.

Keywords: Platelet to lymphocyte ratio, NIHSS, Stroke

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I. Introduction

Stroke is defined as an abrupt onset of focal neurological deficit that is attributable to a vascular cause. Stroke is the second leading cause of death causing 6.2 million deaths in 2011 and third most common cause of disability-adjusted life years in the world.

Thrombosis, platelet activation and inflammation are essential in the pathophysiology of acute ischemic stroke. Platelets represent an important linkage between inflammation, thrombosis, and atherosclerosis in acute ischemic stroke. Increased thrombocyte activation and inflammatory mediator release may result from high platelet numbers.

In contrast, lymphocytes exert anti-inflammatory response in atherosclerosis development. In order to promote tissue healing, lymphocytes stimulate tissue inhibitor of metalloproteinase 1 expression and modify the mononuclear cell phenotype. Physiological stress occurring during ischemic stroke leads to higher level of cortisol which leads to lower lymphocyte counts. Additionally, acute stressful conditions cause activation of sympathetic nervous system which causes redistribution of lymphocytes to lymphatic organs and promotes apoptosis of lymphocytes leading to lymphopenia.

The platelet to lymphocyte ratio is a novel inflammatory marker that can be applied in many diseases for predicting inflammation and mortality. The benefit of platelet to lymphocyte ratio (PLR) is that it reflects the condition of both inflammation and thrombosis pathways and is more valuable than either platelet or lymphocyte counts alone. This novel marker has not been frequently studied with acute ischemic stroke; hence aim of the present study was to find out the role of PLR (Platelet to lymphocyte ratio) in patients of acute ischemic stroke and to correlate with NIHSS for predicting the severity and prognosis.

II. Materials and Methods

Type of study: This is a cross sectional study which was approved by the institutional review board and received the ethics committee approval from the institutional ethics committee.

Study population: Patients admitted with acute ischemic stroke in Medicine department of Govt Medical College, Kottayam, who have fulfilled the inclusion criteria.

Inclusion criteria: Patients aged above 18 years with radiologically diagnosed ischemic stroke presenting within 48 hours of symptom onset

Exclusion criteria:

- Patients with hepatic disease, renal disease, connective tissue disease, autoimmune disease.
- Pregnancy
- Pre-existing platelet disorder
- Patients on antiplatelet drugs.
- Patients on steroids, immunosuppressive therapy.

Methodology: All patients included in the study were subjected to detailed history taking and clinical examination. Patients were subjected to complete blood count and CT brain. NIHSS (National Institute of Health Stroke Scale) score was calculated in each patient at the time of admission. Total NIHSS score ranges from 0 to 42 with higher values reflecting more severe stroke. Patients were categorised using NIHSS into:

Mild stroke = 1-4

Moderate stroke = 5-15

Moderate to severe stroke = 16-20

Severe stroke = 21-42.

Platelet to lymphocyte ratio (PLR) was calculated from complete blood count by dividing absolute value of platelet by absolute value of lymphocyte, in each patient on day of admission. Relationship between stroke severity and Platelet to lymphocyte ratio was assessed using appropriate statistical tests.

Sample Size :

$$\text{Sample size} = \frac{(Z_{1-\alpha/2})^2 SD^2}{d^2}$$

As per the study Role of platelet to lymphocyte ratio and its correlation with NIHSS for prediction of severity in patients of acute ischemic stroke by Deepti sharma et al.,¹ Journal of Association of Physicians of India, January 2021 edition. (Sharma & Gandhi, 2020)

Sample size = 243

{standard deviation from previous study = 93.92}

[mean = 235.98; d=5% of mean]

Data collection procedure: Data was entered in Microsoft excel and analyzed using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. IBM Corp.

III. Confidentiality:

Strict confidentiality was ensured by keeping the patients anonymous with study numbers and the information gathered will only be used for scientific publication.

IV. Ethical Issues

The proposal of the study was presented in front of the Institutional Review board and the approval for the study was obtained from the Institutional Ethics Committee on 02/08/2023 and informed consent was taken from all patients enrolled in the study.

V. Analysis of Data

Data was entered in Microsoft excel and analyzed using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. IBM Corp. Categorical variables were expressed as frequency (percentage) and continuous variables were expressed in mean and standard deviation. Comparison of mean age across the NIHSS severity was done using One-way ANOVA test. Association of categorical variables like Gender, Diabetes status, Hypertension status, Dyslipidemia status, smoking habit and vascular territory with the NIHSS severity were done using Pearson Chi-square test. Correlation of NIHSS score with platelet to lymphocyte ratio was done using

Spearman's rho (Spearman's rank correlation). For all these statistical interpretations, $p < 0.05$ was considered the threshold for statistical significance.

VI. Results

Table 1: Age distribution and population characteristics

Age group (in years)	Frequency	Percent
≤ 40	4	1.6
41 – 50	13	5.3
51 – 60	50	20.6
61 – 70	96	39.5
71 - 80	63	25.9
> 80	17	7.0

Descriptive statistics		
Variable	Levels	Frequency N (%)
Gender	Male	146 (60.1)
	Female	97 (39.9)
GCS score	4	1 (0.4)
	6	5 (2.1)
	7	2 (0.8)
	8	6 (2.5)
	9	5 (2.1)
	10	10 (4.1)
	11	5 (2.1)
	12	9 (3.7)
	13	6 (2.5)
	14	5 (2.1)
	15	189 (77.8)
Diabetes mellitus	Yes	127 (52.3)
	No	116 (47.7)
Hypertension	Yes	155 (63.8)
	No	88 (36.2)
DLP	Yes	114 (46.9)
	No	129 (53.1)
Smoking	Yes	103 (42.4)
	No	140 (57.6)
Alcohol	Yes	93 (38.3)
	No	150 (61.7)
Vascular territory	MCA	161 (66.3)
	ACA	20 (8.2)
	PCA	37 (15.2)
	ACA MCA	22 (9.1)
	MCA PCA	3 (1.2)
NIHSS Severity	Mild	30 (12.3)
	Moderate	109 (44.9)
	Mod- severe	54 (22.2)
	Severe	50 (20.6)

Table 2: Distribution of platelet count, lymphocyte count and platelet to lymphocyte ratio in study population

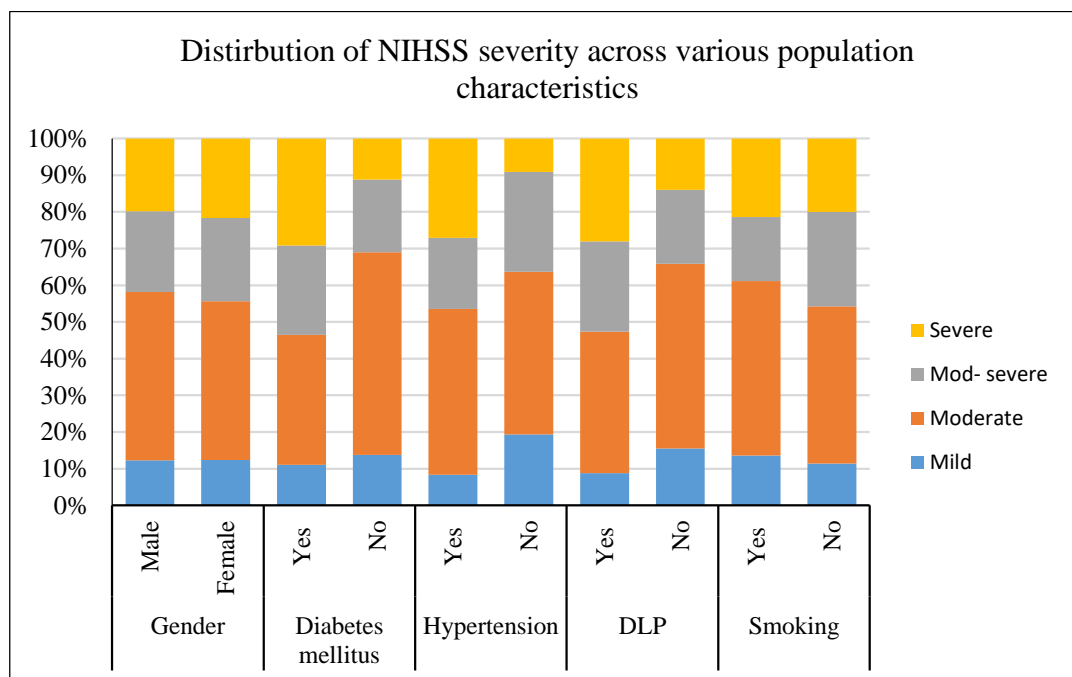
Variables	N	Minimum	Maximum	Mean	Std. Deviation	Median	IQR
Platelet count (lakh/mcl)	243	1.50	5.0	3.03	0.79	3	1.4
Lymphocyte count	243	780	4800	2604.05	901.96	2530	1240
Platelet to Lymphocyte ratio	243	52.82	347.83	132.28	57.59	112.90	64.66

Out of the 243 study population, minimum platelet count was 1.5 lakh/mcl, maximum platelet count was 5 lakh/mcl, with a mean of 3.03 ± 0.79 . Minimum lymphocyte count was 780 cells/mcl, maximum was 4800 cells/mcl and mean of 2604.05 ± 901.96 . Minimum value for Platelet to Lymphocyte ratio was 52.82, maximum value was found to be 347.83 with a mean of 132.28 ± 57.59 .

Table 3: Association of various population characteristics with NIHSS severity

Variables	Levels	NIHSS Severity				χ^2	p value
		Mild N (%)	Moderate N (%)	Mod- severe N (%)	Severe N (%)		
Gender	Male	18 (60.0)	67 (61.5)	32 (59.3)	29 (58.0)	0.19	0.98
	Female	12 (40.0)	42 (38.5)	22 (40.7)	21 (42.0)		
Diabetes mellitus	Yes	14 (46.7)	45 (41.3)	31 (57.4)	37 (74.0)	15.68	0.001*
	No	16 (53.3)	64 (58.7)	23 (42.6)	13 (26.0)		
Hypertension	Yes	13 (43.3)	70 (64.2)	30 (55.6)	42 (84.0)	15.87	0.001*
	No	17 (56.7)	39 (35.8)	24 (44.4)	8 (16.0)		
DLP	Yes	10 (33.3)	44 (40.4)	28 (51.9)	32 (64.0)	10.49	0.015*
	No	20 (66.7)	65 (59.6)	26 (48.1)	18 (36.0)		
Smoking	Yes	14 (46.7)	49 (45.0)	18 (33.3)	22 (44.0)	2.39	0.49
	No	16 (53.3)	60 (55.0)	36 (66.7)	28 (56.0)		

p value <0.05 is considered statistically significant
Pearson Chi- square test



Graph 1: Distribution of NIHSS severity across various population characteristics

Higher proportion patients with NIHSS status moderately severe and severe had Diabetes whereas higher proportion of patients with NIHSS status Mild and moderate didnot.

Higher proportion patients with NIHSS status moderate, moderately severe and severe had hypertension whereas higher proportion of patients with NIHSS status mild didnot.

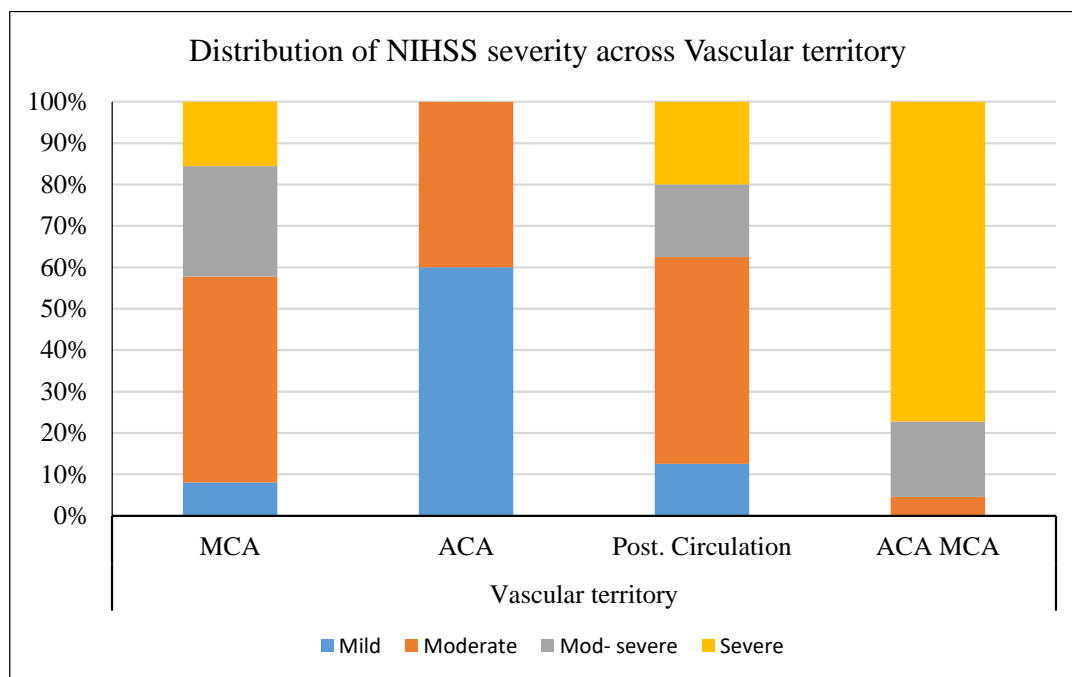
Higher proportion patients with NIHSS status moderately severe and severe had dyslipidemia whereas higher proportion of patients with NIHSS status Mild and moderate didnot.

There is a statistically significant association for diabetes status, hypertension and dyslipidemia with the NIHSS severity.

Table 4: Association of Vascular territory with NIHSS severity

		NIHSS Severity				χ ²	p value
		Mild N (%)	Moderate N (%)	Mod- severe N (%)	Severe N (%)		
Vascular territory	MCA	13 (8.1)	80 (49.7)	43 (26.7)	25 (15.5)	99.24	<0.001*
	ACA	12 (60.0)	8 (40.0)	0 (0.0)	0 (0.0)		
	Posterior circulation	5 (12.5)	20 (50.0)	7 (17.5)	8 (20.9)		
	ACA MCA	0 (0.0)	1 (4.5)	4 (18.2)	17 (77.3)		

p value <0.05 is considered statistically significant
Pearson Chi- square test



Graph 2: Distribution of vascular territory with NIHSS Severity
Majority of patients with territory ACA had NIHSS severity Mild.

Majority of patients with territory MCA had NIHSS severity Moderate while patients with territory ACA MCA had NIHSS status as severe. There is a statistically significant association between vascular territory and the NIHSS status.

Table 5: Comparison of platelet to lymphocyte ratio with NIHSS severity

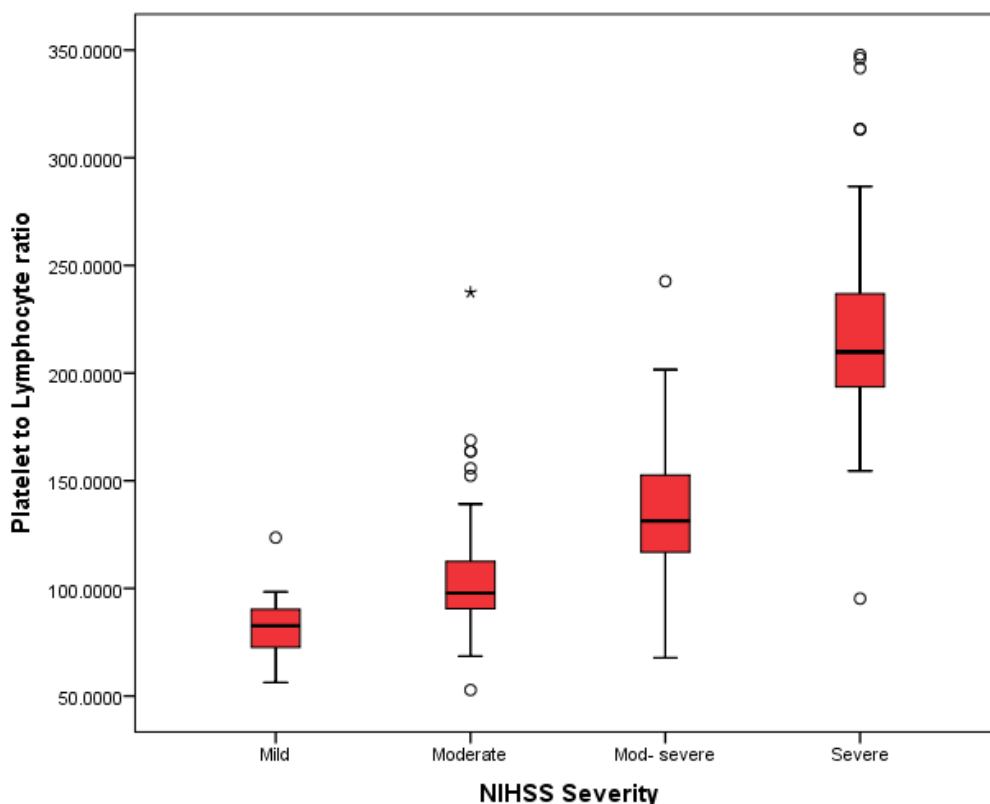
Comparison of mean ranks of platelet to lymphocyte ratio across NIHSS severity						
NIHSS severity	N	Mean (S.D)	Mean rank	df	χ^2	p value
Mild	30	82.09 (13.96)	37.22	3	162.42	<0.001*
Moderate	109	103.62 (23.73)	88.65			
Mod- severe	54	135.02 (29.23)	151.81			
Severe	50	221.90 (50.28)	213.39			

p value <0.05 is considered statistically significant
Kruskal- Wallis AOVA test

Table 6: Pairwise comparison of platelet to lymphocyte ratio with NIHSS severity

Pairwise comparison using Dunn's post hoc test				
NIHSS Severity (I)	NIHSS Severity (J)	Rank Difference (I-J)	p value	
Mild	Moderate	-51.43	0.002*	
Mild	Mod- severe	-114.59	<0.001*	
Mild	Severe	-176.17	<0.001*	
Moderate	Mod- severe	-63.16	<0.001*	
Moderate	Severe	-124.74	<0.001*	
Mod- severe	Severe	-61.58	<0.001*	

p value <0.05 is considered statistically significant



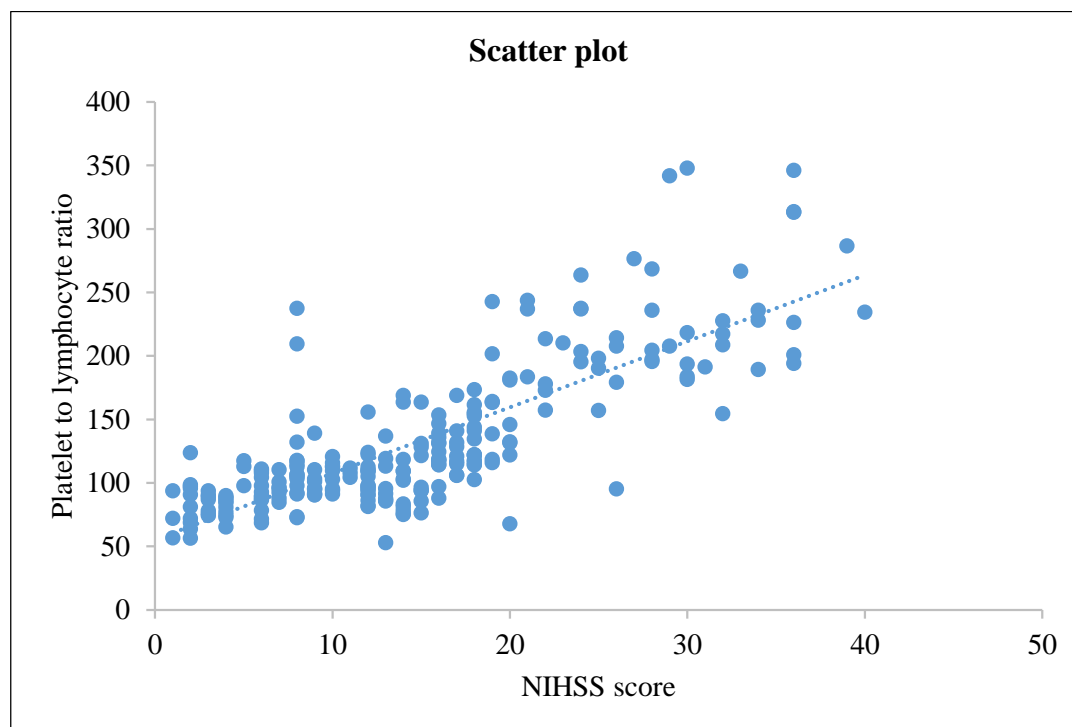
Graph 3: Box plot for platelet to lymphocyte ratio across NIHSS severity

NIHSS severity mild had significantly lesser PLR ratio than all other groups. NIHSS severity moderate have a significantly lesser ratio than the moderately severe group. Those patients with NIHSS severity status as severe had significantly higher platelet to lymphocyte ratio than moderate- severe group. As PLR increases, there is more chance of increase in NIHSS severity and this relation was found to be statistically significant.

Table 7: Correlation of NIHSS Score and Platelet to lymphocyte ratio

Correlation	r	p value
NIHSS score – Platelet to lymphocyte ratio	0.776	<0.001*

p value <0.05 is considered statistically significant
Spearman rho correlation test



Graph 4: Scatter plot of NIHSS score and platelet to lymphocyte ratio

There is a strong positive correlation ($r=0.776$, P value - <0.001) between the NIHSS scores and platelet to lymphocyte ratio.

VII. Discussion

In this study 243 patients with acute ischemic stroke who met the inclusion criteria, admitted in Department of General Medicine, Government Medical College Kottayam during the study period were enrolled. Platelet to lymphocyte ratio was calculated at time of admission and each variable was separately studied. The mean age of patients in this study was 66.5 ± 9.9 years with the maximum cases in the age range of 61-70 years. This was similar to study done by Grau et al² in which mean age of patients was 65.9 ± 14.1 years.

In this study, 60.1% were males and 39.9% were females. Male preponderance was also observed in studies done by Aiyar et al³ and R P Eapen et al⁴.

In our study hypertension (63.8%) was the most common risk factor studied, followed by diabetes (52.3%), dyslipidemia (46.9%), smoking (42.4%). This was similar to studies done by Dalal et al⁵. In a population based study conducted in Rochester, Minn using multiple logistic regression analysis 74% of the study population were hypertensives and the population attributable risk of hypertensives was 26%⁶.

In this study, most common vascular territory involved was MCA territory (66.3%), followed by posterior circulation stroke (15.2%). This was similar to the study by Das SK et al⁷ and Hui et al⁸.

About 44.9% of patients had NIHSS severity as moderate, 22.2% had moderate -severe, 20.6 % had severe and 12.3% had mild stroke. But in study by Reeves m et al⁹ most cases of ischemic stroke were found to be mild with median NIHSS score 3. This difference could be due to the fact that our study was conducted in a tertiary centre where mostly referred cases are admitted.

Hypertension, diabetes and dyslipidemia were found to have a statistically significant association with NIHSS status. Higher proportion patients with NIHSS status moderately severe and severe had Diabetes. Higher proportion patients with NIHSS status moderate, moderately severe and severe had hypertension. Higher proportion patients with NIHSS status moderately severe and severe had dyslipidemia. This was similar to the results of study done by Alloubani A et al¹⁰

The mean platelet to lymphocyte ratio among the patients with acute ischemic stroke was found to be 132 ± 57.59 . According to a large multicentric trial conducted to find out the reference range for platelet to lymphocyte ratio conducted by Luo H et al¹¹ reference interval for PLR in adults was found to be within 49-198.

The mean platelet to lymphocyte ratio in patients with NIHSS severity as mild was 82.09 ± 13.96 , those with moderate severity was 103.62 ± 23.73 , those with moderate -severe stroke was 135 ± 29.23 , and those with severe stroke was 221.9 ± 50.28 .

NIHSS score group Mild had significantly lesser ratio than all other groups. Those patients with NIHSS score group as severe had significantly higher platelet to lymphocyte ratio than all other groups.

According to the study done by Deepthi Sharma et al, on comparing PLR with patients of different NIHSS score, it was found to be lowest in NIHSS score group mild i.e.171.23±48.14 which increased to 229.66±98.57 in NIHSS score group moderate, 296.23±44.09 in NIHSS score group moderate-severe and was highest in NIHSS score group severe amounting to 356.63±43.90 and a statistically significant correlation was found between PLR and NIHSS score at the time of admission.

A strong positive correlation ($r=0.776$, p value < 0.001) was found between the NIHSS scores and platelet to lymphocyte ratio. This was similar to study done by Nijalingappa¹² in which there was positive correlation between PLR with NIHSS($r=0.68$, $p<0.001$). The PLR increased with increasing NIHSS score.

VIII. Conclusion

The mean platelet to lymphocyte ratio in patients with acute ischemic stroke in this study is 132 ± 57.59 . There was statistically significant association between platelet to lymphocyte ratio and NIHSS severity. Higher PLR ratios were associated with more severity of stroke.

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