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ORGINAL ARTICLE

Neutrophil to lymphocyte ratio, and platelet to lymphocyte ratio as a predictor of stroke in patients with COVID-19

Nearmeen M. Rashad[a,*], Waleed M. Reda Ashour[b] , Marwa H.S. Hussien [c] Amira M. El-Helaly[d], Haitham E. Mohamed [e],Magda M. Sherif [a]

[a] Internal Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[b] Neurology, Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[c]Medical Biochemistry and Molecular Biology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[d]Clinical Pathology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt.
[e]Anesthesia and Intensive Care Unit, Faculty of Medicine, Zagazig University, Zagazig, Egypt.

[*]Corresponding author:
Nearmeen M. Rashad

E-mail address:
nrashad78@yahoo.com & n.rashad@zu.edu.eg.

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ABSTRACT

Background: coronavirus disease 2019 (COVID-19), is documented as an emerging global pandemic, representing one of the leading causes of morbidity and mortality worldwide. Stroke is arguably the most important complication of COVID-19. It may be presumed that NLR and PLR could be used as biomarkers of endothelial dysfunction in many diseases including stroke. This study aimed to explore the role of NLR and PLR as predictive markers of stroke in patients with COVID-19.

Methods: 392 confirmed COVID -19 subjects retrospectively analyzed. Among enrolled COVID-19 patients, only 24 patients had a stroke (ischemic stroke= 21 and non-ischemic stroke, n=3). Clinical, laboratory, and radiological parameters were investigated.

Results: Among Covid -19 ,24 (6.1%) had acute ischemic stroke, 3 (0.76%) had non-ischemic stroke. results show that PLR was 271.2±161.4 and NLR was 5.96±2.4 in COVID -19 patients (n=392) There was a significant difference between studied groups as regard NLR, Covid -19 patients without stroke, n= 368 (5.7±3.24), ischemic stroke, n=21(9.2±3.32) and non-ischemic stroke, n=3(8.29±3.12), p <0.001. While as regards PLR, the result of the current study detected that there was a non-significant difference between studied groups; Covid -19 patients without stroke (270.6±168.6), ischemic stroke (302.9±121.71), and non-ischemic stroke (172.7±46.67), p-value =0.387.

Conclusions: These results suggest that NLR may be more used as a biomarker for stroke in particular ischemic stroke in COVID-19 patients. Calculation of NLR could help in the early prediction of high-risk patients with COVID-19 for better management.

Keywords: COVID-19, ischemic stroke, non-ischemic stroke, platelet-to-lymphocyte ratio, Neutrophil-to-lymphocyte ratio.

INTRODUCTION

There is a lot of evidence that stroke is considered the third most common cause of death worldwide and the third main trigger of disability [1]. There is growing evidence that the prevalence of ischemic stroke which is the most popular subtype of stroke is accounting for 80% of all cases of stroke [2].

A preponderance of evidence suggests that endothelial dysfunction is one of the most

important underlying molecular mechanisms of COVID-19 [3]. Intriguing reports are investigating endothelial dysfunction in micro and macrovascular manifestations of COVID-19. It may be assumed that the pathogenesis could be the direct entry of the virus through ACE-2 receptor, hematogenous spread and neuronal spread [4] as well as the indirect mechanisms are inflammatory response, immune dysregulation, and cytokine storm [5].

Neutrophil–lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are cheap, easy, and noninvasive biomarkers that could be used as a biomarker of vascular diseases including stroke. Intriguing reports are investigating PLR and NLR as predictors markers of diseases activity, severity, and mortality [6,7]. Convincing evidence suggests that the inflammatory role of PLR/NLR contributed to the high association between both and high risk of mortality in many diseases. Though some reports are controversial, some recent studies suggested that PLR and NLR could have diagnostic and prognostic influence in many diseases [8,9]. Nowadays we are facing an aggressive pandemic, COVID-19 which is associated with a high risk of morbidity and mortality. Thus, we aimed in the current study to explore the role of NLR and PLR as a predictive marker of stroke in COVID-19.

SUBJECTS AND MATERIAL

This is a retrospective cross-sectional study conducted in a tertiary hospital, Zagazig University hospitals Egypt. Of 654 patients included at the beginning of the study, 392 were confirmed cases of COVID-19 according to Egyptian protocol. Among Covid -19(n=392) ,21 (5.35%) had acute ischemic stroke, 3 (0.76%) had non-ischemic stroke. A total of 177 (45.1%) patients were males. The study flowchart is shown in figure 1. The study design was accepted by zagazig University Institutional Review Board (IRB) ((ZU-IRB#: 6389).

Ethical Clearance

Written informed consent was obtained from all participants. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

We excluded patients with brain tumor, surgical or accidental trauma, history of the previous stroke, history of use of anticoagulants or anticonvulsants. Imaging including computed tomography (CT) of the chest and brain was done. Blood samples were collected for routine and research investigations including CBC [Blood samples were collected in vacuum tubes with EDTA as an anticoagulant for automated CBC. CBC including differential cell count was measured by automated cell counter Sysmex XN2000 (Sysmex diagnostic, Japan). NLR and PLR were calculated as the ratio of neutrophil cell and platelet count to lymphocyte cell count, respectively. and normal references were the 95% reference range of NLR in normal males and females are 0.43~2.75 and 0.37~2.87, PLR is 36.63~149.13 and 43.36~172.68, respectively. . Other tests were done in biochemical and clinical pathology departments according to zagazig university hospital's COVID-19 protocol.

Statistical analysis

The statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the means if normally distributed or median(range) if not normally distributed. Normality was checked by Kolmogorov Smirnov test. Homogeneity of variance was checked by Levene's test. Categorical variables were presented by the count (percentage). Fisher's Exact Test: for (2X2) (RXC). It is an alternative to the chi-squared test to discover if there is a relationship between two categorical variables when the expected cell count is less than five. • One-way Analysis Of Variance (ANOVA) was used to compare means of the groups followed by LSD test to compare statistical differences between three groups. If the data was nonparametric The Kruskal-Wallis test was used to compare them. The correlations between PLR and NLR parameters were analyzed using Pearson,s correlation. Further evaluation of independent factors correlated with PLR and NLR in covid 19 patients with stroke were

investigated with linear regression analysis. Logistic regression analysis was performed to identify predictors of stroke among COVID V-19 patients. The diagnostic performance of PLR and NLR was investigated by Receiver operating characteristic (ROC) curve analysis. P values < 0.05 were considered to be significant

RESULTS

Demographic, clinical, and laboratory findings characteristics in COVID-19 patients.

Of 654 patients included at the beginning of the study, 262 were excluded (44 Children (age <18 years,42 pregnant,176 patients with incomplete laboratory tests. Thus,392 patients were included in the study according to Egyptian protocol. A total of 177 (45.1%) patients were males and their mean age was 40.21±14.14 years. Clinical data for examples obesity indices including BMI, blood pressure, and current smoker, are shown in table 1. Interestingly, comorbidities associated with COVID-19 patients at admission are described in table 1, among all comorbid conditions associated with COVID-19 patients at admission, diabetes 124 (31.6%), hypertension111(28.3%), were the most prevalent comorbid conditions followed by chronic liver disease, 43(10.9) and malignancy 42(10.7%).

As regard laboratory parameters, the enrolled patients with COVID 19- had metabolic dysfunction as hyperglycemia, dyslipidemia, obesity, and hypertension as shown in table 1. Moreover, there were increase levels of inflammatory and coagulopathy markers including LDH, C-reactive protein, D dimer, ferritin, and serum uric acid. On the contrary, patients with COVID -19 had anemia as well as low SPO2 as shown in table 1.

Neutrophil–lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in all enrolled COVID -19 patients: Our results show that PLR was 271.2±161.4 and NLR was 5.96±2.4 in COVID -19 patients (n=392) as shown in Table 1.

Demographic, clinical, and laboratory findings characteristics in COVID-19 patients

Among enrolled patients with COVID -19 ,368(93.8%) had COVID -19 without stroke, (24 (6.1%) had acute stroke [21 (5.35 %) had ischemic stroke and 3 (0.76%) had non-ischemic stroke]. Excitingly, the ischemic stroke group had meaningfully higher values of BMI, diastolic blood pressure, FPG,2-h plasma glucose, HbA1c, D-dimer, ferritin, and serum uric acid compared to COVID -19 patients with non-ischemic stroke <0.001*, table 2. However, neutrophils count was significantly low in COVID -19 without stroke compared to other groups <0.001*, table 2, On the other hand, there was a non-significant difference between other groups as regard other parameters >0.005 as shown in Table 2.

Comparison between studied groups as regard NLR and PLR

Regards NLR, the result of the recent study detected that there was a significant difference between studied groups; Covid -19 patients without stroke, n= 368 (5.7±3.24), ischemic stroke, n=21(9.2±3.32) and non-ischemic stroke, n=3(8.29±3.12) figure 2a, p <0.001. While as regards PLR, the result of the present study detected that there was a non-significant difference between studied groups; Covid -19 patients without stroke (270.6±168.6), ischemic stroke (302.9±121.71) and non-ischemic stroke (172.7±46.67), p-value =0.387 figure 2b.

Pearson correlation between NLR and PLR values with clinical and laboratory parameters among COVID -19 patients with stroke (n=24) patients

Regards NLR, our results revealed significant positive correlations with LDH, C-reactive protein, D-dimer, ferritin, serum uric acid P<0.05) (Table 3). Interestingly, PLR our results revealed significant positive correlations with C-reactive protein, D-dimer, ferritin, serum uric acid (P<0.001) (Table 3).

Linear Regression Analysis in COVID -19 patients with stroke

We evaluated the main effectors of NLR and PLR among COVID -19 patients with stroke. Linear regression analysis showed that D-dimer and ferritin I were independently correlated with NLR (P< 0.001) (Table 4). While

only D-dimer was independently correlated with NLR P< 0.001) (Table 4).

Logistic regression analysis for prediction of stroke among COVID-19 patients

To find the predictors of stroke among COVID -19 patients, we analyzed our findings using logistic regression analysis (Table 5). Interestingly, we found that NLR, PLR and D-dimer levels were the only predictors of stroke among COVID-19 patients (OR = 1.484; OR = 0.995; OR = 1.005 respectively,), table 5, P <0.05*.

The accuracy of NLR and PLR in differentiating ischemic stroke and non-ischemic stroke by Receiver operating characteristic curve (ROC).

The power of NLR in ischemic stroke and non-ischemic stroke by ROC analysis, the AUC was 0.701 (95% CI = 0.600-0.802) with sensitivity = 75%, specificity = 57.2%, and the cutoff values (5.3), figure 3a, p <0.001. However, the power of PLR in ischemic stroke and non-ischemic stroke by ROC analysis, the AUC was 0.668 (95% CI = 0.524-0.793) with sensitivity = 70.8%, specificity = 68.1%, and the cutoff values (198.3), figure 3a, p <0.001.

Table 1 Demographic, clinical and laboratory findings characteristics in COVID-19 patients

Characteristics, symptoms	COVID-19 patients (N=392), n (%)
Age (years), (mean ±SD)	40.21± 14.14
Male, n (%)	177 (45.1%)
Body mass index (kg/m$^{2)}$	33.13± 4.7
Systolic blood pressure (mm Hg)	140.7±27.4
Diastolic blood pressure (mm Hg)	85.2±6.28
Current smoker, n (%)	78(19.8%)
Coexisting condition	
No, n (%)	33(8.4%)
Hypertension, n (%)	111(28.3%)
Diabetes, n (%)	124(31.6%)
Chronic liver disease, n (%)	43(10.9)
Malignancy, n (%)	42(10.7%)
COPD, n (%)	78(19.8%)
Immunosuppression, n (%)	33(8.4%)
Leukocytes, $\times10^9$/L	5.9±1.691
Neutrophils, $\times10^9$/L	4.31±0.98
Lymphocytes $\times10^9$/L	1.01±0.77
Platelets, $\times10^9$/L	202.3±66.5
PLR	271.2±161.4
NLR	5.96±3.4
Hemoglobin, g/L	10.51± 3.4
TC (mg/dL)	288.07±60.3
TG (mg/dL)	213.6± 87.8
LDL cholesterol (mg/dL)	140.2± 43.28
HDL cholesterol (mg/dL)	45.5±9.78
FPG (mg/dl)	130.6± 36.92

Characteristics, symptoms	COVID-19 patients (N=392), n (%)
2-h plasma glucose (mg/dL)	205.08±50.3
HbA1c	7.5±2.795
Blood urea nitrogen, (mg/dl)	31.17± 9.22
Serum creatinine (mg/dl)	1.72±0.94
Lactate dehydrogenase, U/L	276.3± 114.7
C-reactive protein, mg/L	39.92± 30.7
D-dimer (ng/mL)	5.7±3.07
Ferritin (ng/mL)	452.1± 187.1
Serum uric acid (mg/dl)	5.36±2.6
Pulse oxygen saturation	74.8±11.19

WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low density lipoprotein.

Table 2: Demographic, clinical and laboratory findings characteristics in COVID-19 patients

Characteristics, symptoms	Without stroke (N=368)	Ischemic stroke (N=21)	Non ischemic stroke (N=3)	P value
Age (years), (mean ±SD)	40.2±14.6	52.1±23.06	41.1±16.85	0.773
Male, n (%)	166 (45.1%)	10 (47.6%)	1(33.3%)	0.104
BMI, kg/m^2	32.6±4.2	35.6±4.2 [a]	30.6±7.1[c]	<0.05
SBP (mm Hg)	145.9±25.6	150.7±28.4	149.7±20.1	0.325
DBP (mm Hg)	86.2±4.6	95.2±1.34[a]	80.2±9.76	<0.001*
Current smoker	69(18.7%)	8(38.1%)[a]	1(33.3%)[b]	<0.001*
Coexisting condition				
No, n (%)	31(8.4%)	2(9.5%)	0	<0.001*
Hypertension, n (%)	93(25.3%)	15(71.4%) [a]	3(100%)[b ,c]	<0.001*
Diabetes, n (%)	110(29.9%)	11(52.4%) [a]	3(100%) [b,c]	<0.001*
Chronic liver disease, n (%)	42(11.4%)	1(10.9)	0	<0.001*
Malignancy, n (%)	38 (10.3%)	4 (4.7%)	0	<0.001*
COPD, n (%)	72(19.6%)	6(28.6%) [a]	0	<0.001*
Immunosuppression, n (%)	30(8.2%)	3(14.2%) [a]	0	<0.001*
Leukocytes, ×10^9/L	5.8±1.14	6.6±1.11	10.8±4.31 [b,c]	<0.001*
Neutrophils, ×10^9/L	4.3±0.84	6.25±1.1[a]	6.021±0.7[b]	<0.001*
Lymphocytes ×10^9/L	1.12±0.79	0.75±0.28	0.96±0.45	0.318
Platelets, ×10^9/L	256.3±81.5	206.3±61.5	135.3±26.5	0.205
Hemoglobin, g/L	10.68±3.7	9.51±3.1	10.11±2.4	0.095
TC (mg/dL)	259.07±24.3	261.07±24.3	235.07±33.3	0.121
TG (mg/dL)	217.6±45.6	226.6±65.1	206.6±55.9	0.542
LDL cholesterol (mg/dL)	176.1±9.7	165.2±13.8	134.2±16.7[b]	0.004
HDL cholesterol (mg/dL)	37.33±3.2	35.75±8.18	42.5±6.78	0.124
FPG (mg/dl)	136.6±20.2	155.6±26.03[a]	116.6±17.1[b,c]	<0.001*
2-h plasma glucose (mg/dL)	231.4±32.5	271.08±59.3	187.08±44.3	<0.001*
HbA1c	7.9±1.8	8.5±2.5[a]	7.6±1.3	<0.001*
Blood urea, (mg/dl)	28.9±5.6	26.17±9.27	23±16.7	0.663
Serum creatinine (mg/dl)	1.52±0.4	1.82±0.7[a]	1.32±0.4[c]	0.015
LDH, U/L	309.8±59.6	296.3±124.2	256.3±103.5	0.849
C-reactive protein, mg/L	38.2±17.6	41.92±22.7	35.92±24.7	0.430

Characteristics, symptoms	Without stroke (N=368)	Ischemic stroke (N=21)	Non ischemic stroke (N=3)	P value
D-dimer (ng/mL)	1.9±1.2	6.9±3.07[a]	3.9±3.07[b,c]	<0.017
Ferritin (ng/mL)	393.1±52.4	592.1±117.1[a]	400.1±117.1[b, c]	<0.023
Serum uric acid (mg/dl)	5.76±2.9	7.76±1.9[a]	4.36±1.6[b,c]	<0.001*
Pulse oxygen saturation	80.8±43.1	72.8±11.9	76.8±9.2	0.313

TC; total cholesterol, TG; triacylglycerol. FPG fasting plasma glucose, Hba1c BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure LDH, lactate dehydrogenase. * Significant P values (P < 0.05) between three groups as calculated by ANOVA. LSD was done ;a Significant P values (P < 0.05) when compared between without stroke and ischemic stroke group. b Significant P values (P < 0.05) when compared between without stroke and non-ischemic stroke. C Significant P values (P < 0.05) when compared between ischemic stroke and non-ischemic stroke.

Table 3. Pearson correlation between NLR and PLR values with clinical and laboratory parameters among COVID -19 patients with stroke (n=24) patients

Parameters	NLR		PLR	
	r	P value	r	P value
HbA1c	0.020	0.692	0.023	0.645
Blood urea, (mg/dl)	0.048	0.348	0.065	0.189
Serum creatinine (mg/dl)	0.010	0.841	0.042	0.403
LDH, U/L	0.111	<0.05*	0.004	0.993
C-reactive protein, mg/L	0.169	<0.001*	0.272	<0.001*
D-dimer (ng/mL)	0.420	<0.001*	0.209	<0.001*
Ferritin (ng/mL)	0.142	<0.001*	0.178	<0.001*
Serum uric acid (mg/dl)	0.715	<0.001*	0.264	<0.001*
Pulse oxygen saturation	-0.015	0.765	-0.007	0.392

Table 4: Linear Regression Analysis in COVID -19 patients with stroke to assess the main independent factors correlated with NLR and PLR

Model		Unstandardized Coefficients		Standardized Coefficients	t	P value	95% C.I. for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
NLR	(Constant)	-14.828	8.070		-1.837	0.067	-30.695	1.039
	D-dimer	0.054	0.021	0.133	2.576	0.010	0.013	.094
	Ferritin	19.055	5.653	0.167	3.371	0.001	7.941	30.169
	Serum uric acid	-0.020	0.010	-0.134	-1.897	0.059	-0.040	.001
	Creatinine	0.792	0.523	0.110	1.513	0.131	-0.237	1.821
PLR	(Constant)	218.961	29.233		7.490	0.000	161.486	276.436

Model		Unstandardized Coefficients		Standardized Coefficients	t	P value	95% C.I. for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
	D-dimer	-0.337	0.075	-0.231	-4.474	0.000	-0.485	-0.189
	Ferritin	15.937	20.476	0.039	0.778	0.437	-24.321	56.195
	Serum uric acid	-0.026	0.038	-0.048	-0.677	0.499	-0.100	0.049
	Creatinine	3.404	1.896	0.131	1.795	0.073	-0.324	7.132

Table 5: Logistic regression analysis for prediction of stroke among COVID-19 patients

	B	S.E.	Wald	P value	OR	95% C.I.	
						Lower	Upper
Ferritin	-0.003	0.003	0.804	0.370	0.997	0.992	1.003
D-dimer	0.005	0.002	5.739	0.017	1.005	1.001	1.009
C-reactive protein,	0.009	.009	0.947	0.330	1.009	0.991	1.027
LDH, U/L	-0.006	00.005	1.549	0.213	0.994	0.985	1.003
PLR	-0.005	0.002	5.727	0.017	0.995	0.991	.999
NLR	0.395	0.075	27.389	0.000	1.484	1.280	1.721
Constant	-4.150	1.742	5.677	0.017	0.016		

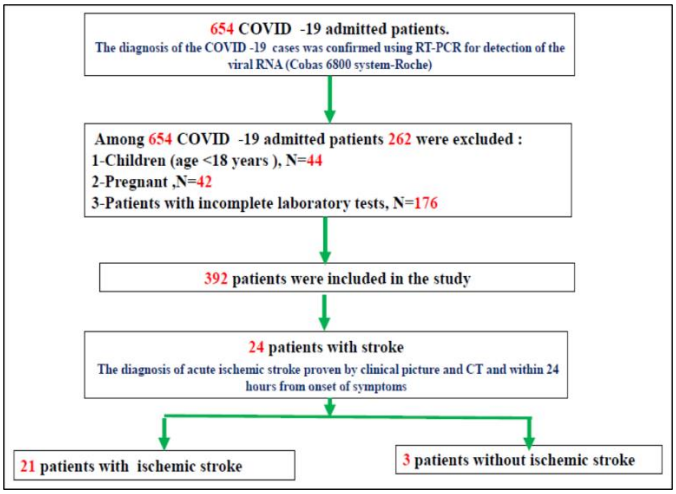

Figure 1: Study flowchart showing the patient selection.

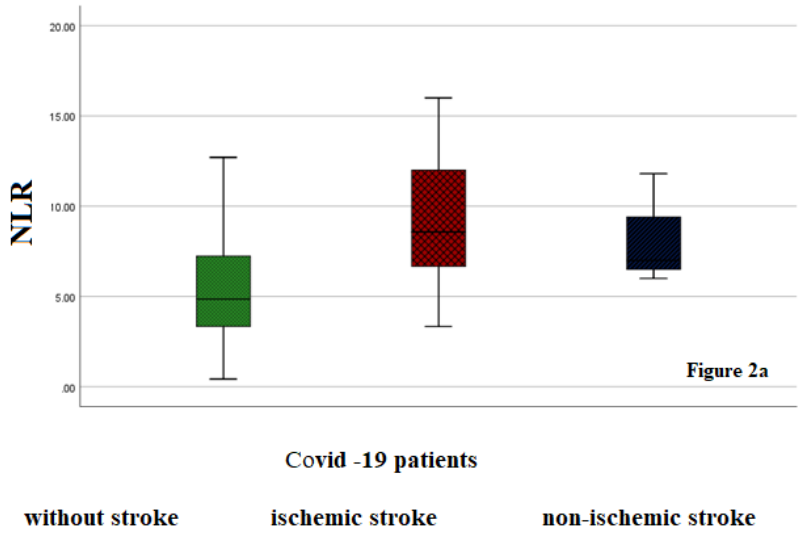

Figure 2a:Comparison between studied groups as regard NLR

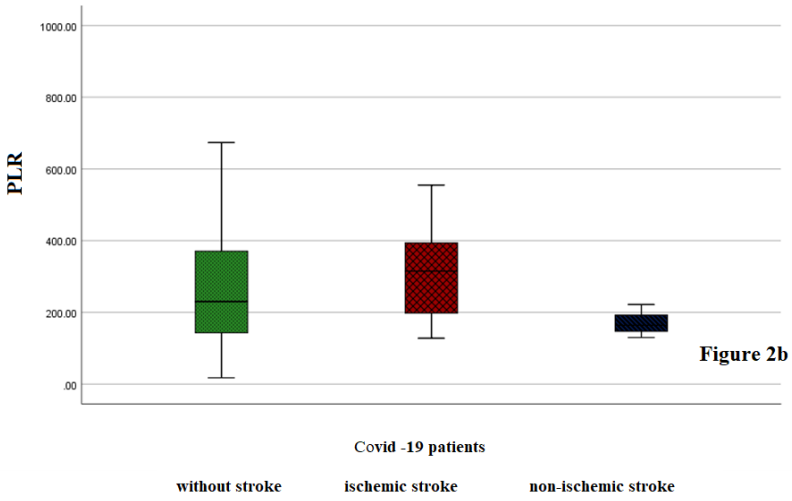

Figure 2b:Comparison between studied groups as regard \ PLR

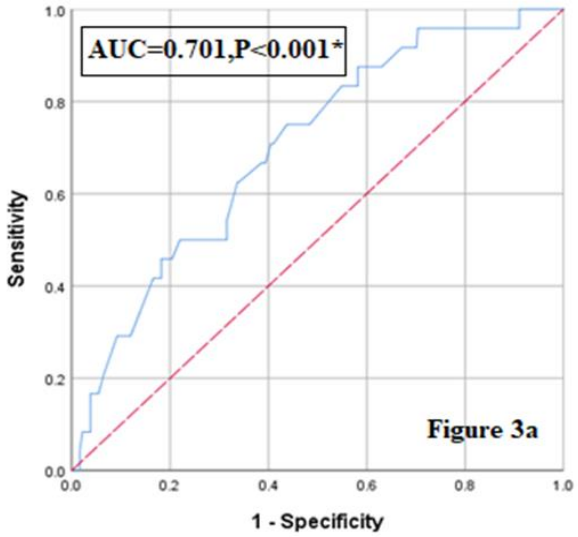

Figure 3a: The accuracy of NLR in differentiating ischemic stroke and non-ischemic stroke by Receiver operating characteristic curve (ROC)

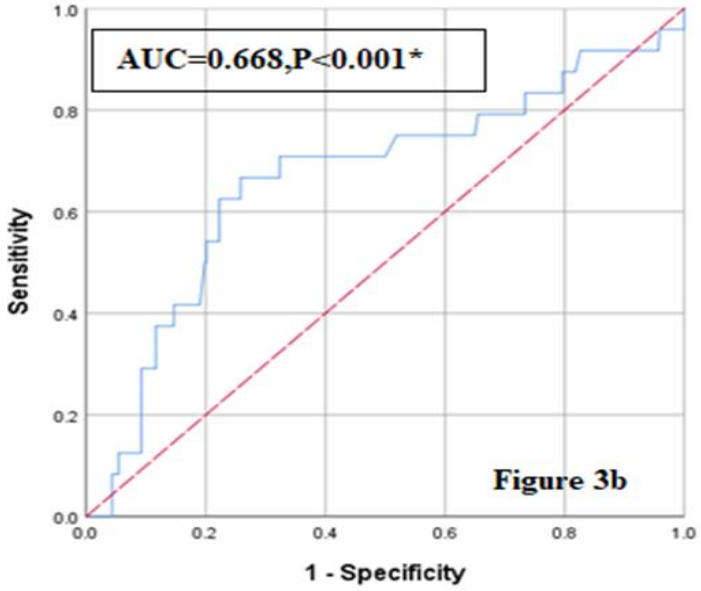

Figure 3b: The accuracy of PLR in differentiating ischemic stroke and non-ischemic stroke by Receiver operating characteristic curve (ROC)

DISCUSSION

Mounting evidence indicates that is widespread COVID-19 worldwide and is still a major threat to humanity. Even more importantly, COVID-19 like many pathogens including viruses can invade and destroy the brain leading to multiple diseases of CNS [10]. Recently published studies highlighted many pathogens attack CNS and caused many chronic disabilities [11,12]. Emerging evidence demonstrated that stroke is still a leading cause of morbidity and mortality, during this pandemic, its associations with COVID-19 and its clinical course in infected people are gradually increasing. Even more importantly, the prevalence of stroke in the pandemic era can be evaluated in two different perspectives; for the general population and in cases diagnosed with COVID-19 [13].

In this report, we have demonstrated that among enrolled Covid -19 patients,24 (6.1%) had an acute stroke [21 (5.35 %) had ischemic stroke and 3 (0.76%) had non-ischemic stroke]. We observed a substantial increase of metabolic and inflammatory disorders parameters in COVID -19 patients with ischemic stroke including BMI, diastolic blood pressure, platelets, PLR, FPG,2-h plasma glucose, HbA1c, D-dimer, ferritin, and serum uric acid compared to the non-ischemic group of strokes. Though, neutrophils count and NLR levels were significantly low in ischemic stroke compared to non-ischemic stroke.

Similar results were confirmed by Shahjouei et al study, they observed a high prevalence of stroke especially ischemic stroke in COVID-19 participants compared to general inhabitants. Interestingly, they observed a high prevalence of stroke in young patients and even in asymptomatic subjects with COVID -19 at stroke beginning [14].

The results of Helms et al detected that the frequency of stroke is reported between 2.8% and 5.4% among in-patient COVID-19 cases [15]. In another study conducted by Klok et al to evaluate COVI D-19 patients in an intensive care unit (ICU), the frequency of ischemic stroke was found to be 1.6% [16].

Supporting our results Sharifi-Razavi et al observed that most of the reported cases are diagnosed with ischemic stroke [17]. Also, we noticed that these findings could be contributed to the higher prevalence of stroke risk factors in these patients such as hypertension and diabetes, which are also indicative of poor outcomes in COVID-19 infection. Also, there might be several explanations for underlying pathophysiological mechanisms leading to stroke in the course of COVID-19 infection. The unrestrained cytokine storm in critical COVID-19 presentations leads to multi-organ failure. [18].

Against present results, research conducted by Balestrino et al study detected a marked decrease in the prevalence of diagnosed transient ischemic attack during peaks and outbreaks of COVID -19 at the large Italian university hospital in comparison with a similar time in 2019. They explained their finding that they did not notice any difference between 2020 and 2019 in the prevalence of stroke in their city could be contributed to the small number of populations in their city [19]. Also, Hoyer et al data demonstrate and quantifies the low prevalence of in-patient admission of recent cases of stroke during the COVID-19 pandemic and they suggested that the social distance during this pandemic could be the reason for this low prevalence of stroke patient hospitalization [20].

According to Rudilosso and his colleagues, they observed about a 25% reduction in ischemic stroke admission in hospitals and centers of stroke [21].

In contrast to our results, Rudilosso et al [21]and Hoyer et al [20] observed a reduction in the prevalence of ischemic stroke admission in hospitals and centers of stroke and these differences could be due to the small number of populations in their city and social distance during this COVID -19 pandemic could be the reason for this low prevalence of stroke patient hospitalization

This study provides evidence that among studied clinical and laboratory parameters, there were significant positive correlations between NLR and PLR values with LDH, C-reactive protein, D-dimer, ferritin, serum uric acid. For further evaluation of study correlations results we analyzed our results by linear regression test in COVID -19 patients with stroke, we detected that D-dimer and ferritin were independently correlated with NLR ($P< 0.001$). While only D-dimer was independently correlated with NLR. Interestingly the current study results observed that NLR, PLR and D-dimer levels were the only predictors of stroke among COVID-19 patients (OR = 1.484; OR = 0.995; OR = 1.005 respectively,) by logistic regression analysis test.

The interesting findings of our study were that there was a considerable difference among studied groups; Covid -19 patients without stroke, ischemic stroke, and non-ischemic stroke as regard NLR. While, PLR, the result of the present study detected that there was

a non-considerable variation between studied groups as regard PLR. Moreover, the power of NLR in ischemic stroke and non-ischemic stroke by ROC analysis, the AUC was 0.701 (95% CI = 0.600-0.802) with sensitivity = 75%, specificity = 57.2%, and the cutoff values (5.3), however, the power of PLR in ischemic stroke and non-ischemic stroke by ROC analysis, the area under the curve was 0.668 (95% CI = 0.524-0.793) with sensitivity = 70.8%, specificity = 68.1%, and the cutoff values (198.3).

Similar findings were observed by another Egyptian study conducted by Shahin et al et evaluate the prognostic value of NLR in acute patients with IS either treated by intervention methods or not and they observed that NLR among ischemic stroke patients with bad prognosis was significantly higher than patients who had a good prognosis. Interestingly, they detected that the optimal limit value of NLR for the prediction of unfavorable outcomes was 4.15 with a sensitivity of 100% and a specificity of 88.5%.

Some limitations should be considered. the small sample size of the study in particular in the non-ischemic stroke group of COVID -19 patients as this study was a retrospective cross-sectional study thus further studies with a larger sample size should be performed in the future to validate our results.

In conclusion, the present research observed that NLR had significant power in the prediction of ischemic stroke and could be used as an easy, cheap, and noninvasive marker of stroke in the particular ischemic subgroup for proper management of patients with COVID-19 complications.

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