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Study of the Predictive Value of Neutrophil/Lymphocyte Ratio in Diagnosis of COVID-19 Infection

Ayman Mohammed Ellehleh[1], Mohsen Mohamed Elkhayat[1], Reham Salah EL Zaiat[2], Mervat Hussein Kamel Habib[1], Ahmed Ragab El-Gazzarah[1]

Departments of [1]Tropical Medicine and [2]Clinical Pathology,
Faculty of Medicine, Menoufia University, Menoufia, Egypt

***Corresponding author:** Mervat Hussein Kamel, **Mobile:** (+20) 01010096261, **E-mail:** waleedkhedr1991@gmail.com

ABSTRACT

Background: Early diagnosis of COVID-19 infection can prevent the lethal clinical course of the disease and result -instead- in a better outcome. Thus, there was an urging need for rapid and simple laboratory tests for early prediction of infection that will eventually improve morbidity and mortality of the disease.

Objective: The study aimed to assess the predictive value of neutrophil/lymphocyte ratio in the diagnosis of COVID-19 infection in terms of sensitivity and specificity.

Patients and methods: In this retrospective study, we analyzed the clinical data of 150 participants divided into three equal groups; 50 patients with a positive reverse transcription polymerase chain reaction (RT-PCR) oronasopharyngeal swab for SARS-CoV-2 (Group I), 50 patients with non-COVID-19-related fevers and/or respiratory illness (negative swab and CT chest) (Group II) and 50 healthy controls (Group III).

Results: There was a high statistically significant difference between the studied groups regarding absolute neutrophil count, absolute lymphocyte count, NLR, CRP and serum ferritin. In this study there was a significant correlation between NLR and CRP while, there were no significant correlations between NLR and other parameters like BMI, heart rate, Hb, platelet count and serum ferritin. Thus, the NLR can be considered as a dependable predictor of COVID-19 infection at a cutoff point of more than 3.06 with sensitivity 61% and specificity 86%

Conclusion: NLR could be a useful, cheap, simple marker for early prediction of patients infected with COVID-19 with cutoff point more than 3.06. NLR could be used as a dependable risk predictor in the diagnosis of COVID-19 infections apart from its cut-off point.

Keywords: COVID-19, Lymphocyte, Neutrophil, NLR, Cutoff point.

INTRODUCTION

COVID-19 caused catastrophic effects on the world's demographics as the disease has a high rate of infection and mortality. It was first discovered in Wuhan, China, in December 2019 as an infectious disease in which patients suffered from ARDS of unknown cause [1]. The disease, which was found to be caused by one of beta-corona viruses was considered as a pandemic in March 2020 [2], as the virus was of a highly infectious deadly strain [3]. This new coronavirus can spread from person to person mainly by aerosol and contact routes [4]. The main target for COVID-19 infection was to bind to angiotensin-converting enzyme 2 (ACE2) receptor in the host cell membrane so, it can enter the host cell. COVID- 19 disease has been rapidly distributed around the world and caused a lot of deaths so, many countries had to impose quarantine in different places [5]. The clinical presentation of this disease ranged from asymptomatic infection to severe symptomatic cases with acute respiratory failure, which was lethal in some cases [6].

COVID -19 affects many systems and organs in the body leading to their failure. It can also cause endothelial damage and cytokine storm. The early detection of COVID-19 infection has a great effect on clinical outcome of the patients so there was a need for rapid available laboratory tests for early detection of infection. Multiple hematological abnormalities and acute phase reactants have been well correlated with disease severity and progression[7].

Several prior research on neutrophils, lymphocytes, CRP, serum ferritin, and other reactive proteins in COVID-19 patients have been conducted [5-8]. However, nothing is known regarding their relationship with early illness prediction in Egypt.

Because of the low cost and ease of access to the neutrophil-to-lymphocyte ratio (NLR), many researches declared that it could be used as a prognostic factor in different diseases like solid cancer, cardiovascular diseases, chronic obstructive pulmonary diseases, rheumatic diseases, traumatic brain injury and hepatic and pancreatic diseases. So, it can also be used as a diagnostic factor in COVID -19 infection [9-12].

The aim of the present study was to assess the predictive value of the NLR in the diagnosis of COVID-19 infection in terms of sensitivity and specificity.

PATIENTS AND METHODS

Study Design: In this retrospective study we analyzed the clinical data of 100 patients. Fifty of them were COVID-19 patients [diagnosed with a positive reverse transcription polymerase chain reaction (RT-PCR) oronasopharyngeal swab for SARS-CoV-2] (**Group I**; COVID group).

Another 50 patients with non-COVID-19-related fevers and/or respiratory illness (negative swab and

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CT chest) (**Group II**; Non COVID group). The laboratory data of another 50 healthy volunteers age- and sex-matched were included as a control group (**Group III**). Patients' data were collected from the patients' clinical records of Zaweit Alnaora Central Hospital, Menofia Governorate.

Inclusion criteria: Patients with COVID-19 with positive oronasopharyngeal swab for SARS-CoV-2, or non-COVID-19-related fevers and/or respiratory illness (negative swab and CT chest) and aged > 18 years old.

Exclusion criteria: Patients < 18 years old, pregnant women and patients with lab evidence- or history of chronic kidney, hematological or liver diseases and malignancies or patients receiving immune-suppressant drugs.

The data records of the included patients were tabulated with special interest on:
The clinical presenting symptoms and signs of the included patients at the time of admission especially respiratory symptoms. The existence of chronic diseases especially cardiovascular, respiratory, kidney, liver, hematological diseases, malignancies and immune suppressant drugs.

Clinical examination: Vital signs records, O^2 saturation at the time of admission, cardiac and chest and abdominal examination findings. **Laboratory investigations: Complete blood count** including haemoglobin concentration (Hb), RBCs count, WBCs count, absolute neutrophil count, absolute lymphocyte count, NLR and platelet count. **Liver function tests** including serum total and direct bilirubin, serum albumin, ALT, AST and Prothrombin time and concentration. **Renal function tests** including blood urea and serum creatinine. **C-reactive protein** and **Imaging studies** including CT chest.

Ethical approval: Menoufia Medical Ethics Committee of Menoufia Faculty of Medicine gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis

SPSS version 23 was used to gather and analyse data. Statistics were separated into two categories: Descriptive statistics: quantitative data was provided as a median and range, while qualitative data was presented as numbers (N) and percentages (%). Chi-square test (X^2), Student-t test (t), Mann-Whitney (U) test and ANOVA test (F) were used. P value ≤ 0.05 was deemed statistically significant.

RESULTS

Patients' Socio-Demographics: There were no statistically significant differences between the analysed groups in terms of age or gender, however there was a statistically significant difference in terms of BMI and smoking ($p<0.05$) (Table 1).

Table (1): Socio-demographic data among the studied groups

	Group I (n = 50)		**Group II (n=50)**		**Group III (n = 50)**		**Test of sig.**	**p**
	No.	**%**	**No.**	**%**	**No.**	**%**		
Age (years)								
Min. – Max.	21-80		19-90		19-77		F=	
Mean ± SD.	53.300±14.417		52.380±16.787		50.580±16.469		0.377	0.686
Sex								
Female	28	56.00	25	50.00	18	36.00	χ^2=	0.121
Male	22	44.00	25	50.00	32	64.00	4.225	
BMI (kg/m^2)								
Min. – Max.	22.5-32.4		17.4-29.6		17.5-24.8		F=	<0.001*
Mean ± SD.	27.014±2.519		23.192±3.514		20.758±1.886		67.051	
Tukey test	**p1** <0.001, **p2** <0.001, **p3** <0.001							
Smoking								
Smoker	22	44.00	20	40.00	8	16.00	χ^2=	0.006*
Non-smoker	28	56.00	30	60.00	42	84.00	10.320	

*p1=Group I, II p2=Group I, III p3=Group II, III

In terms of hypertension, there was a statistically significant difference between the tested groups, while there was a statistically insignificant difference between the studied groups regarding COPD, diabetes, heart failure, chronic kidney disease, malignancy and immunosuppressive therapy (p>0.05) (Table 2).

Table (2): Prevalence of chronic diseases among the studied groups

		Group I (n=50)		Group II (n=50)		Total		X^2	P-value
		N	%	N	%	N	%		
COPD	**Yes**	22	44.00	27	54.00	49	49.00	1.000	0.317
	No	28	56.00	23	46.00	51	51.00		
Diabetes	**Yes**	18	36.00	17	34.00	35	35.00	0.044	0.834
	No	32	64.00	33	66.00	65	65.00		
Hypertension	**Yes**	28	56.00	12	24.00	40	40.00	10.667	0.001*
	No	22	44.00	38	76.00	60	60.00		
Heart failure	**Yes**	3	6.00	1	2.00	4	4.00	1.042	0.307
	No	47	94.00	49	98.00	96	96.00		
Chronic kidney disease	**Yes**	3	6.00	1	2.00	4	4.00	1.042	0.307
	No	47	94.00	49	98.00	96	96.00		
Immunosuppressive therapy	**Yes**	1	2.00	1	2.00	2	2.00	0.000	1.000
	No	49	98.00	49	98.00	98	98.00		
Malignancy	**Yes**	1	2.00	1	2.00	2	2.00	0.000	1.000
	No	49	98.00	49	98.00	98	98.00		

There was high statistically-significant difference between the studied groups regarding the prevalence of anosmia and loss of taste ($p < 0.001$), while there was a statistically-significant difference between the studied groups regarding abdominal pain ($p < 0.05$). There was no significant difference between the studied groups regarding fever, headache, dyspnea, cough, diarrhea and hemoptysis (p>0.05) (Table 3).

Table (3): Clinical data among the studied groups

		Study group						Chi-Square	
		Group I (N=50)		Group II (N=50)		Total (n=100)			
		N	%	N	%	N	%	X^2	P-value
Fever	**Yes**	35	70.00	39	78.00	74	74.00	0.832	0.362
	No	15	30.00	11	22.00	26	26.00		
Headache	**Yes**	22	44.00	18	36.00	40	40.00	0.667	0.414
	No	28	56.00	32	64.00	60	60.00		
Anosmia	**Yes**	31	62.00	8	16.00	39	39.00	22.236	<0.001*
	No	19	38.00	42	84.00	61	61.00		
Loss of taste	**Yes**	28	56.00	6	12.00	34	34.00	21.569	<0.001*
	No	22	44.00	44	88.00	66	66.00		
Dyspnea	**Yes**	18	36.00	26	52.00	44	44.00	2.597	0.107
	No	32	64.00	24	48.00	56	56.00		
Cough	**Yes**	37	74.00	36	72.00	73	73.00	0.051	0.822
	No	13	26.00	14	28.00	27	27.00		
Diarrhea	**Yes**	24	48.00	19	38.00	43	43.00	1.020	0.313
	No	26	52.00	31	62.00	57	57.00		
Epigastric pain	**Yes**	43	86.00	28	56.00	71	71.00	10.928	0.001*
	No	7	14.00	22	44.00	29	29.00		
Hemoptysis	**Yes**	11	22.00	16	32.00	27	27.00	1.268	0.260
	No	39	78.00	34	68.00	73	73.00		

There was high statistically-significant difference between the studied groups regarding SBP, DBP, respiratory rate, oxygen saturation ($p<0.001$), while there was no significant difference between the studied groups regarding heart rate ($p>0.05$) (Table 4).

Table (4): Vital signs among the studied groups

		Study group									**ANOVA**		**TUKEY'S Test**		
		Group I (n=50)			**Group II (n=50)**			**Group III (n=50)**			**F**	**P-value**	**I&III**	**I&III**	**II&III**
Heart rate (bpm)	**Range**	63	-	125	60	-	98	64	-	98	1.517	0.223			
	Mean ±SD	85.70	±	18.39	81.280	±	9.85	82.38	±	9.38					
SBP (mmHg)	**Range**	90	-	170	90	-	130	90	-	120	11.224	<0.001*	0.001*	<0.001*	0.870
	Mean ±SD	115.40	±	16.56	105.500	±	11.44	104.20	±	9.81					
DBP (mmHg)	**Range**	60	-	110	60	-	100	60	-	80	11.220	<0.001*	0.007	<0.001*	0.255
	Mean ±SD	74.60	±	12.48	68.400	±	9.97	65.20	±	7.06					
Respiratory rate	**Range**	12	-	32	21	-	32	11	-	19	179.558	<0.001*	<0.001*	<0.001*	<0.001*
	Mean ±SD	18.04	±	4.83	26.480	±	2.49	14.22	±	1.81					
Oxygen saturation	**Range**	64	-	99	89	-	99	90	-	99	18.245	<0.001*	<0.001*	<0.001*	0.958
	Mean ±SD	88.72	±	9.15	94.580	±	3.08	94.90	±	2.47					

Patients' Laboratory and imaging data:

Absolute lymphocyte count, absolute neutrophil count, NLR, CRP, serum ferritin, D-dimer, LDH, procalcitonin and serum creatinine showed highly significant differences among the studied groups ($p<0.001$), while platelet count, WBCs, blood urea, total bilirubin and serum albumin were significantly different among the studied group ($p<0.05$). On the other hand, there were no significant differences between the studied groups regarding Hb, prothrombin time, ALT and AST ($p>0.05$) (Table 5).

Table (5): Laboratory investigations among the studied groups

		Study group			ANOVA		TUKEY'S Test		
		Group I (n=50)	Group II (n=50)	Group III (n=50)	F	P-value	I&II	I&III	II&III
(Hb) (g/dl)	**Mean ±SD**	12.142 ± 1.876	12.640 ± 1.809	12.498 ± 1.519	1.087	0.340			
Platelet count×10^3	**Mean ±SD**	272.380 ± 67.83	218.020 ± 52.12	229.160 ± 56.821	4.230	0.016*	0.018*	0.076	0.839
White blood cells ×10^3	**Mean ±SD**	9.028 ± 2.14	9.133 ± 2.09	6.902 ± 1.65	3.714	0.027*	0.993	0.059	0.044*
Absolute lymphocyte count ×10^3	**Mean ±SD**	1.516 ± 0.281	2.641 ± 0.551	2.280 ± 0.54	14.049	<0.001*	<0.001*	0.002*	0.221
Absolute neutrophil count ×10^3	**Mean ±SD**	7.072 ± 1.63	6.913 ± 1.55	4.033 ± 0.981	11.585	<0.001*	0.973	<0.001*	<0.001*
NLR	**Mean ±SD**	5.299 ± 1.201	3.066 ± 0.740	1.863 ± 0.45	36.983	<0.001*	<0.001*	<0.001*	0.010*
CRP (mg/L)	**Mean ±SD**	51.360 ± 12.611	16.620 ± 3.981	11.220 ± 2.601	31.866	<0.001*	<0.001*	<0.001*	0.585
Serum ferritin (ng/ m L)	**Mean ±SD**	381.880 ± 9.93	98.220 ± 23.401	86.180 ± 20.132	59.899	<0.001*	<0.001*	<0.001*	0.918
D-dimer(mg/L)	**Mean ±SD**	1.800 ± 0.431	0.638 ± 0.141	0.234 ± 0.041	104.991	<0.001*	<0.001*	<0.001*	0.001*
LDH (U/L)	**Mean ±SD**	293.080 ± 47.664	266.820 ± 32.199	162.680 ± 38. 618	135.899	<0.001*	0.006*	<0.001*	<0.001*
Procalcitonin (ng/mL)	**Mean ±SD**	3.188 ± 0.773	1.592 ± 0.313	0.227 ± 0.054	470.566	<0.001*	<0.001*	<0.001*	<0.001*
Prothrombin time (seconds) and concentration	**Mean ±SD**	90.300 ± 6.309	91.060 ± 5.032	89.180 ± 5.944	1.335	0.266			
Serum creatinine (mg/dl)	**Mean ±SD**	1.074 ± 0.240	0.764 ± 0.187	0.786 ± 0.152	12.026	<0.001*	<0.001*	<0.001*	0.949
Blood urea (mg/dl)	**Mean ±SD**	40.120 ± 9.921	31.160 ± 4.400	29.460 ± 4.987	5.598	0.005*	0.026*	0.006*	0.873
ALT (U/L)	**Mean ±SD**	27.040 ± 6.486	24.740 ± 5.731	25.180 ± 5.557	1.814	0.167			
AST (U/L)	**Mean ±SD**	21.020 ± 5.120	20.760 ± 4.891	20.040 ± 4.853	0.331	0.719			
Total bilirubin (mg/dl)	**Mean ±SD**	0.709 ± 0.160	0.634 ± 0.156	0.597 ± 0.147	3.470	0.034*	0.196	0.029*	0.673
Serum albumin (g/ L)	**Mean ±SD**	4.355 ± 0.619	4.671 ± 0.304	4.441 ± 0.473	5.750	0.004*	0.004*	0.646	0.048*

There was a high statistically-significant difference between the studied groups regarding the CORAD degree of the CT chest and the prevalence of ground glass opacities and/or consolidation (p<0.001). There was no significant difference among the studied groups regarding pleural effusion, cardiac effusion, cardiomegaly, mediastinal mass & L.N, pneumothorax and clinical outcome (p>0.05) (Table 6).

Table (6): CT chest and clinical outcome among the studied groups

Study group		Group I (n=50)		Group II (n=50)		Total (n=100)			
		N	%	N	%	N	%	X^2	P-value
CT chest CORAD	CORAD 1	0	0.00	15	30.00	15	15.00	88.879	<0.001*
	CORAD 2	0	0.00	8	16.00	8	8.00		
	CORAD 3	2	4.00	26	52.00	28	28.00		
	CORAD 4	12	24.00	1	2.00	13	13.00		
	CORAD 5	36	72.00	0	0.00	36	36.00		
GGO or consolidation	Yes	32	64.00	13	26.00	45	45.00	14.586	<0.001*
	No	18	36.00	37	74.00	55	55.00		
Complication	Pleural effusion	3	6.00	1	2.00	4	4.00	1.042	0.307
	Cardiac effusion	2	4.00	1	2.00	3	3.00	0.344	0.558
	Cardiomegaly	3	6.00	1	2.00	4	4.00	1.042	0.307
	Mediastinal mass	1	2.00	0	0.00	1	1.00	1.010	0.315
	Mediastinal L.N	1	2.00	1	2.00	2	2.00	0.000	1.000
	Pneumothorax	1	2.00	0	0.00	1	1.00	1.010	0.315
Outcome	Died	3	6.00	2	4.00	5	5.00	4.027	0.134
	Still admitted	18	36.00	28	56.00	46	46.00		
	Discharge	29	58.00	20	40.00	49	49.00		

There was a significant correlation between NLR and CRP, lymphopenia and absolute neutrophil count. On the other hand, there were no significant correlations between NLR and other parameters like BMI, heart rate, SBP, DBP, respiratory rate, oxygen saturation, Hb, platelet count, serum ferritin, prothrombin time and concentration, serum creatinine, blood urea, ALT, AST, total bilirubin and serum albumin (p>0.05) (Table 7).

Table (7): Correlation between socio-demographics, lab investigation and NLR among the studied groups

Correlations				
	NLR			
	Group I (n=50)		Group II (n=50)	
	r	P-value	r	P-value
Age (Years)	0.177	0.219	-0.288	0.043*
BMI (kg/m^2)	-0.009	0.950	-0.023	0.872
Heart rate(bpm)	0.141	0.330	-0.032	0.826
SBP (mmHg)	0.156	0.279	-0.059	0.682
DBP (mmHg)	0.095	0.512	-0.039	0.786
Respiratory rate	0.167	0.247	0.099	0.493
Oxygen saturation	-0.233	0.104	0.217	0.130
Hb (mg/dl)	-0.060	0.678	-0.047	0.743
Platelet count×10^3	-0.149	0.301	0.007	0.964
White blood cells ×10^3	0.132	0.362	0.427	0.002*
Absolute lymphocyte count ×10^3	-0.325	0.021*	-0.460	0.001*
Absolute neutrophil count) ×10^3	0.375	0.007*	0.685	<0.001*
CRP (mg/L)	0.290	0.041*	0.314	0.027*
Serum ferritin (ng/ m L)	0.101	0.483	0.243	0.090
D-dimer(mg/L)	-0.098	0.498	0.165	0.252
LDH (U/L)	0.023	0.875	-0.091	0.531
Procalcitonin(ng/mL)	0.090	0.532	-0.007	0.959
Prothrombin time and concentration	0.221	0.123	-0.141	0.330
Serum creatinine (mg/dl)	0.008	0.957	-0.018	0.902
Blood urea (mg/dl)	0.010	0.946	-0.019	0.895
ALT (U/L)	0.062	0.669	-0.105	0.468
AST (U/L)	-0.117	0.419	-0.089	0.537
Total bilirubin (mg/dl)	0.239	0.094	-0.138	0.338
Serum albumin (g/L)	-0.096	0.508	0.009	0.952

The cutoff values of NLR:

At a cutoff point of >3.06, NLR could discriminate COVID-19 patients from healthy individuals with sensitivity of 61% and specificity of 86% (Table 8 and figure 1).

Table (8): ROC curve between group I and group III

ROC curve between Cases and Control						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
NLR	>3.06	61.0	86.0	89.7	52.4	81.7%

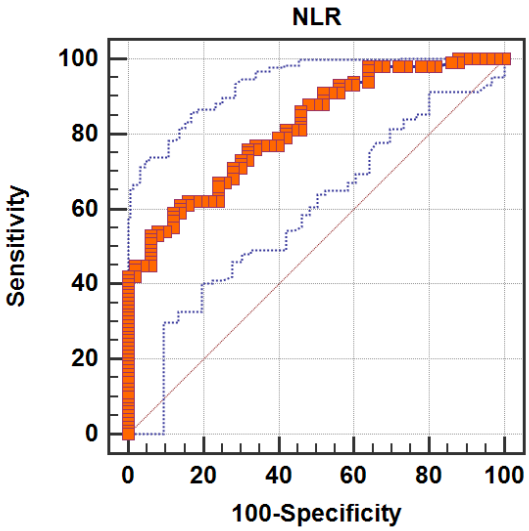

Figure (1): ROC curve between group I and group III

The cutoff point of NLR between cases (COVID-19 patients and patients with fever related respiratory illness) and control (healthy group) was > 2.96 with sensitivity and specificity of 86% and 84% respectively (Table 9 and figure 2)).

Table (9): ROC curve between patient groups (I&II) and Group III

ROC curve between Group I and Group III						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
NLR	>2.96	86.0	84.0	84.3	85.7	92.1%

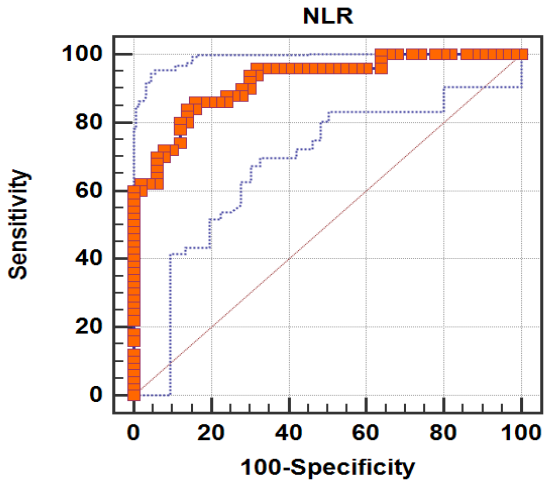

Figure (2): ROC curve between Cases and Control.

At a cutoff point of > 2.69, NLR could discriminate COVID-19 patients from other non-COVID respiratory illness with sensitivity and specificity of 88% and 62% respectively (Table 10 and figure 3).

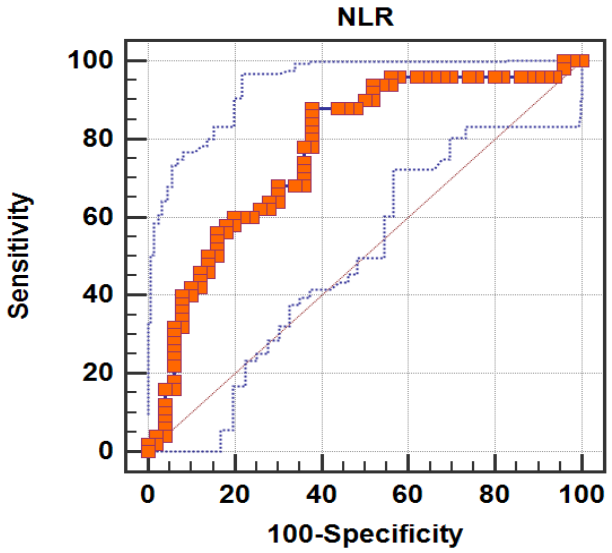

Figure (3): ROC curve between group 1 and group 2

Table (10): ROC curve between Group I and Group II

ROC curve between Group I and Group II						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
NLR	>2.69	88.0	62.0	69.8	83.8	77.3%

At a cutoff point of > 1.36, NLR could discriminate non-COVID-19 patients from healthy individuals with sensitivity and specificity of 90% and 44% respectively (Table 11 and figure 4)).

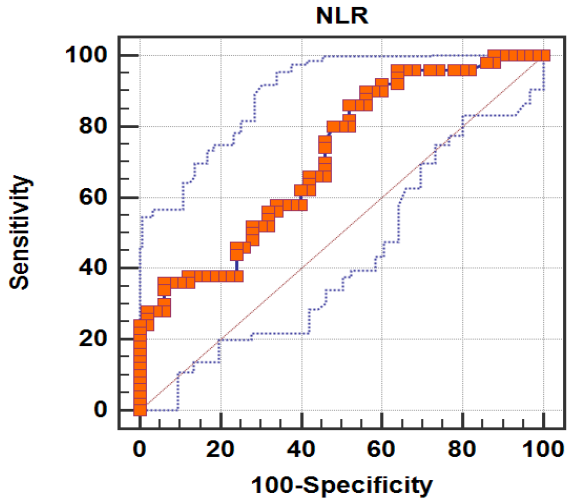

Figure (4): ROC curve between Group II and Group III

Table (11): ROC curve between Group II and Group III

ROC curve between Group II and Group III						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
NLR	>1.36	90.0	44.0	61.6	81.5	71.3%

DISCUSSION

COVID-19 infection spread rapidly all over the world and caused many social and medical problems therefore, early detection of infection by different inflammatory markers, among them the NLR could help [13]. With these ideas, we aimed to detect the changes that occur in the hematological profile of coronavirus-positive cases and also compare them with patients affected by non-COVID related fevers and/or respiratory illness and with the healthy controls so that early isolation could be considered.

In the current study, there was a statistically negligible difference in age and sex between the analysed groups, which is consistent with the findings of **Kabak *et al.*** [14] and **Mousavi-Nasab *et al.*** [15]. In contrast to our findings, there was a statistically significant difference between the studied groups in terms of age and gender in the study of **Tahtasakal *et al.*** [16], where 534 patients were divided into two unequal groups and his study included a large number of ICU patients.

In the current study, there was a statistically significant difference between the studied groups in terms of BMI and smoking, which is consistent with **Cai *et al.*** [17] and **Nicholas *et al.*** [18] who concluded a statistically significant difference between the studied groups in terms of BMI and smoking.

In this study, there was a statistically significant difference in the prevalence of chronic illnesses across the analysed groups in terms of hypertension, while there was a statistically insignificant difference between the studied groups regarding COPD, diabetes, heart failure, chronic kidney disease, malignancy and immunosuppressive therapy and these results agree with those of the study of **Liu *et al.*** [19].

In our study, groups I and II did not vary statistically in terms of fever, headache, dyspnea, cough, diarrhoea, or hemoptysis. This agrees with **Kabak *et al.*** [14]. Meanwhile, in terms of anosmia, loss of taste, and epigastric discomfort, there was a statistically significant difference between the groups investigated and this is in disagreement with **Tahtasakal *et al.*** [16]**.** This can be rationalized by the fact that the study compared between mild-moderate- and severe-critical ICU patients on mechanical ventilation and there was no control group.

There was a high statistical difference between the comparative groups as regards SBP and DBP. This is similar with the findings of the research by **Prozan *et al.*** [20].

In our study, respiratory rate and oxygen saturation showed high statistically significant difference and this is in agreement with **Mejía *et al.*** [21] in his retrospective cohort study on 369 patients.

In the present study heart rate had a statistically insignificant difference between the patients' groups (I & II). This is in agreement with **Ikram *et al.*** [22] in his study that was conducted at South Africa on 236 participants. In contrast with our result, **Tahtasakal *et al.*** [16] revealed a statistically significant difference, which could be rationalized by the fact that his study included large number of ICU patients.

In the present study platelet count, WBCs, blood urea, total bilirubin and serum albumin were significantly different among the studied groups. This is in contrast with **Cai *et al.*** study [17] that included 455 COVID-19 patients and showed that platelet count, WBCs, blood urea, total bilirubin and serum albumin had no significant differences. This could be due to the study design that was tightly dependent on body mass index of the patients and racial bias (most of the included patients were Chinese).

There were no statistically significant changes between the examined groups in Hb, prothrombin time, ALT, and AST, which is consistent with the findings of the **Liu *et al.*** [19] research.

There was a substantial statistical difference between the examined groups in terms of CT chest CORAD and GGO or consolidation, while there was a statistically insignificant difference among the studied groups regarding pleural effusion, cardiac effusion, cardiomegaly, mediastinal mass, mediastinal L.N, and pneumothorax. Our results agree with those of **Grassi *et al.*** [23] (134 patients included, in Italy) who concluded that GGO, with areas of consolidations were present in high percentage (96.8%) in COVID-19 patients and additional CT signs such as discrete pulmonary nodules, mediastinal lymphadenopathy, pericardial and pleural effusions were found in low percentage of cases.

There was a strong association between NLR and CRP in this investigation. Also, there were strong correlations between NLR and lymphopenia & absolute neutrophil count. This is in agreement with **Kulkarni *et al.*** [24] in his study on 60 patients and with **Sukrisman *et al.*** [25] in his study involving 41 COVID-19 patients.

There were no significant connections between NLR and other study characteristics such as BMI, heart rate, SBP, DBP, respiratory rate, oxygen saturation, Hb, platelet count, serum ferritin, prothrombin time and concentration, serum creatinine, blood urea, ALT, AST, total bilirubin and serum albumin. This important finding indicates that NLR was not affected by some important laboratory parameters that it could be used as a marker for detection of COVID-19 infection. This is in agreement with **Caillon *et al.*** [26] in his study on 157 COVID-19 patients. In contrast**, Al-Humairi *et al.*** [27] reported a significant correlation between NLR and other lab parameters in their study that was

conducted on 139 COVID-19 patients at Baghdad Teaching Hospital (Baghdad, Iraq). This can be rationalized by the fact that their study was done on group of COVID-19 patients that were randomly selected and with no control group.

As the NLR is considered rapid and economical test to detect the degree of inflammation, so it could help physicians in early detection of inflammation despite of its variable cutoff values. Several studies showed high cutoff values and others with low values so, we tried to make a more comprehensive analysis about the cutoff point of NLR. In the present study NLR at a cutoff point of > 3.06 could discriminate COVID-19 patients from healthy individuals with a sensitivity of 61%, specificity of 86%, PPV of 89.7%, NPV of 52.4% and accuracy of 81.7%. This result is very close to that reported by **Liu *et al.*** [19] in his prospective study, which included 61 patients in China and stated that the incidence of critically ill patients with NLR ≥ 3.13 was 50%, and 9.1% with NLR < 3.13.

Also, in the present study NLR at a cutoff point of more than 2.96 could discriminate the included cases (COVID-19 and non-COVID patients with respiratory tract infection) from healthy controls with a sensitivity of 86%, specificity of 84%, PPV of 84.3%, NPV of 85.7% and accuracy of 92.1%. This result is so close to that of **Sukrisman *et al.*** [25] that showed two values for NLR: 2.62 for non-severe patients and 7.06 for severe disease, which showed the importance of NLR in early detection of COVID-19 infection. But this result is quite far from that reported in **Al-Humairi *et al.*** [27] study that declared that an NLR at 12.9 had a sensitivity of 82.4% and specificity of 81.9%. This difference because their study was done on a group of COVID-19 patients randomly-selected with no control group and presence of ICU patients.

ROC curve analysis of NLR between COVID-19 patients and patients with non-COVID respiratory tract infections revealed that NLR at a cutoff point of more than 2.69 could discriminate both groups with a sensitivity of 88%, specificity of 62%, PPV of 69.8%, NPV of 83.8% and accuracy of 77.3%. Yet, this result is quite away from the study of **Prozan *et al.*** [20], which declared that NLR at a cutoff value of > 6.82 had an odds ratio of 2.88 and p-value of < 0.001.

At a cutoff point of >1.36, NLR could discriminate non-COVID-19 patients with respiratory tract infection from healthy individuals with a sensitivity, specificity, PPV, NPV, and accuracy of 90%, 44%, 61.6%, 81.5% and 71.3% respectively. This result is away from that reported by **Taylan *et al.*** [28] in their study done in Turkey, as they declared an NLR cutoff for detecting exacerbation of COPD of 3.29 with a sensitivity and specificity of 80.8% and 77.7% respectively (AUC 0.894, P = 0.001). This difference in the cutoff value can be rationalized by the fact that their study included a low number of patients and included a large number of COPD patients with no consideration of other acute respiratory illnesses.

CONCLUSION

NLR could be used as a dependent risk predictor in diagnosis of COVID-19 infections apart from its cutoff point.

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