Original Article

Association between Clinical Characteristics and Laboratory Findings of 102 Patients with COVID-19 in Iraq

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Abstract

Background: The coronavirus epidemic (COVID-19) initially appeared in Wuhan, China in December, 2019 and then rapidly spread all over the world. The importance of information about the clinical and non-clinical characteristics of Iraqi COVID-19 patients was highlighted. The aim of this study was to investigate the demographic, clinical, and laboratory data of COVID-19 with assessed the influence of comorbidities on the severity of infections. **Materials and Methods:** We collected medical records of hospitalized 102 patients with COVID-19 at three hospitals from December 2021 to May 2022. Patients in the cohort study were diagnosed with positive COVID-19 by reverse transcription polymerase chain reaction according to nasopharyngeal samples. The cohort study was for separating two groups: non-severe and severe or critical groups. **Results:** The receiver operating characteristic (ROC) curve revealed that patients aged ≥ 48 years had higher levels of D-dimer, white blood cell (WBC) and neutrophils count (NUE), neutrophil-to-lymphocyte ratio (NLR), and platelets-to-lymphocyte ratio (PLR) when compared to non-severe patients. These parameters were used to predict high-risk patients with low lymphocyte counts. A logistic regression model generated results to include D-dimer, NUE, and lymphocytes count (LYM) were identified as independent risk factors for intensive care unit (ICU) patients of COVID-19 whereas WBC was a dependent factor with an odds ratio (8.330, 1.288, 0.225, and 1.534), respectively. Cut-off values by ROC curve for D-dimer, NUE, WBC, LYM, PLR, and NLR parameters were ≥ 0.780, ≥7.7, ≥10.5, ≥1.27, ≥200, and ≥5.4, respectively. **Conclusion:** In conclusion, this study demonstrated that COVID-19 severity can be predicted by analyzing clinical and laboratory data of patients. Comorbidities such as hypertension, diabetes mellitus, cardiac diseases, kidney diseases, malignancy, and hepatic diseases were identified as significant risk factors for COVID-19 severity and progression.

Keywords: COVID-19, D-dimer, logistics regression, ROC curve

Introduction

In early December 2019, pneumonia infection with unclear cause developed in Wuhan, China. The causal agent was identified as a novel encased RNA beta-coronavirus, which was later identified and renamed Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Coronavirus has been found in many hosts including avian hosts, bats, camels, cats, dogs, and mice.[1] The coronavirus disease 2019 (COVID-19) was eventually named by the World Health Organization (WHO).[2] This disease was declared a Public Health Emergency of International Concern by WHO on January 30, 2020.[3] The majority of patients experience only mild to moderate symptoms, while a small proportion develops chronic cases. Life-threatening consequences of this new disease include immune system overreaction, usually known as sepsis, lung problems leading to respiratory failure, coagulopathy complications, and multi-organ failure.[4,5] The post-COVID-19 symptoms are similar to post-SARS and community-acquired pneumonia. All individuals who have recovered from the new COVID-19 should be subjected to long-term surveillance for the assessment and treatment of symptoms and disorders that may arise after recovery.[6] Changes in demographic and clinical features

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have been noted with significant differences among COVID-19 patients in different areas of the world.[7] In the Middle East, few studies have conducted to investigate the variations in clinical characteristics, care, and outcomes of COVID-19 patients as well as in the gulf area.[8] A first case of COVID-19 in Iraq was reported on February 24th, in the Najaf province. Iraq is one of countries with higher rate of COVID-19 (about 2.6%) among other countries.[9] It has been observed that age, presence of comorbidities, lymphopenia, thrombocytopenia, acute renal failure, d-dimer, and interleukin 6 are variables defining the severity of the disease in COVID-19 patients.[10] Some thrombotic consequences have been noted in severe COVID-19 patients such as stroke, ischemic limbs, and venous thromboembolism. In individuals with severe illness, venous thromboembolism was frequent.[10-12] The clinical course and staying in a hospital treating COVID-19 patients are closely linked to their comorbidities and ages.[13] Diabetes mellitus (DM) patients had greater mortality and death rates, as well as longer hospital admission, according to study in Iraq.[14] The goal of this study is to investigate the demographics, comorbidities, clinical features, and laboratory analysis of patients in the severe and non-severe phases of the disease among some Iraqi patients. If could identify high-risk people faster, clinicians could begin and enhance close monitoring and intensive care more easily and rapidly.

Materials and Methods

Study design and participants

From December 15, 2021 to April 30, 2022, the enrolled patients [mean ± standard deviation (SD) ages 52.66 ± 18.82] were admitted to the main hospitals (Al Diwaniyah Teaching Hospital, Al-Hussein Teaching Hospital, and Morjan Hospital) in three Provinces of Iraq (Al Diwaniyah Government, Al Muthanna Government, and Babel Government). Patients were positive for SARS-CoV-2 based on reverse transcription polymerase chain reaction according to guidelines of the WHO criteria.[15] All the data of demographic, clinical, exposure history, and laboratory data were extracted from medical records of cases. The baseline and clinical characteristics help the doctors to decide who were all the patients needed intensive care unit (ICU) and distinguish between asymptomatic and symptomatic and compared between them as needed as to close follow-up

Ethical consideration

The study was conducted in accordance with the declaration of Helsinki. It was carried out with patients' verbal and written approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approval by a local ethics committee according to the document (dated February 2, 2022) to get this approval.

Data collection

Data collection included demographic, symptoms, laboratory values, vaccination status, and medication offered. The number of comorbidities such as diabetes mellitus, hypertension, coronary artery disease, and chronic renal disease was recorded in the medical history. Laboratory investigation in current study comprised complete blood counts (CBC), lymphocytes count (LYM), neutrophil count (NUE), white blood cells (WBCs) count, hemoglobin (Hb) levels, platelets count, and coagulation function indicators [prothrombin time (PT) and D-dimer]. In addition, two important markers recently used in studies neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte count ratio (PLR). Hematology parameters performed using GENEX device (GENEX Laboratories, New York, USA) is fully automated hematology analyzer to rapidly assay whole blood specimens for the CBC and the results include WBC count, platelet count, LYM, NUE, and Hb levels.

Statistical analysis

Statistical analysis was performed using the SPSS 27.0 (SPSS, IBM Company, Chicago, Illinois). For the data included in the current study, descriptive analysis was provided using mean, SD, and median (minimum–maximum value). Depending on the kind of distribution and variables, a Student's *t* test or a Mann–Whitney *U* test was used to compare demographic and laboratory data between the groups. When *P*-value <0.05 was meant rejected null hypothesis and significant difference in results of the study. The receiver operation characteristic (ROC) curve was used to calculate cut-off values for parameters to determined which factor aid in the illness severity diagnosis. Logistic regression was carried out to measure the association among parameters associated with COVID-19 patients.

Results

Demographic and clinical features

A total of 102 patients were included in the study with COVID-19 diagnosis according to WHO criteria. Patients ages range from 18 to 85 years, the median age of 53 years (interquartile range 25–75) of total patients, and the cut-off age of ≥48 years to determine which age may predict high-risk patients accorded ROC cure at area under curve (AUC) (0.93) [Figure 1]. The baseline demographic and characteristics of COVID-19-related hospitalizations are shown in Table 1. The male patients were 48 (47.1%) and female patients were 54 (52.9%) cohort patients in the current study. Forty-nine patients (48%) had comorbidities. The most common comorbidities with COVID-19 infection were cardiovascular disease nine (18.3%), hepatic disease two (4%), hypertension 14 (13.7%), DM 15 (30.6%), kidney diseases six (12.2%), and cancer three (6.1%). The physicians classified the patients

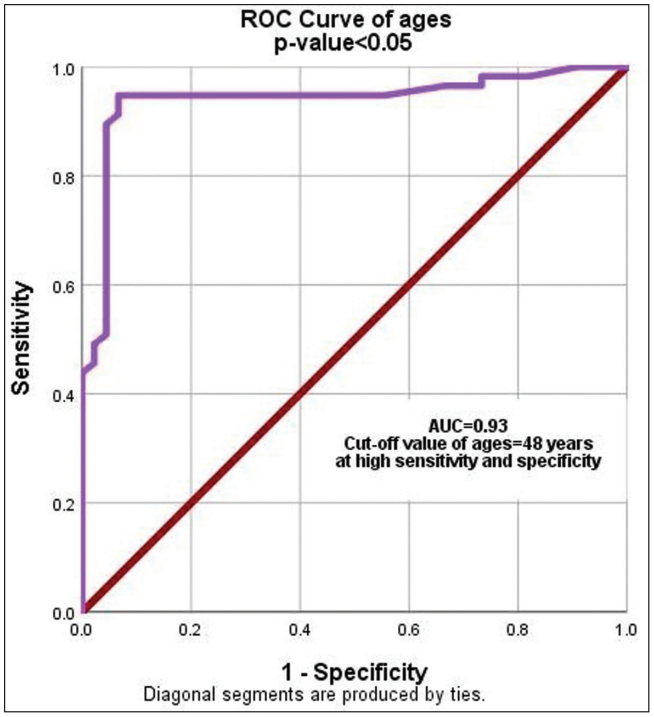

Figure 1: The ROC curve of age in predicting critical illness of COVID-19

Table 1: Demographic and clinical characteristics variables among COVID-19 patients

Characteristics	Total patient $N = 102$	Non-severe group $N = 45$	Severe group $N = 57$
Age, median (IQR)	53 (36–69)	37 (28–42)	67 (60–75)
Gender	Male/48 (47.1%) Female/54 (52.9%)	Male/15 (31.3%) Female/30 (55.6%)	Male/33 (68.8%) Female/24 (44.4%)
Death	5 (4.9%)	0	5 (8.7%)
Comorbidity	49 (48%)	17 (34.6%)	32 (68.3%)
Hypertension	14 (13.7%)	3 (21.42%)	11 (78.5%)
Diabetes meletus	15 (30.6%)	6 (40%)	9 (60%)
Cardiac diseases	9 (18.3%)	5 (55.5%)	4 (44.4%)
Kidney diseases	6 (12.2%)	1 (16%)	5 (83.3%)
Cancer	3 (6.1%)	2 (66.6%)	1 (33.3%)
Hepatic diseases	2 (4%)	0	2 (100%)
Oxygen support	47 (46%)	0	47 (82.4%)
Vaccination status	41 (40.1%)	29 (64.4%)	12 (21%)

IQR, interquartile range

into two groups (severe and non-severe) based on the severity. Severe COVID-19 cases were required to have admitted in ICU and were given oxygen, whereas non-severe patients presented fever, upper respiratory tract symptoms, and non-stayed in hospitals for a long time did not require ICU and oxygen. When the demographic parameters of hospitalized COVID-19 patients and outpatients with confirmed COVID-19 were examined. There was no significant difference in terms of age and gender between the two groups. Among these patients, 57 (55.9%) were isolated in clinical wards and 45 (44.1%) needed ICU support. The median age of critically ill patients who required ICU was 67 years (interquartile range 60-75), whereas the median age of non-ICU patients was 37 (interquartile range 28-42). The current study found cancer, hepatic, and kidney failure were associated with increased of severity. In the current study, all comorbidities had a significant impact on admitted patients in the ICU and increased their mortality rate with a *P*-value of <0.05. Among patients with chronic diseases, five deaths (4.9%) occurred in severe cases.

Treatments profiles

Out of the total number of patients, 82.4% received antibiotics therapy, antiviral therapy, and oxygen support for critical cases as recorded in their hospital medical records. The remaining patients received different types of therapy based on the severity of their condition. Antibiotics therapy included azithromycin, doxycycline, and ceftriaxone. Early anticoagulation may prevent clots formation, and for that reason, anticoagulant medication was routinely administered to all ICU patients.

Laboratory findings in COVID-19 patients admitted to the hospital

Table 2 showed laboratory parameters for two groups since admission, which were then compared. The D-dimer, white blood cells, neutrophiles, PT, NLR ratio, and PLR ratio were higher in severe groups compared with non-severe, whereas low LYM in ICU patients was recorded. There were no significant differences observed in the platelets and hemoglobin markers between both groups. The mean values in LYM, NUE, WBC, D-D, PLR, NLR, and PT were statistically higher in severe cases in contrast with non-severe cases. In this work, the other parameters (such as Hb and PLT) did not seem to be discriminant.

The efficacy of routine blood parameters in diagnosis of COVID-19 infection

The ROC curve is a two-dimensional diagram depicting blood routine parameter cut-off values and ratios based on blood routine findings. The ideal cut-point value determined via ROC curve analysis has different sensitivities and specificities for D-dimer, neutrophils, and WBC in Figure 2, in addition NLR and PLR in Figure 3. Table 3 displays ROC curve values and includes AUC, cut-off, specificity, sensitivity, and *P*-value.

The binary logistic regression model

In this model, we admitted four parameters (LYM, WBC, NUE, and D-D), and the model was correctly classified the cases (severe and non-severe) at 91.2%, it was statistically significant at $P < 0.001$ with $\chi^2 = 101.56$ and this mean model fit with predictor. In addition, the HL test predicted goodness fit to model *P*-value > 0.05. Increasing in D-dimer and neutrophils, and decrease in LYM were

Table 2: Described the changes in clinical hematology parameters in COVID-19 patients

Parameters	Total patient *n* (102) M ± SD	Non-severe group *n* (48)	Severe group *n* (56)	Normal range	*P*-value
White blood cell	13.5×10^9/L ± 5.5	8.54 ± 3.06	17.41 ± 3.55	$4.5–11.0\times10^9$/L	*P* = 0.03 Increase
Lymphocytes	1.55 ± 0.96	2.36 ± 0.62	0.92 ± 0.67	$1.5–4.5\times10^9$/L	*P* = 0.002 Decrease
Neutrophils	10.88 ± 4.35	7.69 ± 2.68	13.39 ± 3.72	$2–8\times10^9$/L	*P* = 0.01 Increase
Platelet	276.6×10^9/L ± 77.45	254.42 ± 33	294 ± 96	$150–450\times10^9$/L	*P* = 0.19 Normal
D-dimer	1.37 ± 1	0.51 ± 0.25	2 ± 1	<0.50 µg/mL	*P* = 0.001 Increase
NLR	11 ± 9	3.54 ± 1.95	16.9 ± 7.9	Less than 0.7 or greater than 3 = abnormal	*P* = 0.002 Increase
PLR	307.96 ± 271.76	116.5 ± 39.98	435 ± 285	Less than 36 or greater than 150 = abnormal	*P* = 0.001 Increase
Prothrombin time	12.47 ± 2.1	12.24 ± 1.81	13.10 ± 2.98	10–13.8 s	*P* = 0.15 Normal
Hemoglobin	13.93 ± 1.49–male 12.74 ± 1.94—female	Male/14.86 ± 1.16 Female/13.54 ± 1.49	Male/13.51 ± 1.44 Female/11.75 ± 2	Male/13.8–17.2 Female/12.1–15.1	*P* = 0.15 Normal

NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, *P*: The *P*-value, M ± SD: mean and standard deviation
* Significant $P < 0.05$

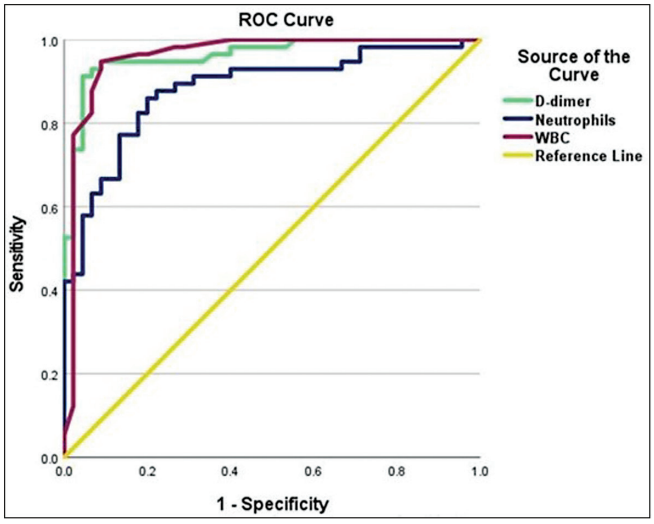

Figure 2: The ROC curves of different parameters of routine laboratory blood tests in predicting severe SARS-CoV-2 infection, on admission D-dimer, Neutrophils, and White blood cells

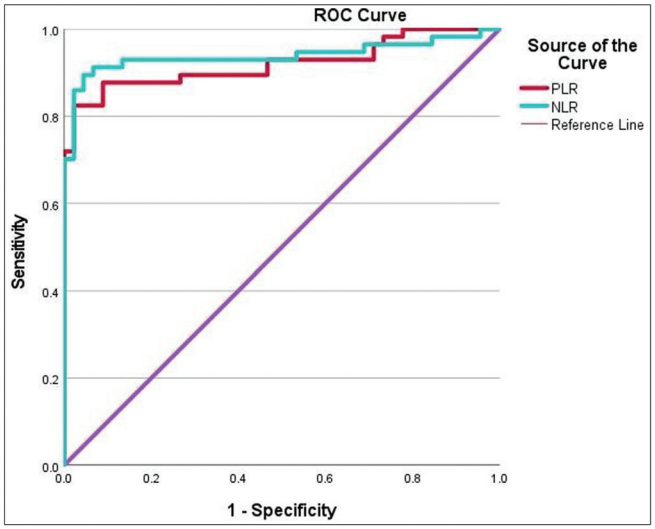

Figure 3: The ROC curves of NLR: neutrophils-to-lymphocytes ratio; PLR: platelet-to-lymphocyte ratio in predicting severe SARS-CoV-2 infection

independent factors in the prediction of COVID-19 whereas WBC was dependent on other parameters to contribute of severity as in Table 4.

Discussion

In this observational analysis, the described the clinical and laboratory features of 102 confirmed SARS-CoV-2 patients in Iraq, categorizing them as severe and non-severe cases based on length of hospital stay, need for oxygen support, and severity of symptoms. The recent results of some studies revealed that male and female patients were equally susceptible to COVID-19 infection.[16,17] Most of the severe cases had comorbidities as the results of many studies on diabetes, hypertension, and cardiovascular diseases related to the severity of COVID-19.[18,19] The COVID-19 outbreak is currently putting significant stress on the healthcare system.

After investigating the results found in present study matched the meta-analysis by Barek *et al.*[20] indicating that older patients (age ≥ 50 years) were at risk of acquiring severity and that comorbidities and clinical manifestations may have a substantial impact on the prognosis and severity of COVID-19. A second study found most of patients ranged from mild to moderate in age group 50–59 years.[21]

Table 3: Analysis of several blood parameters by ROC curve to examine the cut-off value, AUC, specificity, sensitivity, and *P*-value

Parameters	AUC	Cut-off value	Sensitivity	Specificity	*P* value
D-dimer (μg/mL)	0.96	≥0.780	91%	95%	$P < 0.001$*
Neutrophils × 10^9 per L	0.88	≥7.7	86%	80%	$P < 0.001$*
WBC × 10^9 per L	0.96	≥10.5	94%	91%	$P < 0.001$*
Lymphocytes × 10^9 per L	0.91	≥1.27	96%	82%	$P < 0.001$*
PLR	0.92	≥200	82%	96%	$P < 0.001$*
NLR	0.93	≥5.4	89%	95%	$P < 0.001$*

AUC: area under curve, *P*: The *P*-value

* Significant

Table 4: Logistic regression analysis showed the impact of various blood parameters

Parameters	*B*	df	Sig.	Exp(*B*)
Lymphocytes	–1.492	1	0.002*	0.225
Neutrophils	0.253	1	0.035*	1.288
D-dimer	1.673	1	0.034*	8.330
WBC	0.428	1	0.626	1.534

* Significant the *P*-value < 0.05, Exp(*B*):log *B*

According to this study findings, two factors (NLR and PLR) were important to predict the severity of COVID-19. In line with other studies confirmed of the NLR values were found to be considerably greater in COVID-19 patients with severe illness,[22,23] whereas deceased and severe critical patients had higher PLR levels in admitted-to-hospital than surviving and non-severe patients.[24]

In the study on the biomarkers of infection, D-dimer appeared discriminant for severe evolution and increased prognosis of infection, and this was consistent with many studies in the world.[25-27] A study in China showed D-dimer levels are frequently high in COVID-19 patients hospitalized and D-dimer levels correspond with disease severity and were a valid predictive diagnostic for in-hospital death.[28] Study from Egypt by Hashem *et al*.[29] confirmed that D-dimer > 0.9 mg/L in addition increase in NLR > 8 and PLR > 192 might be easily accessible indicators of severe COVID-19 infection needing ICU hospitalization.

Neutrophils are a key part of the immune system's defense against pathogens. However, excessive neutrophil activity can damage tissues and cause acute respiratory distress syndrome. The coronavirus (2019) is linked to a systemic increase in immature neutrophils, but the function of neutrophils in viral infections is poorly understood.[30] The findings of this study located most of the high-risk patients had higher neutrophils and ROC curve confirmed good biomarker at AUC (0.88) predicted at cut-off value >7.7 considered was severe in line with study based on the Bayesian inference analysis quantified the evident pattern of lung damage in accordance with the increase in neutrophils in COVID-19 patients. In a study, the immune cell transcriptome profile also revealed increased neutrophil markers in COVID-19 patients' lung and bronchoalveolar lavage fluid samples. Importantly, 17 of the excessive neutrophil-activated genes were NETosis (a type of programmed cell death and a program for formation of neutrophil extracellular traps) linked genes, and these genes interacted with T and NK cells via negative regulation. As a result, the researchers believe that neutrophil extracellular traps (NETs) in lung tissue causes an inadequate antiviral response in COVID-19 patients.[31] According to study by Tiwari *et al*.[32] increased neutrophil counts were associated with increased COVID-19 disease severity and these results were in line with the results of current study, and the concept that elevated neutrophil counts might be utilized to predict the severity of an infection.

The results of this study showed that most patients admitted to hospitals had a low lymphocyte count, which is consistent with the findings of Wang *et al*.[33] study, according to their research, a decrease in T lymphocyte subsets was associated with a higher likelihood of ICU hospitalization, mechanical ventilation, and death in COVID-19 patients.

In conclusion, the outcomes of this study indicate that a lowering in LYM and increases in D-dimer, NLR, PLR, and WBC are the best laboratory predictors of a severe prognosis for COVID-19. Monitoring severity predictors may aid clinicians in identifying and monitoring patients at higher risk for progression. Patients with a high probability of severe progression could be identified, however, using cut-off values for the majority of discriminant factors. During the epidemic, the comprehensive results of 102 patients admitted to the hospital showed clinical and laboratory features that could predict a high risk of ICU requirement or even death at the time of admission. Age and multiple chronic conditions were independent risk factors to increase rate of mortality among patients.

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Conflicts of interest
There are no conflicts of interest.

Author contributions
All the author conducting experimental design and data analysis. All authors read and approved the final version of the manuscript.

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