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Research Article

D-二聚体是新冠肺炎感染严重程度的危险因素

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【摘要】：
背景：由严重急性呼吸综合征冠状病毒 2（SARS-CoV-2）引起的 2019 冠状病毒病（COVID-19）临床病程多变，死亡风险因素尚不明确。方法：这项回顾性研究包括伊拉克纳杰夫 Al-Sadder 医院和 Alamal 医院的一些经实验室确诊的 COVID-19 成年住院患者（≥20 岁）。这些患者在 2021 年 12 月 1 日至 2022 年 1 月 31 日期间死亡或出院。 从医院数据库中收集了幸存者和死亡者的人口统计学、 临床试验、 治疗和实验室结果数据。 进行了统计分析以确定住院死亡的风险因素。结果：研究共纳入 100 名患者，其中 67 人出院， 33 人在医院死亡。年龄分布显示 45% 的患者年龄在 40 岁以下，而 55% 的患者年龄在 40 岁以上。 该队列中 57% 为男性（37 名幸存者 vs. 20 名死亡者，p=0.024），43% 为女性（30 名幸存者 vs. 13 名死亡者，p=0.010）。66% 的患者患有合并症，其中 55% 的幸存者和 87% 的死亡者患有基础疾病。 值得注意的是，死亡者中糖尿病的患病率更高（85% vs. 18%），其次是哮喘（58% vs. 10%）、中风（48% vs. 10%）、肾衰竭（42% vs. 6%）、心脏病发作（33% vs. 10%）和高血压（18% vs. 15%）。调查结果显示，白细胞（WBC）计数中位数为 8.7 mg/dl（IQR：6.1－15.63 mg/dl），淋巴细胞计数为 57.6（52.8－61.1），D-二聚体水平为 2.35 μg/ml（IQR：1.2－4.72 μg/ml），铁蛋白水平为 775 μg/ml（IQR：720.3－866.4 μg/ml），C 反应蛋白（CRP）水平为 4.55 mg/dl（IQR：1.5－5.3 mg/dl），乳酸脱氢酶（LDH）水平为 341.5 IU/L（IQR：291.3－427 IU/L）。 与幸存者相比， 死亡患者的这些参数明显较高。 D-二聚体与铁蛋白、CRP、LDH、 白细胞及淋巴细胞计数与 LDH 均呈显著正相关。 ROC 分析显示， CRP 的曲线下面积 （AUC） 为 0.802（95%CI： 0.717～0.886）， 临界值为 4.45mg/dl， 灵敏度为 87.9%， 特异度为 37.3%； D-二聚体的曲线下面积（AUC） 为 0.749 （95%CI： 0.652～0.846）， 临界值为 2.40μg/ml，灵敏度为 81.8%， 特异度为 32.8%。 LDH 的 AUC 为 0.70（95% CI：0.587-0.813），临界值为 353.50 IU/L，敏感性为 72.7%，特异性为 37.3%。铁蛋白的 AUC 最低，为 0.684（95% CI：0.555-0.813）， 临界值为 809.50 μg/ml，敏感性为 69.7%，特异性为 37.1%。 结论：本研究发现， 年龄较大与 D-二聚体水平升高以及铁蛋白、CRP 和 LDH 升高有关。这些参数与成年 COVID-19 患者的病情严重程度和死亡风险有关。D-二聚体和 CRP 是病情进展最可靠的两个预测因子。 了解这些生物标志物与病情进展之间的相互作用可能有助于制定更有针对性的治疗干预措施，并在医疗环境中更好地分配资源。
【关键词】： D-二聚体、冠状病毒病、铁蛋白、受试者工作曲线（ROC）、曲线下面积（AUC）

D-Dimer as a Risk Factor for the Severity of COVID-19 Infection

【Abstract】:
Background: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has a variable clinical course, and mortality risk factors are not well established. **Methods**: This retrospective study included adult inpatients (≥20 years old) with laboratory-confirmed COVID-19 from Al-Sadder Hospital and Alamal Hospital in Al-Najaf, Iraq.

The patients either died or were discharged between December 1, 2021, and January 31, 2022. Data on demographics, clinical trials, treatments, and laboratory results were collected from the hospital database for both

survivors and non-survivors. Statistical analyses were performed to identify the risk factors for in-hospital mortality. **Results**: A total of 100 patients were included in the study, of whom 67 were discharged and 33 died in the hospital. The age distribution showed that 45% of the patients were under 40 years of age, while 55% were over 40 years old. The cohort comprised 57% males (37 survivors vs. 20 non-survivors, p=0.024) and 43% females (30 survivors vs. 13 non-survivors, p=0.010). Comorbidities were present in 66% of the patients, with 55% of the survivors and 87% of the non-survivors having underlying conditions. Notably, diabetes mellitus was more prevalent in the non-survivors (85% vs. 18%), followed by asthma (58% vs. 10%), stroke (48% vs. 10%), renal failure (42% vs. 6%), heart attack (33% vs. 10%), and hypertension (18% vs. 15%). The findings revealed a median white blood cell (WBC) count of 8.7 mg/dl (IQR: 6.1–15.63 mg/dl), lymphocyte count of 57.6 (52.8–61.1), D-dimer levels of 2.35 µg/ml (IQR: 1.2–4.72 µg/ml), ferritin levels of 775 µg/ml (IQR: 720.3–866.4 µg/ml), C-reactive protein (CRP) levels of 4.55 mg/dl (IQR: 1.5–5.3 mg/dl), and lactate dehydrogenase (LDH) levels of 341.5 IU/L (IQR: 291.3–427 IU/L). These parameters were significantly higher in the non-survivors than in the survivors. A significant positive correlation was found between D-dimer and ferritin, CRP, and LDH as well as between WBC and lymphocyte counts and LDH. ROC analysis indicated that CRP had an area under the curve (AUC) of 0.802 (95% CI: 0.717-0.886) with a cutoff of 4.45 mg/dl, demonstrating 87.9% sensitivity and 37.3% specificity. D-dimer showed an AUC of 0.749 (95% CI: 0.652-0.846) with cutoff of 2.40 µg/ml, 81.8%, and 32.8%, respectively. LDH had an AUC of 0.70 (95% CI: 0.587-0.813) with a cutoff of 353.50 IU/L and 72.7% sensitivity and 37.3% specificity. Ferritin had the lowest AUC of 0.684 (95% CI: 0.555-0.813), with cutoff of 809.50 µg/ml, 69.7%, and 37.1%, respectively. **Conclusion**: This study found that older age correlates with elevated D-dimer, ferritin, CRP, and LDH levels. These parameters are associated with disease severity and mortality risk in adult COVID-19 patients. D-dimer and CRP levels have emerged as two of the most reliable predictors of disease progression. Understanding the interplay between these biomarkers and disease progression may lead to targeted therapeutic interventions and better resource allocation in healthcare settings.

【Keywords】: D-dimer, coronavirus disease, ferritin, receiver operating curve (ROC), area under the curve (AUC)

1. Introduction

The novel ß-coronavirus Sudden Respiratory Distress Syndrome (SARDS) has been established as the cause of ARDS. Coronavirus-2 is a virus that caused Coronavirus Disease in the Year 2019 (COVID-19) in SARS-CoV-2). The World Health was classified the disease as a public health emergency of worldwide concern in the first month of 2020 [1]-[2]. COVID-19 was categorized into three severity levels. If flu-like symptoms emerge early, they are frequently viral pneumonia, which is the result of a viral infection. Patients were admitted to the hospital for a prolonged stay or placed on a ventilator. Inflammation of the lungs and coagulopathy are two diseases that can occur together. The active phase begins with a combination of physiological and metabolic changes that occur shortly after tissue injury. of an inflammatory process Inflammatory indicators such as C-reactive protein (CRP), ferritin, IL-6, and IL-1 are all high, and D-dimer has also been associated with ARDS, which has poor clinical results. The third stage of the disease is fibrosis [3]. Intracellular ferritin reserves have been intensively studied as indicators of iron metabolism [4]. Ferritin is an acute protein that increases in response to a range of inflammatory conditions, cancer, excess iron, and liver or renal illness. Even if there is a temporary presence of COVID-19, ferritin levels can be monitored. Ferritin levels in hospitalized patients have been found to be significantly higher in several studies. However, there is usually no specific marker for haemophagocytic lympho-histiocytosis [5]. D-dimer is a fibrin breakdown product produced by plasma fibrinolytic enzymes and is a common thrombotic biomarker [6]. It is considered typical for a D-dimer level of less than 0.5 g/mL, and levels increase as people get older and during pregnancy. As the incidence of community-acquired pneumonia increases, so does the severity of the disease, as does the D-dimer level. In patients with COVID-19, D-dimer levels are a possible prognostic predictor. The entrance day D-dimer level has been shown in multiple studies to predict sickness severity [2]. In this early case series, the risk factors for severe disease and mortality were not well understood. This study aimed to identify laboratory biomarkers in individuals with COVID-19 to determine whether biomarkers can distinguish between people who are more likely to develop severe disease and those who are not, as well as between those who are less capable of surviving or are at a high or low risk of dying. Identifying laboratory signs that can distinguish between these patients would also increase clinical situational awareness.

2. Methodology

A retrospective cross-sectional study was conducted on all verified COVID-19 patients admitted to Al-Sadder and Alamal care centers from December 1, 2021, to January 31, 2022, after approval was obtained from the Kufa University and Health Intuition Ethics Committee (November 2021). All patients with COVID-19 aged 20 years or older who were diagnosed by polymerase chain reaction (PCR) were included in the polymerase chain reaction (PCR). The exclusion criteria are also important. Patients with anemia and thalassemia, pregnant women who had already been diagnosed with liver disease, and those with cancer were not included in the study. Severe disease was diagnosed in patients who met any of the following criteria. Dyspnea with a respiratory rate of less than 30 breaths/min. In the resting state, finger oxygen

saturation was 93%. PaO2/FiO2 300 mm Hg. Respiratory failure requiring medical ventilation. Demographic characteristics as well as comorbidities such as chronic obstructive pulmonary disease (COPD), asthma, diabetes mellitus, renal failure, hypertension, heart attack, heart failure, stroke, and clinical and laboratory findings, including white blood cell count (WBC), lymphocyte, D-dimer, ferritin, C-reactive protein (CRP), and lactic dehydrogenase (LDH), were assessed. The tests were performed at the Clinical Pathology Laboratory of the hospital, and the results were acquired from the hospital database. The two groups of patients were survivors and non-survivors. All data were entered into a standardized datasheet.

2.1. Statistical Analysis

The Kolmogorov-Smirnov test was used to analyze the distribution of the variables. Qualitative data were provided as median (interquartile range (IQR) 25 percent-75 percent) values, quantitative data were provided as mean and standard deviation, and qualitative data were presented as percentages, as well as with numbers and percentages. The chi-square test was used to analyze the demographic characteristics. An independent t-test was used to compare the laboratory findings. A receiver operating curve (ROC) was used to determine the cutoff value for potential illness severity predictions, as well as the sensitivity and specificity of the predictors. Pearson's correlation test was used to compare parameters. SPSS version 28, a statistical package for the social sciences (IBM Corp., Armonk, NY, USA), was used to analyze all data. The significance level was set at $p<0.05$ [7].

3. Results

3.1. Characteristics of Patients with COVID-19

This study included 100 COVID-19 patients. The baseline patient characteristics are shown in Table (1).

表 **1**

Table 1 Clinical characteristics of COVID-19 patients

Parameters	Total number of Covid-19 patients n= 100	Survivor n=67(67%)	Non-Survivor n=33(33%)	p-value
	Median (IQR)	Mean ± SD	Mean ± SD	
Age (year)	43 (32–63.75)	44.46±17.74	51.48±15	0.042
< 40 n (%)	45 (45%)	37 (55.2%)	8 (24.2%)	0.0001*
> 40 n (%)	55 (55%)	30 (44.8%)	25 (75.8%)	0.500
Male n (%)	57 (57.0%)	37 (55.2%)	20 (60.6%)	0.024 *
Female n (%)	43 (43.0%)	30 (44.8%)	13 (39.4%)	0.010 *
Hb (g/dl)	12.8 (11.8–13.7)	12.89±1.49	12.58±1.13	0.294
WBC (X10/mm^3)	8.7 (6.1–15.63)	7.74±4.04	15.49±4.68	0.0001 *
< 4 n (%)	19 (19.0%)	17 (25.4%)	2 (6.1%)	
> 4-10 n (%)	38 (38.0%)	36 (53.7%)	2 (6.1%)	0.0001 *
> 10 n (%)	43 (43.0%)	14 (20.9%)	29 (87.9%)	
Lymphocyte	57.6 (52.8–61.1)	55.56±6.13	59.13±3.5	0.003 *
D. dimer (µg/ml)	2.35 (1.2–4.72)	2.62±2.1	3.86±2.12	0.007 *
Ferritin (µg/ml)	775 (720–866.4)	766.74±91.21	831.4±146.03	0.008 *
CRP (mg/dl)	4.55 (1.5–5.3)	3.14±2.39	5.58±1.43	0.0001 *
LDH (IU/L)	341.5 (291–427)	332.37±94.06	403.06±99.06	<0.001 *

*Significant difference at p-value <0.05. IQR, interquartile range; COVID-19, coronavirus disease 2019; Hb, hemoglobin; WBC, leukocytes; CRP, C-reactive protein; LDH, lactate dehydrogenase.

The number of COVID-19 survivors was 67%, and 33% were non-survivors. The age of all the patients ranged from 22 to 75 years (median (IQR) 43 (32–63.75) years). The average age of non-survivors was substantially higher than that of survivors (51.48±15 vs. 44.46±17.74, p=0.042). Patients were divided into groups according to age, including 45% of patients in the age group < 40 years and 55% of patients in the age group >40 years. A significant proportion of the patients (57%) were males (37 (55.2%) vs. 20 non-survivors (60.6%), p=0.024). More than 43% of the patients were female, with 30 survivors (44.8%) vs. 13 non-survivors (39.4%) (p=0.010).

Patients had underlying comorbidities (66%), with 37 surviving (55%), and 29non-surviving patients (87%) patients. The most prominent comorbidities in non-survivors were diabetes mellitus (85% vs. 18%), asthma (58% vs.10%), stroke (48% vs.10%), renal failure (42% vs. 6%), followed by heart strike (33% vs. 10%), and hypertension (18% vs.15%), as shown in Figure 1.

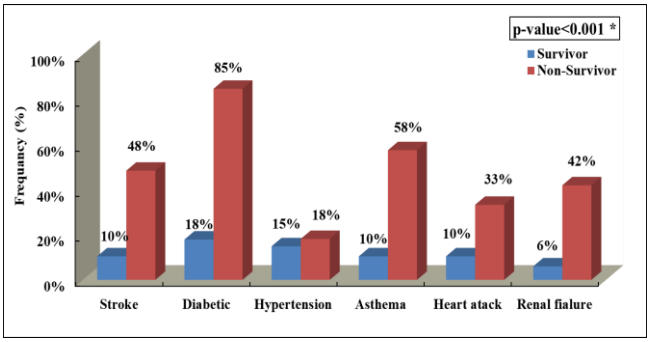

图 **1**

Fig.1 Frequency of comorbidities in survivors and non-survivors of COVID-19

3.2. Laboratory Findings

Major laboratory parameters and markers were tracked for all patients with COVID-19, surviving and non-surviving.

3.2.1. *Hematological Parameters*

The mean Hb level 12.79±1.38 in all patients, and the results showed no significant differences between survivors and non-survivors of COVID-19 (12.89±1.49 vs. 12.58±1.13, p=0.294). The median WBC cell count was (8.7) mg/dl (IQR: 6.1–15.63 mg/dl). The mean WBC in non-survivor patients was markedly higher than that in survivors (15.49±4.68 vs. 7.74±4.04, p=0.0001); 2(6.1%) of non-survivor patients had WBC <4 mg/dl, but 87.9% had WBC >10 mg/dl as compared to survivor patients 17 (25.4%) and 14 (20.9%), respectively. The median (IQR) value 57.6 (52.8–61.1)) was significantly lower in survivors than in non-survivors (p=0.003).

3.2.2. *D-dimer, Ferritin, CRP, and LDH*

The average value of D-dimer was (2.35) µg/ml with (IQR: (1.2–4.72) µg/ml, highly significant in non-survivors when compared with survivor (3.86±2.12 vs. 2.62±2.1, p=0.007). The normal level of ferritin (20.0–300.0 lg/mL) was also elevated with COVID19 a median value was (775) µg/ml (IQR: 720.3–866.4) µg/ml. Ferritin levels were significantly elevated in non-survivors mean value was (831.4±146.03) µg/ml) compared to survivors (766.74±91.21) µg/ml, (p=0.008).

The highest CRP level was achieved with COVID-19 (4.55) mg/dl, (IQR:1.5–5.3 mg/dl), and CRP (normal value: <0.5 mg/dl). A significantly increased mean value of (5.58±1.43) mg/dl was observed in non-survivors compared to (3.14±2.39) mg/dl in survivors (p=0.0001). Moreover, the median serum LDH level was (341.5) IU/L, (IQR: 291.3–427 IU/L), which is significantly higher in non-survivor than survivor mean value of (403.06±99.06 vs. 332.37±94.06, p=0.0001).

3.2.3. *Analysis of the Correlation between Laboratory Parameters*

The connections between inflammatory biomarkers and D-dimer (ferritin, CRP, and LDH), in addition to WBC and lymphocyte counts, are presented in Table 2 and Figure 2.

表 **2**

Table 2 Correlations of D-dimer, CRP, and ferritin levels in COVID-19 patients

Parameters		D. dimer (µg/ml)	Ferritin (µg/ml)	CRP (mg/dl)	LDH (IU/L)	WBC (X10 mm3)
Ferritin	**R**	0.355**	--			
	P-value	<0.001				
CRP	**R**	0.646**	0.244*	--		
	P-value	<0.001	0.015			
LDH	**R**	0.457**	0.667**	0.457**	--	
	P-value	<0.001	<0.001	<0.001		
WBC	**R**	0.437**	0.315**	0.444**	0.360**	--
	P-value	<0.001	0.001	<0.001	<0.001	
Lymphocyte	**R**	0.374**	0.159	0.436**	0.250*	0.400**
	P-value	<0.001	0.114	<0.001	0.012	<0.001

No. of COVID19 patients = 100; WBC, leukocytes; CRP, C-reactive protein; LDH, lactate dehydrogenase. * Correlation is significant at p-value < 0.05; **. at p-value < 0.01.

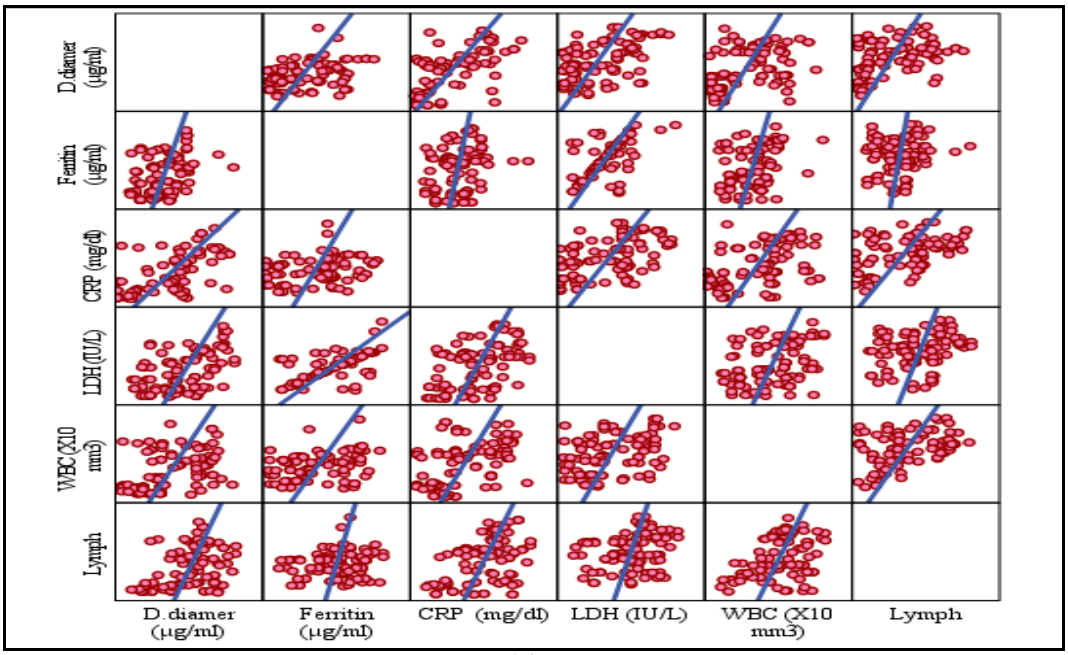

图 **2**

Fig.2 *Multipule* scatter plots showing correlations between D. dimer, ferritin, CRP, LDH, WBC, and lymphocyte counts in patients with COVID-19. WBC, white blood cells; CRP, C-reactive protein; LDH, lactate dehydrogenase

The results revealed a significant positive correlation between D-dimer and ferritin (r=0.355, p<0.001), but a high correlation with CRP (r=0.646, p<0.001), LDH (r= 0.457, p<0.001), WBC count

(r=0.437, p<0.001), and weak correlation with lymphocyte count (r=0.374, p<0.001). A significant weak correlation between ferritin and CRP (r=0.244, p=0.015) and WBC (r=0.315, p=0.001), but no significant correlation with lymphocyte (r=0.159, p=0.114), also a positive correlation with LDH (r=0.667, p=<0.001). CRP was significantly positively correlated with LDH (r=0.457, p<0.001), WBC (r=0.444, p=0.001), and lymphocytes (r=0.436, p=0.114).

3.2.4. The Area under the Curve (AUC)

A receiver operating characteristic (ROC) curve analysis showed that CRP as a marker of COVID-19 severity in non-survivors compared with survivors had a cut-off value of 4.45 mg/dl, with 87.9% sensitivity and 37.3% specificity, and high significant AUC = 0.802 (95% CI: 0.717-0.886). In comparison, the AUC for D-dimer as a marker of COVID-19 severity was 0.749 (95% CI: 0.652-0.846). and a cut-off for D- dimer of 2.40 µg/ml, with 81.8% sensitivity and 32.8% specificity. The area under the curve (AUC) of LDH was 0.70 (95% CI: 0.587-0.813), with a cutoff value of 353.50 (IU/L, 72.7% sensitivity, and 37.3% specificity. However, ferritin showed the lowest AUC of 0.684 (95% CI: 0.555-0.813), with a cutoff of 809.50 (µg/ml), 69.7% sensitivity, and 37.1% specificity (Table 3 and Figure 3).

表 **3**

Table 3 Area under the curve for study parameters to predict marker effectiveness for COVID-19 between survivors and non-survivors

Parameters	AUC	Std. Error	p-value	95% CI	Cut-off	Sensitivity	1 - Specificity
CRP (mg/dl)	0.802	0.043	0.0001	0.717-0.886	4.450	0.879	0.373
D. dimer (µg/ml)	0.749	0.050	0.0001	0.652-0.846	2.40	0.818	0.328
LDH (IU/L)	0.700	0.058	0.001	0.587-0.813	353.50	0.727	0.373
Ferritin (µg/ml)	0.684	0.066	0.003	0.555-0.813	809.50	0.697	0.371

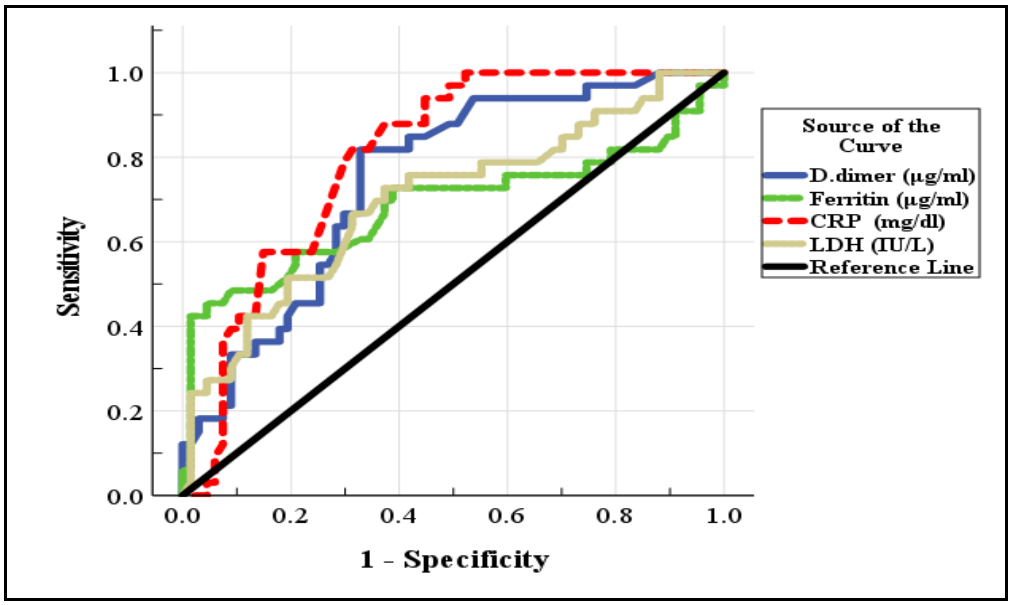

图 **3**

Fig.3 ROC curve for the D-dimer, Ferritin, CRP, and LDH to predict COVID-19 severity ROC, receiver operating characteristic; CRP, C-reactive protein; COVID-19, coronavirus disease 2019.

4. Discussion

4.1. Characteristics of Patients with COVID-19

This retrospective study determined several risk factors for death among adults in Iraq who were hospitalized for COVID-19. In the current study, we assessed 100 COVID-19-positive patients, of which 67 were survivors and 33 were non-survivors. In particular, older age and D-dimer levels greater than 1 µg/mL were associated with a higher risk of non-survivor hospital death. Additionally, elevated levels of blood ferritin, CRP, LDH, leukocytosis, and lymphocytopenia were more commonly observed in association with disease severity in patients with diagnostic COVID-19. Both viral survivors and non-survivors were identified in throat samples. In SARS and MERS, older age is a substantial independent predictor of mortality [8]. According to the current study, older age is linked to death in patients with covid-19, according to the current study. Age-related impairments in T-cell and B-cell activity, as well as the overproduction of type 2 cytokines, could result in a lack of viral replication control and extended proinflammatory responses, potentially leading to poor outcomes [9].

Diabetes, hypertension, heart attack, asthma, stroke, and renal disease were all found to be comorbid in this study, and may play an important role in disease severity and death. An increase in comorbidities with increasing age could explain the higher mortality rate in the elderly population [10]. The prevalence of diabetes mellitus among COVID-19 patients varies according to previous reports. As reported in [11], diabetes was two times more common in severe cases than in moderate cases, and 9.7% of patients had diabetes. The results of the current study comply with those of [10], and we found that 85% of the non-survivors had diabetes. The immune system is believed to be affected by blood glucose levels, which increase its susceptibility to SARS-CoV-2 infection and other infectious diseases [12].

When comparing non-survivors with survivors of COVID-19, the current study found a greater rate of asthma, stroke, and heart attacks. In patients with severe COVID-19, heart failure and coronary artery disease (CAD) were more common than in individuals with moderate COVID-19, as well as in those closely linked to the occurrence of diabetes and hypertension. Previous studies have shown that cardiovascular disorders worsen the severity of covid-19, as well as mortality, among patients with COVID-19 [10], [13].

4.2. Laboratory Findings

4.2.1. White Blood Cell and Lymphocyte Counts

Laboratory and biochemical parameters were significantly different between the survivor and non-survivor groups: WBC, lymphocytes, D-dimer, ferritin, CRP, and LDH levels were pathologically increased. The status and degree of multiorgan failure are reflected in sepsis and septic shock [14]. Although bacterial infections are the most common cause of sepsis, viral illnesses can also cause it. This could also explain why a low lymphocyte count is linked to a poor prognosis and a higher complication rate [15]. A rapid increase in neutrophil count may also result in lymphocyte apoptosis. Additionally, lymphocytes have ACE receptors, which may be responsible for the direct cytotoxic action of the virus [16]. In this study, we discovered that more than 87.9% of non-survivors had a WBC count of >10.0 cell/L. Although bacterial infections are the most common cause of sepsis, viral infections can also cause sepsis [17].

4.2.2. Serum D-Dimer Level

The non-survivor group had much higher D-dimer values, which was consistent with the findings of other studies that examined D-dimer levels [18]–[19]. A D-dimer level >2000 mg/L upon hospital admission was a predictor of mortality in COVID-19 patients, according to [15]. When comparing non-surviving COVID-19 patients to survivors, a recent study found that higher fibrin-relevant (D-dimer and fibrin degradation product) levels were significantly associated with non-survival in COVID-19 patients. In severe SARS-CoV-2-infected patients with increased D-dimer or sepsis-induced disseminated intravascular coagulation, low-molecular-weight heparin was also used. Increased D-dimer levels in hospital admissions may be a good predictor of COVID-19 severe and fatal COVID-19 cases [20]. A similar study found that D-dimer can distinguish between patients with and without significant COVID-19 forms, although it lacked mortality data [21]. This could be due to a hypercoagulable state induced by a cytokine storm and viremia, which leads to fibrin polymerization, thrombus formation, and ultimately, a negative consequence [22]. In addition, a significant positive correlation was observed between D-dimer and CRP levels (r=0.646; p0.001) in this study. Comparable findings were obtained in a previous study [23]. In patients with COVID-19, there is also a strong positive correlation between D-dimer and CRP levels. In contrast, the weak relationship between D-dimer and serum ferritin (r=0.355; p0.001) was significant. These data imply that during the immunological response to COVID-19, hyperinflammation stimulates the coagulation pathways [24].

4.2.3. Serum Ferritin Level

Non-survivors of COVID-19 had significantly higher serum ferritin levels. Non-survivors had higher ferritin levels than survivors [25]. Furthermore, ferritin levels were observed to increase in correlation with the severity of the condition [11]. The hospital death rate is higher in patients with serum ferritin levels >300 ng/mL than in those with serum ferritin levels of 300 ng/mL [2]. Ferritin level 809.5 was also shown to predict non-survivors, with a sensitivity of 69.7.9% and specificity of 37.1.2% (AUC = 0.684). When all of these observations were combined and analyzed, hyperferritinemia was found to be an independent risk factor for COVID-19 as well as a predictor of illness severity. There are two possible explanations for the relevance of ferritin level. According to [26], the clinical course of severe COVID-19 is similar to that of macrophage-activating syndrome, which is characterized by elevated ferritin levels and the presence of a cytokine storm. In patients with covid-19, the H-chain of ferritin-activating macrophages is responsible for the increased inflammatory cytokine output. Another possibility is that an increase in ferritin helps the immune system respond to invading bacteria by supporting iron metabolism, including in viral infections. For viral replication, the host cells must have improved cellular metabolism and optimal iron levels. Thus, restricting iron bioavailability is critical to interfere with viral replication. Despite the underlying etiology, Patients with COVID-19 have high blood ferritin levels. It would be beneficial to determine whether serum ferritin can be utilized as a biomarker of the severity of inflammation in COVID-19 patients [27]. Nonetheless, ferritin levels are thought to be a good predictor of poor outcomes.

4.2.4. Serum CRP and LDH Levels

CRP is a well-known inflammatory biomarker that is elevated in most people with COVID-19. In comparison with non-severe cases, more severe cases showed a more obvious increase in CRP levels (81.5% vs. 56.4%, respectively) [28]. Higher CRP levels have also been associated with the development of acute respiratory distress syndrome, increased troponin T levels, and myocardial damage in patients with severe COVID-19 [29]-[30]. This finding can be interpreted as an indication of severe inflammation. Elevated serum CRP levels were associated with an increased risk of death. Non-survivors have a gradual increase in CRP levels during their hospital stay [17]. We discovered that non-survivors of COVID-19 had higher CRP levels than survivors; moreover, the analysis of AUC showed a higher CRP level (AUC= 0.802 (95% CI: 0.717-0.886).

5. Conclusions and Recommendations

The study concluded that older age and higher D-dimer, ferritin, CRP, and LDH levels were associated

with disease severity, and that adult patients with COVID-19 had a higher risk of dying. D-dimer and CRP levels are among the best predictors of disease progression.

These biomarkers could be utilized to separate patients who need intensive care at the time of admission, allowing for risk stratification and, hence, better patient management. This will also help reduce patient mortality by allowing early detection of signs of disease progression.

Declarations

Author Contributions

Dhamya Kadhim Sarhan contributed to the research conceptualization, methodology, data curation, and investigation. **Intisar R. Sharba** contributed by writing the abstract, introduction, and visualization of the research findings. **Zainab Basim Mohammed** contributed to the validation and statistical analysis of the data, writing the research methods and discussion section, and overall supervision.

Ethical Approval and Consent to Participate

The ethics committee of Kufa University and Health Intuition granted all necessary clearances and ethical approval in November 2021.

Conflict of interest

The authors declare that they have no conflicts of interest.

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