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ORIGINAL ARTICLE

Determinants of Hospitalization and Mortality in COVID-19 Patients Admitted to the Emergency Department

Acil Servise Başvuran Covid-19 Hastalarında Hastaneye Yatış ve Mortalitenin Belirleyicileri

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ABSTRACT

Aim: We aim to elucidate the clinical traits, comorbidities, and prognostic factors associated with intensive care unit (ICU) admission and in-hospital mortality in a group of COVID-19 patients admitted to a university hospital.
Methods: This study was conducted in the Erciyes University Hospital. Retrospective cohort study of patients admitted to the Emergency Department between April 1, 2020, to October 30, 2020, and received the International Classification of Diseases (ICD)-10 diagnostic code of COVID-19. We separated the patients into three groups: outpatients, patients admitted to COVID-19 wards, and patients admitted to ICUs. We performed multivariate regression analyses to identify the variables predicting hospital mortality.
Results: Of the 194 patients included in the study, 54.6% were male, and the median age was 49 (interquartile range, 37–63). The study admitted 128 (66%) patients to wards, 37 (19.1%) to ICUs, and 29 (14.9%) as outpatients. The most frequent comorbidities were hypertension (25.3%), diabetes mellitus (19.1%), and malignancy (11.9%). Compared with the non-ICU group, ICU patients had older ages ($p<0.001$) and had more comorbidities. In the multivariate analysis, age (odds ratio [OR], 1.139; 95% confidence interval [CI]: 1.003–1.293), ferritin (OR, 1.004; 95% CI: 1.000–1.008), and red cell distribution width (RDW) (OR, 2.085; 95% CI: 1.181–3.682) on admission were significant factors predicting mortality in the hospital.
Conclusions: In-hospital mortality rate was 16.5% among all patients. The older age, increased ferritin, and RDW are the most important factors associated with a higher risk of death during hospital stays for COVID-19.

Keywords: COVID-19, critical care, emergency department, intensive care unit, mortality

ÖZ

Amaç: Bir üniversite hastanesine başvuran COVID-19 hastaları ile ilgili klinik özellikleri, komorbiditeleri ve prognostik değişkenleri, yoğun bakım ünitesine (YBÜ) yatışı ve hastane içi mortaliteyi öngören faktörleri tanımlamak.
Gereç ve Yöntemler: Bu çalışma Erciyes Üniversitesi Hastanesi'nde yapılmıştır. 1 Nisan 2020 ile 30 Ekim 2020 tarihleri arasında Acil Servise başvuran ve COVID-19 tanı kodunu alan hastaların retrospektif kohort çalışmasıdır. Hastalar; ayaktan hastalar, COVID-19 servislerine yatan hastalar ve YBÜ'ye yatan hastalar olarak üç gruba ayrıldı. Hastanede mortaliteyi öngören değişkenleri belirlemek için çok değişkenli regresyon analizleri yapıldı.
Bulgular: Çalışmaya dahil edilen 194 hastanın %54.6'sı erkekti ve medyan yaş 49'du (çeyrekler arası aralık, 37-63). Hastaların 128'i (%66) servise, 37'si (%19.1) YBÜ'ye yatırıldı, 29'u (%14.9) ayaktan tedavi edildi. En sık eşlik eden hastalıklar hipertansiyon (%25.3), diabetes mellitus (%19.1) malignite (%11.9) idi. Yoğun bakımda olmayan grupla karşılaştırıldığında, yoğun bakım hastalarının yaşı daha büyüktü ($p<0.001$); ve daha fazla yandaş hastalığı vardı. Çok değişkenli analizde yaş (Odds oranı, 1.139; %95 güven aralığı: 1.003–1.293), ferritin (Odds oranı, 1.004; %95 güven aralığı: 1.001–1.008) ve kırmızı hücre dağılım genişliği (RDW) (Odds oranı, 2.085; %95 güven aralığı: 1.181–3.682) hastanedeki mortaliteyi öngören önemli faktörlerdi.
Sonuçlar: Tüm hastalarda hastane içi mortalite oranı %16.5 idi. İleri yaş, artan ferritin ve RDW, COVID-19 nedeniyle hastanede kalış sırasında daha yüksek ölüm riski ile ilişkili en önemli faktörlerdir.

Anahtar Kelimeler: Acil servis, COVID-19, kritik bakım, mortalite, yoğun bakım ünitesi

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INTRODUCTION

The SARS-CoV-2 virus causes coronavirus disease (COVID-19), a viral infection that affects the respiratory system (1). The COVID-19 pandemic has resulted in a rise in the number of patients in critical condition (2). Twenty percent of COVID-19 patients develop severe hypoxia or respiratory failure (3). The majority of severely sick patients received care in emergency rooms and general wards, lacking access to specialized treatment in intensive care units (ICUs) (2, 3). This situation strained emergency department (ED) resources and bed capacity (1). Rapid and accurate triage of critical COVID-19 patients from EDs to hospital units is essential (4). To forecast the mortality of critical COVID-19 patients admitted to the ED, there is a need for readily available biomarkers.

There is already researchs (5-7) that shows how some biomarkers are linked to how well COVID-19 patients do in the hospital, but it hasn't been used much when combined with other factors. Due to the virus's potential to seriously disrupt many vital organs such as the heart, liver, and kidneys, researchers are also investigating blood parameters as prognostic factors, especially tests that investigate complete blood count, coagulation and fibrinolysis steps, and measurements related to inflammation (7). In particular, the prognostic value of simple but effective biomarkers such as ferritin (8) and red cell distribution width (RDW) (9) has emerged as a powerful tool for predicting COVID-19-related mortality.

In the early days of the pandemic, patients had to wait in emergency rooms due to hospital bed occupancy. Especially in settings where beds and resources are limited, the burden of patient triage for hospitalization and close monitoring of patients at risk of death is becoming more critical. The aim of this study is to examine the impact of biomarkers such as ferritin and RDW on ICU admission and in-hospital mortality in COVID-19 patients admitted to the ED of a university hospital. The study also aims to provide useful information to quickly understand who is at greatest risk in EDs by looking at how well these biomarkers can predict the future.

MATERIALS and METHODS

This retrospective study included patients over 18 who applied to the ED of Erciyes University Hospital between April 01, 2020 and October 30, 2020 and whose International Classification of Diseases (ICD)-10 diagnosis code was COVID-19. We obtained the relevant information from the Hospital Data Processing Center, Patient Information Management System, Hospital Archive, and Department of Emergency Medicine records. We excluded patients with incomplete data from the study. The Erciyes University School of Medicine's ethical committee (dated January 20, 2021 and numbered 2021/67) and the Ministry of Health approved the study. We conducted the study in accordance with the Declaration of Helsinki.

Study Design

The ED, where the study was conducted, had a bed capacity of 45 and had three rooms (one room and 15 beds for trauma). The COVID-19 examination room and the observation room (six beds) were separate. Suspected and confirmed COVID-19 patients were taken to the COVID-19 examination room. The COVID-19 national guidelines were used to diagnose suspected and confirmed cases (10). Whether the patients

were treated as outpatients or hospitalized in the ward or ICU was determined by the consultation of infectious and/or pulmonary diseases. Polymerase Chain Reaction (PCR) tests were performed in the Ministry of Health authorised Molecular Virology Laboratory, Microbiology Department. Since this was the first COVID-19 pandemic in Türkiye, vaccination had not commenced; therefore, the patients in the study were unvaccinated. Only the first applications of patients diagnosed with more than one COVID-19 were considered.

We divided the patients into three groups. Group 1 consisted of mild cases treated as outpatients. Group 2 consisted of patients admitted to COVID-19 wards. Group 3 consisted of patients requiring ICU admission. Patients in the COVID-19 examination room who were diagnosed with COVID-19 and were not hospitalized were included in the 'Outpatient' group and in the 'Ward' group if they were admitted to the ward from the ED and in the 'ICU' group if they were admitted to the ICU from the ED. If patients died in the hospital after admission, the outcome was considered mortality.

Group I (outpatients): Patients with typical or atypical COVID-19 symptoms or asymptomatic patients with positive COVID-19 PCR test results and considered vitally stable (oxygen saturation >94%, respiratory rate <20/min, pulse <100/min, blood pressure >120/80 mmHg) were included in this group. We obtained PCR test results from patient files, following up on an outpatient basis, and selected cases that met the inclusion criteria.

Group II (patients requiring COVID-19 ward admission): This group included patients who required hospitalization in COVID-19 wards, presented with typical or atypical COVID-19 symptoms, had positive COVID-19 PCR test results, or had typical involvement in thoracic computed tomography (CT).

Group III (patients requiring ICU admission): This group included patients who presented with typical or atypical COVID-19 symptoms, had a positive COVID-19 PCR test result or typical involvement in thoracic CT, had unstable vital findings, and required close noninvasive or invasive follow-up in the ICU.

A qualified team of doctors examined and gathered data on patient demographics, clinical symptoms, comorbidities, preliminary laboratory results, radiological findings, and outcomes.

Statistical Analysis

Continuous variables were presented as median (IQR) values. Categorical variables were presented as frequency (n) and percentage (%) values. Conformity to normal distribution was evaluated with Skewness and Kurtosis coefficients, the Kolmogorov-Smirnov test, and Histograms. The Mann-Whitney U test was used to compare non-normally distributed continuous variables between two groups. The Kruskal-Wallis test was used to compare variables between three or more groups. For variables with a significant P-value in the Kruskal-Wallis test, the Mann-Whitney U test with Bonferroni correction was used to determine which groups the difference originated from. Chi-square/Fisher's exact analysis examined relationships between categorical variables. A post-hoc Bonferroni test was performed to identify the source of significant differences. Associations between continuous variables were analyzed using Spearman's correlation analysis. A binary logistic regression model was constructed to define the factors predicting hospital mortality. Variables with a P value below 0.10 and not correlated with each other were included in the

multivariate logistic regression model. The logistic regression model included age, sex, hypertension, troponin, hemoglobin, lymphocytes, lymphopenia, procalcitonin, C-Reactive Protein (CRP), fibrinogen, pro b-type natriuretic peptide (proBNP), D-Dimer, prothrombin time (PT), red cell distribution width (RDW), and ferritin levels. Groups were not included in the analysis if there were fewer than 20 patients in a group and if small groups overlapped. The variance was assessed using Nagelkerke R^2 and goodness of fit using the Hosmer-Lemeshow test, which describes the odds ratio with its respective 95% confidence intervals. To determine the predictive power of age, ferritin and RDW for in-hospital mortality, receiver operating characteristic (ROC) analysis was performed. Youden's index (sensitivity +1- specificity) was used to determine the optimal cut-off values. The parameters' sensitivity, specificity, positive and negative likelihood ratio, and positive and negative predictive values were calculated for the optimum cut-off levels. SPSS version 23 and MedCalc programs were used in all analyses, and $p<0.05$ was accepted as statistically significant.

To evaluate whether the sample size was sufficient to detect significant effects in our multivariate logistic regression model, a post hoc power analysis was conducted using the F-test-based method in G Power 3.1 program. The effect size (f^2) was derived from the Nagelkerke R^2 value (0.857), calculated as $f^2 = R^2 / (1 - R^2)$. Given a total sample size of 194 and 16 independent variables, the power analysis yielded a statistical power of 1.0, indicating that the study had adequate power to detect significant effects within the model.

RESULTS

The study included 194 patients who met the inclusion criteria out of 1200 admitted to the ED. The median age was 49 (IQR 37–63), and 54.6% were male. Ninety-two patients (47.4%) had at least one other disease. The most common comorbidities were hypertension (49, 25.3%), diabetes mellitus (37, 19.1%), and malignancy (23, 11.9%). The most frequent symptoms reported were fever (58.8%), myalgia or fatigue (53.6%), sore throat (47.9%), and dry cough (44.8%) (Table 1). One hundred fifty-three patients (78.9%) had positive PCR results, and 72.2% (n=140) had typical radiological findings. The overall mortality rate was 16.5% (n=32) among all patients (Table 2).

Table 2 presents a comparative analysis of Group I, II, and III patients. Of the patients, 15% (n=29) were in Group I, 66% (n=128) were in Group II, and 19% (n=37) were in Group III. We evaluated factors predicting mortality across the groups (Table 3). These three variables—age [OR: 1.139 (95% CI 1.003–1.293), P = 0.045], ferritin [OR: 1.004 (95% CI 1.001–1.008), P = 0.019], and RDW on hospital admission [OR: 2.085 (95% CI 1.181–3.682), P = 0.011]—were all found to be significant in predicting COVID-19 mortality (Table 4). Figure 1 presents the ROC curves of age, RDW, and ferritin, while Table 5 presents the sensitivity and selectivity values.

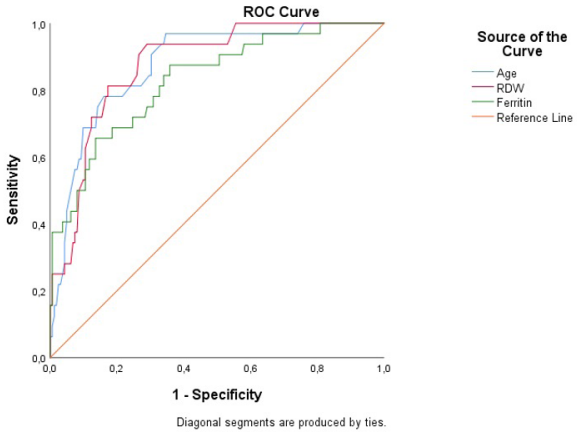

Figure 1. ROC Curves of Age, RDW, and Ferritin for Predicting In-Hospital Mortality in COVID-19 Patients.

Table 1. Baseline demographic, clinical, and comorbidity characteristics of patients on admission

Total (n=194)		n (%)[a]
Demographic information		
Age, median (IQR)		49 (37-63)
Sex	Male	106 (54.6)
	Female	88 (45.4)
Comorbidities		
	At least one comorbid disease	92 (47.4)
	At least two comorbid diseases	60 (30.9)
	Hypertension	49 (25.3)
	Diabetes Mellitus	37 (19.1)
	Malignancy	23 (11.9)
	Cardiovascular Disease	20 (10.3)
	Chronic Renal Disease	13 (6.7)
	Chronic Obstructive Pulmonary Disease	13 (6.7)
	Coronary Artery Disease	11 (5.7)
	Congestive Heart Failure	10 (5.2)
	Asthma	8 (4.1)
Symptoms on admission		
	Fever, >38°C	114 (58.8)
	Myalgia or Fatigue	104 (53.6)
	Sore Throat	93 (47.9)
	Dry Cough	87 (44.8)
	Headache	64 (33)
	Shortness of Breath	45 (23.2)
	Diarrhea	23 (11.9)
	Nausea	13 (6.7)
Outcomes		
	Ward	128 (66.0)
	Intensive Care Unit	37 (19.1)
	Outpatient	29 (14.9)
	Mortality	32 (16.5)

[a]Percentages are calculated on the total number of patients. IQR: Interquartile range

DISCUSSION

The identification and application of reliable biomarkers remain pivotal in clinical decision-making, particularly in critical care settings. Ferritin and RDW, extensively studied during the COVID-19 pandemic, have demonstrated significant prognostic value in predicting disease severity and mortality. Their utility, however, extends beyond COVID-19, warranting exploration in other critical and chronic conditions. The point of this talk is to put ferritin and RDW in a bigger picture of clinical situations, focusing on their use as signs of prognosis and their ability to help with treatment plans.

Ferritin is an acute-phase reactant and a critical indicator of iron metabolism (11). High serum ferritin levels have been associated with mortality and the development of severe outcomes in COVID-19 (8, 12). A meta-analysis showed that high ferritin was associated with poor outcomes in COVID-19 and acute respiratory distress syndrome (ARDS) development (13). While its elevation in COVID-19 patients has been linked to cytokine storm and poor outcomes, similar associations are observed in other inflammatory and infectious diseases: Sepsis and Septic Shock: Studies show a correlation between elevated ferritin levels and worse outcomes in sepsis, a reflection of hyperinflammatory responses and macrophage activation syndrome (MAS) (14, 15). Researchers have found that hyperferritinemia is a part of the "sepsis-associated hyperferritinemic syndrome," which means that multiple organs are failing and people are dying. Hemophagocytic Lymphohistiocytosis (HLH): Ferritin is a diagnostic criterion for HLH, a life-threatening hyperinflammatory syndrome. Extreme ferritin levels (>10,000 ng/mL) strongly suggest HLH, aiding early diagnosis and treatment (16). Autoimmune Diseases: Conditions such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) often show elevated ferritin

Table 2. Comparison of clinical, laboratory, and outcome parameters across COVID-19 patient groups

Parameters*	Outpatient (n=29)	ICU (n=37)	Ward (n=128)	p
Age	39 (31-48)	72 (63-77)	46,5 (37-60)	<.001[a]
Gender (Male)	12 (41.4)	24 (64.9)	70 (54.7)	.164[b]
Lymphocyte (103/µL)	1.7 (1.15-2.31)	0.66 (0.40-1.17)	1.45 (1.02-1.98)	<.001[a]
CRP (mg/L)	7.70 (1.94-18)	85 (44-174)	8.80 (3.45-32)	<.001[a]
Ferritin (ng/mL)	67 (32-102)	625 (240-1318)	161 (65.8-322)	<.001[a]
D-dimer (µg/L)	370 (190-580)	2300 (930-6640)	405 (258-630)	<.001[a]
Hemoglobin (g/dL)	13.6 (12.5-14.8)	11.2 (9.40-13.1)	13.8 (12.1-15.1)	<.001[a]
Leukocyt (103/µL)	5.88 (4.63-7.90)	11.46 (7.92-16.38)	5.73 (4.39-7.38)	<.001[a]
Thrombocyte (103/µL)	274 (230-319)	198 (156-250)	225 (182-290)	.012[a]
RDW (%)	13.1 (12.1-14.2)	16 (15.3-16.9)	13.1 (12.4-13.9)	<.001[a]
Neutrophil (103/µL)	3.41 (4.90-2.88)	11.50 (8.85-16.03)	3.30 (2.40-4.60)	<.001[a]
MPV (%)	10.9 (9.90-11.5)	10.6 (9.90-11.3)	10.4 (9.90-11.1)	.713[a]
Procalcitonin (ng/mL)	0.05 (0.03-0.07)	0.41 (0.15-1.22)	0.05 (0.02-0.10)	<.001[a]
ProBNP (pg/mL)	29 (12-84)	1384 (558-4009)	38 (17.3-90)	<.001[a]
Creatine Kinase (U/L)	55 (29-96)	96 (69-216)	78.5 (48-115)	.002[a]
Troponin (ng/mL)	0.003 (0.003-0.004)	0.031 (0.015-0.067)	0.004 (0.003-0.007)	<.001[a]
Fibrinogen (mg/dL)	348 (240-421)	480 (372-633)	346 (270-453)	.001[a]
Creatinine (mg/L)	0.85 (0.68-0.95)	1.15 (0.88-1.73)	0.88 (0.72-1.07)	<.001[a]
ALT (u/L)	20 (17-31)	23 (14-59)	22 (16-31)	.781[a]
AST (u/L)	26 (19-38)	32 (23-57)	24 (19-34.3)	.088[a]
Prothrombin Time (sec)	11.7 (11.2-12)	12.9 (12-16)	12.1 (11.5-12.9)	<.001[a]
At least one comorbid disease	7 (24.1)	37 (100)	48 (37.5)	<.001[b]
At least two comorbid diseases	4 (13.8)	30 (81.1)	26 (20.3)	<.001[b]
Hypertension	1 (3.4)	28 (75.7)	20 (15.6)	<.001[b]
Diabetes Mellitus	3 (10.3)	22 (59.5)	12 (9.4)	<.001[b]
Malignancy	3 (10.3)	9 (24.3)	11 (8.6)	.043[b]
Cardiovascular Disease	1 (3.4)	7 (18.9)	12 (9.4)	.114[b]
Chronic Renal Disease	0 (0)	8 (21.6)	5 (3.9)	<.001[b]
COPD	0 (0)	10 (27)	3 (2.3)	<.001[b]
Coronary Artery Disease	0 (0)	7 (18.9)	4 (3.1)	.003[b]
Congestive Heart Failure	0 (0)	6 (16.2)	4 (3.1)	.007[b]
Asthma	0 (0)	2 (5.4)	6 (4.7)	.653[b]
Fever, >38°C	16 (55.2)	22 (59.5)	76 (59.4)	.913[a]
Myalgia or Fatigue	16 (55.2)	20 (54.1)	68 (53.1)	.978[a]
Sore Throat	14 (48.3)	18 (48.6)	61 (47.7)	.994[a]
Dry Cough	12 (41.4)	28 (75.7)	47 (36.7)	<.001[a]
Headeche	8 (27.6)	12 (35.1)	43 (33.6)	.786[a]
Shortness of breath	0 (0)	26 (70.3)	19 (14.8)	<.001[a]
Diarrhea	3 (10.3)	4 (10.8)	16 (12.5)	.926[a]
Nausea	3 (10.3)	4 (10.8)	6 (4.7)	.294[a]
Mortality	0 (0)	31 (83.8)	1 (0.8)	<.001[b]

CRP: C-reactive protein; RDW: Red cell distribution width; MPV: Mean platelet volüme; COPD: Chronic Obstructive Pulmonary Disease; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ICU: Intensive care unit; IQR: Interquartile range; BNP: Brain natriuretic peptide.

[a]Kruskal-Wallis test was used. Values are expressed as median (IQR).

[b]The chi-square test was used. Values are given as continuous data (percentage).

Table 3. Comparison of demographic and clinical features between survivor and non-survivor COVID-19 patients

	Total (n=194)	Survivor (n=162)	Nonsurvivor (n=32)	P
Male Gender, n (%)	106 (54.6)	84 (51.9)	22 (61.8)	0.079[b]
Age, Median (IQR)	49 (37.3–63)	44.5 (35–59)	72.5 (63.8–77)	<0.001a
Positive RT-PCR Test, n (%)	153 (78.9)	132 (81.5)	21 (65.6)	0.045[b]
Pneumonia on Thorax CT, n (%)	140 (72.2)	117 (72.2)	23 (71.9)	0.968[b]
Comorbidity, n (%)				
At least one comorbid disease	92 (47.4)	60 (37)	32 (100)	<0.001[b]
At least two comorbid diseases	60 (30.9)	33 (20.4)	27 (84.4)	<0.001[b]
Hypertension	49 (25.3)	25 (15.4)	24 (75)	<0.001[b]
Diabetes Mellitus	37 (19.1)	18 (11.1)	19 (59.4)	<0.001[b]
Malignancy	23 (11.9)	15 (9.3)	8 (25)	0.012[b]
Cardiovascular Disease	20 (10.3)	13 (8.0)	7 (21.9)	0.019[b]
Chronic Renal Disease	13 (6.7)	4 (2.5)	9 (28.1)	<0.001[b]
Chronic Obstructive Pulmonary Disease	13 (6.7)	4 (2.5)	9 (28.1)	<0.001[b]
Coronary Artery Disease	11 (5.7)	4 (2.5)	7 (21.9)	<0.001[b]
Congestive Heart Failure	10 (5.2)	3 (1.9)	7 (21.9)	<0.001[b]
Asthma	8 (4.1)	6 (3.7)	2 (6.3)	0.508[b]
Laboratory Findings at ED admission, median (IQR)				
Hemoglobin (g/dL)	13.4 (11.7-14.8)	13.8 (12.1-15.1)	11.3 (9.4-13)	<0.001[a]
Leukocyt (103/µL)	6.04 (4.53-9.38)	5.92 (4.51-7.89)	11.51 (5.33-17.89)	<0.001[a]
Neutrophil (103/µL)	3.78 (2.61-6.47)	3.39 (2.54-4.76)	11.48 (6.84-18.21)	<0.001[a]
Lypmphcyt (103/µL)	1.40 (0.86-1.99)	1.52 (1.04-2.09)	0.61 (0.39-0.95)	<0.001[a]
Thrombocyt (103/µL)	229 (181-294)	233 (188-299)	195 (144-250)	0.017[a]
Creatinine (mg/L)	0.90 (0.74-1.12)	0.87 (0.72-1.05)	1.16 (0.89-1.97)	<0.001[a]
ALT (U/L)	22 (16-33.8)	22 (16-31)	23 (14-45.5)	0.512[a]
AST (U/L)	25 (19-37)	24 (19-34.8)	34.5 (23-57.3)	0.015[a]
Creatine Kinase (U/L)	76 (48.3-123)	73.5 (46.3-115)	95.5 (68.5-191)	0.025[a]
Troponin (ng/mL)	0.005 (0.003-0.012)	0.004 (0.003-0.007)	0.040 (0.014-0.068)	<0.001[a]
CRP (mg/L)	11.8 (4.58-52.8)	8.66 (3.28-30.8)	98 (43.8-174)	<0.001[a]
Procalcitonin (ng/mL)	0.06 (0.03-0.15)	0.05 (0.03-0.09)	0.37 (0.14-1.16)	<0.001[a]
D-dimer (µg/L)	455 (270-1038)	405 (240-638)	2170 (920-5930)	<0.001[a]
Fibrinogen (mg/dL)	363 (284-483)	348 (268-461)	445 (360-637)	0.003[a]
Ferritin (ng/mL)	166 (66.3-397)	134 (53.3-298)	659 (270-1489)	<0.001[a]
ProBNP (pg/mL)	53.3 (19.3-307)	38.5 (16.4-118)	1980 (639-4432)	<0.001[a]
Prothrombin Time (sec)	12 (11.5-13)	12 (11.4-12.7)	12.9 (12-15.2)	<0.001[a]
RDW (%)	13.3 (12.5-15)	13.1 (12.4-14.1)	15.9 (15.0-17.8)	<0.001[a]
MPV (%)	10.5 (9.90-11.2)	10.4 (9.90-11.1)	10.6 (10.1-11.6)	0.144[a]
Symptoms on admission, n (%)				
Fever, > 38 °C	114 (58.8)	96 (59.3)	18 (56.3)	0.752[b]
Myalgia or fatigue	104 (53.6)	86 (53.1)	18 (56.3)	0.743[b]
Sore throat	93 (47.9)	78 (48.1)	15 (46.9)	0.895[b]
Dry cough	87 (44.8)	62 (38.3)	25 (78.1)	<0.001[b]
Headeche	64 (33)	52 (32.1)	12 (37.5)	0.553[b]
Shortness of Breath	45 (23.2)	19 (11.7)	26 (81.3)	<0.001[b]
Diarrhea	23 (11.9)	19 (11.7)	4 (12.5)	0.902[b]
Nausea	13 (6.7)	9 (5.6)	4 (12.5)	0.151[b]
Length of Hospital Stay (days), Median (IQR)	6 (4-10)	6 (3-9)	10 (5-15.5)	<0.001[a]

CRP: C-reactive protein; RDW: Red cell distribution width; MPV: Mean platelet volüme; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ICU: intensive care unit; IQR: Interquartile range; RT-PCR: Real-time reverse transcriptase polymerase chain reaction; BNP: Brain natriuretic peptide.

[a]Mann–Whitney U test was used. Values are expressed as median (IQR)

[b]The chi-square test was used. Values are given as continuous data (percentage).

Table 4. Multivariate Logistic Regression Analysis Results Predicting In-Hospital Mortality

Variables	B	SE	Wald	df	p-value	OR	95% CI for OR	
							Lower	Upper
Male gender	0.856	1.123	0.582	1	0.446	2.354	0.261	21.254
Age	0.130	0.065	4.027	1	**0.045**	1.139	1.003	1.293
Troponin	0.997	1.299	0.589	1	0.443	2.711	0.212	34.591
Lypmphcyt	0.000	0.000	0.783	1	0.376	1.000	0.999	1.000
Hemoglobin	0.272	0.302	0.810	1	0.368	1.312	0.726	2.373
Thrombocyt	-0.006	0.005	1.573	1	0.210	0.994	0.984	1.004
Procalcitonin	0.367	0.937	0.153	1	0.695	1.443	0.230	9.052
CRP	0.006	0.010	0.382	1	0.537	1.006	0.987	1.026
Ferritin	0.004	0.002	5.522	1	**0.019**	1.004	1.001	1.008
ProBNP	0.000	0.000	1.488	1	0.222	1.000	1.000	1.000
D-dimer	0.000	0.000	0.183	1	0.669	1.000	1.000	1.001
Fibrinogen	0.001	0.004	0.133	1	0.716	1.001	0.994	1.009
PT	0.078	0.143	0.299	1	0.585	1.082	0.816	1.433
RDW	0.735	0.290	6.417	1	**0.011**	2.085	1.181	3.682
AST	0.005	0.006	0.750	1	0.386	1.005	0.994	1.017
Hypertension	1.441	1.396	1.065	1	0.302	4.225	0.274	65.239
Constant	-28.439	11.152	6.503	1	0.011	0.000		

Hosmer and Lemeshow Test: P=0.998, Nagelkerke R^2: 0.857

B: Unstandardized regression weight; CI: Confidence interval; OR: Odds ratio; SE: Standard error; CRP: C-reactive protein; AST: Aspartate aminotransferase; RDW: Red cell distribution width; PT: Protrombin time; BNP: Brain natriuretic peptide.

Table 5. Predictive Performance of Age, RDW, and Ferritin for Mortality in COVID-19 Patients

(%95 CI)	Age	RDW	Ferritin
Cut-off Level	>60 years	>14.5 %	>276 ng/mL
AUC	0.877 (0.816-0.938)	0,875 (0.818-0.932)	0,829 (0.750-0.907)
Sensitivity	81.25 (63.56-92.79)	81.25 (63.56-92.79)	71.88 (53.25-86.25)
Specificity	75.93 (68.59-82.29)	79.63 (72.6-85.54)	71.60 (64.0-78.4)
+LR	3.38 (2.45-4.66)	3.99 (2.82-5.65)	2.53 (1.82-3.51)
-LR	0.25 (0.12-0.52)	0.24 (0.12-0.50)	0.39 (0.22- 0.68)
PPV	40 (32.62-47.87)	44.07 (35.77-52.71)	33.33 (26.5-40.94)
NPV	95.35 (90.84-97.7)	95.56 (91.23-97.8)	92.8 (88.02-95.77)

CI: Confidence interval; AUC: Area under the curve; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio; PPV: Positive predictive value; NPV: Negative predictive value; RDW: Red cell distribution width.

levels, particularly during disease flares. Monitoring ferritin may provide insights into disease activity and therapeutic responses (17). Chronic Kidney Disease (CKD): Ferritin serves as an indicator of inflammation and iron status in CKD patients, aiding in the management of anemia. Elevated ferritin in these patients may signal poor prognosis due to chronic inflammation (18).

Our findings show that RDW significantly predicts the severity of COVID-19 infection in patients, which is not surprising. The RDW has been crucial because it can accurately predict the probability of death in the general population. RDW measures the variety of red blood cell sizes and shows changes in the body's underlying health, like inflammation, oxidative stress, and poor erythropoiesis (19). Its prognostic significance extends to numerous conditions: Cardiovascular Diseases: Research has established RDW as a predictor of mortality in heart failure, acute coronary syndrome, and atrial fibrillation. Elevated RDW is associated with poor cardiac function, increased inflammation, and adverse outcomes (20). Respiratory Diseases: Higher RDW values are linked to worsening disease, low oxygen levels, and a higher risk of death in people with chronic obstructive pulmonary disease (COPD) and pneumonia (21). Cancer: Various malignancies, including colorectal and lung cancers, have reported RDW elevation. We hypothesize that it reflects tumor-induced inflammation and systemic stress. Sepsis: RDW is a robust predictor of sepsis outcomes, with higher values indicating increased risk of mortality. Its integration into sepsis scoring systems enhances the early identification of high-risk patients (19).

Numerous studies have demonstrated a significant correlation between elevated RDW (9, 22, 23) and hyperferritinaemia (8, 24, 25) in relation to COVID-19 mortality. Moreover, elevated RDW (26) and serum ferritin (24, 27) levels in COVID-19 patients have been demonstrated to forecast not only in-hospital mortality but also illness severity and deterioration of clinical status, resulting in ICU admission. Consequently, in critically COVID-19 patients, these biomarkers may offer guidance and alerts to mitigate morbidity and mortality. Considering that RDW and ferritin evaluations have been incorporated into standard hematological screening in the ED and ICU during the pandemic, their application may serve as an auxiliary instrument for clinicians to categorize COVID-19 patients at an early stage, facilitating more judicious resource allocation.

Ferritin and RDW, as markers of systemic inflammation and metabolic derangements, can complement each other in prognostic modeling. For instance: (I) Chronic Inflammatory States: When someone has a disease like inflammatory bowel disease (IBD), having high levels of ferritin and RDW at the same time may mean they have severe inflammatory activity and anemia from a long-term illness. (II) Critical Illness: Together, these biomarkers give a full picture of the amount of inflammation and the movement of red blood cells in intensive care, which helps in figuring out who is at risk.

Our study has limitations due to single-center and retrospective study design. Coupled with the lack of vaccination data restricts applicability to other settings or patient populations. Additionally, our study hospital was not designated as a pandemic center in the region.

CONCLUSION

In conclusion, the present study, which evaluated blood parameters as predictors of hospitalization and mortality, yielded significant results. The identification of predictors for COVID-19 mortality is crucial for enhancing treatment strategies and preventing patient fatalities. An accurate analysis of COVID-19 predictors can significantly enhance the clinical decision-making process and facilitate quicker diagnoses for patients at heightened risk of mortality. Ferritin and RDW have emerged as critical biomarkers with prognostic significance beyond COVID-19. Their ability to reflect systemic inflammation, oxidative stress, and disease severity underscores their versatility across a range of conditions. By using these biomarkers in regular clinical practice and research, doctors can make diagnoses more accurately, get better at predicting how patients will do in critical and long-term illnesses, and improve their patients' outcomes.

Conflict of interest

The authors declare that there is no conflict of interest.

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