

Assessment of Clinical Characteristics and Mortality-Associated Factors in COVID-19 Critical Cases in Kuwait

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Highlights of the Study

- No significant difference in age and sex was found among critically ill patients with COVID-19.
- This study suggests that the risk factors that can be used to predict mortality include preexisting hypertension, severe acute respiratory distress syndrome, renal replacement therapy, procalcitonin level, serum albumin, lymphocyte count, and D-dimer.
- Early identification of risk factors for mortality might help achieve better outcomes.

Keywords

SARS-CoV-2 · Coronavirus infection · Pneumonia · Acute respiratory distress syndrome

Abstract

Objective: The objective of this study was to assess the clinical characteristics and identify mortality risk factors in intensive care unit (ICU)-admitted COVID-19 patients. **Methods:** We recruited and analyzed SARS-CoV-2-infected adult patients (age ≥ 18 years) who were admitted to the ICU at Jaber Al-Ahmad Al Sabah Hospital, Kuwait, between March 1, 2020, and April 30, 2020. The risk factors associated with in-hospital mortality were assessed using multiple regression

analysis. **Results:** We recruited a total of 103 ICU patients in this retrospective cohort. The median age of the patients was 53 years and the fatality rate was 45.6%; majority (85.5%) were males and 37% patients had more than 2 comorbidities. Preexisting hypertension, moderate/severe acute respiratory distress syndrome, lymphocyte count $<0.5 \times 10^9$, serum albumin <22 g/L, procalcitonin >0.2 ng/mL, D-dimer $>1,200$ ng/mL, and the need for continuous renal replacement therapy were significantly associated with mortality. **Conclusion:** This study describes the clinical characteristics and risk factors for mortality among ICU patients with COVID-19. Early identification of risk factors for mortality might help improve outcomes.

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Introduction

The outbreak of novel coronavirus disease began with a simple case of pneumonia in Wuhan, China, in late December, 2019. By January 30, 2020, the World Health Organization declared the disease as a Public Health Emergency of International Concern and renamed it as COVID-19 [1]. Less than a month later, on February 24, the State of Kuwait confirmed 3 patients on a flight coming from Islamic Republic of Iran to have contracted the virus, marking the start of the outbreak in the country [2]. By March 3, 2020, the first COVID-19 patient was admitted to the intensive care unit (ICU). In the next 2 months, >100 confirmed cases of COVID-19 were admitted to the ICU.

The COVID-19 pandemic is considered one of the greatest global public health crises since the 1918 influenza pandemic [3]. Although the clinical spectrum of the infection appears to be broad, patients infected with COVID-19 are found to be at high risk of developing pneumonia, acute respiratory distress syndrome (ARDS), or multi-organ failure, requiring hospitalization and admission in a critical care unit [4–6]. The lack of adequate preparedness and late implementation of the countermeasures led to a drastic global spread of COVID-19 within a short period of time. Furthermore, the lack of an appropriate vaccine has also contributed to the spread and the high mortality of this disease, despite the low mortality rate of the infection itself. Several epidemiological studies have shown that advanced age and presence and history of severe comorbidities, such as cardiovascular diseases, are significantly associated with COVID-19-related mortality. Moreover, COVID-19-related mortality has been attributed to virus-activated “cytokine storm syndrome” [7].

The high rate of spread of this disease has put a lot of burden on an already overwhelmed health-care system. This has led to development of new COVID-19-specific treatment centers and prioritizing the use of medical resources based on patient characteristics. Understanding the risk factors of ICU admission is an important factor in triage decision-making and identification of patients who might benefit more from critical care services [8]. We assessed the clinical characteristics and identified the mortality-associated predictive factors in COVID-19 patients who were admitted to the ICU in Kuwait.

Methods

Study Design and Settings

We conducted a retrospective study consisting of patients admitted to the ICU at Jaber Al-Ahmad Hospital, between March 1,

2020, and April 30, 2020. Jaber Al-Ahmad Al Sabah hospital was designated as the national hospital for the management of COVID-19-infected patients in Kuwait. The hospital initially had 3 ICUs (60 beds), and as the pandemic progressed, the ICU bed capacity was subsequently increased to 145 beds.

Patient Criteria

We enrolled patients aged ≥ 18 years admitted to ICU with SARS-Cov-2 infection as confirmed by real-time reverse transcriptase PCR assay of nasopharyngeal swab specimens. Management and treatment of COVID-19 ICU patients were according to the published international and local guidelines [9].

Data Collection and Definition

Patient data were extracted from the electronic medical records using standardized data collection sheet. We recorded information on age, gender, preexisting medical conditions, including hypertension, diabetes, ischemic heart disease, hyperlipidemia, bronchial asthma, chronic renal failure, malignancy, and autoimmune diseases, home medications, and presenting symptoms prior to admission. We collected laboratory and radiological test results upon admission to ICU. Chest X-ray findings were categorized as normal, unilateral infiltrate, and bilateral infiltrate, and CT-scan findings were categorized as normal, ground glass appearance, and mixed pattern of consolidation. CT scan of the chest and echocardiographs were requested as clinically indicated and at the discretion of the treating physicians. We also recorded data on maximum respiratory support (i.e., low-flow nasal cannula, noninvasive mechanical ventilation, and intubation) and additional adjunctive support, including inhaled nitric oxide, inotropes, renal replacement therapy (RRT), and extracorporeal membrane oxygenation. Information on patient-specific therapies, such as administration of hydroxychloroquine, antivirals, and convalescent plasma, was also collected.

ARDS was defined according to the Berlin guidelines on ARDS [10], and the quick Sequential Failure Assessment (qSOFA) score was calculated upon admission according to the Third International Consensus Definitions Task Force for sepsis and septic shock [11]. Secondary infection was defined as clinical signs of pneumonia or bacteremia and positive culture on blood or body fluid or endotracheal or bronchoalveolar lavage specimens. The study protocol was approved by the Ethics Committee of the Ministry of Health of Kuwait.

Statistical Analysis

We reported continuous variables as median (interquartile range [IQR]) and categorical variables as number and percentage. With mortality as the outcome of interest, differences between deceased patients and discharged patients were analyzed using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables.

We dichotomized the laboratory findings based on the clinical assessment and normal references. We used multivariate logistic regression model to identify risk factors of mortality. Variables that were found to be significant during the univariate analysis were included in the multivariate regression model. Age was included in the final model as it had been described to be a risk factor for mortality in previous studies [7]. Variables with >50% missing values were not included in the model (such as high-sensitivity

[HS] cardiac troponin). The results of the multivariable regression model are expressed as odds ratio (OR) with 95% confidence interval (95% CI). The area under the receiver operating characteristic curve was used to assess the performance of the regression model, and the Hosmer-Lemeshow test was used to test the goodness of fit. Statistical analysis was performed using STATA/IC 14 (STATA Corp., College Station, TX, USA), and 2-tailed $p < 0.05$ was considered statistically significant without adjustment for multiple testing.

Results

Demographic and Clinical Characteristics

During the study period, a total of 103 patients were admitted. Of those, 56 (54.3%) patients have been discharged and 47 (45.6%) patients died. The median age was 53 years [IQR: 44–63] and majority 85.4% (88/103) of the patients were male. Two or more comorbidities were present in 37% (38/103) of the patients with diabetes mellitus being the most common (39.2%) followed by hypertension (35%). The most common presenting symptoms were fever (61%) followed by cough/chest pain (48%). The median duration of symptoms was 2 days [IQR: 1–5] and 5 days [IQR: 1–8] prior to hospital and ICU admission, respectively (Table 1).

There were no significant differences in age and gender between the discharged and deceased patients. Deceased patients were more likely to have >2 comorbidities compared to the discharged patients (53 vs. 21.6%; $p = 0.005$). A higher proportion of deceased patients were hypertensive compared to the discharged group (51 vs. 21.4%; $p = 0.002$). Moreover, deceased patients tended to exhibit higher qSOFA score than the discharged patients ($p = 0.05$) (Table 1).

Laboratory and Radiological Findings

Table 2 shows the laboratory and radiological findings of the patients on admission to ICU. Total lymphocyte counts and serum albumin levels were significantly lower among the deceased patients. Levels of Cr, procalcitonin (PCT), C-reactive protein (CRP), D-dimer, and HS cardiac troponin were significantly elevated in the deceased patients compared to the discharged patients.

The majority of the patients (84.6%) exhibited bilateral infiltrates on chest X-ray (Table 2). Only 10 patients had CT scan results of the chest, with 6 of them showing mixed pattern of consolidation and ground glass appearance and 4 showing mainly ground glass appearance. There was no significant difference between the groups on the basis of the radiological findings.

Treatment and Clinical Course

The treatment and clinical course are shown in Table 3. Most patients (96%) were treated with antibiotics. Antiviral therapy (ritonavir-lopinavir) was used for 82.5% of the patients, while oseltamivir was used for 27% of the patients. Hydroxychloroquine was administered in 78% of the patients. Among the 103 patients, only 14.6% received systemic steroids. Majority of the patients (76.7%) were intubated and mechanically ventilated, and 54% of the patients were prone positioned. A total of 9 patients (8.7%) required extracorporeal membrane oxygenation, 11 patients (10.7%) received inhaled nitric oxide, and 3 patients (2.9%) received convalescent plasma.

Moderate/severe ARDS was present in 76% of the patients, and 25% of the patients developed secondary bacterial infection. Inotropic support was used for 71% of the patients, and the proportion of deceased patients who required inotropic support was significantly higher than that in the discharged patients (89.4 vs. 58.5%; $p < 0.001$). RRT was used in 20.4% of the patients, and 2 of the patients who had preexisting CKD needed RRT. Moreover, among the deceased patients, intubation, RRT, moderate/severe ARDS, and secondary bacterial infection were observed more frequently than among the discharged patients. Median time to discharge from ICU was 10 days (IQR: 6–15), and median time to death was 13 days (IQR: 7–23).

Risk Factors of Mortality

The multivariate logistic regression analysis showed that the risk factors associated with mortality were preexisting hypertension (OR: 3.2, 95% CI: 1.2–8.9), moderate/severe ARDS (OR: 3.4, 95% CI: 1.1–10.8), lymphocyte counts $< 0.5 \times 10^9/L$ (OR: 6.1, 95% CI: 1.2–29.8), albumin < 22 g/L (OR: 7.5, 95% CI: 2.1–26.2), PCT > 0.2 ng/mL (OR: 3.8, 95% CI: 1.3–7.8), D-dimer $> 1,200$ ng/mL (OR: 5.1, 95% CI: 1.2–21.6), and the need for RRT (OR: 9.3, 95% CI: 2.4–36.2) (Table 4). The area under the receiver operating characteristic curve showed a good accuracy in predicting mortality with an AUC equal to 0.82 (95% CI 0.74–0.90) and an overall accuracy of 76.7%. The Hosmer-Lemeshow test showed a good model adequacy ($p = 0.56$).

Discussion

In this retrospective case series, we described the clinical characteristics and mortality-related risk factors in adult patients with confirmed COVID-19 who were ad-

Table 1. Baseline demographics and clinical characteristics

	All patients N = 103	Discharged group N = 56	Death group N = 47	p value
Age, median (IQR)	53 [44–63]	51 (40–61)	56 (48–63)	0.057
Age groups, n (%)				
<40	17 (16.5)	15 (26.8)	2 (4.2)	
41–50	29 (28.2)	14 (25)	15 (32)	
51–60	30 (29)	14 (25)	15 (33)	0.052
61–70	19 (18.4)	10 (17.8)	9 (19.1)	
>71	8 (7.7)	3 (5.3)	5 (10.6)	
Sex, n (%)				
Male	88 (85.5)	46 (82.1)	42 (89.4)	0.403
Female	15 (14.5)	10 (17.7)	5 (10.6)	
Number of comorbidities, n (%)				
None	37 (36.3)	27 (49.1)	10 (21.3)	
One comorbidity	27 (26.5)	15 (27.3)	12 (25.5)	0.004
Two or more comorbidities	38 (37.2)	13 (23.6)	25 (53.2)	
Comorbidities, n (%)				
Diabetes mellitus	40 (39.2)	17 (30.9)	23 (48.9)	0.058
Hypertension	36 (35)	12 (21.4)	24 (51.1)	0.002
Ischemic heart disease	12 (11.8)	6 (11)	8 (17)	0.119
Dyslipidemia	11 (10.8)	6 (11)	5 (10.5)	1
Asthma	13 (12.7)	4 (7.3)	8 (17)	0.231
Malignancy	3 (2.9)	2 (3.7)	1 (2)	1
Chronic renal failure	4 (3.9)	0	4 (8.5)	0.056
Others (autoimmune, hypothyroidism)	8 (7.8)	5 (9.2)	3 (6.4)	0.714
Home medications, n (%)				
Insulin	34 (33.3)	15 (26.8)	19 (41.3)	0.122
Beta blockers	13 (12.7)	4 (7.1)	9 (19.6)	0.061
ACEI	10 (9.8)	5 (8.9)	5 (10.8)	0.734
Aspirin	7 (6.8)	2 (3.6)	5 (10.8)	0.147
Cholesterol-lowering agents	10 (9.8)	6 (10.7)	4 (8.7)	0.487
Inhalation bronchodilators	5 (4.9)	3 (5.4)	2 (4.3)	0.814
Steroids	2 (1.9)	0	2 (4.3)	0.231
Presenting symptoms, n (%)				
Sore throat/nasal congestion	32 (32)	14 (26)	13 (27.6)	1
Cough/chest pain	48 (48)	18 (33.3)	25 (53.2)	0.139
Fever	61 (61)	28 (51.8)	26 (55)	1
Vomiting/diarrhea	1 (1)	0	0	
Fatigue/myalgia	15 (15)	6 (11)	6 (12.7)	1
Travel history prior to admission, n (%)	12 (11.6)	10 (17.8)	2 (4.2)	0.068
Contact with COVID-19-positive patient, n (%)	16 (15.5)	7 (12.5)	9 (19)	0.584
Duration of symptoms prior to hospital admission, days, median (IQR)	2 (1–5)	1.5 (1–5)	2 (1–5)	0.876
Duration of symptoms prior to ICU admission, days, median (IQR)	5 (1–8)	5 (1–8)	4 (1–8)	0.987
qSOFA points, n (%)				
1 point	55 (53.4)	31 (55.3)	22 (46.8)	
2 points	24 (23.3)	10 (17.8)	14 (29.8)	0.05
3 points	24 (23.3)	13 (23.2)	11 (23.4)	
>2 points	48 (46.6)	23 (41)	25 (53.2)	0.240

Data expressed as n (%) and median (IQR). ACEI, angiotensin-converting enzyme inhibitors; qSOFA, quick Sequential Failure Assessment; IQR, interquartile range; ICU, intensive care unit.

Table 2. Laboratory and radiological findings on admission

	All	Discharged group	Death group	<i>p</i> value
<i>Laboratory values</i>				
WBC ($\times 10^9/L$), median (IQR)	8.2 (6.3, 10.2)	8.4 (5.5–10)	7.5 (6.3–10.6)	0.837
Neutrophils ($\times 10^9/L$), median (IQR)	6.4 (4.7, 8.7)	6.9 (4–8.8)	5.7 (4.9–10.1)	0.788
Lymphocytes ($\times 10^9/L$), median (IQR)	0.9 (0.7, 1.2)	1 (0.8–1.2)	0.8 (0.5–1.1)	0.005
Lymphocytes < 0.5 , <i>n</i> (%)	15 (15.3%)	3 (5.7%)	12 (26.1%)	0.005
Hemoglobin (g/L), median (IQR)	122 (102–135)	125 (109–135)	116 (91–135)	0.181
Platelets ($\times 10^9/L$), median (IQR)	238 (192–303)	258 (204–327)	215 (167–269)	0.067
PT INR, median (IQR)	1.04 (0.9–1.1)	1.03 (0.97–1.1)	1.07 (0.99–1.5)	0.164
aPTT, seconds, median (IQR)	41.5 (20.5–56)	40 (21–54)	45 (17–59)	0.658
D-dimer, ng/mL, <i>N</i> = 56, median (IQR)	1,234 (566–2,855)	809 (555–1,344)	2,346 (893–3,940)	0.029
D-dimer $> 1,200$ ng/mL, <i>n</i> (%)	28 (50%)	9 (32%)	19 (67.9%)	0.015
Fibrinogen, g/L, median (IQR)	7 (6–7.8)	7 (6–7)	6.5 (3.5–9)	0.913
Cr, mmol/L, median (IQR)	85 (68–116)	82 (68–97)	97 (77–176)	0.01
Cr > 120 mmol/L, <i>n</i> (%)	22 (22.4%)	8 (15%)	14 (31%)	0.03
Albumin, g/L, median (IQR)	25.4 (22–29)	26 (23.6–29.8)	24.5 (20.6–28.5)	0.007
Albumin < 22 g/L, <i>n</i> (%)	24 (23.3%)	7 (13.5%)	17 (40.5%)	0.006
ALT, IU/L, median (IQR)	42 (24–57)	39 (23–54)	44 (23–65)	0.318
AST, IU/L, median (IQR)	50 (38–74)	45 (33–69)	49 (40–76)	0.184
LDH, IU/L, median (IQR)	447 (346–561)	445.5 (332–633)	453 (366–547)	0.527
Troponin I (HS), ng/L, <i>N</i> = 28, median (IQR)	22 (9–84.7)	9 (6–17)	73 (23–146)	0.009
Troponin I, ng/L, median (IQR)	0.013 (0.01–0.03)	0.03 (0.01–0.04)	0.013 (0.003–0.05)	0.538
CK, IU/L, median (IQR)	296 (97–604)	384 (87–404)	128.5 (104–282)	0.668
Ferritin, ng/mL, median (IQR)	1,164 (681–1,571)	1,425 (883–1,588)	1,153 (454–1,556)	0.171
PCT, ng/mL, median (IQR)	0.41 (0.2–1.5)	0.29 (0.09–0.52)	0.81 (0.32–3.2)	0.0004
PCT > 0.2 ng/mL, <i>n</i> (%)	52 (49.5%)	18 (33.3%)	28 (59.6%)	0.036
CRP, mg/L, median (IQR)	139 (95–232)	125 (95–166)	164 (107–340)	0.009
CRP > 200 mg/L, <i>n</i> (%)	35 (34%)	8 (14.8%)	22 (46.8%)	0.002
<i>Radiological findings, n</i> (%)				
Chest X-ray				
Unilateral infiltrate	6 (5.7)	3 (6.4)	3 (6.7)	0.725
Bilateral infiltrate	88 (84.6)	41 (87.2)	36 (80)	
Chest CT scan, <i>N</i> = 10				
Ground glass appearance plus consolidation	6 (60)	2 (66.7)	3 (50)	1
Ground glass appearance	4 (40)	1 (33.3)	3 (50)	

Values are presented in median (IQR) and *n* (%). WBC, white blood count; PT INR, prothrombin time international normalized ratio; aPTT, activated partial thromboplastin time; ALT, alanine transaminase; AST, aspartate transaminase; LDH, lactate dehydrogenase; CK, Cr kinase; PCT, procalcitonin; CRP, C-reactive protein; IQR, interquartile range.

mitted to the critical care unit. The major outcome assessed here was patient mortality. We evaluated the association between the patient's demographic, laboratory, and clinical data and mortality. The median age of our patients was 53 years and majority were male. The relationship between gender and mortality in sepsis remained controversial. Results from meta-analysis indicated that males constituted a significantly higher proportion of those who had adverse clinical outcomes and died from COVID-19 [12]. In contrast, no correlation between mortality and gender were observed in other studies. However, unlike other studies, we did not find any sig-

nificant correlation between advancing age and patient mortality. This finding could be attributed to the fact that most of the patients recruited in the current study were aged between 44 and 63 years, while other studies include higher proportions of individuals > 65 years of age, which results in a more significant association between age and mortality [7, 13].

Several studies have shown that presence of comorbidities, such as cardiovascular disease and secondary infections, contributes significantly to disease severity and mortality among COVID-19 patients [7, 14, 15]. In an earlier study, hypertension was the most common co-

Table 3. Treatment and clinical course

	All	Discharged	Death	<i>p</i> value
Lopinavir-ritonavir, <i>n</i> (%)	82 (79.6)	47 (83.9)	38 (80.8)	0.184
Oseltamivir, <i>n</i> (%)	28 (27.2)	18 (32)	10 (21.2)	0.251
Hydroxychloroquine, <i>n</i> (%)	79 (76.7)	41 (73.2)	40 (85)	0.151
Antibiotics, <i>n</i> (%)	99 (96)	45 (96)	45 (100)	0.495
Inotropic support, <i>n</i> (%)	73 (70.9)	31 (55.3)	42 (89.4)	0.001
Systemic steroid, <i>n</i> (%)	15 (14.6)	7 (12.9)	8 (17)	0.782
Convalescent plasma transfusion, <i>n</i> (%)	3 (3)	0	3 (2)	0.092
Maximum respiratory support, <i>n</i> (%)				
High-flow nasal cannula	22 (21.4)	17 (30.3)	0	
Noninvasive ventilation	2 (1.9)	2 (4.2)	0	
Intubation	79 (76.7)	35 (62.5)	47 (100)	0.001
Prone positioning, <i>N</i> = 95, <i>n</i> (%)	51 (53.7)	27 (51.9)	27 (60)	0.518
ECMO, <i>n</i> (%)	9 (8.7)	7 (12.5)	2 (4.3)	0.176
iNO, <i>n</i> (%)	11 (0.7)	6 (10.7)	5 (10.6)	0.737
RRT, <i>n</i> (%)	28 (27.2)	9 (16.1)	19 (40.4)	0.006
ARDS, <i>N</i> = 96, <i>n</i> (%)				
None	11 (11.5)	11 (21.6)	0	
Mild	12 (12.5)	8 (15.7)	4 (8.9)	0.002
Moderate	53 (55)	24 (47)	29 (64.4)	
Severe	20 (21)	8 (15.7)	12 (26.7)	
Moderate-severe ARDS, <i>n</i> (%)	73 (76)	32 (62.7)	41 (91.1)	0.001
Secondary bacterial infection, <i>n</i> (%)	26 (25.2)	7 (12.5)	16 (34)	0.03
Length of ICU stay, days, median (IQR)	11 (6–18.5)	10 (6–15)	13 (7–23)	0.244

Data are presented in *n* (%) and median (IQR). ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide; RRT, renal replacement therapy; ARDS, acute respiratory distress syndrome; IQR, interquartile range; ICU, intensive care unit.

Table 4. Multivariate analysis for the risk factors of mortality

Risk factor	OR (95% CI); <i>p</i> value
Age	
Less than 40 years	Reference
41–50	5.5 (0.95–31.9); 0.057
51–60	5.4 (9.95–31.2); 0.058
61–70	3.5 (0.55–21.8); 0.187
More than 71 years	4.7 (0.51–44.2); 0.174
More than 2 comorbidities	2.9 (0.9–9.2); 0.072
Preexisting hypertension	3.2 (1.2–8.9); 0.02
qSOFA >2 points	2.2 (0.95–5.2); 0.065
Moderate to severe ARDS	3.4 (1.1–10.8); 0.038
Cr >120 mmol/L	3.1 (0.92–9.9); 0.069
Albumin <22 g/L	7.5 (2.1–26.2); 0.002
Lymphocyte counts <0.5 ×10 ⁹	6.1 (1.2–29.8); 0.026
PCT >0.2 ng/mL	3.8 (1.3–7.8); 0.014
CRP >200 ng/mL	2.3 (0.78–6.8); 0.133
D-dimer >1,200 ng/mL	5.1 (1.2–21.6); 0.026
Sepsis	2.7 (0.96–7.9); 0.057
Intubation	2.1 (0.95–4.6); 0.064
Inotropic support	3.5 (0.87–14.1); 0.078
RRT	9.3 (2.4–36.2); 0.001

morbidity, affecting 509 (49% [95% CI, 46–52%]) of 1,043 patients with available data [16]. We found that 37% of the patients who were admitted to the ICU exhibited presence of previous comorbidities, the most common being diabetes (39.2%) and hypertension (35%). Similarly, half of the patients who died suffered from hypertension (51.1%) and diabetes (48.9%). This finding was consistent with those of the previous studies [15]. Furthermore, our results also indicated hypertension to be an independent risk factor for mortality (adjusted OR: 3.2, 95% CI: 1.2–8.9). Moreover, compared to the discharge group, more than double the number of patients in the death group suffered from 2 or more comorbidities.

In several studies, ICU mortality has been associated with organ dysfunction. qSOFA is a recently developed scoring system used to assess the organ dysfunction. Although qSOFA score does not directly evaluate patient mortality, previous studies have demonstrated the relationship between mortality and dysfunction [17]. In our study as well, a higher proportion of the patients who died showed higher qSOFA scores compared to the patients in

the discharged group (53.2 vs. 41.1%, respectively); however, the difference was not statistically significant ($p = 0.24$).

Our results also indicated that patient mortality was significantly associated with higher levels of HS troponin, PCT, and CRP. Elevated levels of HS troponin have been associated with acute coronary syndrome, reduced left ventricular function, and higher levels of IL-6 and TNF-alpha, which ultimately leads to mortality among the ICU patients [18]. PCT, a precursor of calcitonin, is mainly released during bacterial sepsis and tissue injury. It has previously been recognized as an indicator of severity of organ failure and mortality among the ICU patients [19, 20]. It is noteworthy that high levels of PCT are associated with bacterial infection, which indicates that the death among the COVID-19 patients with elevated PCT might be due to secondary bacterial infections. This assumption was supported by our results which showed that compared to the discharge group, a higher proportion of patients who died suffered from bacterial infections. CRP is involved in inflammatory reactions, and elevated CRP levels have been significantly associated with several cardiovascular disorders, organ failure, and mortality among the ICU patients [21, 22].

Lower levels of lymphocytes (lymphopenia) and albumin (hypoalbuminemia) have also been associated with patient mortality. Within the death group, 40.5 and 13.5% of the patients exhibited albumin <22 g/L and lymphocytes $<0.5 \times 10^9/L$, which was significantly higher compared to the discharge group (26.1 and 5.7%, respectively) ($p < 0.05$). Our results corroborated with those of the previous studies [23, 24]. Furthermore, D-dimer has been previously shown to be a sensitive independent predictor of mortality among ICU patients [25], which was consistent with our results. Compared to the discharged patients, a significantly higher proportion of patients who died had D-dimer $>1,200$ ng/mL ($p = 0.015$). However, a few studies have discouraged the use of D-dimer quantification for mortality prediction in ICU patients [25, 26]. In addition, requirement of RRT was also found to be significantly associated with patient mortality, even after adjusting for the confounding factors (adjusted OR: 9.3, 95% CI: 2.4–36.2). It is worth mentioning that although high-flow nasal cannula and noninvasive mechanical ventilation were used in only 21 and 2% of our patients, respectively, none of them died, which could indicate a survival benefit for patients who receive noninvasive ventilation; however, it is very difficult to draw this conclusion at this point due to the nature of our study, and such

results could be confounded. To our knowledge, this is the first study in our region describing the characteristics of critically ill COVID-19 patients and their predictors for mortality.

Limitations

There were several limitations for our study. Firstly, the sample size in our study was relatively small. Recruitment of a higher number of patients could have provided a clearer picture. Secondly, the patient data were collected retrospectively from their electronic records, which were often incomplete. This could lead to information bias. Thirdly, there was no standard protocol for laboratory workup of the patients during ICU admission. This led to the absence of the results for some laboratory tests for some patients. Due to this, the laboratory-based data for some patients could not be included in the regression model, which might have led to discrepancy with respect to mortality predictors. In future studies, we propose to recruit larger numbers of patients and to follow them up for a longer duration to further elucidate the factors that contribute to mortality among COVID-19 patients.

Conclusions

Our observational study involving critically ill patients with confirmed COVID-19 showed no significant differences in mortality based on age and gender. Several risk factors were identified to predict mortality. With the increasing surge of critical care patients, early identification of risk factors for mortality is crucial in triage decision-making and for proper utilization of resources. More multicentric large studies are needed to validate the significance of these predictors with respect to patient mortality.

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Statement of Ethics

The study was approved by the Ethics Committee of the Ministry of Health of Kuwait (2020/1411)

Conflict of Interest Statement

The authors declare to have no conflicts of interests.

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Author Contributions

Study design: Mariam Ayed, Abdulwahab A. Borahmah, Anwar Yazdani, Ahmad Sultan, Ahmad Mossad, and Hanouf Rawdhan; data collection: Mariam Ayed, Abdulwahab A. Borahmah, Anwar Yazdani, Ahmad Sultan, Ahmad Mossad, and Hanouf Rawdhan; data analysis: Mariam Ayed; drafting of manuscript: Mariam Ayed; revision of manuscript: Mariam Ayed, Abdulwahab A. Borahmah, Anwar Yazdani, Ahmad Sultan, Ahmad Mossad, and Hanouf Rawdhan; consent for final manuscript: Mariam Ayed, Abdulwahab A. Borahmah, Anwar Yazdani, Ahmad Sultan, Ahmad Mossad, and Hanouf Rawdhan.

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