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The Primary Outcomes and Epidemiological and Clinical Features of Coronavirus Disease 2019 (COVID-19) in Iran

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Abstract

Aim

We aimed to describe the epidemiological and clinical characteristics of Iranian patients with COVID-19.

Methods

In this single-center and retrospective study, patients with confirmed COVID-19 infections were enrolled. Univariate and multivariate logistic regression methods were used to explore the risk factors associated with outcomes.

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Results
Of 179 patients with confirmed COVID-19 infection, 12 remained hospitalized at the end of the study and 167 were included in the final analysis. Of these, 153 (91.6%) were discharged and 14 (8.38%) died in hospital. Approximately half (50.9%) of patients suffered from a comorbidity, with diabetes or coronary heart disease being the most common in 20 patients. The most common symptoms on admission were fever, dyspnea, and cough. The mean durations from first symptoms to hospital admission was 8.64 ± 4.14 days, whereas the mean hospitalization time to discharge or death was 5.19 ± 2.42 and 4.35 ± 2.70 days, respectively. There was a significantly higher age in non-survivor patients compared with survivor patients. Multivariate regression showed increasing odds ratio (OR) of in-hospital death associated with respiratory rates >20 breaths/min (OR: 5.14, 95% CI: 1.19–22.15, p = 0.028) and blood urea nitrogen (BUN) >19 mg/dL (OR: 4.54, 95% CI: 1.30–15.85, $p = 0.017$) on admission. In addition, higher respiratory rate was associated with continuous fever (OR: 4.08, 95% CI: 1.18–14.08, $p = 0.026$) and other clinical symptoms (OR: 3.52, 95% CI: 1.05–11.87, $p = 0.04$).
Conclusion
The potential risk factors including high respiratory rate and BUN levels could help to identify COVID-19 patients with poor prognosis at an early stage in the Iranian population.

Keywords

COVID-19 · SARS · MERS · Iran · Respiratory rate · Blood urea nitrogen

17.1 Introduction

Novel coronavirus disease (COVID-19) was first reported in Wuhan, China, in December 2019, not long before the lead up to the Lunar New Year when China undertakes the world's largest mass travel event [1]. The COVID-19 outbreak has spread rapidly throughout the world as well as in Iran. Iran was the first Middle East country to report a death due to this coronavirus, which was officially announced on February 20 in Qom [2].

The clinical spectrum of COVID-19 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalized with pneumonia [3, 4]. Previous studies in China have shown acute symptoms of severe respiratory infection in the early stages of this virus, with some patients rapidly developing acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications that can lead to death [5–7].

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As COVID-19 is a newly identified pathogen, the information on the clinical characteristics of affected patients is limited. A few studies on epidemiological and clinical characteristics of cases with novel coronavirus pneumonia have been conducted in China [8–10]. Despite the increasing number of confirmed cases in Iran, no clinical study of Iranian patients has yet been published. Additionally, details of the clinical and course of illness have not yet been well described. A better understanding of the clinical features of COVID-19 can be helpful in preventing and controlling the epidemic and understanding future developments and the potential effect of various interventions. In this paper, we have described the clinical characteristics, laboratory findings, and risk factors of in-hospital death for infected patients with COVID-19 during hospitalization to provide potential insights into the prevention and treatment.

17.2 Methods

17.2.1 Study Design and Participants

This single-center and retrospective study by focusing on the clinical characteristics of confirmed cases of COVID-19 was conducted on 179 adult patients, who referred to the Baqiyatallah Hospital in Tehran, Iran, between February 26 and March 15, 2020. All patients with COVID-19 enrolled in this study were diagnosed according to the World Health Organization interim guidance [11]. The patients were suspected to have COVID-19 infection according to the symptoms like fever, dry cough, shortness of breath, and aches. Upon admission, patients underwent chest computed tomography (CT) scans plus swab-based PCR tests. Since the scan results were readily available (compared to swab tests which took at least 24 h for the results), diagnosis was made based on the CT results. Moreover, the PCR results were dependent on methods of sampling, storage, handling, and transfer of specimens, which may cause a significant rate of false-negative results. All patients were monitored up to March 15, 2020, as the final date of follow-up. The study was approved by the Research Ethics Committee of the Baqiyatallah University of Medical Sciences, and written informed consent was obtained from patients before enrolment and data were collected retrospectively.

17.2.2 Data Collection

All demographic characteristics and clinical data for this retrospective study were collected from medical records of patients with COVID-19. Data recorded include demographics (age, gender, and occupation), smoking history, exposure history (details regarding infection), family history, comorbidities (coronary heart disease, hypertension, diabetes, lung disease, and malignancy), symptoms (fever, fatigue, dry cough, sore throat, headache, myalgia, dyspnea, chest pain, rhinorrhea, nausea, and vomiting), clinical features (respiratory rate, heart rate, blood pressure rate, and body temperature), laboratory findings [white blood cell (WBC) count, lymphocytopenia (lymphocyte count), platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), prothrombin time (PT), partial thromboplastin time (PTT), creatinine (Cr), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), lactic acid dehydrogenase (LDH)], blood gas analysis (saturated pressure of oxygen (SPO2), partial pressure of carbon dioxide ($PaCO_2$) and bicarbonate (HCO_3), clinical outcomes (respiratory failure, heart failure, ARDS, acute cardiac injury, and acute kidney injury), and treatment measures (antiviral therapy, respiratory support, and mechanical ventilation). In addition, the durations from first symptoms to hospital admission, hospitalization days, intensive care unit (ICU) admission, and patient status (death or recovery) at the end of study were recorded.

17.2.3 Definitions

The date of disease onset was defined as the day when the symptom was noticed. Acute respiratory distress syndrome (ARDS) was defined according to the Berlin definition [12]. Acute kidney injury was identified according to the Kidney Disease Improving Global Outcomes (KDIGO) definition [13]. Acute cardiac injury was diagnosed if serum levels of cardiac biomarkers [high sensitivity cardiac troponin I (cTnI)] were above the 99th percentile upper reference limit or if new abnormalities were shown in electrocardiography or echocardiography [14]. Fever was defined as axillary temperature of at least 37.3 °C.

17.2.4 Statistical Analysis

Categorical variables were described as frequency rates and percentages, and continuous variables were described using mean, median, and interquartile range (IQR) values. Means for continuous variables were compared using independent group t tests. In case of limited data or non-normality, the Mann-Whitney test was used. Chi-square test or Fisher exact test (in case of low sample numbers) were used to compare the distribution of categorical data. To explore the risk factors associated with in-hospital death, as well as the COVID-19 swab PCR test and symptom status at the end of hospitalization, univariate and multivariate logistic regression models were used. To avoid over-fitting in the multivariate model, only those factors which resulted in a p-value less than 0.2 in univariate analysis were selected for the multivariate model. The final model was selected according to forward conditional. All statistical analyses were performed using R version 3.6.1 software. A two-sided α of less than 0.05 was considered statistically significant.

17.3 Results

17.3.1 Demographic and Clinical Characteristics

All 179 hospitalized patients with confirmed COVID-19 were monitored up to March 15, 2020, and 12 patients were excluded from the study because they were still hospitalized up to the final date of follow-up. Therefore, we included 167 patients in the final analysis. The mean age of the 167 patients was 55.26 ± 13.01 years (range: 22–89 years), and 133 (79.5%) were men. Of the 167 patients, 153 (91.6%) were discharged, and 14 (8.38%) died in hospital. In 85 patients (50.9%), comorbidities were present which included diabetes (12%), coronary heart disease (12%), diabetes with hypertension (9.6%), and hypertension (8.4%). In addition, 26 (15.6%) patients had history of lung disease that included chronic obstructive pulmonary disease (COPD) (30.7%), history of chemical ventilators (30.7%), pneumonia (23.2%), and asthma (15.4%).

The most common symptoms on admission were fever (90.4%), dyspnea (85.6%), cough (83.8%), myalgia (68.9%), fatigue (50.9%), and headache (37.7%). Less common symptoms were sputum, chest pain, rhinorrhea, sore throat, nausea, and vomiting (Table 17.1). Compared to patients discharged from hospital (n = 153), patients who died in hospital (n = 14) were significantly older (64.78 ± 9.36 vs. 54.39 ± 12.96, p = 0.004). In terms of gender, family history, symptoms, and comorbidities, no statistically significant differences were found between survivor and non-survivor groups (p > 0.05) (Table 17.1).

According to chest CT scans, 58 (34.7%) patients showed consolidation, 52 (34.1%) showed bilateral pulmonary infiltration, and 52 (31.1%) had ground-glass opacity. Nasal swab PCR analysis for COVID-19 was positive in 108

Table 17.1 Baseline demographic and clinical characteristics of patients infected with COVID-19 on admission in survivor and non-survivor patients

Variables	Total (n = 167)	Survivor (n = 153)	Non-survivor (n = 14)	*P*-value
Age				
Mean ± SD (range)	55.26 ± 13.01 (22–89)	54.39 ± 12.96 (22–89)	64.78 ± 9.36 (53–87)	0.004[a]
Gender no (%)				
Male	133 (79.5)	121 (79.1)	12 (85.7)	0.737
Female	34 (20.4)	32 (20.9)	2 (14.3)	
Occupation no (%)				
Employee	52 (31.1)	51 (33.3)	1 (7.1)	0.265
Retired	58 (34.7)	51 (33.3)	7 (50)	
Housewife	29 (17.4)	27 (17.6)	2 (14.3)	
Unemployed	24 (14.4)	20 (13.1)	4 (28.6)	
Soldier	2 (1.2)	2 (1.3)	0	
Doctor	2 (1.2)	2 (1.3)	0	
Exposure history no (%)				
Community	138 (82.6)	124 (81)	14 (100)	0.360
Contact with confirmed cases	13 (7.8)	13 (8.5)	0	
Travel	14 (8.4)	14 (9.2)	0	
Hospital	2 (1.2)	2 (1.3)	0	
Family history no (%)				
Yes	40 (24.0)	39 (25.5)	1 (7.1)	0.191
Symptoms no (%)				
Fever	151 (90.4)	138 (90.2)	13 (92.9)	1.000
Cough	140 (83.8)	128 (83.7)	12 (85.7)	1.000
Sputum	43 (25.7)	41 (26.8)	2 (14.3)	0.523
Dyspnea	143 (85.6)	130 (85)	13 (92.9)	0.695
Myalgia	115 (68.9)	105 (68.6)	10 (71.4)	1.000
Headache	63 (37.7)	60 (39.2)	3 (21.4)	0.254
Fatigue	85 (50.9)	79 (51.6)	6 (42.9)	0.586
Chest pain	23 (13.8)	23 (15)	0	0.221
Rhinorrhea	23 (13.8)	22 (14.4)	1 (7.1)	0.695
Sore throat	23 (13.8)	22 (14.4)	1 (7.1)	0.695
Nausea/vomiting	33 (19.8)	30 (19.6)	3 (21.4)	1.000
Smoking history no (%)				
Yes	14 (8.4)	14 (9.2)	0	0.610
Duration onset of clinical symptoms to hospital admission, days				
Mean ± SD (range)	8.64 ± 4.14 (1–22)	8.69 ± 4.19 (1–22)	8.14 ± 3.63 (2–16)	0.636
Hospitalization, days				
Mean ± SD (range)	5.12 ± 2.45 (1–12)	5.19 ± 2.42 (1–12)	4.35 ± 2.70 (1–8)	0.222
Comorbidities no (%)				
Yes	85 (50.9)	77 (50.3)	8 (57.1)	0.625
The type of comorbidities no (%)				
Kidney disease	2 (1.2)	2 (1.3)	0	
Diabetes	20 (12.0)	17 (11.1)	3 (21.4)	
Hypertension	14 (8.4)	13 (8.5)	1 (7.1)	0.699
Coronary heart disease	20 (12.0)	18 (11.8)	2 (14.3)	
Diabetes and hypertension	16 (9.6)	16 (10.5)	0	
Others	13 (7.8)	11 (7.2)	2(14.3)	
Underlying lung disease no (%)				

(continued)

Table 17.1 (continued)

Variables	Total (n = 167)	Survivor (n = 153)	Non-survivor (n = 14)	*P*-value
Yes	26 (15.6)	23 (15)	3 (21.4)	0.460
The type of lung disease no (%)				
COPD	8 (4.8)	7 (4.6)	1 (7.1)	
Asthma	4 (2.4)	4 (2.6)	0	0.402
Pneumonia	6 (3.6)	6 (3.9)	0	
History of mechanical ventilators	8 (4.8)	6 (3.9)	2 (14.3)	
COVID-19 swab nose no (%)				0.363
Positive	108 (64.7)	97 (63.4)	11 (78.6)	
Negative	37 (22.2)	36 (23.5)	1 (7.1)	
Suspicious	22 (13.2)	20 (13.1)	2 (14.3)	
CT scan findings no (%)				
Consolidation	58 (34.7)	50 (32.7)	8 (57.1)	0.080
Ground-glass opacity	52 (31.1)	51 (33.3)	1 (7.1)	
Bilateral pulmonary infiltration	57 (34.1)	52 (34)	5 (35.7)	
Admitted situation no (%)				
Isolation wards	157 (94)	148 (96.7)	5 (35.7)	<0.001[a]
ICU	13 (7.8)	5 (3.3)	9 (64.3)	<0.001[a]
Antiviral therapy no (%)				
Monotherapy[a]	1 (0.6)	1 (0.7)	0	
Triple therapy[a]	68 (40.7)	64 (41.8)	4 (28.6)	0.586
Fourth therapy[a]	98 (58.7)	88 (57.5)	10 (71.4)	
Treatment no (%)				
Supplemental oxygen	139 (83.2)	125 (81.7)	14 (100)	0.130
NIV	14 (8.4)	6 (3.9)	8 (57.1)	<0.001[a]
IMV	11 (6.6)	1 (0.7)	10 (71.4)	<0.001[a]

[a]Monotherapy: oseltamivir + hydroxychloroquine; triple therapy: oseltamivir + hydroxychloroquine + lopinavir/ritonavir; fourth therapy: oseltamivir + hydroxychloroquine + lopinavir/ritonavir + ribavirin. Abbreviation: *NIV* noninvasive ventilation, *IMV* invasive mechanical ventilation

(64.4%) patients, negative in 37 (22.2%), and suspicious in 22 (13.2%) patients on the day of hospital admission. From 167 patients with COVID-19, 157 (94%) were admitted to isolation wards, and 13 (7.8%) were admitted and transferred to the ICU. The mean durations from first symptoms to hospital admission was 8.64 ± 4.14 (range: 1–22) days, whereas the mean hospitalization time to discharge and death were 5.19 ± 2.42 (range: 1–12) and 4.35 ± 2.70 (range: 1–8) days, respectively (Table 17.1).

17.3.2 Vital Signs, Laboratory Parameters, and Blood Gas Analysis

Heart rate, blood pressure, and body temperature on the day of hospital admission did not differ between survivor and non-survivor patients ($p > 0.05$). However, the median respiratory rate of non-survivor patients was significantly higher than survivor patients (18 vs. 20, $p = 0.031$). Baseline lymphocytopenia occurred in 123 patients (73.7%), with no significant difference between the two groups ($p = 0.732$). In addition, analyses of WBC and platelet count, ESR, CRP, LDH, BUN, Cr, ALT, AST, PTT, PT, INR, and PH showed no significant differences between survivor and non-survivor groups ($P > 0.05$) (Table 17.2). The median of SpO_2 was 90 mm Hg (IQR, 87–93), and the median of $PaCO_2$was 46.6 mm Hg (IQR, 34.6–59.9). The ratio of SpO2 was significantly lower in non-survivor patients than survivor cases (90 vs. 74 mm Hg, $p < 0.001$). However, the median of $PaCO_2$ was not significantly different between survivor and non-survivor groups ($p > 0.05$).

Table 17.2 Vital signs, laboratory parameters, and blood gas analysis of patients with COVID-19 on admission in survivor and non-survivor patients

Variables	Normal range	Total	Survivor	Non-survivor	*P*-value
Respiratory rate	12–20 min	18 (17–20)	18 (17–20)	20 (17–22)	0.031[a]
Heart rate	60–100 BPM	92 (82–106)	92 (84–106)	92.5 (80–102.5)	0.910
Blood pressure	120/80 mmHg	120/80 (110/70–135-80)	120/80 (110/70–135/80)	115/75 (110/67–136/57)	0.398
Temperature	36.1–37.2 C	38 (37–38.4)	38 (37–38.4)	38 (37.1–38.2)	0.712
SpO_2	90–92%	90 (87–93)	90 (88–93)	74 (55–85)	<0.001[a]
WBC	4-10 × 10^3 /L	6.2 (4.8–7.7)	6 (4.7–7.6)	7.4 (5.9–11.8)	0.282
Lymphocyte	1–3 × 10^3 /L	1.1 (0.89–1.5)	1.2 (0.86–1.5)	1.1 (0.98–1.6)	0.732
Platelet	145–45 × 10^3/L	169 (132–217)	169 (133–214)	162 (110–275)	0.395
ESR	Up to 15 mm/hr	39 (24–57)	40 (24–58)	35 (26.7–58)	0.952
CRP	Up to 5 mg/L	60 (24.2–94.7)	57.9 (23–94.7)	67.2 (49–94.7)	0.355
LDH	207–414 U/L	660 (252–824)	657 (508–819)	676 (557–852)	0.978
BUN	7–19 mg/dL	14 (11–18)	13 (11–17)	17.5 (11.7–23.5)	0.064
Cr	0.9–1.3 mg/dL	1.1 (0.9–1.3)	1.1 (0.9–1.3)	1.3 (0.9–1.4)	0.618
ALT	< 45 U/L	46 (29–77)	37 (23–73.5)	48 (24.2–95)	0.744
AST	<35 U/L	37 (23–76)	45 (29–76)	63 (40.5–89)	0.350
PTT	25–35 s	56 (35–76)	55 (35–76)	60 (35.5–76.5)	0.720
PT	≤ 13.5 s	14.2 (13–16.5)	13.8 (12.9–16.5)	15.1 (12.9–19.8)	0.073
INR	≤ 1	1.2 (1–1.3)	1.2 (1–1.4)	1.2 (1–1.3)	0.837
PH	7.38–7.42	7.39 (7.21–7.43)	7.39 (7.18–7.44)	7.4 (7.22–7.43)	0.814
$PaCO_2$	35–45 mm hg	46.6 (34.6–59.9)	47.3 (35.9–60.3)	37.9 (30.3–59.8)	0.440
HCO3	22–26 mEq/L	24.6 (21.3–27)	24.8 (21.3–27.5)	22 (15.7–24.1)	0.091

[a]Data are expressed as the median (IQR), *WBC* white blood cell, *SPO2* saturated pressure of oxygen, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *LDH* lactic acid dehydrogenase, *BUN* blood urea nitrogen, *Cr* creatinine, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *PTT* partial thromboplastin time, *PT* prothrombin time, *INR* international normalized ratio, *PH* pulmonary hypertension past history, *PaCO2* partial pressure of carbon dioxide, HCO_3 bicarbonate

17.3.3 Main Intervention and Complication

All patients in the current study received antiviral treatment, but the types of combination therapy varied among patients. Quadruple combination therapy (oseltamivir + hydroxychloroquine + lopinavir/ritonavir + ribavirin) was administered to 98 (58.7%) patients, 68 (40.7%) patients received triple combination therapy (oseltamivir + hydroxychloroquine + lopinavir/ritonavir), and only one patient received dual combination therapy (oseltamivir + hydroxychloroquine). Invasive mechanical ventilation (IMV) was required in 11 (6.6%) patients, 14 (8.4%) of patients received noninvasive ventilation (NIV), and the majority of patients, 139 (83.2%), received extracorporeal membrane oxygenation as rescue therapy. Compared with survivors, non-survivors were more likely to receive mechanical ventilation, either invasively or noninvasively ($p < 0.001$) (Table 17.1). In terms of complications, all patients developed ARDS, but no other complications such as acute cardiac injury and acute kidney injury were found in these patients.

17.3.4 Univariate and Multivariate Analysis

In univariate analysis, odds of in-hospital death were higher for older patients (OR = 1.07, 95%

Table 17.3 Risk factors associated with in-hospital death and COVID-19 swab test status

	In-hospital death (survive vs. non-survive)				COVID-19 swab test status (positive vs negative)			
Variable	Univariate OR (95%CI)	*P* value	Multivariate OR (95%CI)	*P* value	Univariate OR (95%CI)	*P* value	Multivariate OR (95%CI)	*P* value
Age, years	1.07 (1.02–1.12)	0.006			0.97 (0.95–1.00)	0.051	0.97 (0.95–1.00)	0.051
Female (vs. male)	0.63 (0.13–2.96)	0.56			0.99 (0.44–2.23)	0.98		
Smoker (vs. non-smoker)	–	–			0.44 (0.14–1.33)	0.15		
Underlying disease	1.31 (0.43–3.97)	0.63			0.43 (0.22–0.84)	0.14		
Chronic lung disease	1.54 (0.39–5.95)	0.53			1.72 (0.65–4.56)	0.27		
Respiratory rate (>20 vs. <20 per min)	5.72 (1.52–21.51)	0.01	5.14 (1.19–22.15)	0.028	1.21 (0.36–4.06)	0.75		
Temperature in admission (Celsius)	0.87 (0.45–1.70)	0.71			1.57 (1.03–2.38)	0.03		
SpO2 (<90 vs. >90)	5.47 (1.18–25.28)	0.03	4.33 (0.90–22.79)	0.067	0.97 (0.51–1.87)	0.93		
Lymphocytopenia (<1500 vs. >1500)	1.13 (0.33–3.81)	0.84			1.03 (0.49–2.16)	0.93		
Blood urea nitrogen (>19 vs. <19	5.62 (1.75–18.07)	0.004	4.54 (1.30–15.84)	0.017	0.62 (0.25–1.51)	0.29		
AST (>35 vs. <35)	3.76 (0.81–17.42)	0.09			0.63 (0.31–1.27)	0.20		
PTA (>13.5 vs. <13.5)	1.48 (0.47–4.61)	0.50			1.01 (0.52–1.93)	0.98		
INR (>1 vs. <1)	1.94 (0.58–6.48)	0.27			1.25 (0.65–2.41)	0.49		

CI: 1.02–1.12) (Table 17.3). For those patients with respiratory rates>20/min, the odds of mortality were 5.72 times more than for others (95% CI: 1.52–21.51). Low SpO_2 and high BUN were also found to be associated with a higher risk for in-hospital death according to univariate analysis, whereas multivariate analysis only revealed respiratory rate and BUN as risk factors of in-hospital mortality. For the results of COVID-19 swab PCR tests at the end of hospitalization, univariate analysis revealed that increased temperature on admission (1 °C) could increase the risk of having a positive COVID-19 swab test.

Table 17.4 presents the associated factors with fever and other symptoms at the end of hospitalization. Age still showed a significant factor in univariate analysis, but no significance was observed in multivariate analysis. Patients with higher respiratory rates had a higher chance of continuing fever (or other symptoms) in both univariate and multivariate models. SpO_2 also indicated a potential association with fever in the univariate model, and for those with SpO_2 less than 90 at admission, the odds of continuing fever were 2.52 times higher (95% CI: 1.001–6.39).

BUN was a risk factor for other clinical symptoms in univariate analysis (Table 17.4). However, the results for fever were only borderline (p = 0.054). Moreover, INR increased the chance

Table 17.4 Risk factors associated with fever and other clinical symptoms status at the end of hospitalization

	Fever (finish vs. continue)				Other clinical symptoms (finish vs. continue)			
Variables	Univariate OR (95%CI)	*P* value	Multivariate OR (95%CI)	*P* value	Univariate OR (95%CI)	*P* value	Multivariate OR (95%CI)	*P* value
Age, year	1.04 (1.003–1.07)	0.03			1.02 (0.98–1.05)	0.31		
Female (vs. male)					0.49 (0.13–1.73)	0.27		
Smoker (vs. nonsmoker)	0.39 (0.05–3.14)	0.38			0.94 (0.19–4.48)	0.94		
Underlying disease	0.95 (0.41–2.21)	0.92			0.72 (0.31–1.69)	0.45		
Chronic lung disease	0.98 (0.31–3.13)	0.97			0.71 (0.19–2.55)	0.59		
Respiratory rate (>20 vs. <20 per min)	3.49 (1.06–11.43)	0.04	4.08 (1.18–14.08)	0.026	3.69 (1.12–12.14)	0.03	3.52 (1.05–11.87)	0.04
Temperature in admission (Celsius)	0.88 (0.53–1.46)	0.63			0.89 (0.54–1.47)	0.65		
SpO2 (<90 vs. >90)	2.52 (1.001–6.39)	0.049			2.36 (0.92–6.007)	0.07		
Lymphocytopenia (<1500 vs. >1500)	1.60 (0.65–3.92)	0.30			1.10 (0.42–2.85)	0.84		
Blood urea nitrogen (<19 vs. >19)	2.68 (0.98–7.33)	0.054			2.85 (1.04–7.84)	0.04	2.74 (0.98–7.69)	0.055
AST (>35 vs. <35)	1.10 (0.46–2.65)	0.83			2.01 (0.75–5.32)	0.16		
PTA (>13.5 vs. <13.5)	1.98 (0.81–4.85)	0.13			1.84 (0.75–4.55)	0.18		
INR (>1 vs. <1)	2.85 (1.08–7.52)	0.03	3.12 (1.15–8.46)	0.025	2.11 (0.83–5.36)	0.12		

of continuous fever according to both univariate and multivariate models.

17.4 Discussion

This single-center retrospective study focused on the clinical characteristics of 167 confirmed cases with COVID-19, out of which 153 were discharged and 14 died in hospital. Diabetes and coronary heart disease were the most common comorbidities in these patients, and fever, dyspnea, and cough were the most common symptoms on admission. Our results showed significantly higher age in non-survivor patients compared with survivors, whereas gender, family history, symptoms, or comorbidities did not significantly alter survival. These findings contrast with more recent studies which found that male gender and the presence of comorbidities such as diabetes, hypertension, and heart disease are associated with poorer survival outcomes, including higher death rates [15, 16]. However, this report identified several risk factors for in-hospital death, continuous or completion of fever, and other clinical symptoms at the end of hospitalization up to the final date of follow-up. In particular, high respiratory rates of more than 20 per min and BUN levels greater than 19 mg/dL on admission were associated with a higher risk of death in-hospital. Additionally, a higher respiratory rate of more than 20 breaths per min on admission was associated with continuous fever and other clinical symptoms at the end of hospi-

talization. This is most likely linked with increased demand for oxygen due to the pneumonia-like symptoms.

The SARS-CoV-2 virus which causes COVID-19 disease is similar to the severe acute respiratory syndrome (SARS-CoV) and Middle Eastern respiratory syndrome (MERS-CoV) coronaviruses which resulted in 8096 and 2519 cases worldwide, respectively [17]. However, SARS-CoV-2 has had a much higher rate of infectivity with an estimated 11.9 million cases worldwide, as of July 7, 2020. Overall, global mortality rate in patients with COVID-19 is lower than that previously seen in patients with SARS and MERS [17–22]. According to the results of this study, 138 (82.6%) of patients were infected with the virus through contacts in the community, 14 (8.4%) by travelling, and 13 (7.3%) by contact with confirmed cases, and 2 (1.2%) patients were infected in hospital. Contrary to our study, the rate of hospital transmission was higher in China, which may be explained by low knowledge and experience in dealing with the virus in the early stages. A study by Wang et al. of 138 hospitalized patients with COVID-19 showed that nearly half of patients, 57 (41.3%), were infected in hospital [8]. However, 1 month after the outbreak of COVID-19, China gained increased control over the spread of the virus by adopting measures such as isolation of confirmed and suspected cases and lockdown and quarantine of Wuhan and surrounding areas. This kept the mortality rate less at less than 1% outside of the Hubei province [23, 24].

Our univariate analysis showed that age was the only demographic factor associated with increased death outcomes of COVID-19 infections although this was just outside of significance in the multivariate model. Previous studies showed that older age was an important independent predictor of mortality in SARS-CoV and MERS-CoV [14, 18], and it has been confirmed that increasing age is also associated with increased risk of death in patients with SARS-CoV-2 infections [4, 8, 15, 16]. In a study similar to our study in China by Zhou et al. [4], older age was associated with the high risk of mortality (OR:1.10, 95% CI: 1.03–1.17, $p < 0.001$).

In the current study, all patients developed ARDS, but we did not find other outcomes. In contrast, a previous study from China showed that sepsis was a common complication (59%) as well as other outcomes such as respiratory failure (54%), ARDS (31%), heart failure (23%), septic shock (20%), acute cardiac injury (17%), acute kidney injury (15%), and secondary infection (15%) [4]. In terms of treatment, all patients in the current study received antiviral treatments, but the types of combination therapies used varied between patients. Given the small numbers of patients studied and the lack of a control group, it is impossible to determine whether or not these treatments led to improved outcomes and increased survival. Additionally, the majority of patients (83.2%) received supplemental oxygen as a rescue therapy. Invasive mechanical ventilation (IMV) was required in 11 patients, and 14 patients received noninvasive ventilation (NIV). Compared with survivors, non-survivors were more likely to receive mechanical ventilation, either invasively or noninvasively.

Our study has some limitations. First, due to the retrospective study design, not all laboratory tests were done in all patients, including measurements of D-dimer, IL-6, and serum ferritin. Therefore, their role might be underestimated in predicting in-hospital death. Second, due to the lack of degree of organ dysfunction in the patients, we were not able to calculate the sequential organ failure assessments (SOFA) score. Third, the interpretation of our findings might be limited by the small sample size.

17.5 Conclusions

We found that a high respiratory rate more than 20 breaths per min and BUN levels greater than 19 (mg/dL) on admission were associated with a higher risk of death in hospital. Additionally, higher respiratory rate more than 20 per min on admission was associated with continuous fever and other clinical symptoms at the end of hospitalization. Further studies are needed to increase our understanding of this virus and to aid in the control of future outbreaks. As it

stands now, it is still not certain when this pandemic will diminish to negligible levels as the infection rate is still on the rise in some countries such as Iran, the United States, Brazil, Mexico, and India [21, 22]. Therefore, a more complete understanding of COVID-19 which could be used to inform world policies and help prevent future outbreaks might not be achievable for several years to come.

Declarations Ethics Approval and Consent to Participate

The study was approved by the Research Ethics Committee of the Baqiyatallah University of Medical Sciences, and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively. Thanks to guidance and advice from the Clinical Research Development Unit of Baqiyatallah Hospital.

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Availability of Data and Materials Data associated with this study is available from the corresponding authors on a reasonable request.

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