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Clinical and epidemiological characteristics and outcomes of Coronavirus disease-19 patients in a large longitudinal study

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ABSTRACT

Objective: This study aimed to determine the clinical and epidemiological characteristics and outcomes of Coronavirus disease (COVID)-19 patients.

Methods: In this large cohort study, 15,409 confirmed patients with the COVID-19 of different severities were followed-up from three specialized COVID-19 hospitals between March 18 and October 11, 2020 in Iraqi Kurdistan. The predictors of mortality and severity were examined in binary logistic regression analysis.

Results: The incidence rate of severe/critical status was 12.3% with a median age of 36.0 and case fatality rate (CFR) of 1.98%. The incidence rate of severe/critical conditions and CFR rose with increased age groups; except for 0–14 years (11.9%). The incidence rate of severe/critical patients and CFR was 8.3% and 0.5%, 21.1% and 4.0%, and 23.7% and 8.7% in 15–49 years, 50–64 years, and 65 and older age groups, respectively. The severity of the disease and CFR was associated with coexisting chronic diseases such as cardiovascular diseases (18.2% and 3.1%) and diabetes mellitus (19.8% and 3.4%). The asymptomatic patients (8400 and 54.5%) had statistically higher CFR; 2.3% versus 1.6% ($P = 0.006$). The most common symptoms on diagnosis were fever (31.9%), cough (23.5%), loss of smell/taste (16.3%), sore throat (15.7%), shortness of breath (9.8%), and headache (9.5%). The results showed that being older was the only predictor of mortality and severity in COVID-19 patients.

Conclusions: This region has a low incidence of severe-critic status and CFR. The patients with coexisting medical conditions are more likely to have severe conditions and die of COVID-19. The older age predicts severe/critic status and higher CFR.

Keywords: COVID-19, case fatality rate, outcome, severity

Introduction

The novel coronavirus infection outbreak known as Coronavirus disease (COVID)-19 emerged from Wuhan in China in December 2019.[1] The coronavirus has been spread to other countries, including Iraqi Kurdistan.[2,3] Globally by November 11, 2020, there have been 50,810,763 confirmed cases of COVID-19, including 1,263,844 deaths, reported to the World Health Organization (WHO).[4] The WHO has presented deep concern about the spread of this pandemic.[5]

Health-care systems are encountered with rapidly increasing demands due to the COVID-19 pandemic. The health systems are being overwhelmed, both directly from the coronavirus outbreak and indirectly from vaccine-preventable and treatable medical conditions. Maintaining the population's trust in the capability of the health system is important to provide the safe essential required medical necessities and to control infection risk in medical settings. Infection control is a key step to ensuring appropriate care-seeking behavior and adherence to preventive measures.

The Kurdistan Regional Government (KRG) reported the first confirmed cases of the COVID-19 among the persons who returned from Iran in early February 2020. After that, the KRG released preventive health measures for travelers and community members. In this regard, public and private schools and universities were closed from February 26 to May 2, 2020. The curfew was applied between March 13 and April 23, 2020. The KRG has applied some other preventive measures; including reducing business hours; referring

suspected cases of the COVID-19 to special medical settings; quarantining the persons with close contact with the suspected cases; and increasing awareness about preventive measures through mass media.[6]

The current disease has occurred by a different virus than previously known one. The clinical course of the COVID-19 disease caused by this new virus could be different and was not known completely.[7] The common clinical features are fever, dry cough, shortness of breath (SOB), and pneumonia. The less common clinical features are headache, diarrhea, productive cough, runny nose, and hemoptysis.[8] The clinical outcomes of the patients are different from mild to severe illnesses. The persons aged 65 years and older, smokers, and those with comorbid diseases such as diabetes mellitus (DM) and hypertension are more likely to have a severe situation.[9] The median incubation period of the COVID-19 is between 5 and 6 days, but it could take up to 24 days[10] with an uncertain period of infectivity.[11] The primary goal of controlling this virus is preventing transmission. The patients with COVID-19 show various degrees of laboratory abnormalities such as leukopenia, leukocytosis, and lymphopenia.[12]

The studies have shown that preventive measures such as lockdown and social distance are effective strategies to impede the COVID-19 outbreak across the countries.[13-15] In England, many areas with previously high case incidence reduce sharply. However, the lockdown had not the same effect in every region. For instance, in Kent, the cases were continuously increased during the lockdown, despite having the same restrictions as other regions.[16] Viruses constantly change by mutation result in new variants of a virus over time and sometimes the new variants emerge and disappear. Multiple variants of the virus caused by COVID-19 have been documented in the United States and globally during this pandemic. A new variant of Severe acute respiratory syndrome-coronavirus (SARS-CoV-2) emerged has been responsible for up to 70% more transmissible than the previously known virus. In September 2020, the new variant represented one in four new diagnoses, while by mid-December, this rate was increased to almost two-thirds of new cases in London.[17] A similar pattern was observed in South Africa as well.[18]

The demographic and anthropometric characteristics of the diseases are different across geographic locations[19] and these differences could affect clinical outcomes. We need to analyze the data from a large investigation to find out the disease, establish a specific treatment plan, and optimize resource allocation. There are several studies about COVID-19 from countries over all continents characterizing the nature of the disease. However, we have only one small study in Iraqi Kurdistan focused on the demographic and clinical outcomes of the COVID-19 patients published at the early stage of the outbreak.[3] This study aimed to determine the clinical and epidemiological characteristics of COVID-19 patients. Besides, the association of clinical and epidemiological characteristics of COVID-19 patients with mortality rate was examined in this study.

Methods

Study design and patients

In this large follow-up study, the confirmed patients with the COVID-19 of different severities were followed up by the discharge date from three specialized COVID-19 hospitals. The patients with non-severe medical status who were not admitted to the hospitals were followed up by the mobile medical teams. The patients whose medical conditions were escalated were admitted to the hospital as well. The patients were diagnosed by a certified physician in medical settings in the Duhok governorate of Iraqi Kurdistan between March 18 and October 11, 2020. The governorates of Iraqi Kurdistan are presented in a map in Figure 1.[20] A total of 15,409 patients were diagnosed during the mentioned time. The medical doctors diagnosed the COVID-19 cases based on the WHO interim guidance for COVID-19[21] and local guidelines of the Ministry of Health. The patients were included in this study regardless of disease severity, coexisting medical conditions, and socio-demographic aspects.

The individuals were tested for the COVID-19 for the following reasons in this region. The patients crossed the international border, had contact with a confirmed case, or became ill following visiting health facilities (suspected case). They returned from other governorates/places or they need a certificate of health to work in the private sector. Several persons were tested for the COVID-19 as a routine random screening/surveillance for the suspected cases included those persons who were in quarantine settings.

The patients who were included in this study were selected from different medical settings in the Duhok governorate. The patients who were diagnosed with severe disease were admitted to the following health settings. In early March 2020, the Burn and Plastic Surgery hospital was assigned for COVID-19. In addition, a new 100 beds hospital was made called "Lalav Infectious Diseases hospital" for treatment of the COVID-19 patients with severe and critical conditions. Thereafter, Azadi Teaching Hospital a main tertiary hospital in this region was devoted to treating the COVID-19 patients in early June 2020.

Classification of the disease severity

An infected case was defined as a SARS-CoV-2 positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) taken from a nasal and/or throat swab together. The cases were defined on having signs, symptoms, or radiological findings suggestive of COVID-19 pneumonia.[22]

The criteria for severity of COVID-19 were defined according to the diagnosis and treatment protocol for novel coronavirus

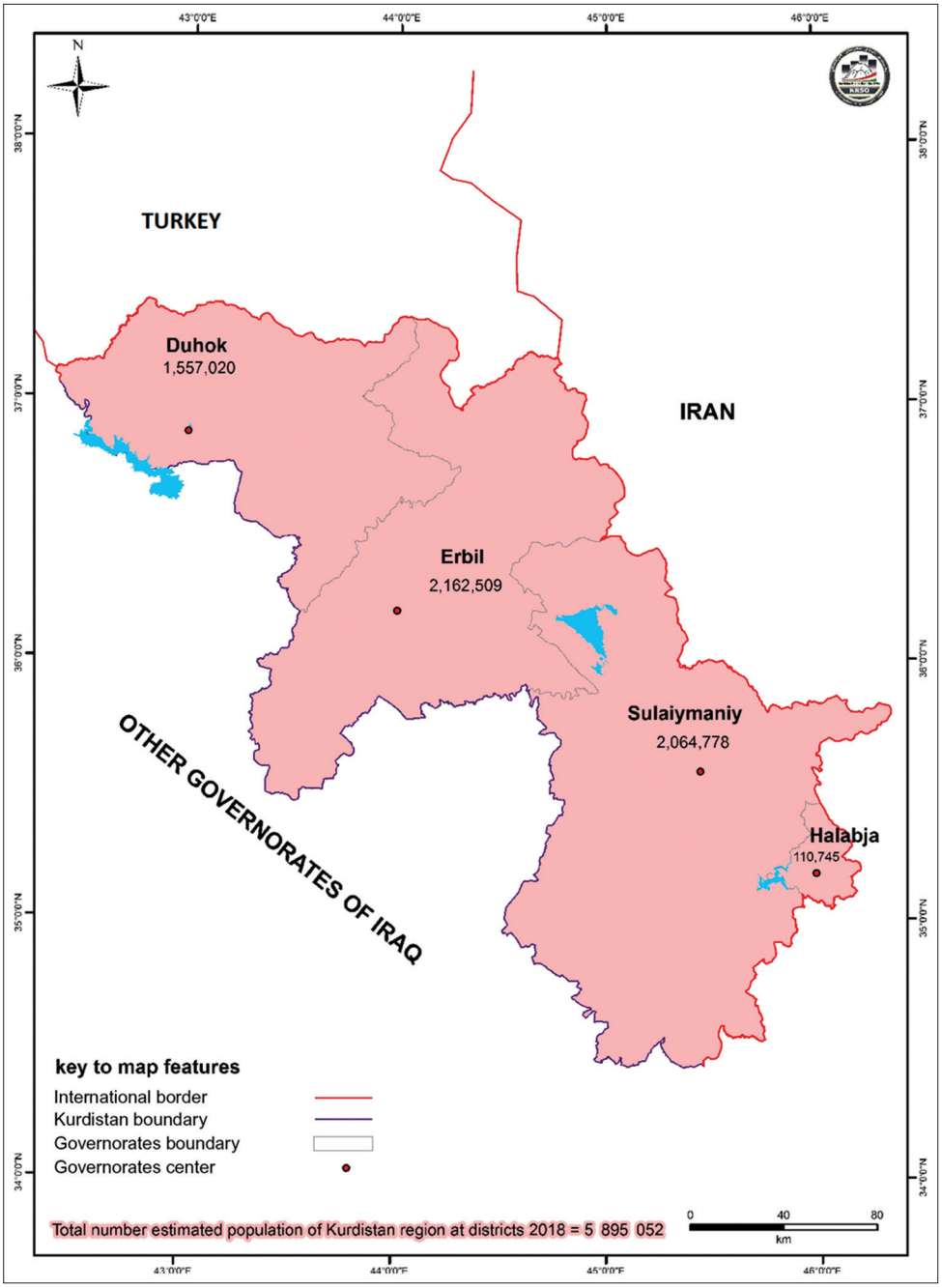

Figure 1: Map of kurdistan region with its estimated population at governorate level

pneumonia (Version 7) as mild, moderate, severe, and critical.[23] We classified as non-severe and severe/critic in this investigation.

The non-severe cases

The non-severe cases compromised mild and moderate cases in this study. The patients with no sign of pneumonia on imaging were considered mild and patients with fever and respiratory symptoms and confirmed radiological outcomes on imaging were considered moderate cases. The severe and critical cases of children and adult populations were determined based on the criteria given in the diagnosis and treatment protocol for novel coronavirus pneumonia (Version 7).[23]

Management

The patients who were diagnosed in this region had different severities and were managed as follows. The management of the cases was performed based on the medical regulation issued by the Ministry of Health of KRG numbered 4504 on February 30, 2020, and the Ministry of Health of Iraq numbered 27,429 on June 1, 2020. The patients were managed according to COVID-19 National Clinical guidelines.[3]

Diagnostic criteria

The RT-PCR diagnostic tests were performed according to the mean recovering time of the patients (14 days). The patients were discharged from the hospital according to the clinical improvement and viral clearance over RT-PCR (two negative results at least 24 h apart). The patients were informed of the possible recurrence of the disease. We did not document the recurrence in this study, because the study was so large.

Data collection

The information of the patients was collected in one of the following categories. The general information of the patients included age, gender, hospital stay (day), occupation (healthcare worker, or non-healthcare worker), and residence was recorded in the first category. The epidemiological and coexisting disorders included pregnancy in childbirth, reasons for testing, and medical conditions were recorded in the second category. At the end, the symptoms of the patients and outcomes were recorded in the third category. The outcomes were documented as recovered or death.

Statistical methods

The general and epidemiological information of the patients was presented in the median (interquartile range) or no. (%). The incidence rates of symptoms and mortality were calculated by dividing the infected or dead patients by the total number of included patients and determined in no. (%). The comparison of incidence rates of severity and mortality in patients with different epidemiological characteristics, coexisting disorders, and symptoms was examined in Pearson Chi-squared tests. The predictors of mortality in patients with COVID-19 were examined in binary logistic regression. The significant level of difference was determined in a $P < 0.05$. The statistical calculations were performed by statistical package for social sciences version 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). The box plots of this study were drawn by JMP SAS 14.3.

Ethical considerations

This study was supported and approved by the institutional ethical board of Duhok General Directorate of Health and Ministry of Health of the KRG registered as 13,878 in 2020. We protected the confidentiality of the personal information of patients through de-identification of the patients' personal information. We did not apply any intervention for patients who were included in this study. The study has no risk to the patents.

Results

The total number of COVID-19 patients was 15,409, of whom 12.3% (n = 1888) were severe/critical. The median age of the patients was 36.0 aged between 0 and 103 years; the majority were 15–49 years. The patients were males (9868, 64.0%) and females (5541, 36.0%). The incidence rate of severe/critical conditions rose with increased age groups; except for 0–14 years (11.9%). The patients with severe/critical disease were older than those with non-severe illness with a median of 9 years. The incidence rate of severe/critical patients was 8.3%, 21.1%, and 23.7% in 15–49 years, 50–64 years, and 65 and older age groups, respectively. Female and non-healthcare worker patients were more likely to have severe/critical condition; 13.0% and 12.4% compared to males and healthcare workers; 11.9% and 9.2%, respectively. Concerning pregnancy, 123 (0.08%) were infected in different trimesters ($P = 0.434$). The patients were from Duhok (97.8%), other Kurdish governorates (1.0%), Iraqi governorates (1.1%), and other countries (0.2%), as shown in Table 1.

The severity of the disease was more likely to be associated with certain coexisting chronic diseases such as cardiovascular diseases (18.2%) and DM (19.8%); however, chronic lung disease, renal impairment, malignancy, and immunodeficiency did not show this association [Table 2].

There were 8400 (54.5%) asymptomatic and 7009 (45.5%) symptomatic patients. The most common symptoms on diagnosis were fever (31.9%), cough (23.5%), loss of smell/taste (16.3%), sore throat (15.7%), SOB (9.8%), and headache (9.5%). Severe COVID-19 was more likely found in patients with SOB (11.6%), loss of appetite (2.7%), or headache (8.0%), Table 3 and Figure 2.

The case fatality rate (CFR) was 1.98%, with a higher rate of aged patients. Lethality increased with age, except for the 0–14 age group (0.7%). The CFR was 0.5%, 4.0%, and 8.7% in 15–49 years, 50–64 years, and 65 and older, respectively. The median hospital stay was 4.0 days in dead patients. The mortality rate was significantly higher in non-healthcare workers compared to healthcare workers; 2.0% versus 0.6; $P = 0.005$. The lethality was higher in pregnant women during the second trimester (2.3%). However, the overall comparison of mortality was not statistically substantial in women with different trimesters. Regarding reasons for COVID-19 testing, there was no significant difference between patients who attended the clinic settings and those in different governorates ($P = 0.258$), Table 4 and Figure 3.

The patients with chronic diseases, cardiovascular diseases, or type 2 DM had a significantly higher CFR rate; 3.1%, 4.4%, and 3.4%, respectively. The patients with other coexisting disorders have not had significantly higher CFR. The asymptomatic patients had statistically higher CFR compared to symptomatic patients; 2.3% versus 1.6 ($P = 0.006$). Furthermore, the patients with SOB had higher CFR compared to patients without SOB; 2.8% versus 1.9%; $P = 0.012$ [Table 5].

The results showed that being older was the only predictor of mortality and severity in COVID-19 patients (Except for

Table 1: Epidemiological characteristics between non-severe and severe COVID-19 patients

Patients' characteristics) (*n*=15409)	All patients (*n*=15,409)	Disease severity		*P*-value
		None-severe (13,521, 87.7%)	Severe/Critic (1888, 12.3%)	
Age (0–103 year)	36.0 (21.0)	36.0 (19.0)	45.0 (28.0)	<0.001[a]
Median (IQR-year)				
Age distribution				
0–14 years	688 (4.5)	606 (88.1)	82 (11.9)	<0.001[b]
15–49 years	10543 (68.4)	9665 (91.7)	878 (8.3)	
50–64 years	2454 (15.9)	1935 (78.9)	519 (21.1)	
65 and older	1724 (11.2)	1315 (76.3)	409 (23.7)	
Hospital stay (1–22 days); Median (IQR-day)	4.0 (6.0)	5.0 (5.0)	3.5 (7.5)	0.965[a]
Sex				
Male	9868 (64.0)	8698 (88.1)	1170 (11.9)	0.045[b]
Female	5541 (36.0)	4823 (87.0)	718 (13.0)	
Occupation				
Healthcare workers	718 (4.7)	652 (90.8)	66 (9.2)	0.010[b]
Non- Healthcare workers	14691 (95.3)	12869 (87.6)	1822 (12.4)	
Residence				
Duhok governorate	15074 (97.8)	13231 (87.8)	1843 (12.2)	0.484[b]
Other Kurdistan governorates	147 (1.0)	131 (89.1)	16 (10.9)	
Other Iraqi governorates	162 (1.1)	136 (84.0)	26 (16.0)	
Other countries	26 (0.2)	23 (88.5)	3 (11.5)	
Pregnancy in childbearing women	123 (0.8)			
First trimester	26 (0.2)	23 (88.5)	3 (11.5)	0.434[b]
Second trimester	44 (0.3)	37 (84.1)	7 (15.9)	
Third trimester	53 (0.3)	49 (92.5)	4 (7.5)	
Reasons for testing COVID-19				
Border crossing	600 (3.89	543 (90.5)	57 (9.5)	0.195[b]
Contact with a confirmed case	8040 (52.18	7000 (87.1)	1040 (12.9)	
Ill person and visited health facilities (Suspect)	5802 (37.65	5114 (88.1)	688 (11.9)	
Return from other governorates	58 (0.38	48 (82.8)	10 (17.2)	
Random screening/surveillance	425 (2.76	385 (90.6)	40 (9.4)	
Get a certificate of health	97 (0.63	88 (90.7)	9 (9.3)	
Others	72 (0.47	62 (86.1)	10 (13.9)	
Contact with a confirmed case and become ill	304 (1.97	270 (88.8)	34 (11.2)	
Contact with a confirmed case in other governorates	1 (0.01	1 (100.0)	0 (0.0)	
Crossed the border and visited health facilities	2 (0.01	2 (100.0)	0 (0.0)	
Contact with a confirmed case and crossed the border	1 (0.01	1 (100.0)	0 (0.0)	
Visited health facilities and need a certificate	2 (0.01	2 (100.0)	0 (0.0)	
Screening of returnees from other governorates	5 (0.03	5 (100.0)	0 (0.0)	

A Mann–Whitney U-test and b Pearson Chi-squared tests were performed for statistical analyses. The bold numbers show a significant difference. COVID: Coronavirus disease, IQR: Interquartile range

15–49 years old). Ironically, being severe or non-severe, asymptomatic or symptomatic, or having coexisting chronic diseases were not predictors for mortality and severity in patients with COVID-19.

A similar pattern was found in the analysis of mortality predictors in patients aged ≥ 65 years old. However, older age was shown to associate with severe/critical medical conditions in patients aged ≥ 65 years old [Table 6].

Discussion

To the best of our knowledge, this is the first large observational study of confirmed COVID-19 patients in Iraq. The median age of the patients was 36.0 aged 0-103 years, though it is different across the world. The median age was lower compared to studies from Italy (65.0 between 18 and ≥75 years);[22] China (47.0 between 0 and ≥65 years);[24] and (56.0 between 18 and 87 years);[25] and the United States (63.0 between 0 and

Table 2: Comparison of prevalence rates of coexisting disorders between non-severe and severe/critic patients

Coexisting disorders (*n*=15409)	All patients (*n*=15,409)	Disease severity		*P*-value
		None-severe (13,521, 87.7%)	Severe/Critic (1888, 12.3%)	
Patients with chronic disease				
Yes	1998 (13.0)	1653 (82.7)	345 (17.3)	<0.001
No	13,411 (87.0)	11,868 (88.5)	1543 (11.5)	
Patients with Cardiovascular diseases				
Yes	1150 (7.5)	941 (81.8)	209 (18.2)	<0.001
No	14,259 (92.5)	12,580 (88.2)	1679 (11.8)	
Patients with diabetes				
Yes	832 (5.4)	667 (80.2)	165 (19.8)	<0.001
No	14,577 (94.6)	12,854 (88.2)	1723 (11.8)	
Patients with Chronic lung disease including asthma and COPD, TB				
Yes	124 (0.8)	103 (83.1)	21 (16.9)	0.110
No	15,285 (99.2)	13,418 (87.8)	1867 (12.2)	
Patients with Renal Impairment				
Yes	129 (0.8)	114 (88.4)	15 (11.6)	0.828
No	15,280 (99.2)	13407 (87.7)	1873 (12.3)	
Patients with malignancy				
Yes	33 (0.2)	28 (84.8)	5 (15.2)	0.611
No	15,376 (99.8)	13,493 (87.8)	1883 (12.2)	
Patients with immunodeficiency				
Yes	46 (0.3)	42 (91.3)	4 (8.7)	0.461
No	15,363 (99.7)	13,479 (87.7)	1884 (12.3)	

Pearson Chi-squared test was performed for statistical analyses. The bold numbers show a significant difference, COPD: Chronic obstructive pulmonary disease

107 years).[26] The lower median age of the affected persons could be due to the median age of 20 in Iraq's population.[27]

In this study, the incidence rate of severe/critical COVID-19 patients was 12.3% and it was linked with increasing age group except for 0–14 years old. It is well documented in the literature that worse outcomes are associated with increasing age.[24,28] Overall, increasing age is associated with impaired immunity and there is an increased prevalence of comorbid diseases such as DM and hypertension. The different rates of severe/critical conditions were reported in the literature, for instance, 15.74%.[24] The studies have reported that COVID-19 patients with severe/critical conditions are older with different median years, 9 years in this study (Iraqi Kurdistan), 7 years in China.[24]

The study showed that healthcare workers (HCWs) are at risk of getting an infection by the COVID-19. In our study, 4.7% of the affected patients were HCWs. The different infection rates have been reported in the literature, 3.5%.[24] Nguyen *et al*.[29] followed up the general community in the UK and USA including front-line HCWs, using the self-reported technique. At the end of the follow-up time, they included 2,035,395 community individuals and 99,795 front-line healthcare workers. They recorded 5545 incident reports of a positive COVID-19 test over 34,435,272 person-days. The front-line HCWs had an increased risk for reporting a positive COVID-19 test (adjusted HR 11·61, 95% confidence interval [CI] 10·93–12·33). Therefore, health policymakers must pay special attention to protect the medical staff against the COVID-19 outbreak. The shortage of medical staff leads to a remarkable burden on health-care services in this region. Importantly, the risk of infection is doubled in household members of front-facing workers, in adjustment for age, gender, comorbidity, and other epidemiological factors.[30] In agreement with this study, the literature has reported similar findings.[29-31]

This study reveals that 54.5% of the patients were asymptomatic on visiting a medical doctor. Fever, cough, loss of smell/taste, sore throat, SOB, and headache are prevalent symptoms in COVID-19 patients. Those with SOB, loss of appetite, or headache are more likely to have severe/critical situations. The literature has reported that fever and cough on admission are the most prevalent symptoms in COVID-19 patients. Guan *et al*.[24] reported that 43.8% and 88.7% had a fever on admission and during hospitalization, respectively, and 67.8% had a cough. In addition, the patients with coexisting illness were more likely to have the severe disease compared to non-severe patients, 38.7% versus 21.0%, respectively.[24] Similar findings were reported in other parts of the words in terms of symptoms.[22,32]

Table 3: Incidence rates of symptoms in patients with confirmed cases of COVID-19

Patients' characteristics) (*n*=15409)	All patients (*n*=15409)	Disease severity		*P*-value
		None-severe (13,521, 87.7%)	Severe (13,521, 87.7%)	
Symptom presence				0.329
Asymptomatic	8400 (54.5)	7351 (54.4)	1049 (55.6)	
Symptomatic	7009 (45.5)	6170 (45.6)	839 (44.4)	
Fever	4915 (31.9)	4314 (31.9)	601 (31.8)	0.949
Chill and rigors	45 (0.3)	39 (0.3)	6 (0.3)	0.825
Sore throat	2414 (15.7)	2140 (15.8)	274 (14.5)	0.141
Cough	3615 (23.5)	3173 (23.5)	442 (23.4)	0.957
SOB	1517 (9.8)	1298 (9.6)	219 (11.6)	0.006
Loss of smell and/or taste	2515 (16.3)	2231 (16.5)	284 (15.0)	0.108
Loss of appetite	306 (2.0)	255 (1.9)	51 (2.7)	0.017
Malaise	116 (0.8)	101 (0.7)	15 (0.8)	0.823
Fatigue (including feeling weak)	956 (6.2)	850 (6.3)	106 (5.6)	0.257
Nausea and Vomiting	285 (1.8)	254 (1.9)	31 (1.6)	0.475
Diarrhea	677 (4.4)	599 (4.4)	78 (4.1)	0.553
Headache	1464 (9.5)	1313 (9.7)	151 (8.0)	0.017
loin pain	21 (0.1)	18 (0.1)	3 (0.2)	0.776
Generalized body ache	795 (5.2)	704 (5.2)	91 (4.8)	0.477
Back ache	123 (0.8)	104 (0.8)	19 (1.0)	0.278
Abdominal pain	71 (0.5)	66 (0.5)	5 (0.3)	0.180
Leg pain/Lower Limb	70 (0.5)	63 (0.5)	7 (0.4)	0.565
Joint Pain	21 (0.1)	17 (0.1)	4 (0.2)	0.342
Dizziness	113 (0.7)	93 (0.7)	20 (1.1)	0.076
Chest pain	204 (1.3)	181 (1.3)	23 (1.2)	0.668
Sleep disturbance	2 (0.0)	2 (0.0)	0 (0.0)	1.000
Epigastric pain	27 (0.2)	24 (0.2)	3 (0.2)	0.856
Hemoptysis	4 (0.0)	4 (0.0)	0 (0.0)	1.000
Fainting	4 (0.0)	4 (0.0)	0 (0.0)	1.000
Flu like symptoms	125 (0.8)	112 (0.8)	13 (0.7)	0.526

Pearson Chi-squared test was performed for statistical analyses except for the following symptoms. Fishers' exact test for sleep disturbance, hemoptysis, and flu-like symptoms. The bold numbers show a significant difference. COVID: Coronavirus disease, SOB: Shortness of breath

The common symptoms reported by systematic reviews were fever (85.6%), cough (68.7%), and fatigue (39.4%). The frequent comorbidities are hypertension (17.4%), diabetes (3.8%), and coronary heart disease (3.8%). The critical cases with complications are 9%, intensive care unit admission is required in 7.3%, invasive ventilation in 3.4%, and mortality is 2.4%.[33] Another meta-analysis confirmed that fever and cough are the most frequent symptoms.[34]

A meta-analysis of 148 articles of 24,410 adults with confirmed COVID-19 from nine countries reported that fever 78% [95% CI 75–81%], a cough 57% [95% CI 54–60%], and fatigue 31% [95% CI 27–35%] are the most prevalent symptoms. The main concern of the authors is that a considerable percentage of patients have chronic diseases. These patients are more likely to have severe/critical disease conditions and more likely to die.

The CFR was 1.98% of 15,409 patients who were followed-up and included in this study. The CFR rate was significantly increased with increasing age, and having chronic diseases, including cardiovascular diseases, or type 2 DM. We found that asymptomatic patients had statistically higher CFR compared to symptomatic patients; 2.3% versus 1.6, respectively, except for the patients with SOB. The CFRs are different based on the coexisting chronic conditions, clinical features, and epidemiological factors. A meta-analysis of 148 articles reported a 7% mortality rate.[35]

The early findings reported from China revealed that CFR is 1.4% in laboratory-confirmed COVID-19 patients[24] and 24.0% in Italy.[22] The Italian study reported that patients aged older than 65 years (HR 3.17, 95% CI 1.84–5.44, $P < 0.001$), history of coronary artery disease (HR 2.93, 95% CI 1.77–4.86, $P < 0.001$), and active cancer (HR 2.32, 95% CI 1.15–4.67, $P = 0.001$) as independent factors related to increased mortality risk. Zhou *et al*.[25] performed

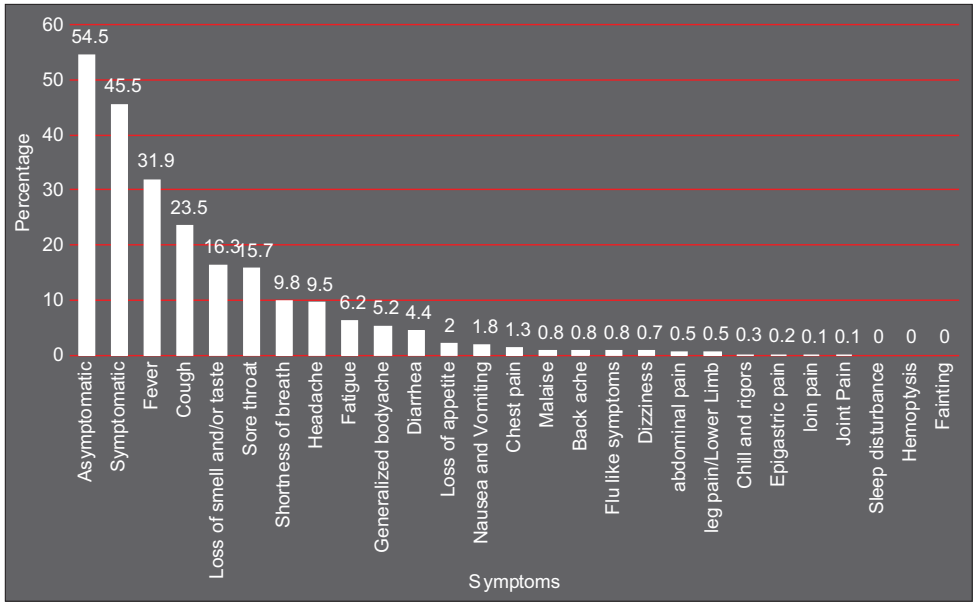

Figure 2: Prevalence rates of symptoms in patients with COVID-19

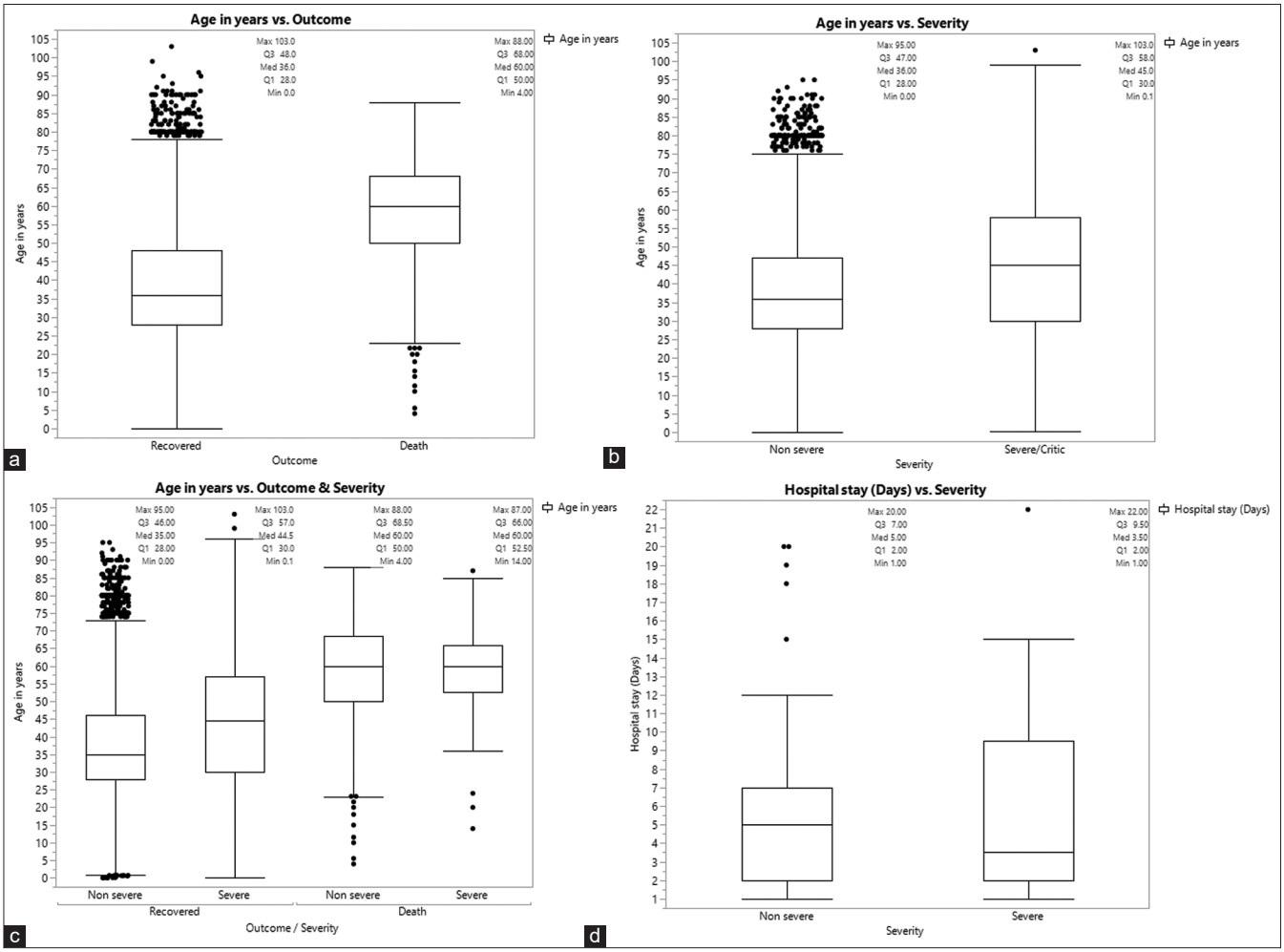

Figure 3: Comparison of median age between patients with different outcomes, (a) age of recovered and dead patients, (b) age of non-severe and severe/critic patients, (c) age of non-severe and severe/critic patients in recovered and dead patients, (d) hospital day of non-sever and sever/critic patients

Table 4: Comparison of outcome of COVID-19 patients with general and epidemiological characteristics

Patients' characteristics) (*n*=15409)	Outcome		*P*-value
	Recovered 15,104 (98.02%)	Dead 305 (1.98%)	
Age (0–103 year)	36.0 (20.0)	60.0 (18.0)	<0.001
Median (IQR-year)			
Age distribution			
0–14 years	683 (99.3)	5 (0.7)	<0.001
15–49 years	10492 (99.5)	51 (0.5)	
50–64 years	2355 (96.0)	99 (4.0)	
65 and older	1574 (91.3)	150 (8.7)	
Hospital stay (1–22 days); Median (IQR-day)		4.0 (6.0)	NA
Sex			0.521
Male	9678 (98.1)	190 (1.9)	
Female	5426 (97.9)	115 (2.1)	
Occupation			0.005
Healthcare workers	714 (99.4)	4 (0.6)	
Non- Healthcare workers	14390 (98.0)	301 (2.0)	
Residence			0.258
Duhok governorate	14771 (98.0)	303 (2.0)	
Other Kurdistan governorates	147 (100.0)	0 (0.0)	
Other Iraqi governorates	160 (98.8)	2 (1.2)	
Other countries	26 (100.0)	0 (0.0)	
Pregnancy in childbearing women			0.405
First trimester	26 (100.0)	0 (0.0)	
Second trimester	43 (97.7)	1 (2.3)	
Third trimester	53 (100.0)	0 (0.0)	
Reasons for testing COVID-19			0.240
Border crossing	595 (99.2)	5 (0.8)	
Contact with a confirmed case	7854 (97.7)	186 (2.3)	
Ill person and visited health facilities (Suspect)	5699 (98.2)	103 (1.8)	
Return from other governorates	58 (100.0)	0 (0.0)	
Random screening/surveillance	419 (98.6)	6 (1.4)	
Get a certificate of health	95 (97.9)	2 (2.1)	
Others	72 (100.0)	0 (0.0)	
Contact with a confirmed case and become ill	301 (99.0)	3 (1.0)	
Contact with a confirmed case in other governorates	1 (100.0)	0 (0.0)	
Crossed the border and visited health facilities	2 (100.0)	0 (0.0)	
Contact with a confirmed case and crossed the border	1 (100.0)	0 (0.0)	
Visited health facilities and need a certificate	2 (100.0)	0 (0.0)	
Screening of returnees from other governorates	5 (100.0)	0 (0.0)	

COVID: Coronavirus disease, IQR: Interquartile range

a multivariable regression and showed that in-hospital mortality is associated with older age (odds ratio 1·10, 95% CI 1·03–1·17), higher Sequential Organ Failure Assessment score (5·65, 2·61–12·23), and d-dimer greater than 1 µg/mL (18·42, 2·64–128·55) on admission.

In agreement with the literature, this study showed that being severe/critical or non-severe or being asymptomatic or symptomatic, or having chronic diseases are not the predictors for mortality and severity in patients with COVID-19. The older age was the only predictor of mortality and severity in COVID-19 patients. However, some other factors have been reported to be predictors for mortality. For example, Fabio *et al*.[22] reported that through multivariable analysis that older age, coronary artery disease, cancer, low lymphocyte count, and high Radiographic Assessment of Lung Edema score as factors independently associated with an increased risk of mortality. Other investigations have reported that older

Table 5: CFR I COVID-19 patients with coexisting disorders and different symptoms

Coexisting disorders (*n*=15,409)	Outcome				*P*-value
	Recovered 15,104 (98.02%)		Dead 305 (1.98%)		
	With coexisting disorder	Without coexisting disorder	With coexisting disorder	Without coexisting disorder	
Patients with chronic disease	1936 (96.9)	13,168 (98.2)	62 (3.1)	243 (1.8)	<0.001
Patients with Cardiovascular diseases	1099 (95.6)	14,005 (98.2)	51 (4.4)	254 (1.8)	<0.001
Patients with diabetes	804 (96.6)	14,300 (98.1)	28 (3.4)	277 (1.9)	0.003
Patients with chronic lung disease including asthma and COPD, TB	122 (98.4)	14,982 (98.0)	2 (1.6)	303 (2.0)	0.769
Patients with Renal Impairment	126 (97.7)	14,978 (98.0)	3 (2.3)	302 (2.0)	0.777
Patients with malignancy	31 (93.9)	15,073 (98.0)	2 (6.1)	303 (2.0)	0.092
Patients with immunodeficiency	45 (97.8)	15,059 (98.0)	1 (2.2)	304 (2.0)	0.924
Symptoms	**With symptom**	**Without symptom**	**With symptom**	**Without symptom**	***P*-value**
Symptom presence	6894 (98.4)	8210 (97.7)	115 (1.6)	190 (2.3)	0.006
Fever	4836 (98.4)	10,268 (97.8)	79 (1.6)	226 (2.2)	0.023
Chill and rigors	43 (95.6)	15,061 (98.0)	2 (4.4)	303 (2.0)	0.234
Sore throat	2370 (98.2)	12,734 (98.0)	44 (1.8)	261 (2.0)	0.547
Cough	3552 (98.3)	11,552 (97.9)	63 (1.7)	242 (2.1)	0.243
SOB	1474 (97.2)	13,630 (98.1)	43 (2.8)	262 (1.9)	0.012
Loss of smell and/or taste	2471 (98.3)	12,633 (98.0)	44 (1.7)	261 (2.0)	0.366
Loss of appetite	298 (97.4)	14,806 (98.0)	8 (2.6)	297 (2.0)	0.421
Malaise	115 (99.1)	14,989 (98.0)	1 (0.9)	304 (2.0)	0.386
Fatigue (including feeling weak)	943 (98.6)	14,161 (98.0)	13 (1.4)	292 (2.0)	0.156
Nausea and vomiting	279 (97.9)	14,825 (98.0)	6 (2.1)	299 (2.0)	0.878
Diarrhea	670 (99.0)	14,434 (98.0)	7 (1.0)	298 (2.0)	0.071
Headache	1442 (98.5)	13,662 (98.0)	22 (1.5)	283 (2.0)	0.169
Loin pain	21 (100.0)	15,083 (98.0)	0 (0.0)	305 (2.0)	0.515
Generalized body ache	783 (98.5)	14,321 (98.0)	12 (1.5)	293 (2.0)	0.329
Back ache	121 (98.4)	14,983 (98.0)	2 (1.6)	303 (2.0)	0.778
Abdominal pain	71 (100.0)	15,033 (98.0)	0 (0.0)	305 (2.0)	0.230
leg pain/Lower Limb	69 (98.6)	15,035 (98.0)	1 (1.4)	304 (2.0)	0.740
Joint Pain	21 (100.0)	15,083 (98.0)	0 (0.0)	305 (2.0)	0.515
Dizziness	113 (100.0)	14,991 (98.0)	0 (0.0)	305 (2.0)	0.129
Chest pain	200 (98.0)	14,904 (98.0)	4 (2.0)	301 (2.0)	0.985
Sleep disturbance	2 (100.0)	15,102 (98.0)	0 (0.0)	305 (2.0)	1.000
Epigastric pain	27 (100.0)	15,077 (98.0)	0 (0.0)	305 (2.0)	0.460
Hemoptysis	4 (100.0)	15,100 (98.0)	0 (0.0)	305 (2.0)	1.000
Fainting	4 (100.0)	15,100 (98.0)	0 (0.0)	305 (2.0)	1.000
Flu like symptoms	123 (98.4)	14,981 (98.0)	2 (1.6)	303 (2.0)	0.760

Pearson Chi-squared test was performed for statistical analyses except for the following symptoms. Fishers' exact test was performed for sleep disturbance, hemoptysis, and fainting. The bold numbers show a significant difference. CFR: Case fatality rate, COVID: Coronavirus disease, SOB: Shortness of breath, COPD: Chronic obstructive pulmonary disease

age and the presence of comorbidities are associated with an increased mortality rate in COVID-19 patients.[25,32,36]

We confirmed the previously published findings in patients from China,[37] United States,[26] and Italy.[22] They reported that older age, coexisting medical conditions such as coronary artery disease, history of hypertension, diabetes, chronic obstructive pulmonary disease, and chronic renal failure, and cancer are related to increased mortality. We back the effect of chronic diseases on increased mortality to their effect on immunity.[38] The current findings give us the utmost importance to reduce the burden of the general health system, targeting the efforts for sufficient screening of the patients at risk.

The role of age in immune system suppression must not be ignored in this disease. The countries with higher infection rates have an older population compared to the countries with low infection rates,[39] France and Italy compared to Iraq and

Table 6: Univariate predictors of mortality in COVID-19 patients

Predictors (n=15,409)	Dependent variable: Outcomes of COVID-19 patients		Dependent variable: Severity	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Severity				
Non-severe	0.996 (0.743–1.335)	0.979		
Severe/critic				
Age distribution				
0–14 years		<0.001		<0.001
15–49 years	0.693 (0.275–1.746)	0.436	0.677 (0.531–0.863)	0.002
50–64 years	5.991 (2.420–14.834)	<0.001	1.984 (1.539–2.557)	<0.001
65 and older	13.190 (5.365–32.426)	<0.001	2.320 (1.791–3.006)	<0.001
Sex at birth				
Male		0.930		0.264
Female	1.011 (0.794–1.287)		1.060 (0.957–1.174)	
Occupation				
Healthcare workers		0.228		0.353
Non–healthcare workers	1.854 (0.679–5.058)		1.133 (0.870–1.476)	
Cardiovascular diseases				
Yes		0.555		0.242
No	0.894 (0.617–1.296)		1.118 (0.927–1.348)	
Type 2 DM				
Yes		0.319		0.053
No	1.251 (0.805–1.943)		0.821 (0.671–1.003)	
Chronic lung disease				
Yes		0.399		0.372
No	1.850 (0.443–7.729)		0.801 (0.492–1.304)	
Renal Impairment				
Yes		0.604		0.198
No	1.366 (0.420–4.439)		1.441 (0.826–2.514)	
Malignancy				
Yes		0.466		0.985
No	0.557 (0.115–2.693)		1.009 (0.372–2.739)	
Immunodeficiency				
Yes		0.637		0.303
No	1.684 (0.193–14.730)		1.754 (0.602–5.111)	
Symptoms presence				
Asymptomatic		0.657		0.551
Symptomatic	0.940 (0.716–1.235)		1.033 (0.928–1.149)	

Binary logistic regression was performed for statistical analysis. The first choice of each variable was considered the reference for the analysis. COVID: Coronavirus disease, DM: Diabetes mellitus, CI: Confidence interval

Saudi Arabia, respectively. Adults aged 65 years and older and patients with coexisting medical conditions are more likely to have a severe-even deadly-coronavirus infection.[40] Therefore, the high infection and mortality rates in high-income countries could be due to aging and accordingly low immunity level.

The effects of aging on the immune system are presented at multiple levels. The production of B and T cells in bone marrow and thymus is decreased first. The functions of mature lymphocytes in secondary lymphoid tissues are diminished accordingly. Therefore, the aged populations unable to respond to the immune challenges as the young populations.[41]

Some other factors have been reported to associate with the mortality rate in the literature. For example, Abdulah and Hassan[42] in a global ecological study reported that the crude mortality rate is increased by raising consuming sugar-sweetened beverages and decreased by increasing fruit consumption and beans and legumes. The anti-inflammatory strategies inside foods, nutrients, or medicines are suggested as viable options for the management of COVID-19[43,44] since the

coronavirus has serious inflammatory consequences for acute pneumonia in persons.[45] The human coronavirus infections cause mild to severe diseases,[3] systemic inflammation, high fever, cough, and acute respiratory tract infection, and dysfunction in internal organs leading to death.

Except for the insufficient age-related micronutrient, the nutritional status of the population has a role in the overall development of the SARS-CoV-2 infection, the clinical status, and outcomes. Therefore, the individuals need the maintenance of host macro- and micronutrient status to avoid the COVID-19 infection.[46]

The older individuals aged 60–65 years old have less ability to respond to the immune challenges and pathogens, antigens, and mitogens decreases due to immune dysregulation.[47] Characteristics of the immune system in older people are a reduction of circulating lymphocytes and loss of immune cells.[48] Besides, the older persons have reduced the production of T cells in the involved thymus. Accordingly, this decreases the function of mature lymphocytes in secondary lymphoid tissues.[41]

Implications and limitations

The main strong point of this study is that we tried to include as much as possible the patients with sufficient information that allowed us to present a clearer picture of clinical features of the COVID-19 in this region. The predictors reported in this study could assist clinicians to determine at an early stage patients with COVID-19 with poor prognosis. However, the study was not exempt from the limitations. We could not record the radiological and laboratory-based information of this large study. Anyhow, we suggest that a large study of radiological and laboratory-based information study be performed in a multi-center investigation.

The world requires serious investment in research and development to find out the current epidemics and prepare for possible future ones. Besides, we need to establish our healthcare system to develop new diagnostic and therapeutic solutions, invest in vaccines and broad-spectrum antivirals. Moreover, we need to take into account the social aspects.[49]

Conclusions

This study showed that patients with COVID-19 have a low incidence rate of severe/critical status in Iraqi Kurdistan. The incidence rate of severe/critical condition was significantly increased with increasing age and was more common in female and non-healthcare worker patients. We found that older COVID-19 patients and those with coexisting medical conditions were more likely to have severe/critical status and a high rate of CFR. Having older age was determined to be the only factor that predicted the severe/critical status and higher mortality.

Authors' Declaration Statements

Availability of data and material

The data used in this study are available and will be provided by the corresponding author on a reasonable request.

Funding statement

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Authors' Contributions

The corresponding author claim that all authors whom their names were reported in this study had sufficient contribution to the concept, design, review, analysis, and final approval.

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