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Clinical characteristics and outcomes of hospitalized COVID-19 patients in a MERS-CoV referral hospital during the peak of the pandemic

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ABSTRACT

Objective: To describe the clinical characteristics and outcomes of hospitalized coronavirus disease 2019 (COVID-19) patients in a middle east respiratory syndrome coronavirus (MERS-CoV) referral hospital during the peak months of the pandemic.
Design: A single-center case series of hospitalized individuals with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in King Saud University Medical City (KSUMC), an academic tertiary care hospital in Riyadh, Saudi Arabia.
Clinical and biochemical markers were documented. Risks for ventilatory support, intensive care unit (ICU) admission and death are presented.
Results: Out of 12,688 individuals tested for SARS-CoV-2 by real time reverse transcriptase polymerase reaction (RT-PCR) from June 1 to August 31, 2020, 2,683 (21%) were positive for COVID-19. Of the latter, 605 (22%) patients required hospitalization with a median age of 55, 368 (61%) were male. The most common comorbidities were hypertension (43%) and diabetes (42%). Most patients presented with fever (66%), dyspnea (65%), cough (61%), elevated IL-6 (93.5%), D-dimer (90.1%), CRP (86.1%), and lymphopenia (41.7%). No MERS-CoV co-infection was detected. Overall, 91 patients (15%) died; risk factors associated with mortality were an age of 65 years or older OR 2.29 [95%CI 1.43–3.67], presence of two or more comorbidities OR 3.17 [95%CI 2.00–5.02], symptoms duration of seven days or less OR 3.189 [95%CI (1.64 – 6.19]) lymphopenia OR 3.388 [95%CI 2.10–5.44], high CRP OR 2.85 [95%CI 1.1–7.32], high AST OR 2.95 [95% CI 1.77–4.90], high creatinine OR 3.71 [95%CI 2.30–5.99], and high troponin-I OR 2.84 [95%CI 1.33–6.05].
Conclusion: There is a significant increase in severe cases of COVID-19. Mortality was associated with older age, shorter symptom duration, high CRP, low lymphocyte count, and end-organ damage.

Introduction

Since the emergence of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in Wuhan, China, in December 2019 and the declaration of the coronavirus 2019 (COVID-19) as a pandemic by the World Health Organization (WHO) on March 11, 2020, it has infected more than 88 million individuals around the world with almost two million deaths as of January 7, 2020 (World Health Organization, n.d.). In the Kingdom of Saudi Arabia (KSA), 363,582 individuals have been infected with 6,282 deaths, with a national case fatality ratio (CFR) of 1.7% (Saudi Arabia Ministry of

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Health, n.d.a, n.d.b), which is less than that reported by the United States (CFR of 2.7%), Italy (CFR of 9.5%), and China (CFR 5.2%) (World Health Organization, n.d.). Many studies have been published describing patient demographics, clinical course, and outcomes from those countries (Argenzian et al., 2020; Docherty et al., 2020; Lechien et al., 2020; Richardson et al., 2020).

The first case of COVID-19 in KSA was reported on March 2, 2020 (Barry et al., 2020b), and the peak of the pandemic was reported in June and July 2020, with 4,919 individuals being the highest number of cases recorded in a single day on June 18, 2020 (Saudi Arabia Ministry of Health, n.d.a, n.d.b; World Health Organization, n.d.).

The Middle East Respiratory Syndrome Corona Virus (MERS-CoV) originated in KSA (Zaki et al., 2012) and is the only country in the world where it is still endemic, causing multiple nosocomial outbreaks (Alenazi et al., 2017; Amer et al., 2018; Assiri et al., 2013; Balkhy et al., 2016; Barry et al., 2020c; Drosten et al., 2015; Fagbo et al., 2015; Oboho et al., 2015). At the time of writing, the most recent reported case of MERS-CoV was on May 31, 2020 (Saudi Arabia Ministry of Health, n.d.a, n.d.b). Per the latest situation update from the WHO, a total of 2,519 laboratory-confirmed MERS-CoV infections, including 866 associated deaths (CFR 34.3%), were reported globally. Most of these cases were in KSA (2,121 cases), including 788 related deaths (CFR 37.1%) between June 2012 and January 2020 (WHO, n.d.).

We describe the clinical characteristics and outcomes of hospitalized patients with COVID-19 in an academic hospital, which serves as a MERS-CoV referral center, during the peak months of the pandemic in KSA. This is a follow-up to our previously published data from the same hospital during the pandemic's early months (Barry et al., 2020a).

Materials and methods

Study design

This is a single-center case series conducted at King Saud University Medical City (KSUMC) of hospitalized COVID-19 patients during the peak of the COVID-19 pandemic, between June 1 to August 31, 2020. We included all individuals aged 14 years or older who were hospitalized for at least 24 h, with real-time reverse transcriptase-polymerase chain reaction (RT-PCR) confirmed COVID-19 during the study period. Patients who were still hospitalized by the end of the study period were followed until discharge or in-hospital death, with the last follow-up event occurring on October 15, 2020.

Disease severity was classified based on the Saudi Ministry of Health (MOH) severity definitions (Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19, n.d.) into asymptomatic, upper respiratory tract illness (URTI), mild to moderate pneumonia, severe pneumonia (in which non-invasive ventilation or mechanical ventilation is required), and critical cases, in which acute respiratory distress syndrome (ARDS), overt sepsis, or multiorgan dysfunction were documented. MERS-CoV RT-PCR was done for all patients who met the case definition as per the MOH (Ministry of Health Command and Control Center, 2018).

All patients were admitted to single rooms under droplet and contact precautions, as per hospital policy, or in airborne infection isolation rooms with 6–12 air-changes per hour, or, when those options were not available, in a single room with a high-efficiency particulate air filter, if aerosol-generating medical procedures were required with the use of fit-tested N95 masks.

This analysis received ethical approval from the KSUMC Institutional Review Board bearing project number E20-4979. Oral informed consent was obtained for data use from all study participants.

Laboratory testing

All hospitalized patients underwent a nasopharyngeal and/or tracheal aspirate upon admission, once obtained it was sent in viral transport medium UTM® (Copan, Brescia, Italy). We defined confirmed COVID-19 as a positive result for both SARS-CoV-2 E and S genes using the RealStar® SARS-CoV-2 real-time Reverse Transcriptase PCR (RT-PCR) kit (Altona®-Diagnostics, Hamburg, Germany) and Rotor-gene Q system (Qiagen®, Santa Clarita, CA, USA) in our institute's molecular laboratory. We confirmed a sample with a cycle threshold (Ct) value $\leq$29 for both SARS-CoV-2 E and S genes as a positive case, whereas a sample with a single gene detection or Ct value $\geq$29 was confirmed by repeating the test on an Xpert® Xpress SARS-CoV-2 kit and GeneXpert XVI system (Cepheid®, Sunnyvale, CA, USA), which detects SARS-CoV-2 E and N genes. When indicated, we used the same samples to test for MERS-CoV RNA in which, after extraction, the RNA was reverse transcribed to cDNA. This was then amplified and screened to detect MERS-CoV upE and ORF1a genes using the specific primers and probes of the RealStar® MERS-CoV RT-PCR kit (Altona® Diagnostics) on the Rotorgene Q instrument (Qiagen®).

Data collection

Patient data was maintained in individual electronic health care records of all those with confirmed COVID-19. The information recorded in health care records included demographic data, medical history, epidemiological exposure, underlying comorbidities, symptoms, physical signs, laboratory results, MERS-CoV PCR, bacterial cultures results, chest X-rays and computed tomographic (CT) scans, treatment measures (i.e., anti-viral therapy, corticosteroids, monoclonal antibody treatment, supportive care), in-hospital complications, admission to the intensive care unit (ICU), and clinical outcomes. The sequential organ failure assessment (SOFA) was determined on the day of ICU admission.

Statistical analysis

Continuous measurements are presented as mean (SD) if they are normally distributed or median [interquartile range (IQR)] if they are not, and categorical variables are counted in percentages. For laboratory results, we assessed whether the measurements were outside the normal range. We used SPSS software (version 25, IBM Corp., Armonk, NY, USA) for statistical analysis, including a univariate analysis to obtain odds ratio (OR) and 95% confidence interval (CI) on the association of the study variables with severity, ICU admission, and mortality. The Haldane–Anscombe correction was used for odds ratio calculation when one of the cells had a value of zero. Pearson's chi-squared test was performed to calculate the p-value in the analysis's categorical variables, and a p-value of <0.05 was considered significant. P-values generated by Fisher's exact test (instead of those generated by Pearson's chi-squared) were used when >20% of the cells had an expected count of less than five.

Results

Demographics

During the peak of the COVID-19 pandemic in KSA from June 1 to August 31, 2020, a total of 12,688 patients aged 14 years and above were tested for COVID-19 by RT-PCR at KSUMC, Riyadh. Of those, 2683 patients (21.1%) tested positive, and of those tested positive, 606 patients (22.6%) required hospitalization. Only one patient was lost to follow-up due to transfer to another hospital;

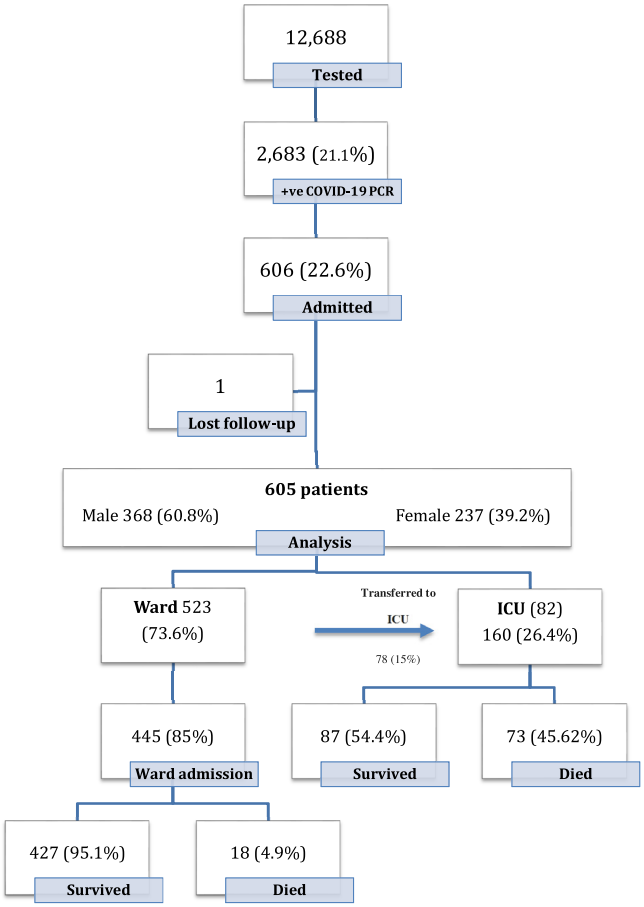

Figure 1. Patients flow.

the remaining 605 patients met the inclusion criteria (Figure 1). Demographic characteristics are shown in Table 1.

Among the 605 patients, 368 (60.8%) were male, and 237 (39.2%) were female. The overall age ranged from 16 to 101 years old with a median age of 55 years. A total of 353 patients (58%) were Saudi nationals. The majority of patients had a high body mass index (BMI), of which 261 were obese (43%). The most frequent comorbidities were hypertension in 262 patients (43%) and diabetes mellitus in 259 patients (43%). Thirty-four patients were pregnant, representing 14% of the sample. Health care workers represented only 4%, one of whom had a history of PCR confirmed MERS-CoV in 2015; none of the other patients had a past history of the disease.

Patients' disposition

Of 445 (73.6%) admitted to the ward, 78 (15%) required transfer to the ICU, while 82 (13.5%) were admitted directly to the ICU, for a total of 160 (26.4%) patients requiring ICU admission. Overall, 514 (85%) were discharged from the hospital, while 91 patients (15%) died during their hospital stay. The median time to discharge or mortality was seven and 13 days, respectively. Reasons for ICU admission included respiratory distress (79.4%), transfer from another hospital on mechanical ventilation (6.3%), hypotension (5.6%), decreased level of consciousness (3.1%), cardiac/respiratory arrest (1.9%), and others (Table 2). Out of those who required ICU admission, 74 patients (46.3%) had two or more comorbid illnesses, while 86 patients (53.7%) had only one or no comorbid illness. Of those who required ICU admission, 32.5% had a temperature of $\geq$38 °C, and 69.4% had a respiratory rate >24/min in the first 24 h of admission. In the ICU, 38.1%, 46.9%, and 45.6% of patients needed vasopressors, mechanical ventilation, and non-invasive ventilation, respectively. One patient in the ICU required extracorporeal membrane oxygenation (ECMO) but did not survive.

Table 1
Demographic data of 605 hospitalized patients with SARS-CoV-2 infection at King Saud University Medical City.

		(n)	(%)
Gender	Female	237	39
	Male	368	61
Age	14–64	455	75
	65 or older	150	25
Occupation	HCWs	26	4
	Non-HCWs	579	96
Nationality	Saudi	353	58
	Non-Saudi	252	42
BMI	Obese	261	43
	Overweight	177	29
	Normal	112	19
	Underweight	10	2
	Not documented	45	7
Comorbid Conditions	HTN	262	43
	DM	259	43
	DLP	92	15
	CAD	64	11
	HF	42	7
	CKD	37	6
	CVA	20	3
	Active cancer	16	3
	Autoimmune diseases	12	2
	COPD	9	2
Pregnancy	Yes	34	14
	No	203	86

HCWs: health care workers, DM: diabetes mellitus, HTN: hypertension, DLP: dyslipidemia, CAD: coronary artery disease, HF: heart failure, CKD: chronic kidney disease, CVA: cerebrovascular accident, COPD: chronic obstructive pulmonary disease.

Clinical presentation

The most common presenting symptoms were fever (65.5%) dyspnea (65%), cough (61%), and gastrointestinal symptoms (37.5%) which included any of the following: nausea, vomiting, diarrhea, (Figure 2). The median duration of symptoms (IQR) was five days.

In the first 24 h of presentation, median oxygen saturation (IQR) was 94%, median temperature (range) was 37.3 °C (36°–40.2 °C), median respiratory rate (IQR) was 23 bpm, and median systolic blood pressure (IQR) was 118 mmHg.

In the first 48 h of admission, laboratory investigations revealed that 9.8% of patients had a WBC count of less than 4.0×10^9/L, while 13.6% of patients had a platelet count less than 150×10^9/L, and 583 (41.7%) had a lymphocyte count less than 1.0×10^9/L. Most patients showed raised Interleukin-6 (IL-6), D-dimer, aspartate aminotransferase (AST), C-reactive protein (CRP), and ferritin levels, in addition to a prolonged QT interval on baseline electrocardiogram (ECG) (Table 3). During admission, chest X-rays (CXR) and CT scans were obtained from 545 and 45 patients, respectively. One hundred and fifty-nine (29.2%) patients had normal CXR, while the other 69.8% had evidence of lung infiltrates. Of those CXR showing infiltrates, 88.5% were bilateral, and 11.5% were unilateral. Of the 45 chest CT scans done, 11.1% were normal, 35.6% showed ground-glass opacification (GGO), 11.1% showed consolidation, 35.5% showed both GGO and consolidation, and 6.7% showed pulmonary embolism. From all COVID-19 confirmed cases, 194 patients (32%) met the case definition for MERS-CoV and were tested for it by RT-PCR. No MERS-CoV co-infection was detected among any of those patients. Additional microbiological testing

Table 2
Clinical characteristics of 160 hospitalized COVID-19 patients who required admission to the ICU at King Saud University Medical City.

Variables		Count n = 160 (%)	Death in ICU n = 73 (45.6%)
Initial admission	Ward then ICU	78 (48.8)	31 (42.5)
	Direct to ICU	82 (51.2)	42 (57.5)
Reason for ICU admission	Cardiac/respiratory arrest	3 (1.9)	1 (1.4)
	Respiratory distress	127 (79.4)	56 (76.7)
	Hypotension	9 (5.6)	4 (5.5)
	Decreased level of consciousness	5 (3.1)	3 (4.1)
	Transferred from another hospital	10 (6.3)	7 (9.6)
	Others (Post-operative, DKA, severe electrolyte disturbances)	6 (3.6)	2 (2.7)
Number of comorbid conditions.	Two or more comorbid conditions	74 (46.3)	42 (57.5)
	One or no comorbid condition	86 (53.8)	31 (42.5)
Temperature in the first 24 hours of hospital admission.	≥38 °C	52 (32.5)	25 (34.2)
	<38 °C	108 (67.5)	48 (65.8)
Respiratory rate in the first 24 hours of hospital admission.	>24 bpm	111 (69.4)	46 (63)
	≤24 bpm	49 (30.6)	27 (37)
Need for vasopressors	Yes	61 (38.1)	52 (71.2)
	No	99 (61.9)	21 (28.8)
Respiratory support	None	6 (3.8)	0 (0)
	Facemask	6 (3.8)	0 (0)
	Non-invasive ventilation : HFNC, BIPAP, CPAP	73 (45.6)	9 (12.3)
	Invasive mechanical ventilation	75 (46.9)	64 (87.7)
	Median ventilator days (IQR)	7 days (15)	
Need for ECMO	Need for ECMO	1 (0.6)	1 (1.4)
Median ICU stay (IQR): 8 days (11)			
Median hospital stay (IQR): 17 days (18)			

IQR: interquartile range, DKA: diabetic ketoacidosis, HFNC: high-flow nasal cannula, BIPAP: bilevel positive airway pressure, CPAP: continuous positive airway pressure, ECMO: extracorporeal membrane oxygenation.

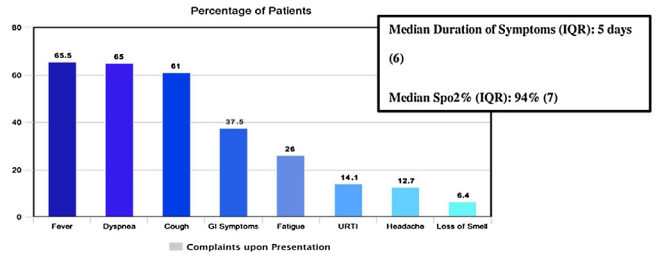

Figure 2. Presenting complaints of hospitalized COVID-19 Patients, King Saud University Medical City, Saudi Arabia.

revealed no influenza-A (184 tested) or influenza-B (185 tested) co-infections. Blood cultures were obtained from 332 patients, and only 20 (6%) were positive, while sputum cultures were obtained from 129 patients, and 18 samples grew various bacteria, while one sample grew *Aspergillus niger*.

Treatment

Treatment of COVID-19 patients varied according to severity and complications, including corticosteroids, interferon beta, anticoagulants, tocilizumab, anti-viral, anti-malaria, and antibacterial agents (Table 4). The most common treatment regimen included hydroxychloroquine, lopinavir/ritonavir, favipiravir, remdesivir, coricosteroids, and tocilizumab (Table 4).

Outcome

Older patients (age group ≥65 years) had high mortality ($p < 0.001$) with an OR = 2.297 [95%CI 1.437–3.671]; however, there was no statistically significant association between age groups and severity of infection or ICU admission. Male patients had more severe disease ($p = 0.004$), but there was no significant association between gender and ICU admission or mortality. BMI showed no significant association with severity of infection, ICU admission, or mortality; mortality was recorded to be higher in patients with BMI ≥ 30 as compared to overweight, normal weight, and underweight patients but did not show statistical significance. Non-health care workers (nHCWs) had more severe infections ($p = 0.003$, OR = 6.880 [95%CI 1.610–29.402]) and were more likely to be admitted to the ICU ($p = 0.035$) compared to HCWs. There were no deaths among the 26 (4%) hospitalized HCWs.

None of the 34 pregnant women admitted with COVID-19 had a severe disease or required ICU admission. Twenty-five women (73.53%) were asymptomatic, three (8.82%) had URTI, and six (17.65%) had mild/moderate pneumonia. Twenty-nine (85.29%) were in their third trimester, four (11.76%) were in the second trimester, and only one was in her first trimester and was presenting with ectopic pregnancy. There was no association observed between gestational age and disease severity. Out of the nine symptomatic patients, six received ceftriaxone, and only one was given dexamethasone due to hypoxia. None were given hydroxychloroquine or anti-viral agents. Most of the patients were admitted for delivery or other obstetric indications, and only one patient was admitted due to symptomatic COVID-19 infection with moderate pneumonia and hypoxia. Regarding obstetrics complications, 15 (44.16%) had an uneventful course, while the rest had different complications, including decelerations in cardiotocography (42.11%), per-vaginal bleeding (21.05%), decreased fetal movement (15.78%), pre-eclampsia (15.78%), and pre-term labor (10.53%). Eighteen (66.67%) pregnant women had a spontaneous vaginal delivery, while nine (33.34%) required emergency cesarean section. The COVID-19 status of the newborns was not well documented; 15 out of 27 (55.56%) newborns tested negative for COVID-19, and the rest were of unknown status due to lack of documentation. All 34 women were discharged with a median hospital stay of seven days.

Nationality had a significant association with severity of infection and ICU admission, with non-Saudis exhibiting more severe disease ($p < 0.001$) and more likely to be admitted to the ICU ($p = 0.004$), although there was no significant impact on mortality

Table 3
Laboratory investigations and radiological findings in hospitalized COVID-19 patients, King Saud University Medical City, Saudi Arabia.

Study variables	Number of patients	Median, (IQR)	Abnormal cutoff	n (%)
Basic investigations				
White blood cells (x10^9/L)	605	7 (4.3)	<4	59 (9.8)
Lymphocytes (x10^9/L)	583	1.1 (0.8)	<1	243 (41.7)
Platelets count (x10^9/L)	605	233 (12)	<150	82 (13.6)
D-dimer (mcg/mL)	534	1.1 (1.34)	>0.45	481 (90.1)
ALT (units/L)	592	38 (36)	>61	146 (24.7)
AST (units/L)	541	42 (39)	>37	291 (53.8)
Serum creatinine (mcmol/L)	604	81 (45)	>115	121 (20)
Inflammatory markers				
Lactate (mmol/L)	345	1.6 (0.8)	>2	84 (24.3)
Ferritin (mcg/L)	529	575 (986)	>400	321 (60.7)
C-reactive protein (CRP) (mg/L)	503	89 (105)	>20	433 (86.1)
Procalcitonin (PCT) (ng/mL)	405	0.12 (0.375)	>0.5	107 (26.4)
Interleukin-6 (IL.6) (pg/mL)	262	57.09 (113.3)	>7	245 (93.5)
Troponin (ng/L)	433	7.4 (21)	>100	33 (7.6)
Creatinine kinase (CK) (units/L)	328	138 (257.5)	>308	87 (26.5)
ECG: QT interval (ms)	122	449.5 (39)	>440	79 (64.8)
Microbiology				
MERS CoV RT-PCR	194		Positive	0 (0)
HIV Ag/Ab	372		Positive	0 (0)
Hepatitis BsAg	407		Positive	10 (2.5)
TB QuantiFERON Gold Plus	316		Positive	12 (3.8)
Sputum culture	129		Positive	18 (14)
Blood culture	332		Positive	20 (6)
Imaging				
Chest X-ray	545		Normal	159 (29.2)
			Infiltration.	381 (69.9)
			Extent	
			Unilateral	44 (11.5)
			Bilateral	337 (88.5)
			Isolated Pleural Effusion	5 (0.9)
CT chest	45		Normal	5 (11.1)
			GGO	16 (35.6)
			Consolidation	5 (11.1)
			Both (GGO and Consolidation)	16 (35.6)
			PE	3 (6.7)

CT: computed tomography, GGO: ground-glass opacity, ECG: electrocardiogram, HIV: human immunodeficiency virus, TB: tuberculosis, IQR: interquartile range, MERS-CoV: Middle East respiratory syndrome coronavirus, RT-PCR: reverse transcription-polymerase chain reaction, ALT: alanine aminotransferase, AST: aspartate aminotransferase, PE: pulmonary embolism.

(p = 0.982). Mortality was significantly higher among patients who were admitted to the ICU directly, compared to those who were admitted initially to the ward (p < 0.001; OR = 10.157 [95%CI 6.018–17.144]). Mortality was also significantly higher among those who reported symptom duration of seven days or fewer in comparison to those who had more than seven days of symptoms prior to presentation (p < 0.001; OR = 3.189 [95%CI 1.643–6.190]). A low saturation of oxygen (SpO_2) of less than 94% in the first 24 h, or a ferritin level of more than 400 mcg/L in the first 48 h, had a significant association with more severe disease and ICU admission; however, these showed no statistically significant association with mortality. High CRP levels (more than 20 mg/L) in the first 48 h had a statistically significant association with more severe infection (p = 0.002) and mortality (p = 0.023; OR = 2.856 [95%CI 1.113–7.327]) but no statistically significant association with ICU admission. Severe infection led to higher mortality (p < 0.001; OR = 35.81 [95%CI 16.15–79.42]) (Table 4).

Other factors, namely having two or more comorbidities, RR of more than 24/min in the first 24 h, low lymphocyte count (<1 × 10^9/L), high PCT (>0.5 ng/mL), markers of end-organ damage: high aspartate transaminase (AST) levels (>37 units/L), high creatinine levels (>115 mcmol/L), high troponin I (>100 ng/L), and CXR infiltrates on arrival were all significantly associated with more severe disease, ICU admission, and mortality (Table 5).

Discussion

This detailed COVID-19 case series from a country endemic with MERS-CoV describes the clinical characteristics and risk factors in hospitalized patients aged 14 years and older with laboratory-confirmed SARS-CoV-2 infection during the peak months of the pandemic. This study is a follow-up to our first detailed case series, which emerged from KSA during the early months of the pandemic (Barry et al., 2020a). It reveals that a fifth of patients tested for COVID-19 were positive, and 23% required hospitalization. Of those, 26% required ICU care, which is a significant rise from the earlier months, in which only a tenth of all patients tested positive, 16% required hospitalization, and 22% required ICU care. In this analysis, the COVID-19 case fatality rate was 3.4% of all those who tested positive in our hospital, which is also a significant rise from 0.2% in the preceding months. Among all hospitalized patients, 15% died, and for the subset of patients requiring ICU admission, 46% died, compared to 12% and 50%, respectively, in the early months. As in the earlier cohort, from 194 (32%) patients who were also tested for MERS-CoV as per case definition, none had any evidence of co-infection.

In-hospital mortality was associated with advanced age (≥65 years), presence of comorbidities, severity of infection upon presentation, and presence of end-organ damage. In a study conducted in Georgia in the United States, the CFR was 17.1% for

Table 4
Diagnosis and treatment among hospitalized COVID-19 patients, King Saud University Medical City, Saudi Arabia.

Study variable	n (%)	Died n = 91 (%)	Survived n = 514 (%)
Diagnosis stratified based on experimental therapy			
Asymptomatic	93 (15.4)	2 (2.2)	91 (97.8)
- Acyclovir	1	0 (0)	1 (100)
- coricosteroids	6	0 (0)	6 (100)
Upper respiratory tract infection	30 (5)	0 (0)	30 (100)
- Hydroxychloroquine	1	0 (0)	1 (100)
- Acyclovir	1	0 (0)	1 (100)
- Favipiravir	1	0 (0)	1 (100)
- Coricosteroids	6	0 (0)	6 (100)
Mildmoderate pneumonia	269 (44.5)	5 (1.9)	264 (98.1)
- Hydroxychloroquine	4	0 (0)	4 (100)
- Lopinavir/Ritonavir.	1	0 (0)	1 (100)
- Favipiravir	2	0 (0)	2 (100)
- Remdesivir	1	0 (0)	1 (100)
- coricosteroids	145	2 (1.4)	143 (98.6)
- Tocilizumab	1	0 (0)	1 (100)
Severe pneumonia	107 (17.7)	12 (11.2)	95 (88.8)
- Hydroxychloroquine	1	0 (0)	1 (100)
- Lopinavir/ritonavir + ribavirin	1	0 (0)	1 (100)
- Favipiravir	1	0 (0)	1 (100)
- Remdesivir	2	0 (0)	2 (100)
- coricosteroids	97	10 (10.3)	87 (89.7)
- Tocilizumab	8	0 (0)	8 (100)
Critical pneumonia	106 (17.5)	72 (67.9)	34 (32.1)
- Lopinavir/ritonavir + ribavirin	5	3 (60)	2 (40)
- Favipiravir	2	2 (100)	0 (0)
- Interferon-beta 1	1	1 (100)	0 (0)
- coricosteroids	97	63 (64.9)	34 (35.1)
- Tocilizumab	28	18 (64.3)	10 (35.7)
Therapy duration			
Steroids, median = 9 days (IQR = 5)			
Favipiravir, median = 9.5 (Range 7–10)			
Remdesivir, duration = 10 days			
Lopinavir/ritonavir + ribavirin, median = 11.5 (IQR = 11)			
Other treatment			
Antibacterial:			
None	113 (18.7)	1 (0.9)	112 (99.1)
One antibacterial	82 (13.6)	8 (9.8)	74 (90.2)
Two or more antibacterial agents	410 (67.8)	82 (20)	328 (80)
Anticoagulant:	558 (92.2)		
- In-hospital DVT prophylactic anticoagulation	432 (77.4)	46 (10.6)	386 (89.4)
- In-hospital therapeutic anticoagulation for suspected PE, ACS, severe disease with high D-dimer	112 (20.1)	41 (36.6)	71 (63.4)
- Already on anticoagulation before COVID-19 diagnosis	14 (2.5)	1 (7.1)	13 (92.9)

IQR: interquartile range, ACS: acute coronary syndrome, PE: pulmonary embolism, DVT: deep venous thrombosis.

non-ICU cases and 30.6% for ICU cases (Gold et al., 2020). Another study from Detroit presented a similar CFR of 5.1% and 39% for general practice and ICU cases, respectively (Suleyman et al., 2020). In China, a meta-analysis of COVID-19 clinical characteristics revealed an overall CFR of 3.6% (Fu et al., 2020), while in the UK, a study of 20,133 patients showed a CFR of 26%, with the median age of victims being 80 years old (Docherty et al., 2020).

Hospital stay was notably longer among patients hospitalized during the peak (median 17 days) in comparison to those hospitalized at the beginning of the pandemic in KSUMC (median five days) (Barry et al., 2020a), which indicates worsening disease severity and an increase in severe/critical cases. These findings are consistent with findings from Wuhan, China, describing the clinical characteristics and outcomes of severe or critical COVID-19, which showed a mean hospital stay of 15 days (Li et al., 2020). Another study from China showed a mean hospital stay of eleven days in general and 21 days for severe/critical cases (Zhou et al., 2020). In the US, it was five days for non-severe cases and 15 days for severe cases requiring ICU admission (Suleyman et al., 2020).

The predominant symptoms were fever, cough, and dyspnea. Our cohort showed a higher percentage of dyspnea (65%) compared to other reports from KSA (27%) (Sarfraz et al., 2020), Turkey (27.8%) (Altunok et al., 2020), and China (6.9%) (Tian et al., 2020). Regarding the 160 patients admitted to the ICU, the fatality rate (CFR) was 47.6%. In comparison, a case series from Kuwait showed a similar CFR of 43.7% (Ayed et al., 2020), but was much less than that reported from Spain (72.9%) (Jiménez et al., 2020). There was no statistically significant difference in age group or gender for ICU admission, which is similar to other studies (Ayed et al., 2020; Jiménez et al., 2020). This could be attributed to a younger population with only 150 patients aged ≥65 years, while other cohorts had higher numbers (Richardson et al., 2020).

Upon admission, infiltrate on CXR was an independent risk factor for ICU admission and death with OR 4.042 [95%CI 2.593–4.848] and

Table 5
Factors associated with ICU admission and outcome among hospitalized COVID-19 patients, King Saud University Medical City, using univariate analysis.

Factors	Severe infection OR (95% CI) *	P value	ICU admission OR (95% CI)*	P value	Death OR (95% CI)*	P value
Demographic data						
Age ≥ 65 (vs. <65)	–	0.156	–	0.255	2.3 (1.4–3.7)	<0.001
Males (vs. Females)	1.7 (1.2–2.4)	0.004	–	0.100	–	0.700
BMI	–	0.502	–	0.342	–	0.365
Non-HCWs (vs. HCWs)	6.89 (1.6–29.4)	0.003	20.3 (1.2–334.7)**	0.035	–	0.109
Non-Saudi (vs. Saudi)	1.9 (1.3–2.6)	<0.001	1.7 (1.2–2.5)	0.004	–	0.982
Clinical data upon Presentation						
Presence of >1 comorbidity (vs. ≤1)	1.6 (1.2–2.3)	0.005	1.7 (1.2–2.5)	0.003	3.2 (2.0–5.0)	<0.001
Admitted initially to ICU (vs. Ward)	–	–	–	–	10.2 (6.0–17.1)	<0.001
Symptoms for ≤7 days (vs. >7 days)	–	–	–	0.418	3.2 (1.6–6.2)	<0.001
RR >24 breaths/min (vs. ≤ 24)	5.3 (3.7–7.7)	<0.001	4.6 (3.1–6.9)	<0.001	2.5 (1.6–4.0)	<0.001
SpO2 < 94 % (vs. ≥ 94%)	3.2 (2.2–4.5)	<0.001	2.4 (1.6–3.5)	<0.001	1.5 (1.0–2.350)	0.083
Laboratory findings and chest X-ray in the first 48 h of admission						
Lymphocyte count < 1 (vs. ≥ 1)	4.3 (3.0–6.2)	<0.001	3.9 (2.7–5.8)	<0.001	3.4 (2.1–5.5)	<0.001
D-dimer > 0.45 (vs. ≤ 0.45)	1.9 (1.0–3.6)	0.043	–	0.231	–	0.154
AST > 37 (vs. ≤ 37)	3.2 (2.2–4.6)	<0.001	2.4 (1.7–3.6)	<0.001	3.0 (1.8–4.9)	<0.001
Creatinine > 115 (vs. ≤ 115)	2.2 (1.5–3.3)	<0.001	2.5 (1.6–3.8)	<0.001	3.7 (2.3–6.0)	<0.001
Ferritin > 400 (vs. ≤ 400)	1.9 (1.3–2.7)	0.001	1.9 (1.3–2.9)	0.002	–	0.312
CRP > 20 (vs. ≤ 20)	2.5 (1.4–4.5)	0.002	1.7 (1.0–3.1)	0.084	2.9 (1.1–7.3)	0.023
PCT ≥ 0.5 (vs. < 0.5)	3.0 (1.9–4.9)	<0.001	3.5 (2.0–6.2)	<0.001	4.7 (2.0–11.2)	<0.001
IL-6 > 7 (vs. ≤ 7)	–	0.637	–	0.441	0.8 (0.7–0.8)	0.013
Trop I > 100 (vs. ≤ 100)	2.7 (1.3–5.8)	0.007	3.2 (1.5–6.6)	0.001	2.8 (1.3–6.1)	0.005
Infiltrate on initial CXR (vs. No infiltrate)	4.0 (2.6–4.8)	<0.001	2.4 (1.5–3.8)	<0.001	2.2 (1.2–3.9)	0.006

OR: odds ratio, CI: confidence interval, Ref: reference value, BMI: body mass index, HCW: health care worker, ICU: intensive care unit, RR: respiratory rate, SpO_2: oxygen saturation, AST: aspartate transaminase, CRP: c-reactive protein, PCT: procalcitonin, IL-6: interleukin-6, Trop-I: troponin I, CXR: chest x-ray.
* OR calculated for severity, ICU admission, and death, respectively
** Haldane-Anscombe corrected odds ratio.

2.192 [95%CI 1.233–3.898], respectively. This was not shown in other studies (Ayed et al., 2020), although they had a significant infiltrate rate upon presentation. Low lymphocyte count, high AST, acute kidney injury (AKI), and raised inflammatory markers (ferritin, CRP, and PCT) were all observed as factors associated with severe disease, ICU admission, and death, which is consistent with other studies (Lechien et al., 2020; Richardson et al., 2020).

The majority of pregnant women included in our study were asymptomatic, with no associations identified between gestational age and disease severity, which is consistent with the results of a large meta-analysis including published data from different countries and populations (Juan et al., 2020). COVID-19 status could not be retrieved for all neonates; however, no neonatal or maternal deaths were recorded.

Multiple drugs were used to manage hospitalized patients' conditions, and coticosteroids were commonly used among different disease spectra. Survival rates were compared between the five groups (asymptomatic, URTI, mild and severe pneumonia, and critically ill), and corticosteroids were found to be successful in the asymptomatic and those with pneumonia in addition to the severe group, compared with the critically ill patients, where the survival rate was poor, which is most likely secondary to hospital stay complications, including pulmonary embolism, cardiopulmonary arrest, and anoxic brain damage. The RECOVERY randomized control trial conducted among COVID-19 patients, where dexamethasone was given to 2104 patients and compared to 4321 patients managed by the standard of care, found that 28-day mortality was lower in the group who received dexamethasone while on oxygen therapy, either supplemental or invasive (The RECOVERY Collaborative Group, 2020). Another prospective meta-analysis in 1703 critically ill patients that compared systemic glucocorticoids with standard care showed that corticosteroids lowered 28-day mortality (Sterne et al., 2020).

Several drugs were used to manage COVID-19, including remdesivir (Sanders et al., 2020). In our center, remdesivir was given as part of the WHO Solidarity trial (WHO Solidarity Trial Consortium, 2020), although the number was quite low, no mortality was observed. A double-blind, randomized, placebo-controlled trial was conducted by Beigel et al. (2020) among 1062 patients who underwent randomization, with 541 assigned to remdesivir and 521 to placebo, it was found that remdesivir predicted a shorter recovery time in those with lower respiratory tract infection compared to the placebo group.

Triple therapy that includes protease inhibitors, interferon, and ribavirin was used for a small number of patients, also as part of the Solidarity trial (WHO Solidarity Trial Consortium, 2020). Of five patients in critical condition who received it, only two survived. A multicenter, prospective, open-label, randomized phase 2 trial in Hong Kong showed that early triple therapy was superior to lopinavir-ritonavir alone regarding shortening symptoms duration and hospital stay (Hung et al., 2020).

Tocilizumab is a monoclonal antibody against interleukin-6 (IL-6) (Luo et al., 2020). It was given to 28 critically ill patients with 18 mortalities. A cohort studying the association between early treatment with tocilizumab and mortality among critically ill patients with COVID-19 was conducted by Gupta et al., and the primary outcome of early treatment with tocilizumab showed lower in-hospital mortality rates (Gupta et al., 2020). Additionally, Salvarani et al. conducted a randomized clinical trial of hospitalized adult patients with COVID-19 pneumonia and did not show any disease progression benefit compared to standard of care (Salvarani et al., 2020). Hydroxychloroquine was also used initially for a few patients as part of the Solidarity trial but was soon discontinued when its use was revoked (US Food and Drug Administration, 2020). None of the six patients who received it died; however, only one had severe disease.

Study limitations

Our study has several limitations, including data emerging from a single-center, lack of data on viral load, and epidemiological data. Only a third of patients were tested for MERS-CoV infections.

Conclusion

In conclusion, this follow-up case series found a significant increase in the number of severe cases of COVID-19, predominantly in male patients younger than 65 years old. Mortality was associated with older age, multiple comorbidities, shorter symptom duration, tachypnea, abnormal CXR on admission, direct admission to ICU, low lymphocyte count, high CRP, and evidence of end-organ damage. No MERS-CoV co-infections were detected.

Availability of data and materials

All the data for this study will be made available upon reasonable request to the corresponding author.

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Conflict of interest

None declared.

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