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Original article

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) coinfection: A unique case series

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ABSTRACT

Introduction: The emergence of the Severe Acute Respiratory Syndrome Coroanvirus 2 (SARS-CoV-2) had raised possibilities of coinfection with the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in countries were these two viruses were reported. In this study, we describe the clinical presentation and demographics of eight patients who were coinfected with SARS-CoV-2 and MERS-CoV.

Materials and methods: This is a case series of hospitalized patients admitted to intensive care units (ICUs). We collected demographics, underlying conditions, presenting symptoms and clinical outcome from the patients' medical records.

Results: During the study period from March 14, 2020 to October 19, 2020, there was a total of 67 SARS-CoV-2 ICU admitted patients who underwent simultaneous SARS-CoV-2 and MERS-CoV testing by PCR. Of those patients, 8 (12%) tested positive for both SARS-CoV-2 and MERS-CoV. There were 6 (75%) males, the mean age ± SD was 44.4 ± 11.8 years, and 7 (87.5%) were obese. Of the patients, 7 (87.5%) were non-smokers, 1 (12.5%) had diabetes mellitus, 1 (12.5%) had heart failure, and 1 (12.5%) had been on anti-platelet therapy. The mean hospital length of stay (LOS) was 21.1 ± 11.6 days and the average ICU LOS was 10.9 ± 6.03 days. All patients received supportive therapy and all were treated with corticosteroid. Of all the patients, 4 (50%) were discharged home and 3 (37.5%) died.

Conclusion: This case series is an important addition to the medical knowledge as it showed the interaction of the coinfection of SARS-CoV-2 and MERS-CoV.

1. Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged at the end of 2019 and had caused the current CoronaVirus Disease 19 (COVID-19) pandemic. COVID-19 had been associated with tremendous medical challenges as well as societal and industrial

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interruption [1]. COVID-19 clinical presentation ranges from asymptomatic to severe disease [2–6]. And the case fatality rate of COVID-19 is variable [7,8]. The clinical characteristics of the disease in Saudi Arabia is similar to other reported presentations [4–6,8,9].

Recently, there had been few reports of coinfection of different micro-organisms with SARS-CoV-2. Coinfections with SARS-CoV-2 were reported with influenza, other respiratory pathogens, herpes simplex virus (HSV) and human immune deficiency virus (HIV) [10–15]. In the Kingdom of Saudi Arabia (KSA), the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is of particular concern as KSA is the country where MERS-CoV had been initially identified in 2012 [16–18]. One particular characteristic of MERS-CoV is the ability to cause healthcare associated outbreaks [19–21].

In addition, MERS-CoV is of particular importance as it has about 35% case fatality rate [22].

The first case of COVID-19 was reported in Saudi Arabia on March 2nd, 2020 [6,9]. However, we are not aware of any reports of coinfection of SARS-CoV-2 and MERS-CoV. In an initial cohort of 99 patients of SARS-CoV-2, none of them had coinfection with MERS-CoV [23]. Here, we describe the clinical and demographics of patients who were coinfected with SARS-CoV-2 and MERS-CoV.

2. Materials and methods

This is a case series of hospitalized patients admitted to intensive care units (ICUs) from March 14, 2020 to October 19, 2020. We collected demographics, underlying conditions, presenting symptoms and clinical outcome from the patients' medical records. Nasopharyngeal swabs were tested for the presence of MERS-CoV *upE* and *orf1a* [24, 25] and for SARS-CoV-2 *E* and *S* genes using the RealStar® SARS-CoV-2 real-time Reverse Transcriptase PCR (RT-PCR) as described previously [6,23,26]. The study was approved by the IRB of the Central IRB of Ministry of Health (Log No: 20-80E).

3. Results

3.1. Case summaries

During the study period, there was a total of 67 SARS-CoV-2 patients who were admitted to the ICUs and underwent simultaneous SARS-CoV-2 and MERS-CoV testing by PCR at the discretion of the treating physicians. Of those patients, 8 (12%) tested positive for both SARS-CoV-2 and MERS-CoV.

3.2. Demographics and clinical characteristics

Of the eight patients, there were 6 (75%) males. The mean age ±SD was 44.4 ± 11.8 years and the mean Body Mass Index (BMI) was 31 ± 4.7. Based on BMI, 1 (12.5%) had normal BMI and 7 (87.5%) were obese and of these 2 (25%) were overweight (BMI 25–29.9), 3 (36.5%) were obese (BMI: 30–34.9), and 2 (25%) had extreme obesity (BMI: > 35) (Table 1).

One patient (12.5%) was Saudi and 1 (12.5%) was a healthcare worker. Of the patients, 7 (87.5%) were non-smokers, 1 (12.5%) had diabetes mellitus, 1 (12.5%) had heart failure, and 1 (12.5%) had antiplatelet therapy. None of the patients had hypertension, ischemic heart disease, chronic obstructive pulmonary disease (COPD), asthma, liver disease; hemoglobinopathy; chronic kidney disease (CKD); renal

Table 1
Characteristics, clinical presentation and outcome of ICU MERS-CoV and SARS-CoV-2 coinfected patients.

Patient Number	1	2	3	4	5	6	7	8
ICU LOS (days)	18	7	12	21	8	3	11	7
Hospital LOS (days)	18	19	39	31	29	4	20	9
Age (years)	48	36	36	39	33	52	69	42
Gender	Male	male	male	female	male	male	female	male
Was patient Saudi or non-Saudi?	non-Saudi	non-Saudi	non-Saudi	non-Saudi	non-Saudi	non-Saudi	non-Saudi	Saudi
BMI	32.8	38.1	31.9	23.9	29.0	31.1	35.2	26.0
Was the case in close contact with a person with fever and/or cough who has been to an affected area?	not indicated	not indicated	not indicated	not indicated	not indicated	No	No	Yes
Current smoker	No	no	no	no	unknown	no	no	no
Diabetes mellitus	No	no	no	no	no	no	yes	no
Hypertension	no	no	no	no	no	no	no	no
Ischemic heart disease	no	no	no	no	no	no	no	no
Heart failure (ejection fraction < 50%)	no	no	no	no	no	no	yes	no
Chronic Lung disease	no	no	no	no	unknown	no	no	no
Duration of symptoms prior to hospital admission	1	4	4	2	2	asymptomatic	4	4
Shortness of breath (Dyspnoea)	yes	yes	yes	yes	yes	yes	yes	yes
Runny nose (rhinorrhoea)	yes	unknown	no	no	unknown	no	yes	no
Gastrointestinal symptoms (Diarrhea/vomiting)	yes	unknown	no	no	unknown	yes	yes	yes
History of fever	yes	yes	yes	yes	yes	yes	no	yes
Altered consciousness/confusion	no	unknown	no	no	unknown	no	no	yes
Cough	yes	yes	yes	yes	yes	yes	no	yes
Hospital Admission Mean BP (mmHg)	101	85		73	129	82	109	91
Heart rate (beats/minute)	86	85		103	110	104	96	90
Respiratory rate (breaths/minute)	32	22		24	20	20	25	17
Oxygen saturation (on room air) (%)	75	81		88	96	88	94	98
Temperature (highest within the first 24 h) (°C)	38	38.3		38.1	39	39.6	37.2	38.6
Glasgow Coma Score (GCS)	15	15		15	10	15	15	15
Chest X-ray - Consolidation	yes	no	yes	yes	yes	no	no	yes
CXR infiltrate on admission	bilateral	no	bilateral	bilateral	bilateral	no	no	bilateral
ICU admission PH value	7.28	7.415	7.37	7.44	7.411		7.49	
PCO2 value (mmHg)	55.9	41.1	36.1	39.9	36.6		51	
PaO2 value (mmHg)	95.9	61.8	207	60	89		71	
O2 Saturation (%)	96.6	91.7	99.8	93	97.7		99	91
Intubated and mechanically ventilated	yes	yes	yes	yes	yes	yes	yes	no
Hospital discharge outcome	death	home	death	home	home	transferred out	death	home

ICU: intensive care unit; LOS: length of stay; BMI: body mass index; CXR: chest x-ray.

replacement; immunocompromised; transplant; malignancy; or recent surgery.

3.3. Symptoms

All patients had shortness of breath, 2 (25%) had runny nose, 4 (50%) had gastrointestinal (GI) symptoms, and 7 (87.5%) had history of fever. Altered consciousness/confusion was present in 1 (12.5%), cough in 7 (87.5%), abdominal pain in 6 (75%), headache in 1 (12.5%), chest pain in 1 (12.5%), arthralgia, myalgia, and fatigue each was present in 12.5%, and sore throat in 3 (37.5%).

3.4. Hospital course

The initial mean and SD of laboratory tests are shown in Table 2. The mean hospital length of stay (LOS) was 21.1 ± 11.6 days, the average ICU LOS was 10.9 ± 6.03 days. The initial mode of oxygen delivery was face mask (1; 12.5%), non-rebreather mask (NRM) (4; 50%), and mechanical ventilation (3; 37.5%). However, eventually 7 (87.5%) required mechanical ventilation and the average duration of mechanical ventilation was 6.67 (±5.9) days. All patients received supportive therapy and all were treated with corticosteroid. The patients did not recieve specific anti-viral therapy. Of all the patients, 1 (12.5%) was transferred to another facility, 4 (50%) were discharged home and 3 (37.5%) died.

4. Discussion

This case series is a unique contribution to the medical literature by examining coinfection of two emerging respiratory pathogens, MERS-CoV and SARS-CoV-2. These two viruses had the chance to cause significant disease in the Kingdom of Saudi Arabia. The country had gained great experience from previous MERS-CoV infection and had adopted a significant infection control and preventative measures [27]. Coinfection of SARS-CoV-2 and other respiratory viruses had been reported [10–15]. In addition, there few cases of coinfection of MERS-CoV and influenza or tuberculosis [28,29]. Here, we report coinfection of MERS-CoV and SARS-CoV-2 in admited patients. In an initial cohort of 99 cases who were tested simultaneously for MERS-CoV and SARS-CoV-2, none of them had SARS-CoV-2 and MERS-CoV coinfection [23]. In the current study, 12% of the tested patients were positive for both SARS-CoV-2 and MERS-CoV. It was reported that in the past few years, MERS-CoV positivity rates among suspected cases was 2–6% [30]. The difference in these two estimates is likely related to the population of patients being tested.

The included patients were relatively young with a mean age ±SD of 44.4 ± 11.8 years. Previously, the mean age of COVID-19 patients in Saudi Arabia was 36–50 years [6,31] and a median age 44 years [23]. The presence of comorbidities in patients with SARS-CoV-2 ranges from 32% to 93% in different studies [32–34]. One half of the included patients had gastrointestinal symptoms. Previously, gastrointestinal symptoms were reported in 33% of MERS-CoV patients [24,25,35–38], and 29% of COVID-19 patients had gastrointestinal symptoms [39] and another study showed higher rate of diarrhea in elderly patients [40]. In addition, the majority of hospitalized MERS-CoV patients had fever, cough and shortness of breath in addition to pneumonia on chest x-ray [24,25,35,41].

This case series showed that 37.5% of ICU coinfected patients had died. Previous studies of MERS-CoV showed a case fatality rate of 30% with increasing rate among those with comorbidities [24], critical ill patients, severe disease, those > 65 years of age, hospital-acquired infections and corticosteroid use [35,42–48]. However, the use of corticosteroid was associated with decreased case fatality rate in randomized controlled trials of COVID-19 patients from 25.7% in standard therapy to 22.9% in the dexamethasone group [49]. In addition, there is a variation in the case fatality rates among different countries and different time intervals and ranged from 60% in March 2020 to 42% in May 2020 [50]. The epidemiology of MERS-CoV infection is Saudi Arabia is well characterized by sporadic cases from camel exposure followed by either hospital [19–21] or community transmission [51–53]. However, we were not able to pinpoint the exact exposure of infection of the included patients.

The initial laboratory findings of the included patients showed normal WBC and lymphocyte counts. However, the mean ± SD of the neutrophils to lymphocyte count ratio (NLCR) was 10.14 (8.77). The NLCR of ≥3.13 is a predictor of ICU admission and a marker of disease severity [32]. A previous study from Saudi Arabia showed that NLCR was significantly higher among ICU admissions than other patients [6]. We did not examine the duration of viral shedding in this study. A previous meta-analysis showed that the mean shedding duration of MERS-CoV was 15·3 days in the upper respiratory tract and 16·3 days in the lower respiratory tract. On the other hand, in COVID-19 patients the shedding of SARS-CoV-2 had a mean duration of 17 days in upper respiratory tract and 14·6 days in lower respiratory tract [54]. It was stated that SARS-CoV-2 viral loads peak about 10 days after symptoms onset [55,56].

In conclusion, this case series is important as it showed the interaction of the coinfection of SARS-CoV-2 and MERS-CoV. However, in this small case-series the combined infection was not associated with increased risk of death in comparison with mono-infection with MERS-CoV. However, as there was one patient who is transferred to another facility and lost to follow-up and if that patient died then the mortality would be 50%. Thus, additional studies are required to confirm or refute this finding and it is not possible to draw a firm conclusion about the mortality in co-infected MERS-CoV and SARS-CoV-2 patients. The presenting symptoms and laboratory data are not different from each of the infection alone. Although, 7 (87.5%) of the coinfection of MERS-CoV and SARS-CoV-2 were in the ICU, this is related to the fact that all tested and included patients were ICU patients. Thus, a firm conclusion could not be drawn in regard to the epidemiology, clinical presentation and outcome of this type of coinfection. With the continued COVID-19 pandemic, there is a continued need to continue precautionary measures including social distancing, hand hygiene and universal masking. These measures continued to be enforced in the Kingdom of Saudi Arabia [9,57]. Moreover, KSA implemented universal masking in public and common areas as these measures are important for the control of COVID-19 [58,59].

Table 2
Initial mean and SD of laboratory tests of patients coinfected with SARS-CoV-2 and MERS-CoV.

Laboratory (normal range)	Mean and Standard Deviation of Data on Hospital Admission
Hgb (13–17 mg/dl)	13.12 (1.96)
WBC (4–11 × 10^9/L)	8.29 (4.03)
Absolute Lymphocyte (0.90–2.90 × 10^9/L)	1.55 (1.23)
Absolute Neutrophil (1.70–7 x 10^9/L)	9.13 (3.26)
Neutrophils/Lymphocyte ratio (1–3)	10.14 (8.77)
Platelets (150–450 × 10^9/L)	247.4 (76.9)
aPTT (30–40 s)	32.23 (5.56)

Hgb: hemoglobin; WBC: white blood celss; aPTT: activated partial thromboplastin time.

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CRediT authorship contribution statement

Alyaa Elhazmi: conceptual design, Data curation, Formal analysis,

Helped with the first draft of the manuscript, All authors finalized and approved the final draft of the manuscript. **Jaffar A. Al-Tawfiq:** conceptual design, Formal analysis, drafted the first manuscriptAll authors finalized and approved the final draft of the manuscript. **Hend Sallam:** Data curation, Formal analysis, All authors finalized and approved the final draft of the manuscript. **Awad Al-Omari:** conceptual design, Data curation, Formal analysis, All authors finalized and approved the final draft of the manuscript. **Saad Alhumaid:** Data curation, Formal analysis, All authors finalized and approved the final draft of the manuscript. **Ahmad Mady:** Data curation, Formal analysis, All authors finalized and approved the final draft of the manuscript. **Abbas Al Mutair:** conceptual design, Data curation, Formal analysis, Helped with the first draft of the manuscript, All authors finalized and approved the final draft of the manuscript.

Declaration of competing interest

None.

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