Journal of Multidisciplinary Healthcare

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Comorbidities and Risk Factors for Severe Outcomes in COVID-19 Patients in Saudi Arabia: A Retrospective Cohort Study

Fatema S Shaikh[1]
Nahier Aldhafferi[1]
Areej Buker[1]
Abdullah Alqahtani[1]
Subhodeep Dey[2]
Saema Abdulhamid[1]
Dalal Ali Mahaii AlBuhairi[1]
Raha Saud Abdulaziz Alkabour[1]
Waad Sami O Atiyah[1]
Sara Bachar Chrouf[1]
Abdussalam Alshehri[3]
Sunday Olusanya Olatunji[1]
Abdullah M Almuhaideb[1]
Mohammed S Alshahrani[4]
Yousof AlMunsour[1]
Vahitha B Abdul-Salam[5]

[1]College of Computer Science and Information Technology, Imam Abdulrahman Bin Faisal University, Dammam, Eastern Province, Saudi Arabia; [2]Indian Institute of Management – Calcutta, Kolkata, India; [3]Prince Mohammed bin Abdulaziz Hospital, Riyadh, Saudi Arabia; [4]College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Eastern Province, Saudi Arabia; [5]Centre for Cardiovascular Medicine and Device Innovation, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Purpose: The first novel coronavirus disease-19 (COVID-19) case in the Kingdom of Saudi Arabia (KSA) was reported in Qatif in March 2020 with continual increase in infection and mortality rates since then. In this study, we aim to determine risk factors which effect severity and mortality rates in a cohort of hospitalized COVID-19 patients in KSA.

Method: We reviewed medical records of hospitalized patients with confirmed COVID-19 positive results via reverse-transcriptase-polymerase-chain-reaction (RT-PCR) tests at Prince Mohammed Bin Abdulaziz Hospital, Riyadh between May and August 2020. Data were obtained for patient's demography, body mass index (BMI), and comorbidities. Additional data on patients that required intensive care unit (ICU) admission and clinical outcomes were recorded and analyzed with Python Pandas.

Results: A total of 565 COVID-19 positive patients were inducted in the study out of which, 63 (11.1%) patients died while 101 (17.9%) patients required ICU admission. Disease incidences were significantly higher in males and non-Saudi nationals. Patients with cardiovascular, respiratory, and renal diseases displayed significantly higher association with ICU admissions ($p<0.001$) while mortality rates were significantly higher in COVID-19 patients with cardiovascular, respiratory, renal and neurological diseases. Univariate cox proportional hazards regression model showed that COVID-19 positive patients requiring ICU admission [Hazard's ratio, HR=4.2 95% confidence interval, CI 2.5–7.2); $p<0.001$] with preexisting cardiovascular [HR=4.1 (CI 2.5–6.7); $p<0.001$] or respiratory [HR=4.0 (CI 2.0–8.1); $p=0.010$] diseases were at significantly higher risk for mortality among the positive patients. There were no significant differences in mortality rates or ICU admissions among males and females, and across different age groups, BMIs and nationalities. Hospitalized patients with cardiovascular comorbidity had the highest risk of death (HR=2.9, CI 1.7–5.0; $p=0.020$).

Conclusion: Independent risk factors for critical outcomes among COVID-19 in KSA include cardiovascular, respiratory and renal comorbidities.

Keywords: COVID-19, SARS-CoV-2, mortality rate, comorbidities, risk factors, KSA

Introduction

The Ministry of Health (MOH) of the Kingdom of Saudi Arabia (KSA) reported 4 new cases of Covid-19 on March 9, 2020, 7 days after the first positive case was identified.[1] COVID-19 infection occurs from airborne exposure to the virus, particularly through droplets/aerosols during coughing or sneezing and physical contact with infected person and objects[5,6] via nasal, oral or fecal route[2] spreading quickly via infected travelers. The first case in KSA was reported in a traveler from Iran to

Correspondence: Fatema S Shaikh
Tel +966-5591660024
Email fsshaikh@iau.edu.sa

Received: 4 May 2021
Accepted: 30 June 2021
Published: 12 August 2021

Qatif[3,4] and confirmed COVID-19 incidences rose to 3717 as of June 10, 2020 with over 308,600 cases and 3600 deaths estimated by August 24, 2020.[5,6] So far, KSA has the highest COVID-19 mortality rate in the Gulf Cooperation Council (GCC) region after Iran and Iraq, and has the third highest positive cases in the Middle East region.[7] Riyadh has the highest number of residents and citizens infected with SARS-CoV-2 in KSA (https://covid19.moh.gov.sa/).

Several complications are associated with COVID-19 infections, which enhance the morbidity and mortality rates.[8] Previous studies have identified poor/weak health-care systems and failure to adhere to precautionary measures as high contributory factors to infection rates especially in poor to low-income countries.[9,10] High risks of severity and mortality have been widely reported in older persons infected with COVID-19, a finding that has been consistent in several countries.[11–13] Surgical procedures especially transplants and pre-existing comorbidities, such as hypertension, obesity, diabetes mellitus (DM), cardiovascular disease, respiratory diseases, malignancies, and other chronic, non-communicable diseases reportedly worsen clinical outcomes in COVID-19 patients, thereby increasing fatality rates.[14,15]

Current global data revealed a 4.8% case fatality ratio (CFR) in China, 5.8% in the USA, 3.5% in Italy, 2.4% in France, 2.7% in the United Kingdom, 2.5% in Brazil, and 1.7% in KSA (https://ourworldindata.org/covid-mortality-risk). About 348 new cases are currently being recorded daily in KSA and total deaths currently stand at 6869 (retrieved 04-24-2021 from Data https://github.com/CSSEGISandData/COVID-19). Decreasing CFR in KSA could be due to multiple swift measures introduced by KSA's government to mitigate the spread of the virus or the recent exposures to MERS-CoV epidemic.[16,17]

In an early data (March 2020) involving 1519 confirmed COVID-19 cases with average mean age of 36 years from KSA, hypertension was the most common comorbidity with a 8.8%, followed by Diabetes Mellitus (DM) with a 7.6% rate.[18] Notwithstanding, despite the increases in fatality rates among COVID-19 patients in KSA, clinical data on contributory risk factors are insufficient. Therefore, this present study aims to describe the demography, clinical characteristics and comorbidities of infected patients, and identify the risks they contribute to the severity and mortality rates for the disease.

Methodology

Study Population

In this retrospective study, all patients above 18 years old who were COVID-19 positive and hospitalized at Prince Mohammed Bin Abdulaziz Hospital (PMAH), Riyadh, KSA from May to August 2020 were included. PMAH is a government-owned 500-bed hospital situated in the eastern part of Riyadh and one of the largest referral hospitals in KSA providing secondary healthcare to various acute or chronic medical conditions that excludes pediatric and gynecological. It houses 2 emergency, 36 medical and 9 intensive care units. These were isolated via HEPA filters during the COVID-19 pandemic to provide emergency services for diagnosed COVID-19 patients. A positive Covid-19 result was determined by reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of specimens collected by a nasopharyngeal swab. The diagnoses followed guidelines approved by the Saudi Center for Disease Prevention and Control. This study has been approved by the Institutional Review Board (IRB) managed by the Deanship of Scientific Research at Imam Abdulrahman Bin Faisal University in Dammam, KSA.

Data Collection and Analysis

The retrieved clinical information included patient's demographics, BMI, and comorbidities, which encompass hypertension, DM, cardiovascular, respiratory, renal, neurological, liver diseases, cancer and other diseases. Data on hospital's Intensive Care Unit (ICU) admission and non-admission were also collected to determine the disease severity. Ages were categorized into seven groups; 20–29; 30–39; 40–49; 50–59; 60–69; 70–79 and >79 years while the BMIs were classified into three groups; ≥30, ≥35 and ≥40.

Analyses were then performed using Python Pandas. Categorical variables evaluated in this study were compared using the Chi Square test. Demographic data in addition to patients' comorbidities were presented as percentages, median and interquartile range (IQR) while the Kaplan-Meier estimator was used to evaluate the survival functions of the different variables. Matplotlib was used for visualization, SciPy for performing Chi Square test, and lifelines for survival analysis. Univariate and multivariate logistic regression methods were used to adjust for the effects of patient's age, gender, comorbidities and the outcomes. *P*-values ≤0.05 were considered significant.

Results

A total of 565 patients hospitalized with COVID-19 at Prince Mohammed Bin Abdulaziz Hospital, Riyadh, KSA were inducted in the study. Patients were stratified based on their ICU admission and mortality rates (Table 1). The majority of the patients were males (75.6%) while distribution based on nationality further revealed that 79.7% of the males were non-nationals (Table 1).

From the total 565 patients, 30.4% had a BMI greater than 30, 14.0% had a BMI greater than 35 while 6.9% had a BMI greater than 40. Comorbidities were present in most of the patients, with respiratory diseases being the most common (46.9%), followed by DM (41.6%). Other reported comorbidities were hypertension (33.8%), cardiovascular (17.0%), renal (14%), neurological (7.3%), cancer (1.8%), and liver (0.4%) diseases. Most patients in the older age-groups required ICU admission which indicated increased disease severity among this group. Requirement for ICU admission was more prevalent in males compared to females (18.2% vs 16.8%) while most patients with BMI ≥ 30 needed ICU admission compared to those with BMI ≥ 35 and BMI ≥ 40 (15.1% vs 13.9% vs 7.8%). A higher proportion of non-Saudi nationals were admitted to the ICU relative to Saudi nationals (18.7% vs 15.3%). However, none of the patients' characteristics significantly determined the need for ICU admission. There was no significant difference in COVID-19 patients with hypertension, DM, cancer, neurological, liver and other comorbidities that required intensive care compared to patients which did not. Relatively, there was a significant need in COVID-19 patients with renal, cardiovascular and respiratory diseases for ICU admission (p<0.001) indicative of higher severities in patients with these comorbidities.

Kaplan-Meier survival analysis curve showed a trend that survival time was shortest in patients in age-group 50–59 years, although not significantly different from other age-groups (Figure 1A–E). Similarly, there were no significant differences in the survival time between Saudi nationals and non-nationals coupled with persons having BMIs <40 and ≥40. Although the trend for survival time seemed to be shorter in females, it is also not significantly different from males (Figure 2B–E). However, survival time is significantly shortened in patients admitted at the ICU (p<0.001). Patients with cardiovascular, respiratory and renal comorbidities had significantly shorter survival time (p<0.001) than those with hypertension, DM and other diseases (Figure 2A–I). Neurological comorbidities also showed increased mortality rates in COVID-19 patients (p=0.04). The overall mortality rate is 11.2% and as observed, none of the patients' characteristics had significant effects on the rate of deaths among the COVID-19 patients. Likewise, there was no significant difference in mortality rates among patients with hypertension, DM, cancer, neurological and liver diseases. However, a higher number of patients with cardiovascular, respiratory and renal diseases died compared to those with other comorbidities (p<0.001). Also, we noted a significant difference in the mortality rate of patients with neurological comorbidities (p=0.04).

Univariate cox proportional hazards regression model revealed that age [HR=1.3 (CI 1.1–1.5)], BMI ≥ 40 [HR=0.2 (CI 0.0–1.5)], nationality [HR=1.3 (CI 0.7–2.2)], and gender [HR=0.7 (CI 0.4–1.3)] were not significant risk factors associated with death among the hospitalized COVID-19 patients. Likewise, hypertension [HR=1.1 (CI 0.7–1.9)], diabetes [HR=1.1 (CI 0.7–1.9)], renal [HR=2.4 (CI 1.4–3.9)], cancer [HR=2.4 (CI 0.9–6.5)], neurological [HR=1.3 (CI 0.7–2.4)], and other [HR=1.3 (CI 0.7–2.5)] comorbidities do not present any significant risk to patients' fatalities (Table 2, Figures 3A, B, D, E, H and I and 4A–D). Comparatively, mortality rates significantly increased among ICU admissions [HR=4.2 (CI 2.5–7.2); p<0.005], patients with cardiovascular diseases [HR=4.1 (CI 2.5–6.7); p<0.005] or respiratory diseases [HR=4.0 (CI 2.0–8.1); p<0.005] (Figure 3C, F and G). Multivariate cox proportional hazards regression model further emphasized cardiovascular disease [HR=2.9 (CI 1.7–5.0); p<0.005] as a major risk factor that significantly contributed to death rates among the hospitalized COVID-19 patients (Figure 5A). This was also supported by the Kaplan Meier Survival function analyses plot for the most significant risk factors (ICU admission, cardiovascular and respiratory diseases) relative to other variables (Figure 5B).

Discussion

This study investigates the demographics, characteristics and comorbidities of COVID-19 patients hospitalized at Prince Mohammed Bin Abdulaziz Hospital, Riyadh, KSA as risk factors or predictors that may contribute to disease severity (defined by admission at the ICU) and death rate. We aimed at identifying the correlation between these variables and how they influence clinical outcomes as previously enumerated in KSA. Hence, to the best of our

Table 1 Patients' Characteristics

Variable	Total Patients	Percent of Total	Non-ICU	ICU	Percent of ICU	p-value (ICU vs Non-ICU)	Died	Mortality Rate	p-value (Died vs Alive)
Total patients	565	100.0%	464	101	17.9%	<0.001	63	11.2%	<0.001
AgeGroup 20–29	30	5.3%	25	5	16.7%	0.946	3	10.0%	0.926
AgeGroup 30–39	82	14.5%	72	10	12.2%	0.195	4	4.9%	0.078
AgeGroup 40–49	131	23.2%	110	21	16.0%	0.618	9	6.9%	0.106
AgeGroup 50–59	152	26.9%	122	30	19.7%	0.564	14	9.2%	0.461
AgeGroup 60–69	106	18.8%	87	19	17.9%	0.900	19	17.9%	0.022
AgeGroup 70–79	48	8.5%	37	11	22.9%	0.450	10	20.8%	0.047
AgeGroup >79	15	2.7%	10	5	33.3%	0.214	4	26.7%	0.129
Gender Female	137	24.3%	114	23	16.8%	0.800	17	12.4%	0.703
Gender Male	428	75.8%	350	78	18.2%	0.800	46	10.8%	0.703
BMI ≥ 30	172	30.4%	146	26	15.1%	0.311	12	7.0%	0.052
BMI ≥ 35	79	14.0%	68	11	13.9%	0.406	5	6.3%	0.202
BMI ≥ 40	39	6.9%	36	3	7.7%	0.133	1	2.6%	0.133
Non Saudi National	434	76.8%	353	81	18.7%	0.448	46	10.6%	0.549
Saudi National	131	23.2%	111	20	15.3%	0.448	17	13.0%	0.549
Hypertension	191	33.8%	154	37	19.4%	0.584	28	14.7%	0.080
Diabetes	235	41.6%	180	55	23.4%	0.005	33	14.0%	0.088
Cardiovascular Diseases	96	17.0%	57	39	40.6%	<0.001	36	37.5%	<0.001
Respiratory Diseases	265	46.9%	192	73	27.6%	<0.001	54	20.4%	<0.001
Renal Diseases	84	14.9%	40	44	52.4%	<0.001	32	38.1%	<0.001
Cancer	10	1.8%	9	1	10.0%	0.811	4	40.0%	0.016
Neurological Diseases	41	7.3%	28	13	31.7%	0.029	12	29.3%	<0.001
Liver Diseases	2	0.4%	1	1	50.0%	0.792	1	50.0%	0.533
Others Diseases	55	9.7%	40	15	27.3%	0.084	13	23.6%	0.004

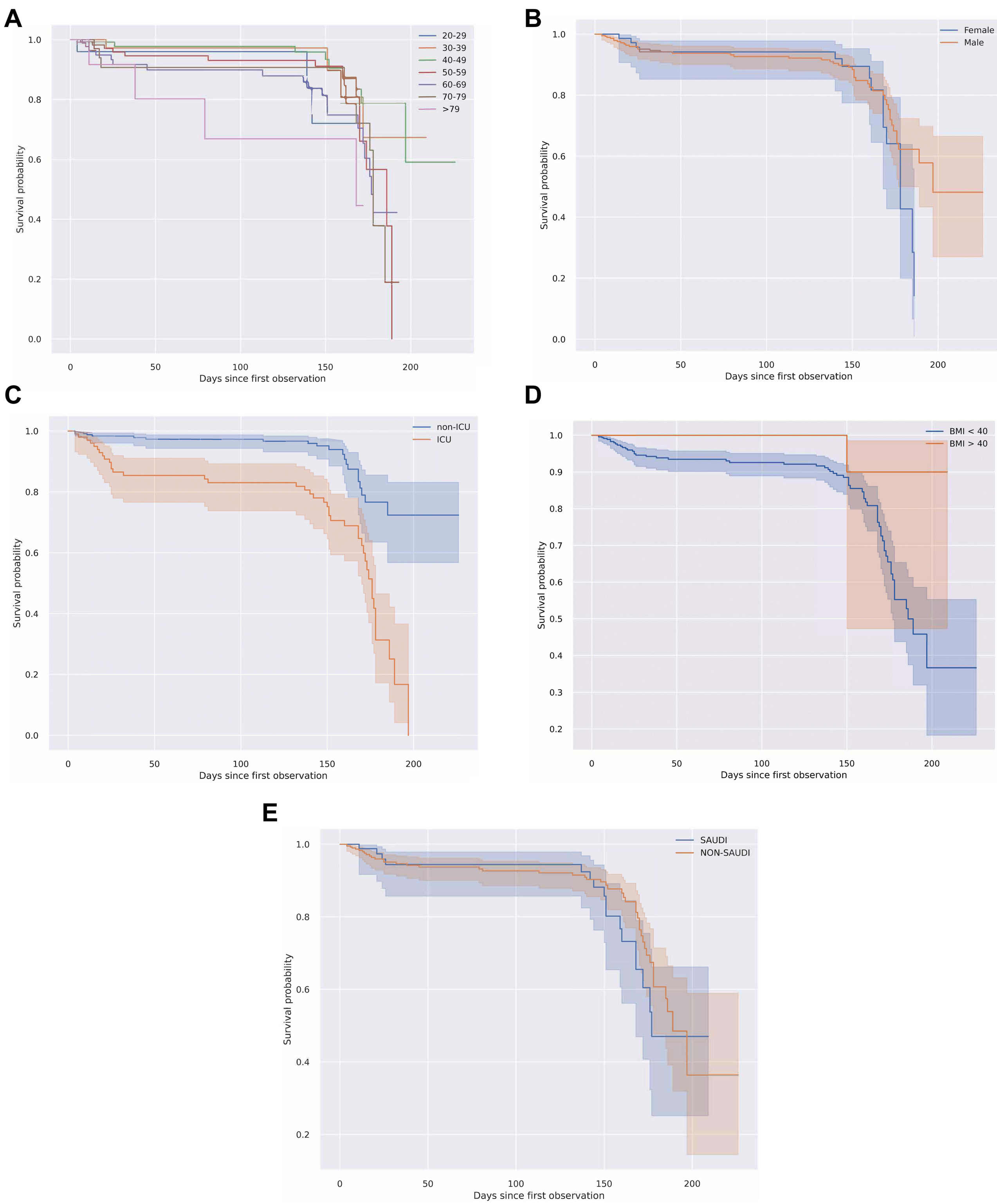

Figure 1 Kaplan Meier survival function analyses of the patients' characteristics investigated for (**A**) Age groups, (**B**) Gender, (**C**) ICU/non-ICU, (**D**) BMI, and (**E**) Nationality.

knowledge, this is first of few studies that succinctly describe the characteristics of a large cohort of hospitalized COVID-19 patients in Riyadh, KSA.

In this study, 75.75% were males compared to the remaining 24.25% that were females, in agreement with recent studies,[19–21] and in contrast to some other studies

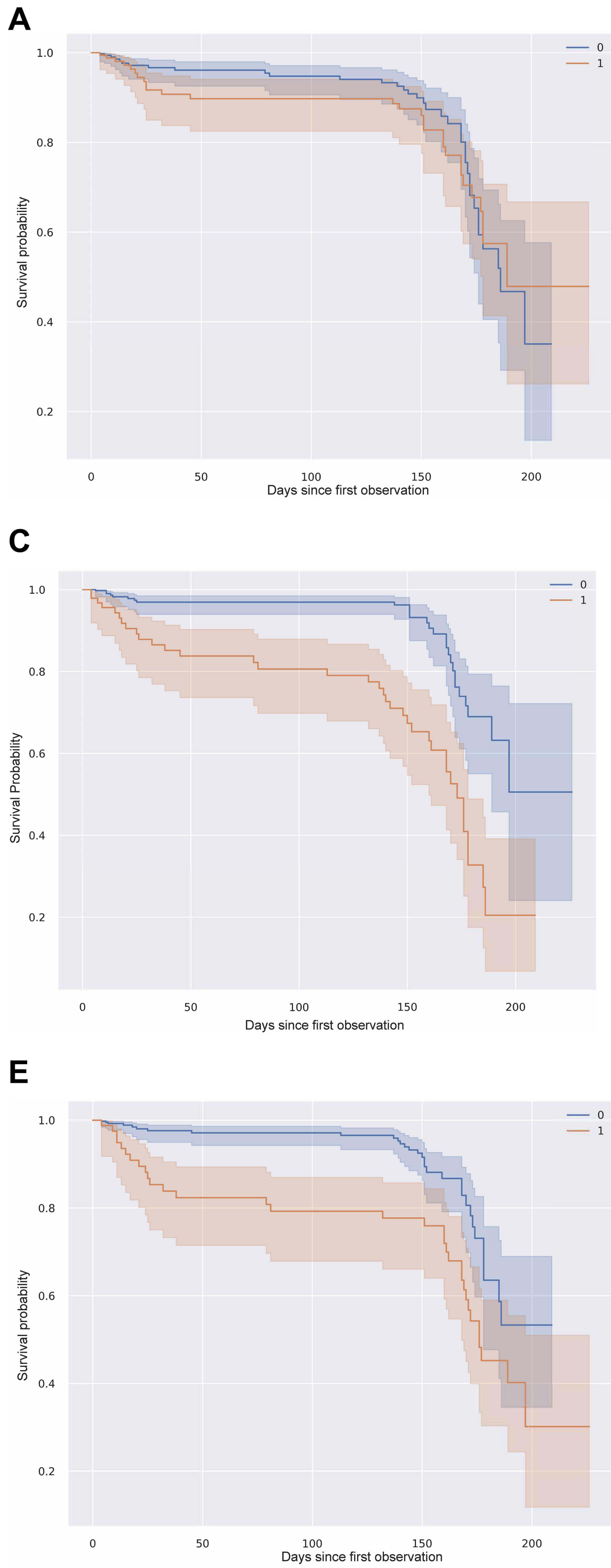

Figure 2 Continue.

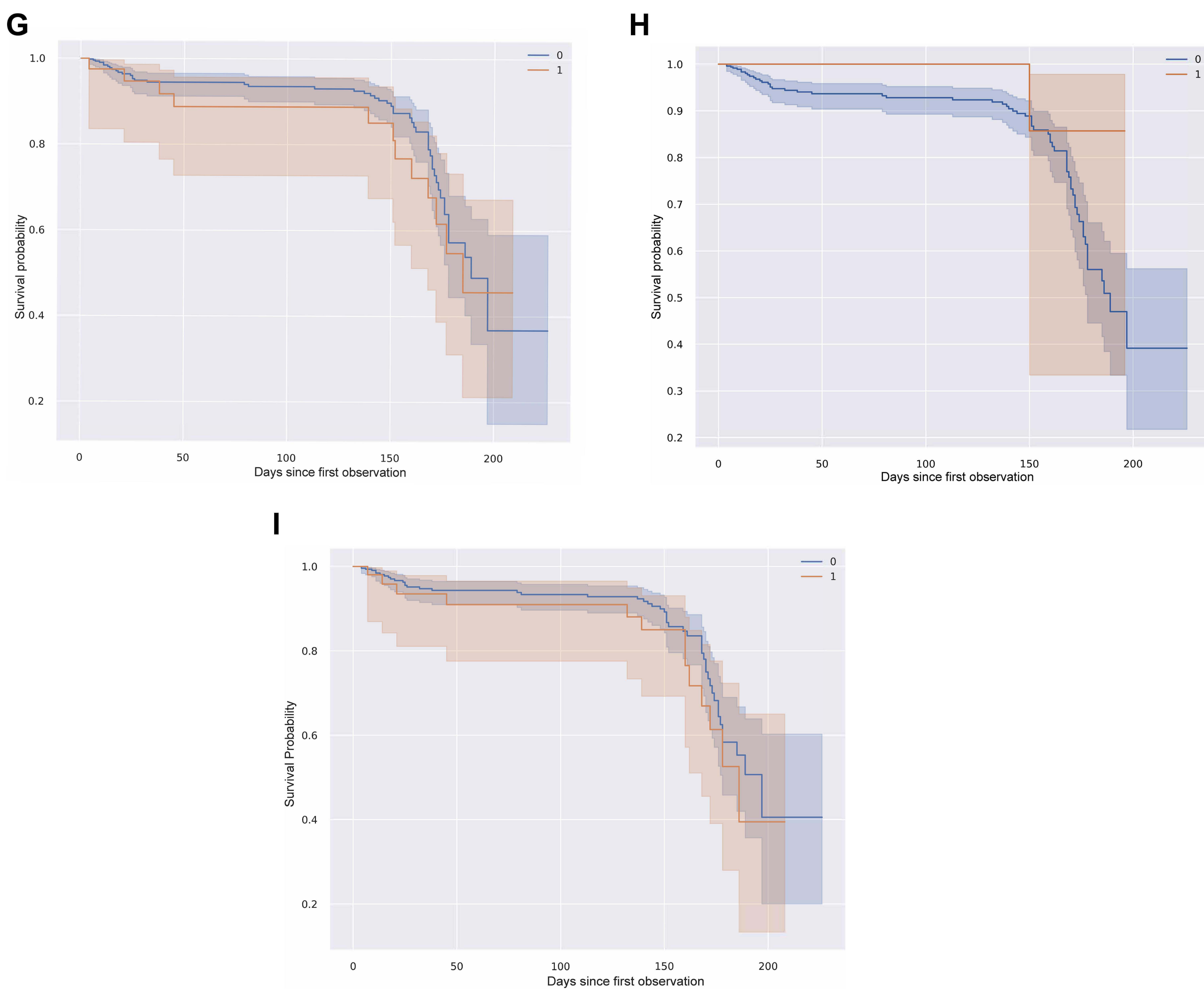

Figure 2 Kaplan Meier survival function analyses of the comorbidities; (**A**) Hypertension, (**B**) Diabetes, (**C**) Cardiovascular diseases, (**D**) Respiratory diseases, (**E**) Renal diseases, (**F**) Cancer (**G**) Neurological diseases, (**H**) Weight, and (**I**) Others.

which showed that females were predominantly infected by SARS-CoV-2.[22,23] High susceptibility among males could be due to the high number of men (Saudi and non-Saudi) in the Saudi population including expatriates, which has a more prevalent male count than female. Recent studies have linked low susceptibility in females to variations in innate immunity, steroid hormones and other factors associated with sex chromosomes.[24] For instance, reduced testosterone levels have been widely linked to high severity in males[25] The regulatory roles played by androgen on transmembrane serine protease 2 (TMPRSS2) coupled with the positioning of the angiotensin converting enzyme 2 (*ACE2*) gene on X-chromosome underlie increased ACE2 levels or rebalancing of ACE1/ ACE2, which altogether, could account for favorable outcomes in females infected with COVID-19.[26] In addition, older males have the obligations to provide for their families, hence they constituted majority of the working population in jobs, such as construction, logistics, delivery and other essential services during the COVID-19 outbreak which increased their contacts and interactions within the society. On the contrary, majority of jobs performed by females enabled them to remain at home and work remotely, including a proportion who are housewives. Moreover, the younger male population have higher tendencies of engaging in more social, sporting and cultural activities which may involve large gatherings. Also common to both young and adult males are social lifestyles or habits, such as smoking compared to females. These socio-cultural factors further account for high susceptibility in the male gender and could therefore shed more light on findings from this study as more males

Table 2 Variables for the Outcomes of Interest Using Univariate and Multivariate Cox Proportional Hazards Regression Model

Variable	Coef (Uni-Variate)	HR (Uni-Variate, exp (Coef))	95% CI Lower (Uni-Variate)	95% CI Upper (Uni-Variate)	p-value (Univariate)	Coef (Multi-Variate)	HR (Multi-Variate, Exp (Coef))	95% CI Lower (Multi-Variate)	95% CI Upper (Multi-Variate)	p-value (Multi-Variate)
ICU	1.44	4.23	2.49	7.18	<0.001	0.98	2.67	1.49	4.78	0.001
Age	0.25	1.29	1.08	1.54	0.006	0.19	1.21	0.98	1.49	0.074
BMI > 40	−1.58	0.21	0.03	1.48	0.117	−0.44	0.65	0.08	5.17	0.681
Hypertension	0.14	1.15	0.70	1.89	0.593	−0.03	0.97	0.55	1.71	0.926
Diabetes	0.12	1.12	0.68	1.86	0.647	−0.35	0.70	0.40	1.22	0.211
Cardiovascular Diseases	1.40	4.07	2.46	6.72	<0.001	1.06	2.88	1.66	4.98	<0.001
Respiratory Diseases	1.38	3.99	1.96	8.11	<0.001	1.11	3.05	1.43	6.47	0.004
Renal Diseases	0.86	2.36	1.42	3.93	0.001	0.45	1.56	0.88	2.78	0.129
Cancer	0.86	2.37	0.86	6.55	0.097	0.53	1.70	0.53	5.50	0.374
Neurological Diseases	0.26	1.29	0.68	2.44	0.429	0.11	1.12	0.56	2.22	0.755
Other Diseases	0.30	1.35	0.73	2.49	0.338	0.16	1.17	0.60	2.28	0.643
Male	−0.33	0.72	0.41	1.26	0.253	0.02	1.02	0.51	2.01	0.966
Saudi National	0.23	1.26	0.72	2.20	0.417	0.39	1.48	0.76	2.87	0.247

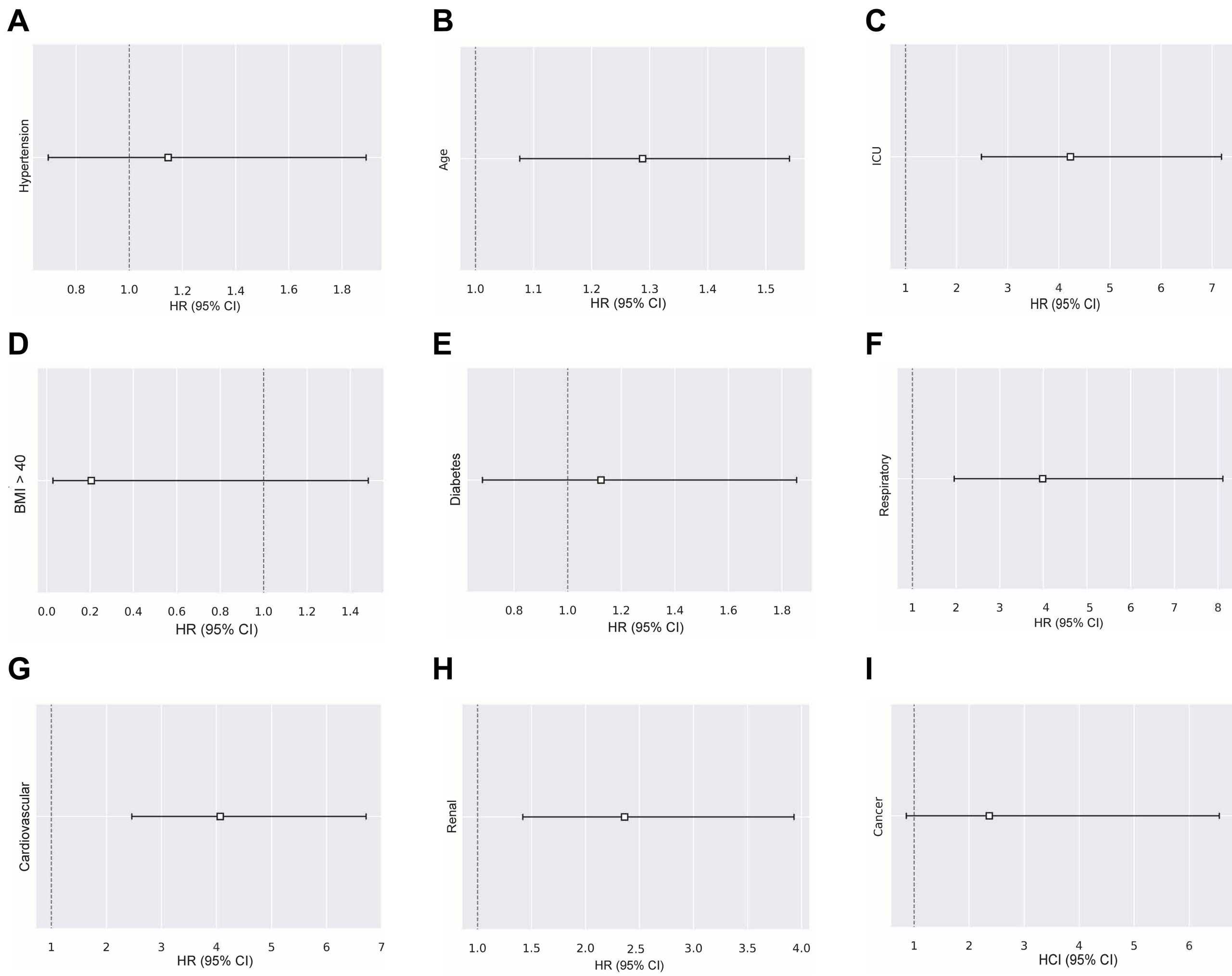

Figure 3 Univariate analyses with forest plots presenting the HR and 95% CI for mortality of COVID-19 based on the patient's characteristics and comorbidities present. (**A**) Hypertension and COVID-19 mortality, (**B**) Age and COVID-19 mortality, (**C**) ICU and COVID-19 mortality (p=0.0010), (**D**) BMI>40 and COVID-19 mortality, (**E**) diabetes and COVID-19 mortality, (**F**) respiratory disease and COVID-19 mortality (p=0.004), (**G**) cardiovascular disease and COVID-19 severity (p<0.001) (**H**), renal disease and COVID-19 mortality, (**I**) cancer and COVID-19 mortality.

required ICU admission. However, death rate was higher in Saudi females than Saudi men, and other non-Saudi males and females. This is an interesting observation as it contradicts current global assertions on COVID-19 mortality rates in females as reported in earlier epidemiological and population-based studies.[27–31]

In this present study, estimated median age for patients was 52 years which was higher than previous studies (44, 36 or 37 years) among infected COVID-19 patients in KSA,[16,18,32,33] while some others reported median ages between 37 and 70.5.[34,35] Our findings, however, contradict with some previous non-Saudi studies that suggested ages above 50 and 60 years as high-risk factors.[35–37] Earlier studies reported that relative to the rest of the world, COVID-19 affects younger persons in KSA.[16,18] Such incidences were observed in our study as COVID-19 cases were prevalent in persons with ages between 30 and 69 years. However, the infection seems to have occurred across our age-groups that ranged from 19 to 102 years indicating disease susceptibility across these ages. High infection and severity rates in adult persons between 50 and 59 years as observed herein may be as a result of high exposures due to work activity, social life-style/habit (eg, smoking) or unstable responses and coordination of the immune system.[38,39]

The BMI has been investigated as a predictor of severity and mortality in COVID-19 patients. According to the World Health Organization's weight classification, BMI ≥ 30 (computed weight (kg)/height (m^2) is classified as obese. An earlier Saudi study revealed 97.8% proportion

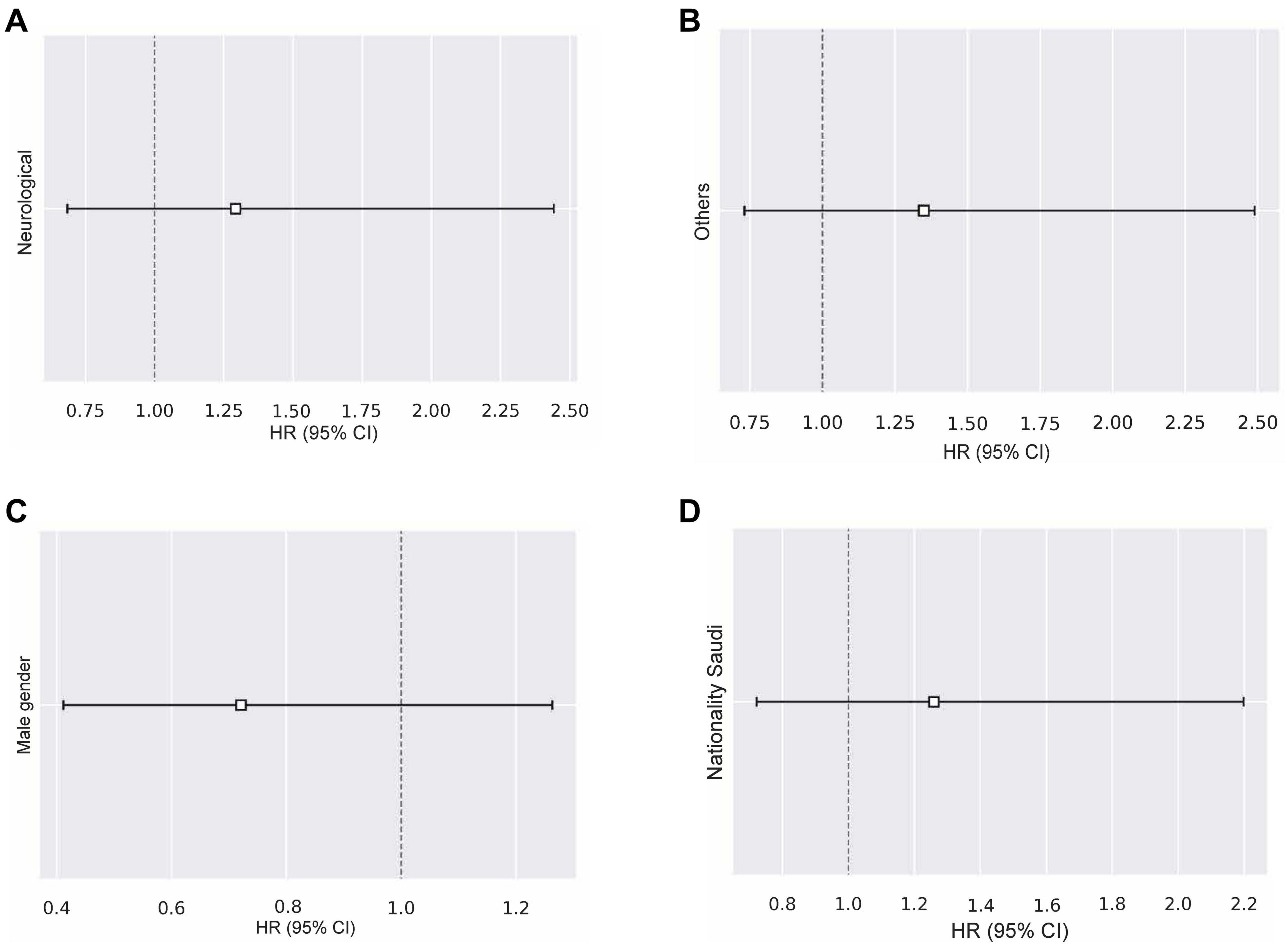

Figure 4 Univariate analyses with forest plots presenting the HR and 95% CI for mortality of COVID-19 based on the patient's characteristics and comorbidities present. (**A**) Neurological diseases and COVID-19 mortality, (**B**) Other diseases and COVID-19 mortality, (**C**) Gender and COVID-19 mortality, (**D**) Nationality and COVID-19 mortality.

of a large cohort of COVID-19 patients had BMI ≥ 30[40] and another recorded obesity in 11.5% of their patients[16] suggesting increases in the incidence rate among Saudi population due to sedentary lifestyles.[41–43] This remains a health concern since it has been pin-pointed as a risk factor for COVID-19, even in younger persons.[44,45] Obesity (BMI ≥30) was recorded in 51.3% of our patients but it was not a defining risk factor to either severity or mortality of the disease.

As observed, COVID-19 infection was high among non-Saudi nationals even though nationality did not contribute significantly to severity. Our finding closely relates to an earlier study that showed that about 80% of their COVID-19 patients were non-Saudi nationals.[40] High infection rates among non-nationals may be as a result of shared housing units increasing disease exposure.[46] This further emphasizes the need for government regulations to reduce residences that are overpopulated thereby reducing the spread of COVID-19 infection and the burden of the pandemic.

The general mortality rate was 11.15% which is lower than the proportion (17.5%) reported in a previous Saudi study,[47] and could reflect a decline in agreement with a recent epidemiological study focused on Saudi population.[33] Mortality rates in some regions of the Gulf nations are reportedly higher; 37.5% for Sudan,[19] 31.7% in North Darfur, 60% in Central Darfur,[48] which could be due to the lack of appropriate health care; testing and treatment facilities.[49] Lower mortality rates have, however, been recently reported in India (2–3%), Italy (0.07%), and the United States of America (6%).[19]

Of all our COVID-19 cases, 101 patients required ICU admission (17.88%) while earlier studies have reported 4.8%,[50] 4.7%[18] and 50%.[51] An interesting observation is that none of the patient's characteristics evaluated in this study presented any significant risk to increasing the need

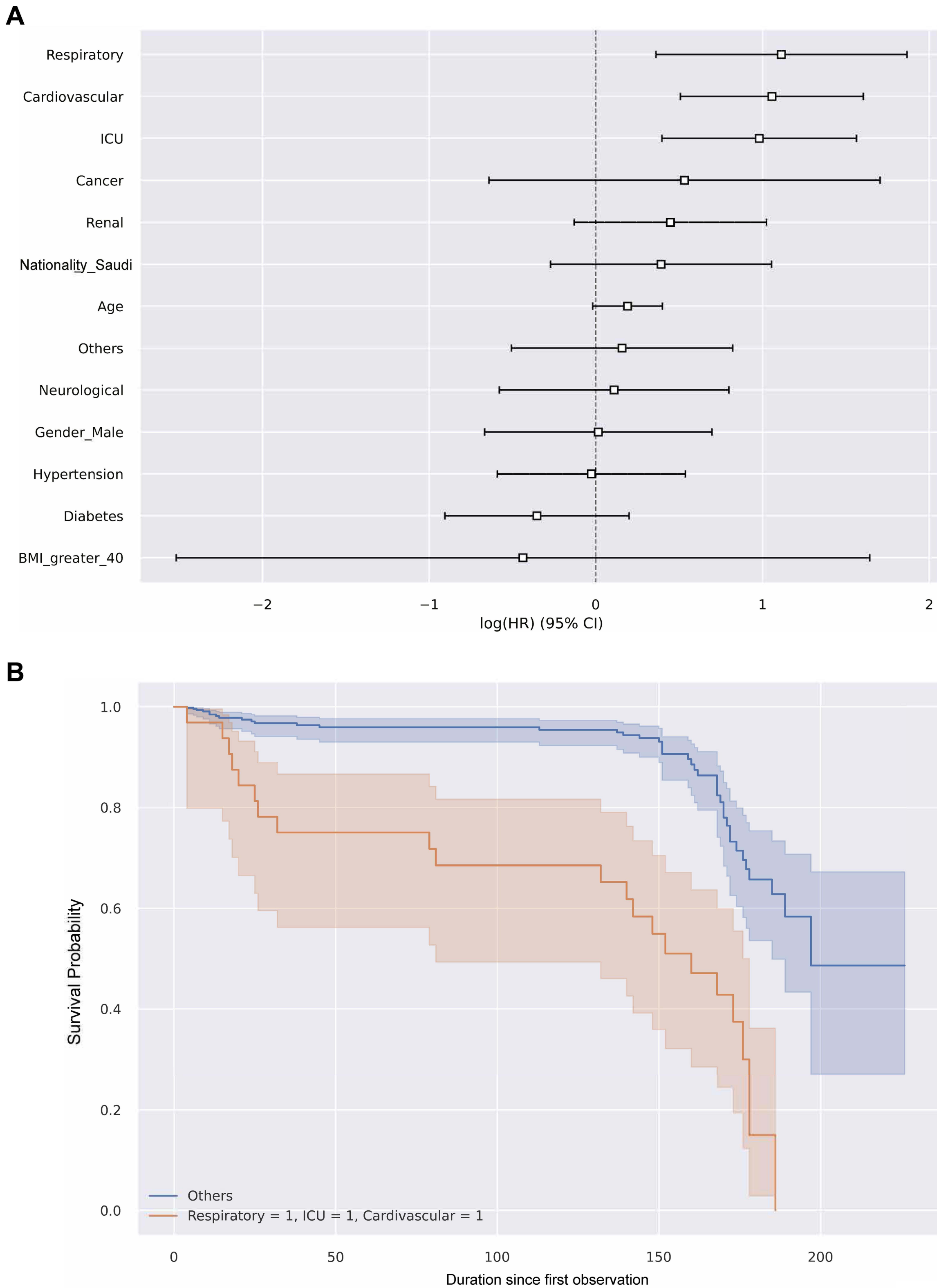

Figure 5 Forest plot from multivariate Cox hazards regression model presenting significant variables, (**A**) HR and 95% CI for COVID-19 mortality. (**B**) Kaplan Meier Survival function analyses for the top three significant variables compared to other factors.

of the patients for intensive care. Over half of the COVID-19 patients investigated herein exhibited various comorbidities, more than reported in previous studies[50] indicating increasing susceptibility among those with pre-existing conditions. In this study, we found that 46.9% of the patients had respiratory diseases, which was the highest comorbidity recorded, followed by diabetes (41.6%) and hypertension (33.8%). Other highly occurring comorbidity include cardiovascular (17.0%), renal (14.9%) and neurological (7.3%) diseases. This is in contrast to many Saudi and non-Saudi studies which showed diabetes and/or hypertension as the most common comorbidities.[16,18,34,52–55] However, contrary to some earlier Saudi and non-Saudi studies,[40,47,56–58] our findings revealed that hypertension and diabetes had no significant effect on the admission of the COVID-19 patients at the ICU, and as well do not affect the death rates. Several studies have also reported that no independent association exists between DM, hypertension and hospital in-death.[59,60] In addition, reduction in COVID-19 fatalities among diabetes patients as observed in this study may have been due to the rapt and attentive care administered to them by the health officials in the hospital since previous reports have already established them as high-risk patients. Moreover, our study identified that patients with respiratory [HR 4.0 (CI 2.0–8.1); p = 0.010], cardiovascular [HR=4.1 (CI 2.5–6.7); p<0.001], and renal comorbidities were at significantly higher risk of COVID-19 severity, which requires admission at the ICU, eventually leading to death. This is in line with a previous study from the UK on a large group of patients the majority of which had chronic pulmonary and kidney diseases.[13] Associations between these diseases and severe COVID-19 outcomes have also been reported in some non-Saudi studies.[61–64] A recent study from the Eastern Saudi province also revealed G6PD deficiency, which may lead to hemolytic anemia, as one of the most prominent comorbidity.[50] Reportedly, SARS-CoV-2 has negatively influenced the outcome of anemic patients by interacting with hemoglobin either by attacking heme group on 1-beta chain leading to hemolysis or by hepcidin-mimetic action of a spike protein causing hyperferritinemia.[65,66] Cardiac and chronic respiratory diseases have also been identified as risk factors associated with worse outcomes in COVID-19 patients[67] while lung and chronic kidney diseases were also recorded as risk factors in an independent study.[68] We also observed that neurological comorbidities contribute significantly to mortality among the hospitalized patients in line with some previous studies which reported cerebrovascular diseases leads to severe outcomes in COVID-19 cases.[64,69,70] However, after adjustments for all variables, admission of COVID-19 patients at ICU [HR 4.2 (CI 2.5–7.2); p<0.001] predicates mortality among the patients while renal and neurological comorbidities were not associated with fatalities.

Limitations

Although our study results succinctly examined various variables with regards to risk factors and clinical outcomes, it has some limitations which we acknowledge. Most importantly, the study population was curated from a single hospital in Riyadh, which is a more multicultural region compared to the rest of KSA. Therefore, findings herein cannot be generalized for all COVID-19 infected persons in the entire Kingdom.

Conclusion

Our study employed a large cohort of hospitalized COVID-19 patients in KSA and examined factors that could contribute to increases in disease severity and deaths. Findings revealed that incidences occurred across all the age-groups and were higher in males compared to females, and in non-Saudi nationals. However, this factors together with the BMI neither significantly determined patients' admittance at the ICU or death. Some commonly reported comorbidities like hypertension and diabetes had no significant influence on fatalities among the patients. On the contrary, cardiovascular, respiratory and renal comorbidities were high-risk factors to worsening outcomes and even death among hospitalized patients. We believe our study results could facilitate health-care providers in identifying patients with risk of fatality. Findings will also be helpful to decision makers to continue deriving and implementing regulations to reduce the spread of COVID-19 and other future infections among nationals and non-nationals living in KSA.

Ethics Approval and Informed Consent

The ethical approval for this study was obtained from the Institutional Review Board (IRB) managed by the Deanship of Scientific Research at Imam Abdulrahman Bin Faisal University in Dammam, KSA. The IRB reference number is IRB-2020-09-185. Permissions were also obtained from the hospital management in order to carry out this study. Patient consent to review the medical records was not required by the IRB as the data received from the hospital was anonymized by removing patient identification information. Statement covering patient data confidentiality was in compliance with the declaration of Helsinki.

Author Contributions

FS participated in all aspects of the paper including securing funding, study design, analysis and writing. ND participated in data acquisition, writing and journal selection. AB participated in data analysis and study design. AQ participated in writing. SD participated in data analysis and literature survey. SA participated in data acquisition, data preparation and literature survey. DA participated in data acquisition, data preparation and literature survey. RA participated in data acquisition and analysis. WA participated in data acquisition and analysis. SC participated in writing and editing. AA participated in study design and critical review. SO participated in journal selection and critical review. AM participated in critical review and editing. MA participated in data analysis and critical review. YA participated in writing and editing. VAS assisted in study design, analysis, writing and critical review of the manuscript. All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, drafted the article or revised it critically for important intellectual content, agreed to submit to the current journal. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Funding

This project is sponsored by the COVID-19 grant from King AbdulAziz City of Science and Technology (Grant No. 5-20-01-0700-00016)

Disclosure

Dr Fatema Shaikh, Dr Nahier Aldhafferi, Dr Abdullah Alqahtani, Dr Abdullah Almuhaideb, Dr Mohammed Alshahrani, Dr Sunday Olatunji, Ms Areej Buker, Miss Saema Abdulhamid, Miss Dalal AlBuhairi, Ms Raha Alkabour, Miss Waad Atiyah, Miss Sara Mhd Bachar Chrouf, and Dr Abdussalam Alshehri report grant from King Abdulaziz City of Science and Technology, during the conduct of the study. Mr Subhodeep Dey reports grant from King Abdulaziz City of Science and Technology, during the conduct of the study and outside the submitted work. Mr Yousof AlMunsour reports grant from King Abdulaziz City of Science and Technology, during the conduct of the study; and equal – validation, equal – visualization, supporting – writing original draft, and equal – writing – reviewing and editing. The authors reported no other potential conflicts of interest for this work.

References

1. Al-Khani AM, Khalifa MA, Almazrou A, Saquib N. The SARS-CoV-2 pandemic course in Saudi Arabia: a dynamic epidemiological model. *Infect Dis Model*. 2020;5:766. doi:10.1016/j.idm.2020.09.006
2. Khan R, Saxena A, Shukla S, Sekar S, Goel P. Effect of COVID-19 lockdown on the water quality index of River Gomti, India, with potential hazard of faecal-oral transmission. *Environ Sci Pollut Res*. 2021:28:33021–33029. doi:10.1007/s11356-021-13096-1
3. Al-Tawfiq JA, Memish ZA. COVID-19 in the eastern Mediterranean region and Saudi Arabia: prevention and therapeutic strategies. *Int J Antimicrob Agents*. 2020;55(5):105968. doi:10.1016/j.ijantimicrob.2020.105968
4. Al-Tawfiq JA, Sattar A, Al-Khadra H, et al. Incidence of COVID-19 among returning travelers in quarantine facilities: a longitudinal study and lessons learned. *Travel Med Infect Dis*. 2020;38:101901. doi:10.1016/j.tmaid.2020.101901
5. World Health Organization. WHO coronavirus disease dashboard. WHO; 2020
6. Li H, Liu L, Zhang D, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet*. 2020;395(10235):1517–1520. doi:10.1016/S0140-6736(20)30920-X
7. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. 2020;20(5):533–534. doi:10.1016/S1473-3099(20)30120-1
8. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: a review. *Fetal Pediatr Pathol*. 2020;39:246–250. doi:10.1080/15513815.2020.1747120
9. Shadmi E, Chen Y, Dourado I, et al. Health equity and COVID-19: global perspectives. *Int J Equity Health*. 2020;19(1):104. doi:10.1186/s12939-020-01218-z
10. Nzaji MK, Mwamba GN, Miema JM, et al. Predictors of non-adherence to public health instructions during the covid-19 pandemic in the democratic republic of the congo. *J Multidiscip Healthc*. 2020;13:2215. doi:10.2147/JMDH.S274944
11. Lai PH, Lancet EA, Weiden MD, et al. Characteristics associated with out-of-hospital cardiac arrests and resuscitations during the novel coronavirus disease 2019 pandemic in New York City. *JAMA Cardiol*. 2020;5:1554.
12. Rezende LFM, Thome B, Schveitzer MC, de Souza-júnior PRB, Szwarcwald CL. Adults at high-risk of severe coronavirus disease-2019 (Covid-19) in Brazil. *Rev Saude Publica*. 2020;54:50. doi:10.11606/S1518-8787.2020054002596
13. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: prospective observational cohort study. *BMJ*. 2020:369. doi:10.1136/bmj.m1985
14. Nanda S, Chacin Suarez AS, Toussaint L, et al. Body mass index, multi-morbidity, and COVID-19 risk factors as predictors of severe COVID-19 outcomes. *J Prim Care Community Health*. 2021;12:215013272110185. doi:10.1177/21501327211018559
15. Sahu KK, Siddiqui AD. A review on recipients of hematopoietic stem cell transplantation patients with COVID-19 infection. *Ther Adv Infect Dis*. 2021;8:20499361211013252. doi:10.1177/20499361211013252.

16. Al-Omari A, Alhuqbani WN, Zaidi ARZ, et al. Clinical characteristics of non-intensive care unit COVID-19 patients in Saudi Arabia: a descriptive cross-sectional study. *J Infect Public Health*. 2020;13:1639–1644. doi:10.1016/j.jiph.2020.09.003
17. Al-Mohaithef M, Padhi BK. Determinants of covid-19 vaccine acceptance in Saudi Arabia: a web-based national survey. *J Multidiscip Healthc*. 2020;13:1657–1663. doi:10.2147/JMDH.S276771
18. Alsofayan YM, Althunayyan SM, Khan AA, Hakawi AM, Assiri AM. Clinical characteristics of COVID-19 in Saudi Arabia: a national retrospective study. *J Infect Public Health*. 2020;13 (7):920–925. doi:10.1016/j.jiph.2020.05.026
19. Omar SM, Musa IR, Salah SE, Elnur MM, Al-Wutayd O, Adam I. High mortality rate in adult covid-19 inpatients in Eastern Sudan: a retrospective study. *J Multidiscip Healthc*. 2020;13:1887–1893. doi:10.2147/JMDH.S283900
20. Argenzian MG, Bruc SL, Slate CL, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. *BMJ*. 2020:m1996. doi:10.1136/bmj.m1996.
21. Ortolan A, Lorenzin M, Felicetti M, Doria A, Ramonda R. Does gender influence clinical expression and disease outcomes in COVID-19? A systematic review and meta-analysis. *Int J Infect Dis*. 2020;99:496–504. doi:10.1016/j.ijid.2020.07.076
22. Yehia BR, Winegar A, Fogel R, et al. Association of race with mortality among patients hospitalized with coronavirus disease 2019 (COVID-19) at 92 US Hospitals. *JAMA Netw open*. 2020;3: e2018039. doi:10.1001/jamanetworkopen.2020.18039
23. Xie J, Zu Y, Alkhatib A, et al. Metabolic syndrome and covid-19 mortality among adult black patients in new orleans. *Diabetes Care*. 2021;44(1):188–193. doi:10.2337/dc20-1714
24. Conti P, Younes A. Coronavirus cov-19/sars-cov-2 affects women less than men: clinical response to viral infection. *J Biol Regul Homeost Agents*. 2020;34:339. doi:10.23812/Editorial-Conti-3
25. Auerbach JM, Khera M. Testosterone's Role in COVID-19. *J Sex Med*. 2021;18(5):843–848. doi:10.1016/j.jsxm.2021.03.004
26. Gemmati D, Bramanti B, Serino ML, Secchiero P, Zauli G, Tisato V. COVID-19 and individual genetic susceptibility/receptivity: role of ACE1/ACE2 genes, immunity, inflammation and coagulation. might the double x-chromosome in females be protective against SARS-COV-2 compared to the single x-chromosome in males? *Int J Mol Sci*. 2020;21(10):3474. doi:10.3390/ijms21103474
27. Jin JM, Bai P, He W, et al. Gender Differences in Patients With COVID-19: focus on Severity and Mortality. *Front Public Heal*. 2020;8:152. doi:10.3389/fpubh.2020.00152
28. Yanez ND, Weiss NS, Romand JA, Treggiari MM. COVID-19 mortality risk for older men and women. *BMC Public Health*. 2020;20:1–7. doi:10.1186/s12889-020-09826-8.
29. Dehingia N, Raj A. Sex differences in COVID-19 case fatality: do we know enough? *Lancet Glob Heal*. 2021;9(1):e14–e15. doi:10.1016/S2214-109X(20)30464-2
30. Pradhan A, Olsson PE. Sex differences in severity and mortality from COVID-19: are males more vulnerable? *Biol Sex Differ*. 2020;11:1–11. doi:10.1186/s13293-020-00330-7.
31. Peckham H, de Gruijter NM, Raine C, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. *Nat Commun*. 2020;11:1. doi:10.1038/s41467-020-19741-6
32. Barry M, AlMohaya AE, AlHijji A, et al. Clinical characteristics and outcome of hospitalized COVID-19 patients in a MERS-CoV endemic area. *J Epidemiol Glob Health*. 2020;10:214. doi:10.2991/jegh.k.200628.001
33. Alyami MH, Naser AY, Orabi MAA, Alwafi H, Alyami HS. Epidemiology of COVID-19 in the kingdom of Saudi Arabia: an ecological study. *Front Public Heal*. 2020:8:506. doi:10.3389/fpubh.2020.00506.
34. Feng Y, Ling Y, Bai T, et al. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med*. 2020;201(11):1380–1388. doi:10.1164/rccm.202002-0445OC
35. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect*. 2020;80:e14–e18. doi:10.1016/j.jinf.2020.03.005
36. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323:1775–1776. doi:10.1001/jama.2020.4683
37. Porcheddu R, Serra C, Kelvin D, Kelvin N, Rubino S. Similarity in case fatality rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. *J Infect Dev Ctries*. 2020;14:125. doi:10.3855/jidc.12600
38. Nikolich-Zugich J, Knox KS, Rios CT, Natt B, Bhattacharya D, Fain MJ. SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. *GeroScience*. 2020;42:505. doi:10.1007/s11357-020-00186-0
39. Joly BS, Siguret V, Veyradier A. Understanding pathophysiology of hemostasis disorders in critically ill patients with COVID-19. *Intensive Care Med*. 2020;46:1603–1606. doi:10.1007/s00134-020-06088-1
40. Alqahtani AM, AlMalki ZS, Alalweet RM, et al. Assessing the severity of illness in patients with coronavirus disease in Saudi Arabia: a retrospective descriptive cross-sectional study. *Front Public Heal*. 2020;8:775. doi:10.3389/fpubh.2020.593256
41. Memish ZA, El Bcheraoui CE, Tuffaha M, et al. Obesity and associated factors - Kingdom of Saudi Arabia, 2013. *Prev Chronic Dis*. 2014;11:1. doi:10.5888/pcd11.140236
42. Alquaiz AM, Siddiqui AR, Kazi A, Batais MA, Al-Hazmi AM. Sedentary lifestyle and Framingham risk scores: a population-based study in Riyadh city, Saudi Arabia. *BMC Cardiovasc Disord*. 2019;19 (1):1. doi:10.1186/s12872-019-1048-9
43. Albawardi NM, Jradi H, Al-Hazzaa HM. Levels and correlates of physical activity, inactivity and body mass index among Saudi women working in office jobs in Riyadh city. *BMC Womens Health*. 2016;16(1):1. doi:10.1186/s12905-016-0312-8
44. Kass DA, Duggal P, Cingolani O. Obesity could shift severe COVID-19 disease to younger ages. *Lancet*. 2020;395:1544–1545. doi:10.1016/S0140-6736(20)31024-2
45. Petrova D, Salamanca-Fernández E, Rodríguez Barranco M, Navarro Pérez P, Jiménez Moleón JJ, Sánchez MJ. Obesity as a risk factor in COVID-19: possible mechanisms and implications. *Aten Primaria*. 2020;52(7):496–500. doi:10.1016/j.aprim.2020.05.003
46. Alkhamis A, Cosgrove P, Mohamed G, Hassan A. The personal and workplace characteristics of uninsured expatriate males in Saudi Arabia. *BMC Health Serv Res*. 2017;17:1. doi:10.1186/s12913-017-1985-x.
47. Alguwaihes AM, Al-Sofiani ME, Megdad M, et al. Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: a single-centre retrospective study. *Cardiovasc Diabetol*. 2020;19:1. doi:10.1186/s12933-020-01184-4
48. Altayb HN, Altayeb NME, Hamadalnil Y, Elsayid M, Mahmoud NE. The current situation of COVID-19 in Sudan. *New Microbes New Infect*. 2020;37:100746. doi:10.1016/j.nmni.2020.100746
49. Caillard S, Anglicheau D, Matignon M, et al. An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants. *Kidney Int*. 2020;98 (6):1549–1558. doi:10.1016/j.kint.2020.08.005
50. AlJishi JM, Alhajjaj AH, Alkhabbaz FL, et al. Clinical characteristics of asymptomatic and symptomatic COVID-19 patients in the Eastern Province of Saudi Arabia. *J Infect Public Health*. 2021;14(1):6–11. doi:10.1016/j.jiph.2020.11.002
51. Al-Tawfiq JA, Leonardi R, Fasoli G, Rigamonti D. Prevalence and fatality rates of COVID-19: what are the reasons for the wide variations worldwide? *Travel Med Infect Dis*. 2020;35:101711. doi:10.1016/j.tmaid.2020.101711

52. Baradaran A, Ebrahimzadeh MH, Baradaran A, Kachooei AR. Prevalence of comorbidities in COVID-19 patients: a systematic review and meta-analysis. *Arch Bone Jt Surg*. 2020;8:247. doi:10.22038/abjs.2020.47754.2346
53. Khamis F, Al-Zakwani I, Al Naamani H, et al. Clinical characteristics and outcomes of the first 63 adult patients hospitalized with COVID-19: an experience from Oman. *J Infect Public Health*. 2020;13 (7):906–913. doi:10.1016/j.jiph.2020.06.002
54. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062. doi:10.1016/S0140-6736(20)30566-3
55. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): early report from the United States. *Diagnosis*. 2020;7(2):91–96. doi:10.1515/dx-2020-0046
56. Varikasuvu SR, Dutt N, Thangappazham B, Varshney S. Diabetes and COVID-19: a pooled analysis related to disease severity and mortality. *Prim Care Diabetes*. 2021;15:24–27. doi:10.1016/j.pcd.2020.08.015
57. Varikasuvu SR, Varshney S, Dutt N. Markers of coagulation dysfunction and inflammation in diabetic and non-diabetic COVID-19. *J Thromb Thrombolysis*. 2020;51:941–946. doi:10.1007/s11239-020-02270-w
58. Hillson R. COVID-19: diabetes and death. A call to action. *Pract Diabetes*. 2020;37:76–78. doi:10.1002/pdi.2271
59. Suleyman G, Fadel RA, Malette KM, et al. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan detroit. *JAMA Netw open*. 2020;3:e2012270. doi:10.1001/jamanetworkopen.2020.12270
60. Shi Q, Zhang X, Jiang F, et al. Clinical characteristics and risk factors for mortality of COVID-19 patients with diabetes in Wuhan, China: a two-center, retrospective study. *Diabetes Care*. 2020;43(7):1382–1391. doi:10.2337/dc20-0598
61. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020;109(5):531–538. doi:10.1007/s00392-020-01626-9
62. Wang X, Fang X, Cai Z, et al. Comorbid chronic diseases and acute organ injuries are strongly correlated with disease severity and mortality among COVID-19 patients: a systemic review and meta-analysis. *Research*. 2020;2020:1–17. doi:10.34133/2020/2402961
63. De Almeida-pititto B, Dualib PM, Zajdenverg L, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr*. 2020;12(1):1–2. doi:10.1186/s13098-020-00586-4
64. Zhang T, Huang W-S, Guan W, et al. Risk factors and predictors associated with the severity of COVID-19 in China: a systematic review, meta-analysis, and meta-regression. *J Thorac Dis*. 2020;12 (12):7429–7441. doi:10.21037/jtd-20-1743
65. Bergamaschi G, Borrelli de Andreis F, Aronico N, et al. Anemia in patients with Covid-19: pathogenesis and clinical significance. *Clin Exp Med*. 2021;21(2):239–246. doi:10.1007/s10238-020-00679-4
66. Hariyanto TI, Kurniawan A. Anemia is associated with severe coronavirus disease 2019 (COVID-19) infection. *Transfus Apher Sci*. 2020;59(6):102926. doi:10.1016/j.transci.2020.102926
67. Khan A, Althunayyan S, Alsofayan Y, et al. Risk factors associated with worse outcomes in COVID-19: a retrospective study in Saudi Arabia. *East Mediterr Heal J*. 2020;26:1371–1380. doi:10.26719/emhj.20.130
68. Abohamr SI, Abazid RM, Aldossari MA, et al. Clinical characteristics and in-hospital mortality of covid-19 adult patients in Saudi Arabia. *Saudi Med J*. 2020;41(11):1217–1226. doi:10.15537/smj.2020.11.25495
69. Starke KR, Petereit-Haack G, Schubert M, et al. The age-related risk of severe outcomes due to covid-19 infection: a rapid review, meta-analysis, and meta-regression. *Int J Environ Res Public Health*. 2020;17:5974. doi:10.3390/ijerph17165974
70. Barek MA, Aziz MA, Islam MS. Impact of age, sex, comorbidities and clinical symptoms on the severity of COVID-19 cases: a meta-analysis with 55 studies and 10014 cases. *Heliyon*. 2020;6(12): e05684. doi:10.1016/j.heliyon.2020.e05684