International Journal of General Medicine

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ORIGINAL RESEARCH

Assessment of Risk Factors Associated with COVID-19 Illness Outcomes in a Tertiary Hospital in Saudi Arabia

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Introduction: The emergence of the coronavirus disease 2019 (COVID-19) pandemic has significantly impacted the globe. Understanding the association between the population's demographical, clinical risk factors, and outcome of COVID-19 is essential for healthcare providers to develop guidelines and future care plans. This study reports all diagnosed COVID-19 and admitted to Johns Hopkins Aramco Healthcare (JHAH) for hospitalization from March to July 2020.

Methods: This is a retrospective study that presents the demographic, epidemiological, clinical, laboratory, and imaging characteristics of our patients and determines risk factors contributing to their COVID-19 outcome.

Results: The study included 656 patients (53% were male, 60% were older than 50 years of age, 87% were Saudi nationals, 5% pregnant, and 92% non-smokers patients). The source of infection was mostly unknown to the patient or healthcare provider (58%), followed by contact transmission (36%) and travel (5%). In addition, we found that the vast majority of hospitalized patients presented with symptoms (76%) with (90.4%) mild to moderate symptoms and have had stable hospital course during their hospitalization (82.1%). Over fifty percent of the patients had abnormal x-ray upon admission, (4.7%) were intubated, (20.3%) were admitted to an intensive care unit (ICU) or a step-down unit (SDU), and finally (5.3%) were deceased.

Conclusion: The majority of the patients in this study had mild disease, and their outcome was associated with some chronic diseases, most significantly hypertension. However, the study did not demonstrate a statistically significant association between smoking and obesity and COVID-19 outcomes.

Keywords: COVID-19, chronic illness, outcome, epidemiology

Introduction

The coronavirus disease 2019 (COVID-19) outbreak started in Wuhan, China, with the first case presenting with pneumonia in December 2019.[1] As of March 2022, COVID-19 has affected more than 462 million cases and caused more than 6 million deaths worldwide.[2] In Saudi Arabia, the first case of COVID-19 was announced on the 2nd of March 2020.[3] Since then, the virus has infected nearly 749,171 with 731,440 (97.6%) recovered individuals and 9023 (1.2%) mortality rate.[4]

The coronavirus 2019 is novel, and little is known about it. Individuals diagnosed with COVID-19 have reported a broad spectrum of symptoms.[5] Clinical presentation of COVID-19 is heterogeneous, ranging from asymptomatic to having mild to severe symptoms. Influenza-like symptoms may present 2 to 14 days after exposure to the virus, mainly targeting the respiratory system.[5,6] Individuals may present with fever, dry cough,

Received: 9 January 2022
Accepted: 7 June 2022
Published: 27 June 2022

headache, sore throat, congestion, nausea, diarrhea, fatigue, muscle aches, loss of smell or taste, and shortness of breath.[6] However, individuals may suffer from more severe symptoms and multi-organ dysfunctions, affecting their lungs, heart, brain, blood vessels, post-traumatic stress syndrome, and many other.[7]

The high infectivity of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and subsequent mortality put the healthcare systems globally in an enormous challenge. Patients who develop severe COVID-19 clinical course require more resources like intensive care unit (ICU) admissions, invasive ventilation, and more extended hospital stay. Although COVID-19 patients are younger than influenza patients, older adults are at higher risk for severe COVID-19 associated illness and death, particularly those with serious underlying health conditions. The majority of Patients known to have been admitted to an ICU were reported among adults ≥65 years. No deaths were reported among persons aged ≤19 years.[8,9] Such findings coincide with our study results, where older patients are more likely to suffer worse outcomes than younger ones.

Understanding the association between the population's demographical and clinical risk factors and the severity of the outcome of COVID-19 is vital for healthcare providers to develop guidelines and future care plans.[10] Studies have proven that the highest risk factors for COVID-19 mortality and severe comorbidities were older age, diabetes mellitus, hypertension, and obesity.[11] However, more research is needed to comprehend the disease and enrich the literature with more evidence-based studies.

This study reports all diagnosed COVID-19 and admitted to Johns Hopkins Aramco Healthcare (JHAH) for hospitalization from March to July 2020. This study presents our patients' demographic, epidemiological, clinical, laboratory, and imaging characteristics. Moreover, we aim to identify and determine risk factors that contribute to and affect COVID-19 clinical outcomes during their course of illness.

Methods

Study Design and Population

This is a retrospective cross-sectional study. All patients were admitted to Johns Hopkins Aramco Healthcare (JHAH) with a confirmed diagnosis of COVID-19 and eligible for treatment at JHAH from March to July 2020.

JHAH is a tertiary hospital located in Dhahran, Eastern Province of Saudi Arabia. It serves Saudi Aramco employees and their dependents, which entails 300,000 people. The study complies with the Declaration of Helsinki and received JHAH's Institutional Review Board's approval (no. 20-33) in October 2020. The patient's consent was waived due to the retrospective study design with the definite anonymity of all participants.

This study included all patients admitted to JHAH from March to July 2020 with a confirmed diagnosis of COVID-19.

We categorized patients into either symptomatic or asymptomatic. The severity of the symptoms was defined as follows: Asymptomatic cases were defined as having a positive PCR without any associated clinical symptoms. Mild cases were defined as having mild symptoms such as fever, malaise, cough, and upper respiratory symptoms. Moderate cases were defined with infiltration on lung imaging without hypoxia (Oxygen saturation in resting-state ≥ 94%). Severe cases are patients with dyspnea and hypoxia with oxygen saturation < 94%. Finally, critical cases were defined with at least one of these presentations: respiratory failure, septic shock, or multi-organ dysfunction.

Outcome Measures

The primary outcome of this study is to assess and study risk factors associated with COVID-19 outcomes during their hospitalization at JHAH. Illness outcome was determined by discharge status and mortality.

Data Collection

Data were collected using patients' electronic health records system (EPIC). EPIC is a fully integrated electronic health records system that provides more versatile and customized reports about patients with any criteria. The data collected include demographic information: age, gender, nationality, travel history, and mode of exposure; medical history: Ischemic heart disease (IHD), congestive heart failure (CHF), diabetes mellitus (DM),

hypertension (HTN), dyslipidemia, obesity, cancer, kidney disease, lung disease, immunocompromised condition, smoking, and pregnancy; clinical data: recent flu shot, hospitalization, PCR swab test, x-ray findings, symptoms upon admission, severity and deterioration of illness, admission date, and discharge date.

Data were collected by family medicine residents and reviewed by their consultants, who determined the severity of illness. Separately, 10% of the data were validated by one of the other co-investigators.

Sample Size

The total number of patients included in the study is 639. All included patients were diagnosed with COVID-19 prior to hospitalization.

All COVID-19 positive cases were hospitalized based on the early national guidelines endorsed by the Ministry of Health (MoH) of Saudi Arabia. Later on, the MoH modified the guidelines and launched a home monitoring program for home isolation of certain COVID-19 patients. This service was offered to asymptomatic or mildly symptomatic (ie, low-risk) patients.

Statistical Analysis

The data analysis was done using the statistical package IBM SPSS Statistics for Windows, Version 25.0 Armonk. Categorical variables were described as frequencies and percentages. The chi-square and Fisher's exact tests assessed the deterioration severity level and other categorical variables. A test was considered significant if the p-value <0.05.

Results

During the study period, 3400 patients had a positive PCR test and confirmed diagnosis of COVID-19. Out of which, 656 patients were hospitalized at JHAH for medical care. We included all hospitalized patients with COVID-19 except for 17 patients who did not meet the inclusion criteria of this study.

Table 1 describes the demographics of hospitalized patients with approximately (53%) male patients, and (60%) were older than 50 years of age, (87%) Saudi nationals, (5%) pregnant, and (92%) non-smokers patients. The source of infection was mostly unknown to the patient or healthcare provider (58%), following that positive contact transmission (36%), traveling (5%), and finally (1%) was a hospital-acquired infection. Moreover, most study participants did not receive the flu shot in the previous year of 2019 (80%) and did not travel within the 14 days prior to hospitalization. It was also found that (18%) of the patients were in the normal range of body mass index (BMI), and (6.6%) were underweight, leading to a crucial risk factor of high BMI levels for overweight and obese patients (76%). In addition, we observed that the vast majority of hospitalized patients presented with

Table 1 Demographical and Clinical Characteristics of Hospitalized Patients with COVID019

		N	%
Gender	Male	340	53.2
	Female	299	46.8
Nationality	Saudi	558	87.3
	Non-Saudi	81	12.7
Smoking	No	554	92.0
	Yes	48	8.0
Pregnancy	No	531	94.8
	Yes	29	5.2

(*Continued*)

Table 1 (Continued).

		N	%
Mode of Exposure	Domestic Travel	12	2.0
	International Travel	18	2.9
	Contact	222	36.2
	Unknown	356	58.0
	Hospital	6	1.0
Flu Shot 2019	No	491	80.2
	Yes	94	15.4
	Unknown	27	4.4
Body mass index groups	Underweight	39	6.0
	Normal weight	118	18.1
	Overweight	194	29.8
	Obese I	187	28.7
	Obese II	71	10.9
	Obese III	43	6.6
CXR Finding (upon diagnosis)	Normal	244	39.7
	Abnormal	345	56.2
	Not Done	25	4.1
Symptoms (upon admission)	Asymptomatic	147	24.0
	Symptomatic	465	76.0
Severity (upon admission)	Mild	289	47.5
	Moderate	261	42.9
	Severe	57	9.4
	Critical	2	0.3
Hospital Course	Stable	495	82.1
	Not Stable	108	17.9
Deterioration Severity	Moderate	65	48.9
	Severe	43	32.3
	Critical	25	18.8
Intubation	No	485	95.3
	Yes	24	4.7
ICU/SD	No	416	79.7
	Yes	106	20.3
Outcome	Discharged	605	94.7
	Deceased	34	5.3

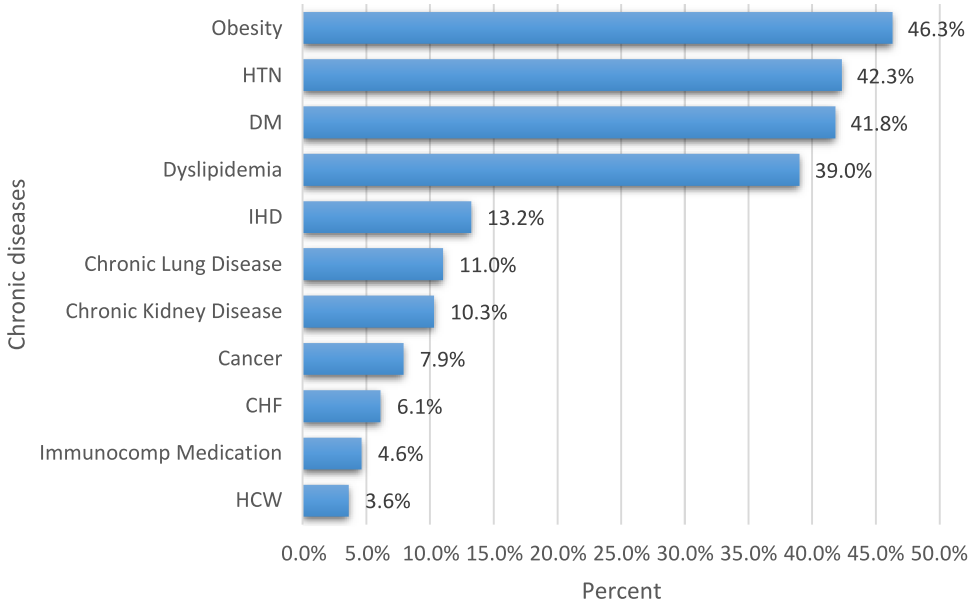

Figure 1 Risk factors associated with hospitalization of COVID-19 patients.

symptoms (76%) with (90.4%) mild to moderate symptoms and had had stable hospital course during their hospitalization (82.1%). More than half of the patients had abnormal x-ray upon admission, (4.7%) were intubated, (20.3%) were admitted to an intensive care unit (ICU) or a step-down unit, and finally (5.3%) were deceased.

Moreover, eleven predetermined risk factors were associated with the patients' condition prior to hospitalization. Nearly half of the patients in our study have a history of obesity, hypertension (HTN), diabetes mellitus (DM), and dyslipidemia (Figure 1).

Demographically, age was the only statistically significant variable with (p=0.018) (Table 2). On the other hand, predetermined clinical risk factors such as DM, HTN, IHD, CHF, cancer, chronic kidney disease, and being on immunocompromising medications were statistically significant (p<0.05) (Table 3). Moreover, the number of chronic diseases the patient suffered from, abnormal chest imaging, the severity of COVID-19 upon admission, the deterioration severity, hospital course, ICU or stepdown ICU admission, and intubation also exhibited statistical significance with (p<0.05) (Table 4).

Table 2 Shows That Age is a Significant Risk Factor in Determining the Outcome of Hospitalized COVID-19 Patients

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
Gender	Male	321	94.4%	19	5.6%	0.748
	Female	284	95.0%	15	5.0%	
Age (years)	18–30	78	100.0%	0	0.0%	0.018
	31–40	72	100.0%	0	0.0%	
	41–50	95	100.0%	0	0.0%	
	51–60	191	97.9%	4	2.1%	
	61–70	97	96.0%	4	4.0%	
	71+	72	93.5%	5	6.5%	

(*Continued*)

Table 2 (Continued).

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
Nationality	Saudi	525	94.1%	33	5.9%	0.108
	Non-Saudi	80	98.8%	1	1.2%	
Smoking	No	522	94.2%	32	5.8%	0.099
	Yes	48	100.0%	0	0.0%	
Pregnancy	No	500	94.2%	31	5.8%	0.395
	Yes	29	100.0%	0	0.0%	
Flu Shot 2019	No	469	95.5%	22	4.5%	0.782
	Yes	91	96.8%	3	3.2%	
Travel History	No	491	94.4%	29	5.6%	1.00
	Yes	32	94.1%	2	5.9%	

Table 3 Shows That Clinical Risk Factors are Significant in Determining Their Impact on the Outcome of Hospitalized COVID-19 Patients

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
HCW	No	561	94.6%	32	5.4%	0.621
	Yes	22	100.0%	0	0.0%	
IHD	No	511	96.1%	21	3.9%	0.001
	Yes	70	86.4%	11	13.6%	
CHF	No	550	96.3%	21	3.7%	<0.001
	Yes	27	73.0%	10	27.0%	
DM	No	350	98.0%	7	2.0%	<0.001
	Yes	231	90.2%	25	9.8%	
HTN	No	350	98.9%	4	1.1%	<0.001
	Yes	232	89.2%	28	10.8%	
Dyslipidemia	No	358	95.7%	16	4.3%	0.190
	Yes	223	93.3%	16	6.7%	
Obesity	No	311	94.5%	18	5.5%	0.764
	Yes	270	95.1%	14	4.9%	

(*Continued*)

Table 3 (Continued).

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
Cancer	No	537	95.7%	24	4.3%	0.002
	Yes	40	83.3%	8	16.7%	
Chronic Kidney Disease	No	528	95.8%	23	4.2%	0.003
	Yes	54	85.7%	9	14.3%	
Chronic Lung Disease	No	492	95.3%	24	4.7%	0.536
	Yes	60	93.8%	4	6.3%	
Immunocompromised Medication	No	530	95.5%	25	4.5%	0.039
	Yes	23	85.2%	4	14.8%	

Table 4 Shows That the Course of Hospitalization Has a Significant Impact on Hospitalized COVID-19 Patients

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
Chronic diseases	0	122	99.2%	1	0.8%	<0.001
	1–3	328	96.8%	11	3.2%	
	4+	135	87.1%	20	12.9%	
CXR Finding (upon diagnosis)	Normal	239	98.0%	5	2.0%	0.012
	Abnormal	319	92.5%	26	7.5%	
	Not Done	24	96.0%	1	4.0%	
Symptoms (upon admission)	Asymptomatic	147	95.5%	7	4.5%	0.660
	Symptomatic	433	94.5%	25	5.5%	
Severity (upon admission)	Mild	286	99.0%	3	1.0%	<0.001
	Moderate	245	93.9%	16	6.1%	
	Severe\Critical	46	78.0%	13	22.0%	
Deterioration Severity	No Deterioration	494	97.6%	12	2.4%	<0.001
	Moderate	63	96.9%	2	3.1%	
	Severe\Critical	48	70.6%	20	29.4%	
Hospital Course	Stable	492	99.4%	3	0.6%	<0.001
	Not Stable	80	74.1%	28	25.9%	

(*Continued*)

Table 4 (Continued).

		Outcome				P-value
		Discharged		Deceased		
		N	%	N	%	
ICU/SD	No	411	98.8%	5	1.2%	<0.001
	Yes	80	75.5%	26	24.5%	
Intubation	No	472	97.3%	13	2.7%	<0.001
	Yes	11	45.8%	13	54.2%	

Discussion

The Pandemic of COVID-19 became an occupational risk that made healthcare workers at more risk of infection and possibly hospitalization. At the beginning of the pandemic, COVID-19 disease appeared to be associated with significant mortality among doctors and health care workers globally.[12] However, a recent systematic review showed a prevalence of hospitalization of 15.1% (95% CI, 5.6–35) and a mortality rate of 1.5% (95% CI, 0.5–3.9) among HCWs.[13] Similarly, in our study, there was no significant impact on HCWs. These differences are probably related to the fact that our healthcare workers are of a younger age group, having fewer comorbidities and obliged with the strict institutional infections control measures. Though a few studies have looked into the relationship of COVID-19 disease outcomes among different ethnic groups, few have shown the link between ethnicity and clinical outcomes, including death. The growing evidence suggests that Asian, Hispanic & American Indians have been associated with more ICU admission and deaths.[14] Such a disparity had also been noted among different ethnicities.[15] The racial and ethnic disparity could not be established in our study as almost all of our sample are Saudi nationals.

In our study, we found no gender difference concerning disease outcomes. Previous data showed differences in the infection rates between males and females. However, the available evidence suggests that male patients have almost three times the odds of ICU admissions.[16] Interestingly enough, more deaths among women are reported in some countries like India. It is needed to explain the gender variance in COVID-19 mortality, especially the presumed batter immunity in women and high lifestyle risk factors in men may define such risk.[16,17]

Behaviors and Practices

Our analysis found that smoking was not associated with COVID-19 severe outcome. This finding is contrary to prior studies. A systemic review concluded that active smoking was moderately linked to severe progression and worse outcomes of COVID-19 infection.[18] However, the analysis was limited because only case series were included, and no randomized trials or retrospective studies were included. A larger systematic review and meta-analysis of forty studies revealed that current and former smokers have an increased risk for a severe COVID-19 infection and a higher mortality rate.[19] This analysis, however, included primarily observational studies. Besides, the severity scale for COVID-19 infection differed across these studies, which may have skewed the results. There may have been missed cases due to labeling smoking status into smoker and non-smoker; not clarifying the method of smoking, the amount of cigarette smoked, period of smoking, and if the cessation of smoking has occurred and for how long. The impact of smoking history on the outcomes of COVID-19 infection needs further studies.

Compared to a study published in July 2020 in Brazil, which found a correlation between getting seasonal Flu vaccine and decreased severity and mortality,[20] our data suggest that the Flu vaccine did not affect the outcome of COVID-19 illness. As there is very limited literature supporting the benefit of the Flu vaccine against COVID-19, we cannot be certain about its effectiveness.[21] Out of the entire study population of 612 people, only 73 people have received the previous year's flu vaccine. This small number is insufficient to determine the impact of the Flu vaccine on the outcomes of COVID-19 infection.

Chronic Illnesses

Patients with pre-existing diabetes have an increased mortality rate compared to non-diabetic patients. A supportive meta-analysis demonstrated a strong association of diabetes with mortality rate,[22] the mechanism of which remains uncertain. Plausible mechanisms include higher affinity cellular binding and efficient virus entry in diabetic patients; decreased viral clearance; diminished T cell immunity; increased susceptibility to hyper-inflammation and dysregulation of the cytokines leading to cytokine storm; and the presence of cardiovascular disease.[23] Furthermore, hyperglycemia and new-onset diabetes mellitus have been observed among COVID-19 patients, a meta-analysis report.[24] Impaired blood glucose regulation in these patients causes downregulation of angiotensin-converting enzyme (ACE-2) receptors leading to high angiotensin II, which has been shown to increase glucose production by the liver and decrease insulin sensitivity.[25] Longstanding hyperglycemia induces metabolic inflammation and impairs the body's immune response and healing process, leading to more severe illness, prolonged recovery, and poor outcomes.[26]

This study found that hypertension was strongly correlated with COVID-19 illness outcomes for hospitalized patients. This finding is consistent with previous studies reporting that hypertension is significantly associated with the increased adverse outcome in patients with coronavirus disease 2019 (COVID-19).[27] This relationship may partly be explained because hypertension is the most common comorbidity among COVID-19 patients. Similarly, our study showed an increased risk of mortality among COVID-19 patients with prior history of congestive heart failure, which is one of the complications of chronic hypertension. This observation is consistent with prior work by Yonas et al.[28] On the other hand, our data showed no association between dyslipidemia and the outcomes of COVID-19 illness. This observation corroborates the findings of a great deal of the previous work by Yang et al. In their meta-analysis, involving twenty-seven studies with a total of 146,364 cases, researchers determined there was no significant relationship between dyslipidemia and COVID-19 morality.[29]

Surprisingly, our data has been unable to demonstrate a significant association between obesity and the outcomes of COVID-19 illness. This study supports evidence from previous systematic reviews and meta-analyses that obesity did not increase hospital mortality among patients admitted with COVID-19 pneumonia.[30] However, these findings are in contrast to a recent meta-analysis suggesting that obese patients are at an increased risk of severe COVID-19 symptoms, acute respiratory distress syndrome (ARDS), hospitalization, intensive care unit (ICU) admission, and undergoing invasive mechanical ventilation.[31]

Compared to non-cancer patients, those admitted for COVID-19 infection and who have a history of cancer were found to have higher mortality. Concordant with this observation, multiple studies reported a mortality rate of 28% among cancer patients.[32,33] Since the median age of cancer diagnosis is 66 years in the USA,[31] we could attribute older age as one of the contributing factors to mortality. Our data does not specify the types of cancer or different therapeutics, so we cannot draw further conclusions. Nonetheless, previous studies have reported that patients with hematological malignancies, such as leukemia, lymphoma, and myeloma, are at a higher risk of mortality.[34]

This study finds that chronic kidney disease (CKD) increases the risk of mortality among COVID-19 patients. Consistent with our observation, a study found that CKD patients deteriorated faster and required ICU admission, especially those on dialysis. Additionally, regardless of their dialysis status, half of those patients died within 28 days of admission.[35] Although we did not further characterize CKD of our study population, a previous study suggests that the mortality correlated to the severity and stage of the kidney disease. Patients with end-stage renal disease (ESRD) and those on hemodialysis are at the most significant risk.[36] This finding could be attributed to the fact that patients with CKD are more likely to have other comorbidities, such as diabetes and hypertension.[37]

Contrary to expectations, this study did not find a significant association between chronic lung disease (CLD) and poor outcomes of COVID-19 illness. We did not, however, specify the type and severity of CLD. This finding differs from the observation of Zhao et al that COVID-19 patients with a pre-existing chronic obstructive pulmonary disease (COPD) had a poorer prognosis than patients without COPD.[18] Furthermore, Shi et al's meta-analysis discovered that asthma was also associated with poor outcomes and higher mortality among COVID-19 patients.[38]

A small prospective study, conducted on patients admitted with COVID-19 in Wuhan, China, showed that patients who received steroids had a poor outcome than those who did not.[39] This study confirms that immunosuppressive medications are associated with poor outcomes among patients admitted with COVID-19 illness. This comes as no surprise as long-term use of these medications, including steroids, will likely alter the immune response to the viral illness. Given the controversy

around the use of Steroids in COVID-19 patients, we take this observation with caution as we did not explore the association of different types of immunosuppressive medications with outcomes of COVID-19 illness.

Clinical Presentation

In our study, the majority (>96%) of mild to moderate disease patients have had a stable hospital course and were ultimately discharged home. On the other hand, nearly one-third (29.4%) of severe to critical illness patients have died. Among patients who required ICU admission, the mortality rate was 24.5%. Our observed mortality rate is lower than what has previously been reported. A systematic review of 32 studies, including more than 69,000 critically-ill COVID-19 patients admitted to the intensive care unit (ICU), revealed that more than half of patients admitted to the ICU did require mechanical ventilation, with an average duration of intubation of 8.4 days and high mortality rate of 58%.[40] A national-scale study of thirteen centers included 156 patients with COVID-19 infection, most of them (89%) with at least one comorbidity, reported that sixty-six percent of patients did require mechanical ventilation and had an average of 10-day length of stay in the ICU. The overall mortality rate was 56%, with the risk increased mainly by older age, sepsis, and more prolonged ICU stays.[41] In a large study from Saudi Arabia, the mortality rate among ICU patients was 27.8 vs 7.8% among non-ICU patients ($p \leq 0.0005$).[42] Despite the heterogeneity in the design of these studies, there seems to be a pattern of certain patients' characteristics and risk factors contributing to poor outcomes of COVID-19 illness.

In conclusion, to our knowledge, this retrospective study is the largest in Saudi Arabia. Our study showed that most of our patients had mild COVID-19, and their disease outcomes were associated with chronic diseases, most significantly hypertension. However, the study did not demonstrate a statistically significant association between smoking and obesity and COVID-19 outcomes.

Disclosure

The authors declare that there is no conflicts of interest in this work.

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