A Retrospective Study of the Factors Associated With Deterioration Severity of COVID-19 Illness at a Tertiary Hospital in Saudi Arabia

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Abstract

Background: COVID-19 has rapidly progressed to a pandemic causing a severe burden on healthcare systems worldwide. It has proven to be a serious threat to certain populations such as elderly and chronically ill people. In this study we aim to determine risk factors contributing and affecting COVID-19 severity and deterioration during the course of illness.

Methods: This is a retrospective cohort study for all hospitalized patients who were diagnosed with COVID-19 from March to July 2020.

Results: A total of 639 patients were included in this study. The majority were Saudi patients (87.3%). 465 (76%) were symptomatic with abnormal x-ray imaging diagnosis (56.2%). Predetermined clinical risk factors were obesity (46.3%), hypertension (42.3%), diabetes mellitus (41.8%), dyslipidemia (39%), Ischemic heart disease (13.2%), chronic lung disease (11%), chronic kidney disease (10.3%), cancer (7.9%), congestive heart failure (6.1%), and immunocompromised patients (4.6%). It was also found that chest x-ray finding upon diagnosis, and presentation of symptoms had a significant impact on the pattern of deterioration.

Conclusion: This study found that elderly and chronically ill patients are at higher risk for more severe COVID-19 infection and risk of deterioration, hospitalization, intensive care unit admission, and probably death when compared to younger and healthier patients.

Background

As of April 2021, there are nearly 138 million cases of Coronavirus Disease 2019 (COVID-19) and nearly 3 million deaths worldwide [1]. Initially, COVID-19 symptoms were not specific, patients presented with flu-like symptoms such as fever and cough that can progress to shortness of breath and pneumonia and may lead to acute respiratory distress syndrome, multi-organ failure, and death [2].

Research efforts have been unified and intensified globally to identify people at greatest risk of developing the infection and progressing from asymptomatic to symptomatic, mild to moderate and severe to critical level causing them to die. Risk factors are better known to the healthcare providers today, these risk factors can vary from demographical attributes such as patient's age, sex, ethnicity, diet, and lifestyle [3] to underlying chronic medical conditions such as obesity, diabetes, hypertension, cardiovascular disease (CVD), kidney disease, and chronic obstructive pulmonary disease (COPD) [4].

It is very helpful for clinicians and healthcare providers to have a clinical prediction model by understanding the possible risk factors within their population in combination to medical conditions associated with COVID-19 severity. Such prediction model will enable them to early classify clinical severity, provide appropriate disposition and prioritize treatment for patients who are at a higher risk of disease progression, prevent their deterioration, and reduce their mortality [3, 2].

Our hospital is a tertiary hospital located in Dhahran, Eastern Province of Saudi Arabia. It serves a population of 300,000 people. Patients from other parts of the Saudi Arabian Kingdom may have different demographic, epidemiologic and clinical characteristics. Determining these indicators and factors could help predict the severity of the illness.

In this study, we report all diagnosed COVID-19 and admitted to our hospital from March to July 2020 for hospitalization. This study presents the demographic, epidemiological, clinical, laboratory, and imaging characteristics of our patients. Moreover, we aim to identify and determine risk factors which contribute and affect COVID-19 severity and deterioration during their illness course.

Methods

Study design and population

This is a retrospective cohort study. All patients were admitted to our hospital with a confirmed diagnosis of COVID-19 and eligible for treatment from March to July 2020. In Saudi Arabia, the Covid-19 confirmed cases reached the peak mid-June 2020. The highest record of more than 2000 COVID-19 critical cases was on mid-April 2020.

The diagnosis of COVID-19 was confirmed by a positive polymerase chain reaction (PCR) test, in addition to the presentation of symptoms, epidemiological and contact history. Patients who were asymptomatic and had no known medical history and risk factors such as pregnancy, chronic diseases and/or on immunocompromised medication were excluded from the study.

Outcome measures

The primary outcome of this study is to assess and study risk factors which contributes illness severity and patients' deterioration during their hospitalization in our hospital. Patients were categorized into either symptomatic or asymptomatic. Symptomatic patients were then subcategorized into: 1) mild, 2) moderate, 3) severe, and 4) critical. Asymptomatic cases were assessed as having a positive PCR with the absence of any associated clinical symptoms. Mild cases were defined with 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 $\geq 94\%$). Severe cases were defined with dyspnea, hypoxia with oxygen saturation $< 94\%$. Finally, critical cases were defined with at least one of these presentations: respiratory failure, septic shock, and/ or multi-organ dysfunction.

Data collection

Data were collected using patients' electronic health records system (EPIC system). EPIC is a fully integrated electronic health records system that provides more versatile and customized reports about patients with any given criteria. Data collected include demographic data (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 whom determined the severity of illness. Separately, 10% of the data were then validated by one of the other co-investigators.

Risk of Bias

All patients admitted to our hospital from March to July 2020 with a confirmed diagnosis of COVID-19 were included in the study without any selection bias.

Sample size

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

At the beginning of the pandemic, all COVID-19 positive cases were hospitalized based on the Saudi Arabian Ministry of Health's (MoH) guidelines. Moving forward and after sufficient understanding of the disease and its behavior, on the 8th of June, the guidelines of the MoH have been modified and home monitoring program was launched for home isolation to specific COVID-19 positive patients. This service was offered to asymptomatic and/ or mildly symptomatic (i.e. low-risk) patients. Thus, our sample has excluded 7 patients who were asymptomatic during their hospitalization.

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 were used to assess the deterioration severity level and other categorical variables. A test was considered significant if the p-value < 0.05. Ordinal logistic regression was performed to predict risk factors for deterioration severity with the baseline characteristics.

Results

The total number of confirm COVID-19 cases were 3400 patients had a positive PCR test and confirmed diagnosis of COVID-19. Out of the total number, 656 patients were hospitalized for medical assistance and monitoring. Out of the 656 patients, 17 patients were excluded for not meeting the inclusion criteria (Fig. 1).

The vast majority of the hospitalized patients were Saudis (87.3%), older than 50 years of age (60.3%), males (53.2%) and non-smokers (92%). The mode of exposure to the virus was mostly unknown to the healthcare providers (58%), following that is contact transmission (36.2%), then international and domestic travelling (4.9%), and (1%) of the patients have acquired it during their hospitalization. The

majority of study participants did not receive the influenza vaccine during the previous year of 2019 (80.2%) and only (6.1%) had travel history within the 14 days prior admission, Table 1 describes the demographical data in details.

It was found that hospitalized patients have had predetermined clinical risk factors associated with their condition at admission, these factors were obesity (46.3%), HTN (42.3%), DM (41.8%), dyslipidemia (39%), IHD (13.2%), chronic lung disease (11%), chronic kidney disease (10.3%), cancer (7.9%), CHF (6.1%), and immunocompromised patients (4.6%). Moreover, only (18%) of the patients were in the normal range of Body mass index (BMI) and (6.6%) were underweight, making overweight and obese patients an obvious risk factor accounting for (76%) of the patients. Another risk factor was associated with hospitalization upon admission was the nature of their job as healthcare worker being a front-liner against the pandemic (3.6%), (Fig. 2). The vast majority of patients were hospitalized because of their presentation of symptoms (76%) and abnormal x-ray findings upon diagnosis (56.2%), however, most of these patients were stable upon admission (82.1%). Symptoms were mostly mild (47.5%) and moderate (42.9%). Severe and critical symptoms accounted for (9.7%) of the cases combined. Moreover, 133 cases deteriorated during the course of hospitalization, out of which 65 (48.9%) patients deteriorated from asymptomatic or mild to moderate, 43 (32.3%) from moderate to severe, and 25 (18.8%) from severe to critical. In addition, 106 (20.3%) of the study patients had required Intensive Care Unit (ICU) admission and only 24 (4.7%) required intubation. By the end of the study, 34 (5.3%) patients died during hospitalization. Table 1 describes both clinical and non-clinical characteristics in details.

Table 2 exhibits the clinical and non-clinical risk factors associated with deterioration severity. The risk factors that had statistically significant impact on patients' condition are age, presentation with symptoms upon admission, severity upon admission, and instability during patients' course of hospitalization, all with p -value <0.05 . Table 3 indicates that medical history has statistically significant impact on the severity of deterioration with p -value <0.05 . In specific, 27.3% of patients who has diabetes, following that 28.4% of hypertension patients, 29.6% chronic lung disease patients, 31.3% of cancer patients, and finally 36.5% of chronic kidney disease patients had their condition deteriorate during their course of hospitalization. Moreover, intubation had a statistically significant ($p<0.001$) impact on the deterioration severity amongst 19 patients, this includes the deterioration of 1 patient to moderate, 4 to severe, and 14 to critical cases. ICU admission had a statistically significant ($p<0.001$) impact as 13 patients have deteriorated to moderate, 40 to severe, and 24 to critical cases. It has also been determined that the longer the patient stays in the hospital the more likely their condition will be deteriorated significantly. And finally, it was found that it is most likely (68%) the patient will die if their condition was critical (Table 2). In addition, it has been found that patients with higher BMI (overweight and Obese) are significantly at a higher risk of condition severity deterioration when associated with older age, diabetes mellitus, hypertension, and dyslipidemia (Table 3).

Table 1
Demographical and clinical characteristics of hospitalized patients
with COVID19

Variable	Category	N	%
Gender	Male	340	53.2
	Female	299	46.8
Age (years)	18–30	78	12.6
	31–40	72	11.7
	41–50	95	15.4
	51–60	195	31.6
	61–70	101	16.3
	71+	77	12.5
Nationality	Saudi	558	87.3
	Non-Saudi	81	12.7
Blood Group	A	143	28.6
	AB	21	4.2
	B	108	21.6
	O	228	45.6
Smoking	No	554	92.0
	Yes	48	8.0
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
Pregnancy	No	531	94.8
	Yes	29	5.2
Mode of Exposure	Domestic Travel	12	2.0
	International Travel	18	2.9

Variable	Category	N	%
	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
Travel History	No	520	93.9
	Yes	34	6.1
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

The severity of deterioration is also affected by the patient's medical history. Preexisting chronic health conditions such as diabetes mellitus, hypertension, cancer, chronic kidney disease, and chronic lung disease had a statistically significant ($p < 0.005$) association with severity of deterioration (Table 4). Ordinal regression analysis was performed at a 95% confidence interval (CI) and revealed that age, chest x-ray (CXR) finding upon diagnosis, and symptoms upon admission had a significant impact on the pattern of deterioration. We found that younger patients, especially those 31–40 years-old, were nearly 1:3 less likely to deteriorate when compared to older patients (71 + years old). Patients with abnormal CXR findings upon diagnosis were three-times more likely to deteriorate compared to those with normal CXR. Furthermore, patients who presented with no symptoms upon admission were 61% less likely to deteriorate when compared to symptomatic patients (Table 5).

Table 2
Presentation of clinical and non-clinical risk factors associated with deterioration severity

		Deterioration Severity								P-value
		No Deterioration		Moderate		Severe		Critical		
		N	%	N	%	N	%	N	%	
Gender	Male	266	78.2	35	10.3	23	6.8	16	4.7	0.738
	Female	240	80.3	30	10.0	20	6.7	9	3.0	
Age (years)	18–30	69	88.5	6	7.7	3	3.8	0	0.0	0.021
	31–40	64	88.9	7	9.7	1	1.4	0	0.0	
	41–50	83	87.4	9	9.5	3	3.2	0	0.0	
	51–60	154	79.0	18	9.2	18	9.2	5	2.6	
	61–70	74	73.3	12	11.9	12	11.9	3	3.0	
	71+	55	71.4	12	15.6	6	7.8	4	5.2	
Nationality	Saudi	440	78.9	55	9.9	40	7.2	23	4.1	0.523
	Non-Saudi	66	81.5	10	12.3	3	3.7	2	2.5	
Smoking	No	435	78.5	58	10.5	38	6.9	23	4.2	0.959
	Yes	37	77.1	5	10.4	4	8.3	2	4.2	
Body Mass Index Groups	Underweight	26	100.0	0	0.0	0	0.0	0	0.0	0.347
	Normal weight	95	81.9	11	9.5	8	6.9	2	1.7	
	Overweight	148	77.1	19	9.9	13	6.8	12	6.3	
	Obese I	142	75.9	25	13.4	14	7.5	6	3.2	
	Obese II	60	84.5	5	7.0	3	4.2	3	4.2	
	Obese III	31	72.1	5	11.6	5	11.6	2	4.7	
Pregnancy	No	409	77.0	58	10.9	41	7.7	23	4.3	0.159
	Yes	20	69.0	7	24.1	2	6.9	0	0.0	
Mode of Exposure	Domestic Travel	10	83.3	1	8.3	0	0.0	1	8.3	0.813
	International Travel	18	100.0	0	0.0	0	0.0	0	0.0	
	Contact	172	77.5	25	11.3	16	7.2	9	4.1	

	Unknown	276	77.5	39	11.0	26	7.3	15	4.2	
	Hospital	5	83.3	0	0.0	1	16.7	0	0.0	
Flu Shot 2019	No	382	77.8	54	11.0	34	6.9	21	4.3	0.744
	Yes	73	77.7	11	11.7	8	8.5	2	2.1	
Travel History	No	394	75.8	61	11.7	43	8.3	22	4.2	0.077
	Yes	31	91.2	1	2.9	0	0.0	2	5.9	
Symptoms (upon admission)	Asymptomatic	135	91.8	5	3.4	4	2.7	3	2.0	< 0.001
	Symptomatic	344	74.0	60	12.9	39	8.4	22	4.7	
Severity (upon admission)	Mild	246	85.1	31	10.7	8	2.8	4	1.4	< 0.001
	Moderate	192	73.6	29	11.1	27	10.3	13	5.0	
	Severe	38	66.7	5	8.8	8	14.0	6	10.5	
	Critical	0	0.0	0	0.0	0	0.0	2	100.0	
Hospital Course	Stable	442	89.3	49	9.9	4	0.8	0	0.0	< 0.001
	Not Stable	28	25.9	16	14.8	39	36.1	25	23.1	
Intubation	No	380	98.7	60	98.4	37	90.2	8	36.4	< 0.001
	Yes	5	1.3	1	1.6	4	9.8	14	63.6	
ICU/SD	No	364	92.6	48	78.7	3	7.0	1	4.0	< 0.001
	Yes	29	7.4	13	21.3	40	93.0	24	96.0	
Hospital Length of Stay	< = 2 days	162	32.1	16	24.6	0	0.0	1	4.0	< 0.001
	3–7 days	206	40.8	25	38.5	4	9.3	6	24.0	
	8 + days	137	27.1	24	36.9	39	90.7	18	72.0	
Outcome	Discharged	494	97.6	63	96.9	40	93.0	8	32.0	< 0.001
	Deceased	12	2.4	2	3.1	3	7.0	17	68.0	

Table 3
Present the significant association between BMI and the risk factors for severity deterioration.

		Obesity
Age (years)	Chi-square	27.971
	df	5
	Sig.	.000*
HCW	Chi-square	.130
	df	1
	Sig.	.719
IHD	Chi-square	.515
	df	1
	Sig.	.473
CHF	Chi-square	.180
	df	1
	Sig.	.672
DM	Chi-square	8.281
	df	1
	Sig.	.004*
HTN	Chi-square	10.715
	df	1
	Sig.	.001*
Dyslipidemia	Chi-square	16.157
	df	1
	Sig.	.000*
Cancer	Chi-square	.484
	df	1
	Sig.	.487
Chronic Kidney Disease	Chi-square	.119

		Obesity
	df	1
	Sig.	.730
Chronic Lung Disease	Chi-square	.757
	df	1
	Sig.	.384
Immunocomp Medication	Chi-square	.042
	df	1
	Sig.	.837

Table 4

Medical history and association with deterioration severity during hospitalization of COVID-19 patients

		Deterioration Severity								P-value
		No Deterioration		Moderate		Severe		Critical		
		N	%	N	%	N	%	N	%	
HCW	No	465	78.4	61	10.3	42	7.1	25	4.2	0.624
	Yes	17	77.3	4	18.2	1	4.5	0	0.0	
IHD	No	421	79.1	55	10.3	36	6.8	20	3.8	0.577
	Yes	59	72.8	10	12.3	7	8.6	5	6.2	
CHF	No	451	79.0	61	10.7	39	6.8	20	3.5	0.092
	Yes	25	67.6	4	10.8	4	10.8	4	10.8	
DM	No	295	82.6	37	10.4	19	5.3	6	1.7	<0.001
	Yes	186	72.7	27	10.5	24	9.4	19	7.4	
HTN	No	295	83.3	35	9.9	20	5.6	4	1.1	<0.001
	Yes	186	71.5	30	11.5	23	8.8	21	8.1	
Dyslipidemia	No	297	79.4	39	10.4	21	5.6	17	4.5	0.338
	Yes	183	76.6	26	10.9	22	9.2	8	3.3	
Obesity	No	263	79.9	33	10.0	20	6.1	13	4.0	0.711
	Yes	217	76.4	32	11.3	23	8.1	12	4.2	
Cancer	No	445	79.3	56	10.0	41	7.3	19	3.4	0.022
	Yes	33	68.8	7	14.6	2	4.2	6	12.5	
Chronic Kidney Disease	No	441	80.0	58	10.5	33	6.0	19	3.4	0.003
	Yes	40	63.5	7	11.1	10	15.9	6	9.5	
Chronic Lung Disease	No	414	80.2	56	10.9	26	5.0	20	3.9	0.023
	Yes	45	70.3	7	10.9	10	15.6	2	3.1	
Immunocomp Medication	No	439	79.1	60	10.8	36	6.5	20	3.6	0.689
	Yes	21	77.8	3	11.1	1	3.7	2	7.4	

Table 5

This table presents the ordinal logistic regression for deterioration severity with the baseline characteristics.

		P-value	OR	95% CI for OR	
				Lower	Upper
Gender	Male	0.336	1.27	0.78	2.09
	Female*	.	1	.	.
Age (years)	18–30	0.166	0.50	0.19	1.34
	31–40	0.044	0.37	0.14	0.98
	41–50	0.057	0.42	0.17	1.03
	51–60	0.604	0.83	0.42	1.66
	61–70	0.87	1.07	0.48	2.38
	71+*	.	1	.	.
Nationality	Saudi	0.776	0.90	0.44	1.84
	Non-Saudi*	.	1	.	.
Blood Group	A	0.929	0.98	0.56	1.70
	AB	0.700	1.24	0.41	3.75
	B	0.659	1.14	0.64	2.05
	O*	.	1	.	.
Smoking	No	0.562	0.78	0.33	1.83
	Yes*	.	1	.	.
Body mass index groups	Overweight	0.170	0.52	0.21	1.32
	Obese I	0.398	0.67	0.26	1.71
	Obese II	0.200	0.49	0.16	1.47
	Obese III*	.	1	.	.
Pregnancy	No	0.326	0.64	0.26	1.57
	Yes*	.	1	.	.
Mode of Exposure	Domestic\International Travel	0.787	1.28	0.22	7.48
	Contact	0.332	1.25	0.80	1.97
	Unknown*	.	1	.	.

		P-value	OR	95% CI for OR	
				Lower	Upper
Flu Shot 2019	No	0.994	1.00	0.56	1.78
	Yes*	.	1	.	.
Travel History	No	0.421	2.27	0.31	16.81
	Yes*	.	1	.	.
CXR Finding (Upon diagnosis)	Normal	0.005	0.36	0.18	0.74
	Abnormal*	.	1	.	.
Symptoms (Upon admission)	Asymptomatic	0.007	0.39	0.19	0.77
	Symptomatic*	.	1	.	.
Severity (Upon admission)	Mild	0.619	0.81	0.35	1.86
	Moderate	0.327	0.73	0.38	1.38
	Severe\Critical*	.	1	.	.
*Reference group					

Discussion

Patient characteristics

The COVID-19 era brought to the medical field many uncertainties about factors that may influence the severity of the infection, further complicating the dilemma of clinical management. The widespread COVID-19 infection, due to the high infectivity of the virus, allowed many healthcare providers to observe and experience different behavior of COVID-19 severity among the different patient populations. Those observations raised the clinical question of what factors can determine COVID-19 disease severity?

Several studies suggest that factors like age, gender, and underlining comorbidities play a significant role in determining COVID-19 severity [5]. In most recent studies that looked into age as a determining factor of disease severity, it was found that older adults are at higher risk for severe COVID-19- associated-illness; hence, they are most vulnerable to the disease and have the most severe form of the illness and the worst outcome. In this study, we could not observe a significant difference between males and females among confirmed cases. However, there are many data in the literature that suggest that males are more prone to get a severe form of COVID-19 infection that may need intensive intervention. Although it is not statistically significant but we found that male patients are (27%) more likely to deteriorate and have severe illness than females (Table 5) [6].

Observational studies demonstrate a higher risk of contracting COVID-19 infection and disease severity among healthcare providers [7, 8, 9]. Such finding did not appear to be significant among our studied population. This could be due to the fact that healthcare workers are mostly of a younger age group, have fewer comorbidities, and are obliged to follow institutional strict infection control measures. Other studies have also linked the disease severity to certain ethnicities [7, 8, 9]. This factor was not evaluated in this study since most of the cohort are Saudi nationals (87.3%).

Moreover, we found that comorbidities such as diabetes mellitus, chronic obstructive lung disease, obesity, and cardiovascular diseases were associated to severe COVID-19 disease, which is similar to what was reported in the literature [10, 11, 12].

Behaviors and practices

We found that smoking was not strongly associated with deterioration severity of COVID-19 infection and severe outcome. This finding is contrary to what Patanavanich & Glantz have reported in their meta-analysis published in 2020, that smoking is a significant risk factor for severe progression of COVID-19 infection compared to non-smokers [13]. In our study, we believe that some smokers might have not disclosed their smoking habits, which might be due to cultural barriers and fear of being judged. Besides, some patients who smoke electronic cigarette classified themselves as non-smokers. Research studying the link between tobacco smoking and COVID-19 infection is still limited. There may have been missed cases in the literature because of mislabeling of smoking status, clarity of smoking methods, the number of cigarettes smoked in general, smoking-status duration, and whether or not smoking cessation has occurred and for how long.

A study in Brazil found that getting the seasonal Flu vaccine decreased the severity and mortality of COVID-19 illness.¹⁰ To the contrary, our data suggest that the flu vaccine did not affect the severity outcome. Amongst our study cohort of 639 individuals, only 73 reported having received the previous year's flu vaccine. Additionally, there is scarcity in literature that examined the impact of the Flu vaccine on COVID-19 illness. Hence, the effect of the Flu vaccine on the severity of COVID-19 disease cannot be fully determined in this study.

Chronic illnesses

In this study, the data strongly suggest that patients with preexisting diabetes mellitus were at an increased risk for severe COVID-19. This finding is supported by several published studies including a meta-analysis by Kumar et al. published in 2020 showed an increase in the severity of Covid-19 infection and mortality by two folds in diabetic patients compared to non-diabetic [14]. Another meta-analysis published in 2020 by Huang, Lim, and Pranata showed that diabetes was associated with adverse outcomes in COVID-19 patients in terms of severity of the infection, rapid disease progression; acute respiratory distress syndrome (ARDS); and mortality. However, the publication was limited by confounding factors such as preexisting risk factors, including older age and hypertension. Diabetes mellitus as a single risk factor was more prominent in studies that include younger diabetic patients without any other comorbidity [15].

Furthermore, the effect of cardiovascular diseases, such as ischemic heart disease (IHD) and congestive heart failure (CHF), on COVID-19 illness was startling and unforeseen. Our data showed no significant correlation between cardiovascular diseases (e.g., IHD and CHF) and deterioration severity in Covid-19 patients. A meta-analysis showed that preexisting chronic diseases, including coronary artery disease (CAD) and cerebrovascular diseases (CVD), increased the risk for developing severe COVID-19 disease and ICU admission [16]. Another meta-analysis indicated that CHF is an independent risk factor that increases the risk for hospitalization, deterioration severity, and mortality in patients infected by COVID-19, however, more data about the stage of CHF was needed [17].

Regarding hypertension, our results suggest a strong correlation with deterioration severity of COVID-19 illness for hospitalized patients. This observation is consistent with previous studies reporting that hypertension is significantly associated with the increased risk of illness progression in patients with COVID-19 [18, 19]. The fact that hypertension is the most common comorbidity among COVID-19 patients may explain this association. A plausible theory is that human pathogenic coronaviruses, namely the severe acute respiratory syndrome coronavirus family (e.g., SARS-CoV, MERS-CoV, and SARS-CoV-2), bind to their target cells through angiotensin-converting enzyme 2 (ACE2). Subsequently, it is expressed by epithelial cells of the lung, intestine, kidney, and blood vessels. However, it remains unclear whether or not poorly controlled blood pressure is a risk factor for getting infected with COVID-19 and developing severe disease [20].

To our surprise, the analysis revealed that dyslipidemia was not significantly correlated with COVID-19 illness severity or progression, but other studies showed otherwise. Dyslipidemia was strongly associated with more severe COVID-19 illness [21]. In this study, different cholesterol levels were not measured, however, it is believed that elevated low-density lipoprotein (LDL) and low high-density lipoprotein (HDL) levels potentiate the inflammatory process caused by the COVID-19 infection [22].

Moreover, our study showed that obesity has a strong correlation between hospital course deterioration of COVID-19 infection especially when associated with age, diabetes mellitus, hypertension, and dyslipidemia. This finding is consistent with previous studies showing that obesity was significantly associated with the increased risk of illness progression in patients with coronavirus disease 2019 (COVID-19) [23]. Additionally, obesity increases the risk for hospitalization, ICU admission, need for invasive ventilation, and death among patients with COVID-19 [24, 25]. About 47.3 % of our population are obese. Out of which patients of the age between 51–60 years (53.6%), patients with DM (53%), patients with HTN (53.9%), and patients with dyslipidemia (56.3%). Obesity is a major healthcare concern due to its associated chronic diseases, including type 2 diabetes, heart diseases, stroke, and certain cancers. Obesity can significantly reduce the patient's quality of life. Recent studies have shown the negative impact on the immune system, making the host vulnerable to infectious diseases. Obesity has appeared as a strong risk factor for disease severity in the current COVID-19 pandemic. Moreover, several studies have demonstrated that obese patients with COVID-19 have a higher risk of severe disease, hospitalization, and increased probability of death [26].

Amongst our study cohort, cancer patients had worse clinical course than non-cancer patients, ranging from moderate to critical. Our result was consistent with multiple studies published globally. A multi-center study has shown that cancer patients infected with COVID19 were more susceptible to severe deterioration of illness and outcomes, with hematological and lung cancers being the highest in adverse events [27]. Another study showed that cancer patients were intubated more frequently than others, which could be attributed to cytokine-associated lung injury in cancer patients with weakened immune systems [28]. Another study found that cancer patients have elevated levels of “Neutrophil, NLR, IL-6, LDH and PCT” [29].

Additionally, our data revealed that patients with chronic kidney disease (CKD) and infected with COVID-19 were more susceptible to more severe illnesses. Previous studies have shown that patients with CKD were at a higher risk for deterioration and poor prognosis [30]. A study by Chan et al that was published in 2021 documented a higher incidence of neutrophilia in such patients. Another study concluded that CKD was a significant predictor of COVID-19 severity among hospitalized patients [31]. The exact mechanism is not precise. Nonetheless, concomitant high blood pressure may play a role due to the decrease in ACE2 by SARS-CoV-2 [32].

Moreover, a significant correlation between chronic lung disease (CLD) and deterioration of COVID-19 illness was found. This finding is supported by a meta-analysis of 19 studies presenting the negative impact of preexisting COPD and tobacco smoking on the severity of COVID-19 infection. Patients with COPD were more likely to have severe COVID-infection by four-folds, compared to those without COPD [33]. However, a significant correlation between the use of immunosuppressive medications and deterioration severity for COVID-19 infection was not found in this study. A cohort study reported a similar finding involving more than 5,000 patients with inflammatory bowel disease (IBD). The use of systemic immunosuppressive therapy in those patients did not increase the risk for COVID-19 infection. While this observation is encouraging, the study had a few limitations. Patients with mild symptoms may not have been tested for COVID-19; the patients who self-discontinued their medications were not classified as non-users. The exact dose of the immunosuppressive medications was not factored in [34].

Clinical presentation

At the beginning of the COVID-19 pandemic, the health authority in Saudi Arabia mandated all COVID-19 positive patients to be admitted to hospitals, regardless of the presence of symptoms. Worth mentioning that in Saudi Arabia, the COVID-19 confirmed cases reached their peak in mid-June 2020 and the highest record of critical cases reached more than 2000 cases in mid-April 2020. Consequently, our study showed a significant correlation between the presence of symptoms upon admission and the deterioration severity. Among those admitted to the hospital with no symptoms, (91.8%) showed no deterioration, (3.4%) showed moderate deterioration, (2.7%) showed severe deterioration, and only (2%) showed critical deterioration. On the other hand, for those who presented with symptoms upon admission, patients were slightly more likely to deteriorate leaving us with (74%) of symptomatic patients showed no deterioration while the remaining (26%) of patients showed moderate (12.9%), severe (8.4%), and critical deterioration (4.7%). Similar findings reported by Chin et al. in their study on patients admitted to the Zhongnan

Hospital of Wuhan University [35]. Chin et al. study showed that patients with severe symptoms and unstable hospital course were more likely to deteriorate. One of the limitations of their study, they only included symptomatic patients since the study was conducted in a center only for those with severe symptoms. Our study included both asymptomatic and symptomatic patients, which gives our study more strength in its findings.

Previous studies showed an association between specific symptoms upon admission and deterioration severity of the COVID-19 illness course. A cohort study by Zhou et al. concluded that of 191 hospitalized patients, the most common presentations were fever in (94%) and cough in (79%) upon admission, which showed an increase in mortality with tachypnea [36]. Another systematic review and meta-analysis by Rodriguez-Morales et al., described the most common symptoms were fever (88.7%), cough (57.6%), dyspnea (45.6%), myalgia or fatigue (29.4%), sore throat (11.0%), headache (8.0%), and diarrhea (6.1%) [37]. Anosmia was associated with a mild clinical course [38]. We are not aware of prior work that studied the correlation between the severity of the symptoms upon admission and the deterioration severity of the COVID-19 illness course. In our study, we looked at the presence and the severity of symptoms upon admission. Among those who presented with mild symptoms majority (85.1%) showed no clinical deterioration in their hospital course, and only (5.4%) of this group showed severe or critical deterioration.

In contrast, for those with moderate symptoms upon admission, (73.6%) showed no deterioration, and up to (15.3%) showed severe to critical deterioration. Whereas if they had severe symptoms upon admission, they had an (8.8%) chance for moderate deterioration and (24.5%) for severe or critical deterioration. This significant finding showed a strong correlation between the severity of the symptoms upon admission and the likelihood of deterioration during the hospital stay.

Hospital course and care complexity

Hospital course and care complexity among hospitalized patients with COVID-19 varied considerably. We evaluated specific indicators of care complexity such as invasive ventilation, admission or transfer to the intensive care unit (ICU) or step down (SD), and the hospital length of stay (LOS) to explore their association with deterioration severity of COVID-19 illness. Expectedly, these indicators correlated positively with the deterioration severity of COVID-19 illness. For instance, patients who required invasive ventilation and admission to the ICU or SD were more likely to have severe to critical deterioration of their illness. Among this study cohort, about 10% of patients who had severe deterioration and two-thirds (63.6%) of those who had critical clinical course were intubated. On the other hand, a third of the patient who had moderate deterioration had to stay in the ICU for some time, while more than 90% of those who had severe to critical course ended up in the ICU. Consistent with prior work, patients who went through moderate to severe deterioration of their illness (e.g., respiratory distress) required invasive ventilation and admission to the ICU. Moreover, those patients had additional risk factors such as old age and obesity, which have led to a more extended hospital stay [39].

According to a meta-analysis published in 2020, the hospital length of stay (LOS) of patients admitted with COVID-19 varied from less than seven days to almost two months [40]. Patients who spent more

time (days) in the hospital were more likely to have gone through more severe deterioration of COVID-19 illness and subsequently unfavorable outcome (death). A hospital LOS of more than seven days was significantly associated with severe or critical clinical course in our study. While more extended hospital stays (more than seven days) tend to be in intensive care (ICU) or step-down (SD) units, we did not further characterize our LOS data based on the location of admission. This limitation was also reported in the meta-analysis by Rees et al.

Conclusion

Similar to what is found in the literature, this study confirms that elder patients and patients with chronic medical conditions (mainly; cardiovascular, chronic kidney disease, chronic lung disease & diabetes) are at higher risk for more severe COVID-19 infection when compared with healthy individuals infected with COVID-19. This population is at higher risk for hospitalization. Even then, they are still at a higher risk of deterioration, ICU admission, ventilation, and death.

Patients who are admitted at early presentation of their symptoms progressed better than those who came with moderate to severe symptoms. Public health authorities and primary care practitioners are expected to raise awareness about this correlation amongst the population as well as healthcare providers. COVID-19 threat on this vulnerable population is an alert for the healthcare industry and governments to develop short and long term plans to reduce the prevalence of modifiable chronic medical conditions. Meanwhile, those who are at a higher risk for acquiring severe COVID-19 should have a strict preventive measure and social distancing to reduce their exposure. Moving forward, we would recommend a post-discharge follow-up study to determine any long term complications or consequences after their course of illness.

Abbreviations

Abbreviation	Stands for
COVID-19	Corona Virus Disease 2019
CVD	cardiovascular disease
COPD	chronic obstructive pulmonary disease
PCR	polymerase chain reaction
IHD	Ischemic heart disease
CHF	congestive heart failure
DM	Diabetes Mellitus
HTN	Hypertension
MoH	Ministry of Health
Intensive Care Unit	ICU
BMI	Body Mass Index
CI	confidence interval
CXR	Chest x-ray

Declarations

Ethics Approval

The study received the Institutional Review Board's approval (no. 20-33) on October 2020.

Consent to Participate

Patients consent form was waived due to the retrospective study design with definite anonymity of all participants.

Availability of data and material

Data is available upon request

Competing Interests

The authors declare that there are no conflict of interests

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Authors' contribution

All authors have contributed in the data collection (YR, NB, WA, AM), data validation (MJ, HM), and writing (HM, MJ, AD, AA, KK, HK) and reviewing (TZ, SM, SQ) of the manuscript.

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Not Applicable

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Figures

Figure 1

Study flow diagram

Figure 2

Risk factors associated with hospitalization of COVID-19 patients