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ORIGINAL RESEARCH

Predictors of Length of Hospital Stay, Mortality, and Outcomes Among Hospitalised COVID-19 Patients in Saudi Arabia: A Cross-Sectional Study

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Background: COVID-19 pandemic is a major strain on health and economic systems, with rapidly increasing demand for in patients' facilities. Disease diagnosis and estimating patients at higher risk is important for the optimal management during the pandemic. This study aimed to identify the predictors of mortality and length of hospital stay in COVID-19 patients.

Methods: A retrospective cross-sectional study was conducted between March 2020 and August 2020 at Al-Noor Specialist Hospital in Mecca, Saudi Arabia. All patients who were admitted and had a confirmed COVID-19 diagnosis by a real-time polymerase chain reaction (PCR) were included in the study. Descriptive statistics were used to describe patients' demographic characteristics, laboratory findings, and clinical outcomes. Multiple logistic/linear regression analysis was used to identify predictors of death and length of stay at the hospital.

Results: A total of 706 patients were hospitalised for COVID-19. The mean age was 48.0 years (SD: 15.6 years). More than half of the patients (68.5%; n= 292) were males. The median duration of stay at the hospital was 6.0 days (IQR: 300–10:00). The prevalence rate of venous thromboembolism (VTE) among the patients was 3.0% (n= 21). In the multivariate logistic regression analysis, age (AOR: 1.05; 1.02–1.09), patients with end-stage renal disease (AOR: 6.44; 2.20–18.87), low Oxygen saturation SPO2 (AOR: 9.92; 4.19–23.50), D.dimer >0.5 (AOR: 13.31; 5.45–32.49), ESR>10 mm/h (AOR: 4.08; 1.72–9.68), Ferritin>400mcg/L (AOR: 18.55; 6.89–49.96), and Procalcitonin>0.5ug/L (AOR: 8.23; 1.81– 37.40) were associated with a higher risk of death among patients with COVID-19. Patients with VTE (AOR: 12.86; 3.07– 53.92) were at higher risk of death due to COVID-19.

Conclusion: Hospitalised COVID-19 patients have multiple negative consequences in terms of their laboratory findings, signs and symptoms. Age and end-stage renal diseases have a significant impact on the mortality rate and the length of hospital stay among COVID-19 patients.

Keywords: COVID-19, hospitalisation, length of stay, survival, ICU, Saudi Arabia

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was discovered in China in 2019, is an ongoing pandemic.[1] In March 2021, it was reported that there are more than 117 million confirmed cases in the world, and the total number of deaths in the world is around 2,600,000 in 220 countries, with a mortality rate of around 2%.[2] In Saudi Arabia, there were around 380,000 confirmed infected cases by January 2021, and a mortality rate of around 1.7%.[3]

Patients with COVID-19 usually complain of fever, cough, fatigue, anorexia, myalgia, and diarrhoea,[4] but in severe illness, usually dyspnoea is the most common symptom often accompanied by hypoxemia.[4] Mortality rates depend on patients who have severe respiratory failure related to interstitial pneumonia and acute respiratory distress syndrome,[5] but higher mortality is found in association with older age, male sex, pre-existing cardiovascular diseases, uncontrolled diabetes, hypertension, asthma, chronic lung disease, and d-dimer greater than 1 μg/mL at admission.[6] Length of hospital stay due to the COVID-19 depends on patients' clinical situation, however, it also depends on local guidelines in the institution or local health authority and the capacity of hospitals.[7,8]

COVID-19 pandemic is a major strain on health and economic systems, and the demand for inpatients' facilities is increasing with the increase in the number of infected cases.[9] Predicting factors associated with the need for hospitalisation and length of stay can be important to help in aid prioritizing patients, decision-making and contingency planning.[10] This study aimed to identify the predictors of mortality and length hospital of stay in COVID-19 patients.

Methods

Study Design and Participants

A retrospective cross-sectional study was conducted at Al-Noor Specialist Hospital in Mecca, Saudi Arabia. Al-Noor Specialist Hospital is a tertiary hospital in Mecca, Saudi Arabia, and it is part of the Ministry of Health. The description of the study settings and the hospital has been described previously.[11] All patients had a confirmed COVID-19 diagnosis by a real-time polymerase chain reaction (PCR). The PCR samples were obtained through a nasopharyngeal swap. All patients were admitted between March 15, 2020, and June 15, 2020 and they were followed up for a time to assess the clinical outcome; and the final date of follow-up was August 15, 2020. Data collection were between March 2020, and August 2020. All patients who were admitted and had a confirmed diagnosis of COVID-19 during the study period were included in the study.

Data Collection and Study Variables

Data were collected from patients' files and electronic records using a unique medical record number (MRN) for each patient. All data were collected, reviewed and checked by a medical team, including medical residents and a consultant pulmonologist. Data included the patient's demographics, clinical symptoms, comorbidity, and laboratory findings. Data were collected at the time of admission to the hospital. Patients were classified according to their severity based on the following category: mild, moderate, severe and, critically severe disease. The definition of these categories has been described previously.[11]

Outcomes

The primary outcome was predictors of patients' admission to an intensive care unit. Secondary outcomes were to identify predictors of length of hospital stay and mortality.

Ethical Approval and Consent-to-Participate

The study protocol and study methodology were approved by the Ministry of Health's Institutional Review Board (IRB), as well as the hospital (No H-02-K-076-0920-386). Patients informed consent were obtained and patients were informed that their clinical data would be used for clinical or research purposes, while keeping all their personal information confidential. The ethical principles of the Declaration of Helsinki were adhered to during collection, handling, and storage of data, and all care was taken to protect patient confidentiality.

Statistical Analysis

Descriptive statistics were used to describe patients' demographics, laboratory findings, and clinical outcomes. Independent sample *t*-test was used to compare the mean value for continuous variables. A Chi-squared test/Fisher test was used to compare proportions for categorical variables. Multiple logistic/linear regression analysis was used to identify predictors of death and length of stay at the hospital, and a confidence interval of 95% ($p < 0.05$) was applied to represent the statistical significance of the results. All statistical analyses were conducted using SPSS (Statistical Package for the Social Sciences) version 25.0 software (SPSS Inc.).

Results

Patients' Clinical Characteristics

Table 1 below shows the characteristics of COVID-19 patients at presentation to the hospital. A total of 706 patients were hospitalised for COVID-19. The mean age was 48.0 years (SD: 15.6 years). More than half of the patients (68.5%; n= 292) were males. The majority of

Table 1 Patients Demographic Characteristics at Presentation

Demographics	All Patients (n=706)	Mild Cases (n= 238)	Moderate Cases (n= 214)	Severe Cases (n= 171)	Critical Cases (n= 83)	P-value
Age (years; mean (SD))	48.0 years (15.6)	41.4 years (14.1)	48.4 years (14.3)	51.5 years (16.0)	58.4 years (14.5)	0.001**
Gender (Total n= 426, Mild n= 168, Moderate n= 154, Severe n= 58, Critical n= 46)						
Male No. (%)	292 (68.5)	116 (69.0)	96 (62.3)	49 (84.5)	31 (67.4)	0.022*
Healthcare worker (Total n= 705, Mild n= 238, Moderate n= 214, Severe n= 170, Critical n= 83)						
Yes No. (%)	25 (3.5)	11 (4.6)	6 (2.8)	6 (3.5)	2 (2.4)	0.691
Nationality No. (%)						
Non-Saudi	435 (61.6)	160 (67.2)	135 (63.1)	90 (52.6)	50 (60.2)	0.026*
Smoking history (Total n= 698, Mild n= 234, Moderate n= 212, Severe n= 169, Critical n= 83)						
Yes No. (%)	122 (17.3)	46 (19.7)	31 (14.6)	36 (21.3)	9 (10.8)	0.102
Body mass index (BMI)						
BMI >30 kg/m^2	88 (15.8)	18 (11.1)	27 (16.7)	30 (18.9)	13 (17.8)	0.250
Comorbidities No. (%)						
Diabetes mellitus	254 (36.0)	55 (23.1)	72 (33.6)	73 (42.7)	54 (65.1)	0.000***
Hypertension	213 (30.2)	38 (16.0)	68 (31.8)	62 (36.3)	45 (54.2)	0.000***
Coronary artery disease	77 (10.9)	4 (1.7)	19 (8.9)	35 (20.5)	19 (22.9)	0.000***
End-Stage Renal Disease	64 (9.1)	8 (3.4)	20 (9.4)	13 (7.6)	23 (27.7)	0.000***
Asthma	28 (4.0)	11 (4.6)	7 (3.3)	8 (4.7)	2 (2.4)	0.730
Congestive heart failure	27 (3.8)	1 (0.4)	5 (2.3)	13 (7.6)	8 (9.6)	0.000***
Cerebrovascular accident	17 (2.4)	1 (0.4)	0	7 (4.1)	9 (10.8)	0.000***
Chronic obstructive pulmonary disease	14 (2.0)	2 (0.8)	4 (1.9)	5 (2.9)	3 (3.6)	0.320
Chronic liver disease	4 (0.6)	0	1 (0.5)	1 (0.6)	2 (2.4)	0.095
Cancer	3 (0.4)	0	1 (0.5)	0	2 (2.4)	0.024*
Tracing history No. (%)						
Recent travel history (Total n= 704, Mild n= 238, Moderate n= 212, Severe n= 171, Critical n= 83) (Yes) No. (%)	69 (9.8)	30 (12.6)	32 (15.1)	6 (3.5)	1 (1.2)	0.000***

(*Continued*)

Table 1 (Continued).

Demographics	All Patients (n=706)	Mild Cases (n= 238)	Moderate Cases (n= 214)	Severe Cases (n= 171)	Critical Cases (n= 83)	P-value
Contact with traveller (Total n= 706, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 83) (Yes) No. (%)	84 (11.9)	38 (16.0)	39 (18.2)	5 (2.9)	2 (2.4)	0.000***
Contact with COVID-19 patient (Total n= 706, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 83) (Yes) No. (%)	324 (45.9)	127 (53.4)	101 (47.2)	65 (38.0)	31 (37.3)	0.007**
Vital signs upon arrival to hospital No. (%)						
Fever (≥ 38°C) (Yes) No. (%)	334 (47.3)	71 (29.8)	84 (39.3)	127 (74.3)	52 (62.7)	0.000***
Respiratory rate > 30 (Yes) No. (%)	67 (9.5)	1 (0.4)	1 (0.5)	38 (22.2)	27 (32.5)	0.000***
SPO2<93 (Yes) No. (%)	156 (22.1)	6 (2.5)	6 (2.8)	97 (56.7)	47 (56.6)	0.000***
Heart rate>125 (Yes) No. (%)	30 (4.2)	0	4 (1.9)	8 (4.7)	18 (21.7)	0.000***
Outcome No. (%) (n= 680)						
Deceased	54 (7.6)	0	0	1 (0.6)	53 (71.6)	0.000***
Not recovered	3 (0.4)	0	0	0	3 (4.1)	0.000***
Recovered	623 (91.6)	235 (100)	214 (100)	156 (99.4)	18 (24.3)	0.000***
Respiratory diseases						
Venous thromboembolism	21 (3.0)	0	3 (1.4)	4 (2.3)	14 (16.9)	0.000***
Pneumonia (radiologically)	450 (63.6)	0	215 (99.5)	155 (90.6)	80 (96.4)	0.000***

Notes: *p < 0.05; **p < 0.01; ***p < 0.001.
Abbreviations: COVID-19, coronavirus disease-2019; SD, standard deviation; No, number (frequency).

them were having mild to moderate cases. Twenty-five patients (3.5%) reported working in the healthcare sector. More than half of them (61.9%; n= 435) were non-Saudi. Around 17.4% (n= 122) reported a history of smoking. The most common comorbidities were diabetes mellitus (DM) (36.0%, n= 254), hypertension (30.2%, n= 213), and coronary heart diseases (10.9%; n= 77). Around 9.8% of the patients (n= 69) reported a recent travel history. Regarding the severity of the patients' case, 33.7% were mild, 30.3% were moderate, and 24.2% were severe, and 11.8% were critical and required intensive care unit (ICU) care. Regarding patients' vital signs upon arrival to hospital, 47.3% (n= 334) had fever (body temperature > 38 °C), 9.5% (n= 67) had respiratory rate (RR) more than 30, 22.1% (n= 156) had SPO2 < 93, and 4.2% (n= 30) had heart rate (HR) > 125.

Fever was the most common symptom at presentation (72.4%, n= 511), followed by cough (63.0%, n= 445), and shortness of breath (56.4%, n= 398) (Table 2). Fever, cough, shortness of breath, nausea/vomiting, headache, loss of taste and smell, sputum were more common across severe and critical cases compared to others.

Laboratory Findings

Around 16.5% (n= 116) of the patients had white blood cell (WBC)> 10,000, 13.9% (n= 98) had WBC< 4000, and 21.0% (n= 148) of them had lymphocyte count <1500. About 12.6% (89) had platelet count < 150 and 29.9% (n= 210) had D.dimer >0.5. The proportion of patients who had WBC >10,000, lymphocyte count <1500, platelet count < 150, and D.dimer >0.5 increase as the severity of the disease increase in a statistically significant pattern (p<0.001). The mean Neutrophil-lymphocyte ratio (NLR) value was 9.9 (SD:33.5). The most common blood groups of COVID-19 patients were A+, O+, and B+ accounting for 35.7%, 28.6%, and 20.5% respectively (Table 3).

Regarding patients' inflammatory measures, around half of the patients had erythrocyte sedimentation rate (ESR)>10 mm/h and C-reactive protein (CRP)>0.3 mg/dl. One-third of the patients had Ferritin>400mcg/L, and 1.8% of them had Procalcitonin>0.5ug/L. Concerning patients' liver function tests, around one-third of the patients had AST>40 and ALT>40. Additionally, 40.1% of them had lactate dehydrogenase (LDH)>230 U/L, and 6.2% had Bilirubin>18.7 umol/L. Regarding patients'

Table 2 Patient Signs and Symptoms Stratified by Severity

Variable	All Patients (n=706)	Mild Cases (n= 238)	Moderate Cases (n= 214)	Severe Cases (n= 171)	Critical Cases (n= 83)	P-value
Fever	511 (72.4)	143 (60.1)	152 (71.0)	150 (87.7)	66 (79.5)	0.000***
Cough	445 (63.0)	140 (58.8)	128 (59.8)	117 (68.4)	60 (72.3)	0.047*
Shortness of breath	398 (56.4)	90 (37.8)	97 (45.3)	143 (83.6)	68 (81.9)	0.000***
Fatigue	176 (25.0)	52 (21.8)	43 (20.1)	61 (35.9)	20 (24.1)	0.002**
Nausea/vomiting	118 (16.7)	38 (16.0)	23 (10.7)	43 (25.1)	14 (16.9)	0.003**
Sore throat	115 (16.3)	54 (22.7)	29 (13.6)	25 (14.6)	7 (8.5)	0.006**
Myalgia	108 (15.3)	31 (13.0)	24 (11.3)	42 (24.6)	11 (13.3)	0.002**
Headache	102 (14.4)	31 (13.0)	28 (13.1)	31 (18.1)	12 (14.5)	0.460
Loss of taste	98 (13.9)	30 (12.6)	21 (9.8)	21 (12.3)	26 (31.3)	0.000***
Loss of smell	90 (12.7)	28 (11.8)	19 (8.9)	18 (10.5)	25 (30.1)	0.000***
Diarrhea	52 (7.4)	19 (8.0)	13 (6.1)	15 (8.8)	5 (6.0)	0.705
Sputum	35 (5.0)	10 (4.2)	8 (3.7)	11 (6.4)	6 (7.2)	0.447
Runny nose	25 (3.5)	16 (6.7)	5 (2.3)	2 (1.2)	2 (2.4)	0.012*
Haemoptysis	2 (0.3)	0	0	1 (0.6)	1 (1.2)	0.228

Notes: *p<0.05; **p<0.01; ***p<0.000.

Table 3 Laboratory Findings of the Study Participants Stratified by Severity

Variable	All Patients (n=706)	Mild Cases (n= 238)	Moderate Cases (n= 214)	Severe Cases (n= 171)	Critical Cases (n= 83)	P-value
Complete Blood Count						
WBC >10,000 (Total n= 701, Mild n= 234, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	116 (16.5)	17 (7.3)	22 (10.3)	32 (18.7)	45 (54.9)	0.000***
WBC <4000 (Total n= 705, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	98 (13.9)	34 (14.3)	34 (15.9)	21 (12.3)	9 (11.0)	0.638
Lymphocyte count <1500 (Total n= 704, Mild n= 237, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	148 (21.0)	25 (10.5)	40 (18.7)	43 (25.1)	40 (48.8)	0.000***
NLR (Mean (SD))	9.9 (33.5)	1.17 (2.33)	1.23 (2.28)	9.2 (66.9)	12.8 (18.8)	0.000***
Platelet < 150 (Total n= 704, Mild n= 238, Moderate n= 214, Severe n= 170, Critical n= 82) (Yes) No. (%)	89 (12.6)	21 (8.8)	23 (10.7)	22 (12.9)	23 (28.0)	0.000***
D.dimer >0.5 (Total n= 703, Mild n= 236, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	210 (29.9)	27 (11.4)	35 (16.4)	91 (53.2)	57 (69.5)	0.000***
Blood Groups (Total n= 322, Mild n= 82, Moderate n= 86, Severe n= 114, Critical n= 40) (Yes) No. (%)						
A+	115 (35.7)	34 (41.5)	21 (24.4)	44 (38.6)	16 (40.0)	0.000***
A-	2 (0.6)	0	0	2 (1.8)	0	
AB+	22 (6.8)	5 (6.1)	5 (5.8)	9 (7.9)	3 (7.5)	
AB-	1 (0.3)	1 (1.2)	0	0	0	
B+	66 (20.5)	16 (19.5)	24 (27.9)	20 (17.5)	6 (15.0)	
B-	3 (0.9)	1 (1.2)	2 (2.3)	0	0	
O+	92 (28.6)	19 (23.2)	27 (31.4)	32 (28.1)	14 (35.0)	
O–	21 (6.5)	6 (7.3)	7 (8.1)	7 (6.1)	1 (2.5)	
Inflammatory measures						
ESR>10 mm/h (Total n= 704, Mild n= 238, Moderate n= 214, Severe n= 170, Critical n= 82) (Yes) No. (%)	366 (52.0)	67 (28.2)	99 (46.3)	139 (81.8)	61 (74.4)	0.000***
CRP>0.3 mg/dl (Total n= 704, Mild n= 238, Moderate n= 213, Severe n= 171, Critical n= 82) (Yes) No. (%)	340 (48.3)	65 (27.3)	97 (45.6)	132 (77.2)	46 (56.1)	0.000***
Ferritin>400mcg/L (Total n= 705, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	204 (28.9)	40 (16.8)	43 (20.1)	76 (44.4)	45 (54.9)	0.000***
Procalcitonin>0.5ug/L (Total n= 705, Mild n= 237, Moderate n= 216, Severe n= 170, Critical n= 82) (Yes) No. (%)	13 (1.8)	1 (0.4)	6 (2.8)	2 (1.2)	4 (4.9)	0.041*
Liver Function Tests (Total n= 705, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)						
AST>40	251 (35.6)	58 (24.4)	61 (28.5)	81 (47.4)	51 (62.2)	0.000***
ALT>40	237 (33.6)	55 (23.1)	56 (26.2)	81 (47.4)	45 (54.9)	0.000***

(*Continued*)

Table 3 (Continued).

Variable	All Patients (n=706)	Mild Cases (n= 238)	Moderate Cases (n= 214)	Severe Cases (n= 171)	Critical Cases (n= 83)	P-value
LDH>230 U/L (Total n= 704, Mild n= 238, Moderate n= 213, Severe n= 171, Critical n= 82) (Yes) No. (%)	282 (40.1)	51 (21.4)	62 (29.1)	108 (63.2)	61 (74.4)	0.000***
Bilirubin>18.7 umol/L	44 (6.2)	6 (2.5)	9 (4.2)	11 (6.4)	18 (22.0)	0.000***
Renal function tests (Total n= 705, Mild n= 238, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)						
Creatinine>115umol/L	121 (17.2)	13 (5.5)	28 (13.1)	34 (19.9)	46 (56.1)	0.000***
Urea>6.04 mmol/L (Total n= 704, Mild n= 237, Moderate n= 214, Severe n= 171, Critical n= 82) (Yes) No. (%)	171 (24.3)	19 (8.0)	46 (21.5)	57 (33.3)	49 (59.8)	0.000***

Notes: *p < 0.05; ***p < 0.001. Reference values; WBC: 4000–1000; lymphocyte: 1500–4000; NLR: 0.78–3.53; platelet: 150–400; D.dimer: 0–0.55; ESR: 0–10; CRP: 0–0.3; ferritin: 10–291; procalcitonin: 0–0.5; AST: 10–34; ALT: 46–120; LDH: 80–230; bilirubin: 0–18.7; creatinine: 44–90; urea: 3.2–8.2.
Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; LDH, lactate dehydrogenase; WBC, white blood cell.

kidney function tests, 17.2% of them had Creatinine>115 umol/L, and 24.3% had Urea>6.04 mmol/L (Table 3).

Factors Associated with Death

The median duration of stay at the hospital was 6.0 days (IQR: 300– 10:00). The duration of stay in the hospital ranged from one day to 55 days. The prevalence rate of venous thromboembolism (VTE) among the patients was 3.0% (n= 21). More than half of the patients (63.6%; n= 450) pneumonia radiologically. At the end of the follow-up period, a total of 623 patients (91.6%) recovered. Three patients (0.4%) did not recover at the end of the follow-up, and 7.6% of the patients (n= 54) deceased while the remaining either transferred to other facility or still in the hospital, at last, follow up. The severity of the cases affected the recovery rate and mortality rate in a statistically significant way (p>0.001) (Table 1).

In the multivariate logistic regression analysis, the following risk factors were associated with a higher risk of death among patients with COVID-19. Age (AOR: 1.05; 1.02–1.09), high respiratory rate (RR) (AOR: 153.90; 9.80–2416.60), low Oxygen saturation SPO2 (AOR: 9.92; 4.19–23.50), D.dimer >0.5 (AOR: 13.31; 5.-45–32.49), ESR>10 mm/h (AOR: 4.08; 1.72–9.68), Ferritin>400mcg/L (AOR: 18.55; 6.89–49.96), and Procalcitonin>0.5ug/L (AOR: 8.23; 1.81–37.40). Patients with VTE (AOR: 12.86; 3.07–53.92) were at higher risk of death due to COVID-19. End-stage renal diseases were identified to increase the risk of COVID-19. For further details, please refer to Table 4.

Factors Associated with Increased Length of Stay

Several factors were associated with increased risk of the length of stay, including comorbidities such as congestive heart failure, cerebrovascular accident, and COPD, fever, D.dimer value of more than >0.5, WBC>10,000, ESR>10 mm/h, CRP>0.3 mg/dl, ferritin > 400 mcg/L, procalcitonin >0.5 ug/L, LDH>230 U/L, creatinine >115 umol/L, and blood group O (p<0.05), for further details, please refer to Table 5.

Discussion

In this cross-sectional study, we investigated the predictors of mortality and length of stay in hospital among hospitalised patients with COVID-19. The key findings of this study are that age, patients with chronic comorbidities, patients with VTE and radiological evidence of pneumonia, and higher D-dimer values were important risk factors that were associated with a higher risk of death and increased length of stay in hospital.

Our findings revealed the significant impact of age and chronic conditions on the mortality rate and the length of hospital stay. It comes as no surprise that the escalated rate of mortality and prolonged hospital stay was associated with older patients. Thus this study substantiates the previous findings of the literature.[12] This may also be due to their weak immune system and some behavioural responses in the measures taken.[13,14] Chronic diseases demonstrate a significant influence on the outcomes; diabetes patients were more vulnerable to fatal consequences

Table 4 Logistic Regression to Identify Risk Factors of Death

Demographics	Odds Ratio for Death[a]	95% CI	Odds Ratio for Death[b]	95% CI
Age	1.06	(1.04 – 1.08)***	1.05	(1.02 – 1.09)**
Gender				
Female (Reference category)	1.00		1.00	
Male	0.77	(0.39 – 1.54)	0.30	(0.11 – 0.81)*
Smoking history				
No (Reference category)	1.00		1.00	
Yes	0.36	(0.13 – 1.02)	0.49	(0.13 – 1.91)
BMI				
BMI <30 kg/m^2 (Reference category)	1.00		1.00	
BMI >30 kg/m^2	1.24	(0.59 – 2.63)	0.25	(0.06 – 1.01)
Comorbidities (not having the disease is the reference category)				
Diabetes mellitus	4.82	(2.63 – 8.85)***	1.64	(0.59 – 4.54)
Hypertension	5.91	(3.24 – 10.77)***	1.63	(0.55 – 4.85)
Coronary artery disease	3.04	(1.54 – 5.99)**	1.08	(0.28 – 4.17)
End-Stage Renal Disease	6.97	(3.69 – 13.17)***	6.44	(2.20 – 18.87)**
Asthma	0.42	(0.06 – 3.13)	0.80	(0.07 – 8.82)
Congestive heart failure	3.59	(1.38 – 9.32)**	0.85	(0.17 – 4.31)
Cerebrovascular accident	10.18	(3.63 – 28.54)***	2.09	(0.37 – 11.92)
Chronic obstructive pulmonary disease	0.89	(0.11 – 6.90)	–	
Chronic liver disease	11.92	(1.65 – 86.38)*	–	
Cancer	23.96	(2.14 – 268.68)*	–	
Vital signs upon arrival to hospital (having the normal range is the reference category)				
Fever (≥ 38°C) (Yes)	1.28	(0.73 – 2.24)	1.46	(0.68 – 3.13)
Respiratory rate > 30 (Yes) SPO2<93 (Yes)	7.09 2.63	(3.66 – 13.73)*** (1.46 – 4.73)**	153.90 9.92	(9.80 – 2416.60)*** (4.19 – 23.50)***
Heart rate>125 (Yes)	12.87	(5.74 – 28.86)***	19.82	(5.22 – 75.25)***
Outcome				
Venous thromboembolism (Yes)	17.54	(6.90 – 44.61)***	12.86	(3.07 – 53.92)***
Pneumonia Radiologically(Yes)	2.35	(1.19 – 4.61)*	1.37	(0.95 – 1.98)
Complete Blood Count (having the normal range is the reference category)				
WBC >10,000 (Yes)	12.36	(6.74 – 22.68)***	16.47	(6.78 – 40.00)***
WBC <4000 (Yes)	0.34	(0.10 – 1.11)	0.31	(0.07 – 1.48)
Lymphocyte count <1500 (Yes)	5.70	(3.19 – 10.17)***	10.17	(4.29 – 24.14)***
NLR (Mean (SD))	1.00	(1.00 – 1.01)	1.23	(1.15 – 1.32)***

(*Continued*)

Table 4 (Continued).

Demographics	Odds Ratio for Death[a]	95% CI	Odds Ratio for Death[b]	95% CI
Platelet < 150 (Yes)	5.73	(3.12 – 10.53)***	9.92	(4.01 – 24.52)***
D.dimer >0.5 (Yes)	8.47	(4.48 – 16.01)***	13.31	(5.45 – 32.49)***
Inflammatory measures (having the normal range is the reference category)				
ESR>10 mm/h (Yes)	2.89	(1.54 – 5.42)**	4.08	(1.72 – 9.68)**
CRP>0.3 mg/dl (Yes)	0.90	(0.52 – 1.55)	0.84	(0.39 – 1.80)
Ferritin>400mcg/L (Yes)	3.89	(2.19 – 6.91)***	18.55	(6.89 – 49.96)***
Procalcitonin>0.5ug/L (Yes)	5.58	(1.66 – 18.77)**	8.23	(1.81 – 37.40)**
Liver Function Tests (having the normal range is the reference category)				
AST>40 (Yes)	3.71	(2.07 – 6.67)***	8.85	(3.64 – 21.50)***
ALT>40 (Yes)	2.41	(1.37 – 4.24)**	4.78	(2.11 – 10.83)***
LDH>230 U/L (Yes)	6.09	(3.13 – 11.82)***	21.26	(7.61 – 59.40)***
Bilirubin>18.7 umol/L (Yes)	1.51	(1.14 – 2.00)**	15.06	(4.63 – 48.99)***
Renal function tests (having the normal range is the reference category)				
Creatinine>115umol/L (Yes)	18.00	(9.46 – 34.25)***	36.33	(13.65 – 96.66)***
Urea>6.04 mmol/L (Yes)	4.48	(2.54 – 7.90)***	15.27	(6.29 – 37.07)***
Blood Groups (blood group A is the reference category)				
B	0.35	(0.08 – 1.47)	0.51	(0.11 – 2.36)
AB	–	–	1.08	(0.02 – 54.95)
O	1.52	(0.77 – 2.99)	1.50	(0.57 – 3.96)

Notes: *p < 0.05; **p < 0.01; ***p < 0.001. [a]Binary logistic regression. [b]Multiple logistic regression adjusted for the following variables (age, gender, and comorbidities). Reference values; WBC: 4000–1000; lymphocyte: 1500–4000; NLR: 0.78–3.53; platelet: 150–400; D.dimer: 0–0.55; ESR: 0–10; CRP: 0–0.3; ferritin: 10–291; procalcitonin: 0–0.5; AST: 10–34; ALT: 46–120; LDH: 80–230; bilirubin: 0–18.7; creatinine: 44–90; urea: 3.2–8.2.

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; LDH, lactate dehydrogenase; WBC, white blood cell.

and longer hospitalisation compared to non-DM patients, which is consistent with results reported from the previous study.[15] Hypertensive patients have a propensity to express high mortality rate and stay hospitalised longer. Likewise, pre-existent cardiovascular and cerebrovascular events carry a high risk of death and a longer duration of hospitalisation. The effect of SARS-COV-2 on the vascular endothelium could be explained by the current understanding that angiotensin-converting enzyme 2 (ACE2) cellular receptors as the entry sites of SARS-COV2 as shown in different studies.[16,17]

There are several explanations for these results, Renin-Angiotensin system (RAAS) and inflammatory cytokines have been mentioned as mediators in severe outcomes among hypertensive patients.[18] Furthermore, the frequent utilisation of angiotensin-converting enzyme inhibitors (ACEIs) can lead to a decrease in angiotensin-converting enzyme (ACE) and an increase in the expression of ACE2 in the lungs which eventually facilitates the invasion of Covid-19 virus,[19,20] nonetheless this still controversial as illustrated by other studies.[21] Further, the severe viral virulence may lead to high oxygen demand, physiological and reflex tachycardia and aggravates the manifestation of coronary artery diseases accompanied by respiratory distress, finally, unfavourable outcomes will present.[22] Patients with chronic liver diseases (CLD) were also more susceptible to fatal consequences either death or a longer hospitalisation period. The confirmed laboratory findings emphasise the negative impact of Covid-19 on liver functions. The previous study elucidated the high mortality rate among CLD

Table 5 Linear Regression to Identify Predictors of Length of Stay

Demographics	Model a			Model b		
	B	SE	ß	B	SE	ß
Age	0.07	0.02	0.145***	−0.013	0.02	−0.03
Gender						
Female	0.93	0.68	−0.07	−1.21	0.66	−0.09
Smoking history						
Yes	3.04	0.71	−0.16***	−1.75	1.03	−0.11
BMI						
BMI >30 kg/m^2	0.12	0.77	0.01	4.27	6.70	0.04
Comorbidities (not having the disease is the reference category)						
Diabetes mellitus	2.46	0.56	0.17***	0.73	0.76	0.05
Hypertension	3.07	0.58	0.20***	0.55	0.82	0.04
Coronary artery disease	3.06	0.86	0.13***	−1.00	1.21	−0.04
End-Stage Renal Disease	7.68	0.91	0.31***	−1.04	2.00	−0.03
Asthma	1.20	1.40	0.03	−0.28	2.16	−0.01
Congestive heart faliure	3.77	1.40	0.10**	−1.04	2.00	−0.03
Cerebrovascular accident	5.31	1.74	0.12**	7.82	2.18	0.17***
Chronic obstructive pulmonary disease	3.93	1.92	0.08*	3.63	3.96	0.05
Chronic liver disease	3.08	3.59	0.03	2.76	4.83	0.03
Cancer	−0.60	4.14	−0.01	−4.88	3.98	−0.06
Vital signs upon arrival to hospital						
Fever (≥ 38°C) (Yes)	2.19	0.54	0.15***	1.83	0.64	0.13**
Respiratory rate > 30 (Yes)	5.15	0.90	0.21***	0.83	2.38	0.02
SPO2<93 (Yes)	1.90	0.48	0.15***	0.21	0.97	0.01
Heart rate>125 (Yes)	4.95	1.32	0.14***	0.54	1.82	0.01
Outcome						
Venous thromboembolism (Yes)	5.04	1.62	0.12**	2.19	2.06	0.05
Pneumonia (Yes)	2.79	0.42	0.24***	1.19	0.44	0.13**
Complete Blood Count						
WBC >10,000 (Yes)	4.02	0.72	0.21***	2.37	0.87	0.13**
WBC <4000 (Yes)	−0.38	0.79	−0.02	1.69	0.93	0.09
Lymphocyte count <1500 (Yes)	1.02	0.67	0.06	1.13	0.89	0.06
NLR (Mean (SD))	0.00	0.01	0.02	0.07	0.06	0.06
Platelet < 150 (Yes)	0.24	0.81	0.01	0.45	1.07	0.02

(*Continued*)

Table 5 (Continued).

Demographics	Model a			Model b		
	B	SE	ß	B	SE	ß
D.dimer >0.5 (Yes)	3.57	0.58	0.23***	2.57	0.87	0.15**
Inflammatory measures						
ESR>10 mm/h (Yes) CRP>0.3 mg/dl (Yes)	2.09 2.10	0.54 0.54	0.15*** 0.15***	1.64 2.74	0.64 0.64	0.12* 0.20***
Ferritin>400mcg/L (Yes)	4.59	0.57	0.29***	3.70	0.72	0.24***
Procalcitonin>0.5ug/L (Yes)	4.46	2.00	0.08*	4.94	1.78	0.13**
Liver Function Tests						
AST>40	−0.27	0.57	−0.02	−0.81	0.69	−0.06
ALT>40	−0.12	0.57	−0.01	−0.82	0.71	−0.06
LDH>230 U/L (Yes)	2.09	0.55	0.14***	2.32	0.70	0.16**
Bilirubin>18.7 umol/L	0.61	0.43	0.05	1.03	1.48	0.04
Renal function tests						
Creatinine>115umol/L	4.90	0.69	0.26***	2.44	1.09	0.13*
Urea>6.04 mmol/L (Yes)	2.89	0.54	0.20***	1.69	0.91	0.10
Blood Groups						
B	−1.38	0.92	−0.06	−1.03	1.12	−0.04
AB	−3.58	3.22	−0.04	2.70	4.83	0.03
O	0.52	0.74	0.03	3.43	0.95	0.17***

Notes: *p < 0.05; **p < 0.01; ***p < 0.001. Model a: Univariate linear regression. Model b: Multiple linear regression adjusted for the following variables (age, gender and comorbidities).

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; LDH, lactate dehydrogenase; WBC, white blood cell; B, the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables; SE, it is the standard deviation of its sampling distribution or an estimate of that standard deviation; ß, a statistical measure that compares the strength of the effect of each individual independent variable to the dependent variable.

patient who they are Covid-19 infected.[23,24] Our findings also highlighted the high mortality rate and the long period of hospitalisation among cancer patients. The nature of cancer and the antineoplastic agents compromise the immune system. Consequently, it spikes the probability of lethal and severe infection of the Covid-19 virus among these patients. Moreover, the redundant clinical visits for follow up and chemotherapy dose also expose the patients to the infection.[25]

The hypercoagulability of Covid-19 patients was observed and confirmed by laboratory findings. Venous thrombus embolism was one of the poor outcomes among covid-19 patients with a significant correlation and high odd ratios. The severe infection and long bed-ridden interval in ICU dysregulate the homeostasis of the cascade system by activating the inflammatory cytokines.[26] Not withstanding, the pathogeneses of VTE-induced by Covid-19 are complex and multifactorial. Our study provides further evidence of Covid-19 pneumonia as a predictor for the high mortality rate and prolonged hospitalisation. These findings support the aggressive preventive measures that be taken to halt the mortality rate among these patients.

In our study, we found no significant difference between blood group type and the risk of death. However, we found a significant difference in the duration of hospital stay for patients with blood group O. Previous reports showed a reduced prevalence of Covid-19

infection in blood group O.[27] However, this was later contradicted, as some other published report suggested that there is no link between Covid-19 infection and type of blood group.[28,29] Future studies on a larger scale and different populations are needed to investigate this association.

In our study and similar to published reports, patients with chronic obstructive pulmonary disease (COPD) were found to be at higher risk for a severe outcome,[30] likely due to the fact that these patients usually have reduced lung function along with various comorbidities.[31] Interestingly, on the other hand, patients with pre-existent asthma did not have a risk of worse outcome,[32] and this could be partly explained by the lower expression of ACE2 in asthmatic bronchial epithelium.[33]

Obesity is one of the major comorbidities to be considered. Above increasing the risk of different complications such as DM, liver diseases and cardiovascular diseases, we observed obesity also increases the mortality rate and the demand on intensive care facilities among SARS-COV-2 patients, which augments the findings in a previous systematic review.[34] Henceforth, obesity is one of the potential predictors for the study outcomes. However, the underlying mechanism behind the bad prognosis of obese patients still unknown.

We believe that our results are similar to the literature, it may help in earlier risk stratification, and triage of COVID-19 patients admitted to the hospital and in reducing the overload on emergency departments visits and intensive care units in order to facilitate COVID-19 cases and other emergency care cases. Some factors identified in this study, such as older age and comorbidities, may help policymakers and guidelines in their recommendations about prioritising patients based on their symptoms and may help to improve the patient's care. Furthermore, the founded risk factors might be helpful in establishing a scoring system that can be applied to predict mortality and appropriate management plan.

This study has some limitations. First, the study population only included patients from a single-centre hospital in Saudi Arabia. Second, the cross-sectional study design restricted our ability to identify causality between study variables.

Conclusion

Hospitalised COVID-19 patients have multiple negative consequences in term of their laboratory findings, signs and symptoms. Age and chronic conditions have a significant impact on the mortality rate and the length of hospital stay among COVID-19 patients. Earlier risk stratification of the COVID-19 patients admitted to the hospital is recommended.

Author Contributions

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Disclosure

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