Scholars LITERATURE

La Prensa Medica Argentina

Research Article

DOI: https://doi.org/10.47275/0032-745X-334
Volume 107 Issue 4

Clinical Aspects and Predictors of Outcome for Hospitalized COVID-19 Patients in Hail, Saudi Arabia

Eman M Abdelsalam[1,2]*, Hessa A Alshammari[2], Safwat AM Eldaboosy[3], Mostafa M Meshref[4], Ehab B Rakha[5,6], Howaida AM Bayomi[6], and Abdulhafeez O Eltoum[2]

[1]Department of Internal Medicine, Faculty of Medicine (for Girls), Al-Azhar University, Cairo, Egypt
[2]Department of Internal Medicine, King Khalid Hospital Hail, Kingdom of Saudi Arabia
[3]Department of Chest Diseases, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[4]Division of Neurology Medicine, Department of Internal Medicine, King Khalid Hospital Hail, Kingdom of Saudi Arabia
[5]Clinical Pathology Department, Mansoura Faculty of Medicine, Mansoura, Egypt
[6]Department of Clinical Pathology, King Khalid Hospital Hail, Kingdom of Saudi Arabia

Abstract

Background: As of December 2020, the documented Corona Virus Disease 2019 (COVID-19) cases have almost reached 360,000 with a case fatality of 1.7%. In this study, we aimed to identify common presentations and complications of the disease and to assess the mortality predicting factors in hospitalized COVID-19 patients.

Patients and Methods: A retrospective study was conducted between 1st June and 31st August 2020 on the confirmed cases of COVID-19 (using RT-PCR) admitted to King Khalid Hospital, Hail, Saudi Arabia. Adult patients aged 18 years or older who were hospitalized for at least 24 hours with confirmed COVID-19 during the study period were included, while patients with an inadequate past medical history and who were still hospitalized were excluded. Data were collected, coded, and analyzed using SPSS software.

Results: Out of 1466 patients tested by RT-PCR, 404 patients (27.55%) were positive for COVID-19. Out of these 404 patients, 131 (32%) were hospitalized and included in our study with a mean age of 57±16 years, and 74 patients (56.5%) were males. Out of 131 patients, there were 28 deaths (21.4%). The most frequent comorbidities were hypertension (80.9%), diabetes mellitus (67.9%), and chronic kidney disease (39.7%). Fever (95.4%), cough (80.9%), dyspnea (65.6%), and body aches & myalgia (35.9%) were the most common symptoms. The significant predictors of mortality were elevated levels of WBC (AOR= 24.2; p=0.06), BUN (AOR= 31.8; p=0.001), AST (AOR= 11.8; p=0.041), INR (AOR= 11.5; p=0.001), D-Dimer (AOR=10.7; 0.005), lactic acid (AOR= 38.3; p<0.001), and creatinine kinase (AOR=2.1; p<0.001). Decreased lymphocyte count and SPO_2 were associated with a high risk of mortality (AOR= 11.9; p=0.037 and AOR= 34.8; p=0.003), respectively. Similarly, patients with COPD were at high risk of mortality (AOR= 18.8; p=0.004).

Conclusion: Among the included patients, the hospitalization mortality rate was 21.4%. Old age and male gender were associated with significant mortality. The independent predictors of COVID-19 mortality were COPD, SPO_2<89, acute Liver Injury, leukocytosis, lymphopenia, and markers of inflammation (ESR, CRP, D- Dimer) and shock (lactate, and creatine Kinase). Further studies are needed to assess definite mortality predictors in hospitalized COVID-19 patients to identify and guide patients' management at risk.

Keywords: COVID-19; SARS-CoV-2; Mortality; Saudi Arabia

Correspondence to: Eman M Abdelsalam, Department of Internal Medicine, Faculty of Medicine (for Girls), Al-Azhar University, Cairo, Egypt; E-mail: emanelgamal92@yahoo.com

Citation: Eldaboosy SAM, Alshammari HA, Safwat AM, et al. (2021) Clinical Aspects and Predictors of Outcome for Hospitalized COVID-19 Patients in Hail, Saudi Arabia. Prensa Med Argent, Volume 107:4. 334. DOI: https://doi.org/10.47275/0032-745X-334

Received: April 29, 2021; **Accepted:** May 13, 2021; **Published:** May 18, 2021

Introduction

The Corona Virus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first discovered in China in December 2019 and due to unexpected rapid spread and thousands of deaths increasing day by day leading to a heavy burden of hospital admissions and high mortality among hospitalized patients, the World Health Organization (WHO) declared COVID-19 as a pandemic infectious disease on 11th March 2020 [1-3].

The COVID-19 virus is a member of the Coronaviruses family, and its genome shared by 70% and 40% homology to SARS-CoV-2 and MERS-CoV, respectively, which resulted in a widespread epidemic [3]. The COVID-19 virus uses its surface glycoprotein "spike" to bind ACE2 receptors on the respiratory tract's epithelial cells, accelerating its access into cells and producing thousands of copies [1]. Although the COVID-19 virus principally targets the respiratory system, other system complications as cardiovascular or renal systems can also contribute to death from COVID-19 disease [4].

The clinical presentation of COVID-19 infection appears to be wide, including asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death [5]. Consequently, early identification of clinical characteristics data and

outcomes of COVID-19 patients is fundamental and valuable for the appropriate management and mortality risk reduction to minimize the patients' suffering and lessen the shortage of medical resources [6]. Numerous case studies describing the clinical characteristics and outcomes of COVID-19 patients have been reported summarizing the experience of the city or regional hospitals and intensive care units (ICU) in different countries. However, population features may vary across the world, even in the same country, affecting the rates for COVID-19 hospitalizations and outcomes [7]. Our study aimed to analyze the clinical and laboratory, and radiological features and detect predictors of the severity and death of hospitalized patients with COVID-19 in King Khalid Hospital, Hail (KK-HH), Saudi Arabia.

Patients and Methods

Study Design

We conducted a retrospective single-center study among the COVID-19 patients presented and admitted to KK-HH, Saudi Arabia. Hail is the capital city of the Hail Region in northwestern Saudi Arabia [8]. It is noteworthy that KK-HH is the main reference hospital in Hail. We used electronic medical record (EMR) data and paper medical files from patients with positive reverse transcriptase-polymerase chain reaction (RT-PCR) nasopharyngeal swab test results for COVID-19 between 1st June and 31st August 2020, who had been admitted and treated in KK-HH. Before beginning the study, approval from the Ethics Committee was obtained (IRB: H-08-L-074-2020-35).

Inclusion and exclusion criteria: Adult patients aged 18 years or older who were hospitalized for at least 24 hours with confirmed COVID-19 during the study period were included, while patients with an inadequate past medical history and who were still hospitalized were excluded.

Data collection: Diagnosis of COVID-19 was based on the history of exposure and clinical manifestations (fever and/or respiratory symptoms) coupled with laboratory and radiological findings. Confirmation was done by detecting COVID-19 nucleic acid in swabs obtained from the respiratory tract via RT-PCR. Sansure Biotech Inc. supplied this kit, Hunan Province, China, with catalog No. S3102E.

The detailed medical history and data at the initial presentation from the ER notes and EMR on patients' admission in terms of demographic variables and clinical characteristics with underlying comorbidities, symptoms, signs, and hospital complications were extracted. Clinical outcomes were recorded in the form of discharge or death. In addition, the details of the chest radiologic examination [X-ray (CXR) and/or computerized tomography (CT)] at the time of admission were obtained.

All laboratory investigations on the day of admission and during hospitalization were collected from the EMR, including complete blood counts, blood chemistry including random blood sugar (RBS) renal and liver function, coagulation profile, inflammatory markers including erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), D-dimer, ferritin, creatinine kinase (CK), lactate dehydrogenase (LDH), and cardiac troponin I. The supportive therapy and medications administered included Kaletra (lopinavir/ritonavir), hydroxychloroquine, pegylated interferon-α, corticosteroid, oxygen therapy, or mechanical ventilation was recorded.

Statistical Analysis

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (version 24). The normality of data was first tested with a one-sample Kolmogorov-Smirnov test. Qualitative data were described using the number and percent. Association between categorical variables was tested using the Chi-square test, while the Fischer exact test and Monte Carlo test were used when the expected cell count less than 5. Continuous variables were presented as mean ± SD (standard deviation) for parametric data and median (min-max) for non-parametric data. The two groups were compared with the Student t-test for parametric data and the Mann Whitney test for non-parametric data. All continuous variables were classified according to the median level. Significant variables entered the Logistic regression model using the forward Wald statistical technique to predict the most significant determinants and control possible interactions and confounding effects. Odds ratios (OR) and 95% confidence intervals (CI) for the tested variables with poor outcomes were calculated in univariate and multivariate logistic regression analysis. Results were considered significant when the p-value is less than 5% ($p \leq 0.05$).

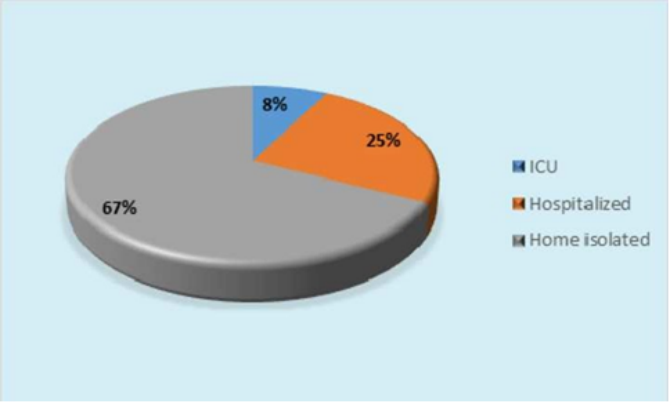

Figure 1: COVID-19 patients in KK-HH.

Results

During our study period, 1466 patients were tested at KK-HH for COVID-19 by RT-PCR, but only 404 patients (27.55%) were positive. Out of these 404 patients, 131 (32%) were hospitalized and included in our study (Figure 1). Regarding the severity of the hospitalized patients, 100 patients (76.3%) had mild to moderate symptoms and received isolation ward care, and 31 patients (23.7%) had severe symptoms, and ICU care was required. All patients were admitted to single rooms under droplet and contact precautions as per hospital policy.

Demographic and clinical characteristics of the hospitalized patients are shown in Table 1. Out of the 131 patients, the hospitalization mortality rate was 21.4%. Briefly, the majority of COVID-19 patients were Saudi citizens (81.7%) *vs.* (18.3%) of other nationalities. The mean ± SD age was (57.69±16.78) years, and 74 patients (56.5%) were males. Furthermore, our data revealed that elderly patients were associated with significant mortality (p=0.003). On the other hand, the hospitalization mortality rate was comparable between males and females (p=0.348).

Contact history showed that 23.7% of the included patients had a close contact history with confirmed COVID-19 patients. Out of the deceased patients, 53.6% had a history of recent travel outside Hail (p<0.001). In terms of occupation, none of the deceased patients were healthcare workers (p=0.017). The smoking history was presented among 43 (32.8%) patients. The most common comorbidities were hypertension (HTN; 80.9%), diabetes mellitus (DM; 67.9%), and

Table 1: Relation between socio-demographic data and outcome of hospitalized COVID- 19 patients KK-HH.

Socio-demographic data		Total	Deceased	Survived	P-value
		(n=131)	(n=28)	(n=103)	
Age (years)		57.69±16.78	65.82±17.29	55.48±16.02	**0.003**
Sex	Male	74 (56.5%)	18 (64.3%)	56 (54.4%)	0.348
	Female	57 (43.5%)	10 (35.7%)	47 (45.6%)	
Nationality	**Saudi**	107 (81.7%)	24(85.7%)	83 (80.6%)	0.533
	Non-Saudi	24 (18.3%)	4 (14.3%)	20 (19.4%)	
Occupation	**Health care Workers**	18 (13.7%)	0 (0%)	18 (17.5%)	**0.017**
	Others	113 (86.3%)	28 (24.8%)	85 (82.5%)	
History of recent travel outside Hail		17 (13.0%)	15 (53.6%)	2 (1.9%)	**<0.001**
Smoking		43 (32.8%)	12 (42.9%)	31 (30.1%)	0.202
History of close contact with Confirmed COVID-19 case		31 (23.7%)	1 (3.6%)	30 (29.1%)	**0.005**
Hypertension (HTN)		106 (80.9%)	26 (92.9%)	80 (77.7%)	0.07
Diabetes Mellitus (DM)		89 (67.9%)	26 (92.9%)	63 (61.2%)	**0.001**
Bronchial Asthma		8 (6.1%)	3 (10.7%)	5 (4.9%)	0.251
Chronic obstructive pulmonary disease (COPD)		10 (7.6%)	8 (28.6%)	2 (1.9%)	**<0.001**
Chronic liver disease (CLD)		2 (1.5%)	1 (3.6%)	1 (1.0%)	1
Chronic Kidney disease (CKD)		52 (39.7%)	16 (57.1%)	36 (35.0%)	**0.033**
Cerebrovascular /Cardiovascular disease		22 (16.8%)	7 (25.0%)	15 (14.6%)	0.19
Thyroid disease		16 (12.2%)	2 (7.1%)	14 (13.6%)	0.355
Cancer/Immunosuppression		6 (4.8%)	4 (14.3%)	1 (1.0%)	**0.007**
Epilepsy		14 (10.7%)	1 (3.6%)	13 (12.6%)	0.169

Table 2: Relation between symptoms, vital signs and outcome of hospitalized COVID-19 patients KK-HH.

Symptoms/ Vital sign	Total	Deceased	Survived	
	(n=131)	(n=28)	(n=103)	P-value
Fever	125 (95.4%)	28 (100.0%)	97 (94.2%)	0.248
Cough	106 (80.9%)	25 (89.3%)	81 (78.6%)	0.204
Dyspnea	86 (65.6%)	25 (89.3%)	61 (59.2%)	**0.003**
Sore throat	20 (15.3%)	1 (3.6%)	19 (18.4%)	0.052
Runny nose	6 (4.6%)	1 (3.6%)	5 (4.9%)	1
Headache	18 (13.7%)	8 (28.6%)	10 (9.7%)	**0.01**
Loss of taste & smell	3 (2.3%)	1 (3.6%)	2 (%1.9)	1
GIT symptoms	9 (6.9%)	4 (14.3%)	5 (4.9%)	0.08
Body aches & myalgia	47 (35.9%)	10 (35.7%)	37 (35.9%)	0.984
Heart Rate (Beat/minute)	100.38±16.23	104.79±19.98	99.18±14.94	0.106
Temperature (°C)	38.43±0.56	38.77±0.42	38.33±0.56	**<0.001**
Systolic Blood Pressure (SBP) (mm-Hg)	124.31±18.49	117.39±21.38	126.19±17.27	**0.025**
Diastolic Blood Pressure (DBP) (mm-Hg)	68.51±11.10	67.32±10.28	68.83±11.34	0.524
Respiratory Rate (RR) (Cycle /minute)	22.19±3.34	26.32±4.62	21.07±1.62	**<0.001**
O2 SAT (%)	92.76±5.34	85.60±7.66	94.59±1.85	**<0.001**

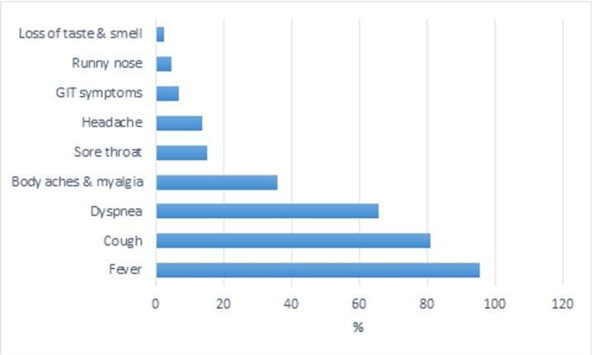

Figure 2: Symptoms among hospitalized COVID-19 patients KK-HH.

chronic kidney disease (CKD; 39.7%). Deceased patients were significantly associated with a higher prevalence of DM (p=0.001), Chronic obstructive pulmonary disease (COPD; p<0.001), CKD (p=0.033), and malignancies (p=0.007).

The most common symptoms among COVID-19 patients were fever (95.4%), cough (80.9%), dyspnea (65.6%), and body aches and myalgia (35.9%) (Table 2, Figure 2). In deceased patients, approximately 89.3% were presented with dyspnea, compared to 59.2% in the survived patients (p=0.003). Body temperature was observed to be higher in the deceased than survived patients (p<0.001). In terms of the SPO_2, a significant reduction (p<0.001) was observed in the deceased group (85.60±7.66) compared to the survived group (94.59±1.85). This reduction in the O_2 saturation was accompanied by a significant elevation (p<0.001) in the respiratory rate (RR) in the deceased group (26.32±4.62) compared to the survived group (21.07±1.62). In addition

to the reduction in systolic blood pressure (SBP) (p<0.025) in the deceased patients (117.39±21.38) when compared to the survivors (126.19±17.27).

Regarding the laboratory findings, we found a significant difference between both groups in all the studied parameters except for the prothrombin time (p=0.127). Within 24 hours of hospital admission, the deceased patients were associated with significant leukocytosis (p<0.001), lymphopenia (p<0.001), hyperglycemia (p=0.002), and elevated renal function tests (urea and creatinine; p<0.001) & liver function tests (AST: p<0.001 and ALT: p=0.002). There was also a prolonged PTT (p<0.001), prolonged INR (p<0.001), and elevated lactate levels (p<0.001) in the deceased patients. Furthermore, our results revealed a significant (p<0.001) high ESR, CRP, D-dimer, ferritin, LDH, CK, and troponin I in the deceased group, compared with the survived group (Table 3).

Fourteen patients (10.7%) had a normal CXR at presentation, while unilateral infiltrates on initial CXR were observed in 27.5% of patients, and 61.8% of patients had bilateral involvement, which mainly involved the lower lobes. Interestingly, all deceased patients were associated with bilateral infiltration compared to only (51.5%) in the survived group (p<0.001). CT chest was done for 13 cases only and confirmed the CXR finding.

Besides supportive management, there were principal types of treatments that were prescribed to COVID-19 patients, including antiviral therapy, antimalarial medications, systemic corticosteroids, anticoagulants, and antibiotics (Table 4). Oxygen therapy was given to all patients, 82 patients thorough nasal cannula or face mask (62.6%), and 23 patients received non-invasive ventilator or high flow oxygen, while ICU admission was required in 23.7%. The most common complications observed during admission were sepsis and septic shock

Table 3: Relation between outcome and laboratory and radiological data of hospitalized COVID-19 patients KK-HH.

Laboratory investigation	Total	Deceased	Survived	
	(n=131)	(n=28)	(n=103)	P-value
White Blood cell (WBCs) count (x 109/L)	8.6 (1.91-30.8)	13.11 (5.78-30.8)	7.76 (1.91-19.60)	**<0.001**
Lymphocytes count (x 109/L)	16.67 (2.09-54.14)	5.67 (2.09-21.96)	18.93 (2.89-54.14)	**<0.001**
Hemoglobin (Hb) (g/dL)	11.97±2.40	10.61±2.28	12.34±2.31	**0.001**
Platelets count (x 109/L)	212.90 (6.60-788.80)	187.2 (63-788.8)	217 (6.60-504.98)	**0.002**
Random Blood Sugar (RBS)(µmol/L)	10.77 (2.90-28.80)	13.75 (5.10-27.90)	8.80 (2.90-28.80)	**0.002**
Blood Urea Nitrogen (BUN) (m mol/L)	6.80 (2.20-76.60)	20.10 (4.10-48.90)	6.45 (2.20-76.60)	**<0.001**
Creatinine (µmol/L)	108 (6.90-1923.00)	292.70 (49.90-1923)	101.01 (6.90-890)	**<0.001**
Aspartate Transaminase (AST) (U/L)	28 (6.4-2179)	50.15 (7.9-2179)	24 (6.40-472.7)	**<0.001**
Alanine Amino Transferase (ALT) (U/L)	25.1 (6.30-857)	39 (6.90-857)	24 (6.30-342.4)	**0.002**
Prothrombin Time (PT) (Sec)	12.78±3.52	13.68±3.36	12.53±3.53	0.127
Partial Thromboplastin Time (PTT) (Sec)	35.15±10.15	43.23±17.03	32.95±5.64	**<0.001**
International Normalised Ratio (INR)	1.09±0.18	1.23±0.27	1.05±0.12	**<0.001**
Erythrocyte Sedimentation Rate (ESR) (mm/h)	61 (8-150)	89.5 (15-150)	53.00 (8-150)	**<0.001**
C-reactive Protein (CRP) (mg/L)	4.80 (0.50-64)	13.05 (2.10-64)	3.80 (0.50-31.20)	**<0.001**
D-dimer (mg/L)	1.40 (0.50-10.90)	2.50 (0.75-10.90)	1.30 (0.50-4.90)	**<0.001**
Ferritin (ng/mL)	479 (59.87-2090)	883 (380.20-2090)	429 (59.87-2000)	**<0.001**
Lactate (mmol/L)	1.9 (0.9-5.40)	2.75 (1.40-5.4)	1.80 (0.90-4.90)	**<0.001**
Lactate Dehydrogenase (LDH) (U/L)	352 (155-1470)	521.50 (229-1470)	312 (155-981)	**<0.001**
Creatinine Kinase (CK) (U/L)	163 (50-5611)	455(104-5611)	150 (50-799)	**<0.001**
Cardiac Troponin I (ng/L)	0.01 (0.01-7.70)	0.02 (0.01-7.70)	0.01 (0.01-1.80)	**<0.001**
Normal Chest X-ray	14 (10.7%)	0(0%)	14(13.6%)	**0.039**
Unilateral infiltration	36 (27.5%)	0(0%)	36 (35.0%)	**<0.001**
Bilateral infiltration	81 (61.8%)	28 (100.0%)	53 (51.5%)	**<0.001**

Table 4: Relation between Supportive therapy, medications, complications, and outcome of hospitalized COVID-19 patients KK-HH.

Medications/Therapy/Complication	Total	Deceased	Survived	
	(n=131)	(n=28)	(n=103)	P-value
Hydroxychloroquine	80 (61.1%)	2 (7.1%)	78 (75.7%)	**<0.001**
Kaletra (lopinavir/ritonavir),	55 (42%)	27 (96.4%)	28 (27.2%)	**<0.001**
Ribavirin	56 (42.70%)	28 (100.0%)	28 (27.2%)	**<0.001**
Dexamethasone	76 (58.0%)	26 (92.9%)	50(48.5%)	**<0.001**
Intrferon Beta-1b	15 (11.5%)	4 (14.3%)	11 (10.7%)	0.595
O2 therapy (Facemask/nasal cannula)	82 (62.6%)	0 (0%)	82 (82%)	**<0.001**
Invasive ventilation	31 (23.7%)	28 (100%)	3 (2.9%)	**<0.001**
Non-invasive ventilation	23 (17.6%)	0 (0%)	23 (22.3%)	**0.006**
Acute respiratory distress syndrome (ARDS)	27 (20.6%)	26 (92.9%)	1 (1.0%)	**<0.001**
Respiratory Failure	29 (22.1%)	28 (100.0%)	1 (1.0%)	**<0.001**
Acute kidney injury (AKI)	24 (18.3%)	11 (39.3%)	13 (12.6%)	**0.001**
Acute liver injury (ALI)	7 (5.3%)	6 (21.4%)	1 (1.0%)	**<0.001**
Sepsis/Septic Shock	34 (26.0%)	19 (67.9%)	15 (14.6%)	**<0.001**
Cardiac complication (HF/MI)	3 (2.3%)	3 (10.7%)	0(0%)	**0.001**

Table 5: Logistic regression analysis for independent predictors of mortality of hospitalized COVID-19 patients KK-HH.

Independent predictors Cut-off point	Univariate regression		Multivariate regression	
	P-value	COR (95% CI)	P-value	AOR (95% CI)
Age (years) > 66 y	0.007	3.2 (1.4-7.7)	0.154	2.6 (0.7-9.6)
DM	0.006	8.3 (1.8-36)	0.151	4.8 (0.5-41)
COPD	≤0.001	20.2 (3.9-102)	0.004	18.8 (2.5-141)
CKD	0.036	2.5 (1.1-5.8)	0.842	1.1 (0.3-4.2)
Cancer	0.013	17 (1.8-159)	0.08	15 (0.7-344)
Temperature >38.8	0.01	3.1 (1.3-7.3)	0.363	2.7 (0.3-22)
RR >25	≤0.001	58 (11.9-284)	0.008	42 (2.7-670)
O2 saturation <89	≤0.001	41 (13-129)	0.003	34.8 (3.4-360)
ARDS	≤0.001	132 (11.5-519)	0.997	1.6 (0.3-472)
AKI	0.002	4.5 (1.7-11.6)	0.134	10.5 (0.48-226)
ALI	0.003	27.8 (3.2-242)	0.029	46 (1.5-144)
Sepsis/ Septic Shock	≤0.001	12.4 (4.7-32)	0.252	7.6 (0.23-242)
WBCs >13	≤0.001	11.8 (4.2-33)	0.016	24.2 (1.8-323)
Lymphocytes <5.6	≤0.001	28.9 (7.4-113)	0.037	11.9 (1.2-122)
Hb <10	0.002	4.04 (1.6-9.9)	0.137	6.18 (0.56-68)
Platelets <187	0.055	2.3 (0.9-5.5)	-	-
RBS >13.75	0.014	2.9 (1.2-7.02)	0.419	2.16 (0.33-13.9)
BUN >20	≤0.001	18.6 (6.1-56)	0.001	31.8 (4.3-236)
Creat.> 292	0.002	4.2 (1.7-10.1)	0.158	1.30 (0.6-1.9)
AST>50	≤0.001	7.3 (2.9-18.6)	0.041	11.8 (1.1-126)
ALT > 39	0.004	3.7 (1.5-8.8)	0.927	1.1 (0.12-10)
PTT >39.5	≤0.001	7.6 (2.9-19.6)	0.732	0.68 (0.08-5.9)
INR >1.2	≤0.001	12.4 (4.7-32)	0.001	11.5 (1.8-39)
ESR >89.5	≤0.001	5.8 (2.3-14.7)	0.006	8.46 (2.8-41)
CRP >13	≤0.001	8.4 (3.2-22)	0.049	5.76 (1.01-33)
D-dimer >2.5	≤0.001	11.9 (4.2-33)	0.005	10.7 (2.1-56)
Ferritin >883	0.001	4.7 (1.9-11.6)	0.861	1.86 (0.17-4.36)
Lactate >2.75	≤0.001	16.2 (5.3-48.9)	≤0.001	38.3 (5.9-247)
LDH >521	≤0.001	16.2 (5.3-48.9)	0.82	1.81 (0.14-4.7)
creatinie kinase >455	≤0.001	33 (8.5-130)	≤0.001	40.5 (5.8-283)
Troponine I >0.02	≤0.001	10.3 (3.8-27.6)	0.362	2.1 (0.42-10.2)

in 34 patients (26%), respiratory failure in 29 patients (22.1%), ARDS in 27 patients (20.6%), and AKI in 24 patients (18.3%). All deceased patients (100%) developed respiratory failure and required intensive ventilation, compared to only 2.9% of the survived group who required intensive ventilation (p<0.001) (Table 4).

Independent predictors of death in the different groups of variables are shown in Table 5, showing crude odds ratio (COR), adjusted odds ratio (AOR), confidence interval (CI), and cut-off point. In univariate regression analysis for predicting the mortality of COVID-19 patients, COR in deceased patients was higher in patients with DM (COR= 8.3, 95% CI: 1.8, 36; p=0.006), COPD (COR= 20.2, 95% CI: 3.9, 102; p<0.001), CKD (COR= 2.5, 95% CI: 1.1, 5.8; p=0.036), cancer (COR= 17, 95% CI: 1.8, 159; p=0.013), acute liver injury (COR= 27.8, 95% CI: 3.2, 242; p=0.003), acute kidney injury (COR= 4.5, 95% CI: 1.7, 11.6; p=0.002), and ARDS (COR= 132, 95% CI: 11.5, 519; p<0.001). After adjusting to covariates, only COPD and acute liver injury were found to be a significant independent predictor of COVID-19 mortality (AOR= 18.8, 95% CI: 2.5, 141; p=0.004) and (AOR= 46, 95% CI: 1.5, 144; p=0.029), respectively. Likewise, many significant predictors were identified, including WBCs >13×109/L (AOR= 24.2, 95% CI: 1.8, 323; p=0.016), and lymphocyte count <5.6×109/L (AOR= 11.9, 95% CI: 1.2, 122; p=0.037), BUN >20 mmol/L (AOR= 31.8, 95% CI: 4.3, 236; p=0.001), AST >50 IU/L (AOR= 11.8, 95% CI: 1.1, 126; p=0.041), INR >1.2 (AOR= 11.5, 95% CI: 1.8, 39; p=0.001), ESR>89.5 mm/h (AOR= 8.46, 95% CI: 2.8, 41; p=0.006), CRP>13 mg/L (AOR= 5.76, 95% CI: 1.01, 33; p=0.049), D-dimer >2.5 mg/L (AOR= 10.7, 95% CI: 2.1, 56; p=0.005), lactic acid >2.75 mmol/L (AOR= 38.3, 95% CI: 5.9, 247; p<0.001), and CK >455 U/L (AOR= 40.5, 95% CI: 5.8, 283; p<0.001).

Where: COR: Crude Odds ratio, AOR: Adjusted odds ratio, CI: confidence interval

Reference values: WBCs (3.5-10 x 10^9/L), Lymphocytes count (1.5-4 x 10^9/L), Hb (13-18 gm/L), RBCs (4.5-6.5$10^9$/L), Platelets (130-400 10^9/L), CRP (up to 6 mg/L), ferritin (13-400 ng/L), ALT (0-37IU/L), AST (0-37IU/L), BUN (2.5-6.4 mmol/L), creatinine (53-115nmol/L), Lactic acid (0.5-2.2 mmol/L), LDH (83-231 U/L), CK (21-232 U/L, D-dimer (up to 0.5 mg/L) and troponin I (up to 0.01 ng/mL).

Discussion

COVID-19 is a recently recognized infection, with no definitive therapy or vaccine to interrupt or diminish its uncontrolled spread. Many studies about the characteristics of COVID-19 disease; however, there are still some underlying issues that remained unknown [9]. This study described the clinical features, outcomes (discharge or death), and risk factors for the death of 131 patients with COVID-19 admitted to KK-HH. In our study, males were more commonly infected than females, agreeing with the current literature [4,8, and 10-12]. Females usually have a lower vulnerability to viral infections due to protection from the X chromosome and sex hormones that play a crucial role in innate and adaptive immunity [13]. In contrast, a recent report revealed no difference in the percentage of men and women between

ICU patients and non-ICU patients [14]. Our study revealed that the COVID-19 disease was more frequent in older age, especially in deceased patients. These findings were similar to those of Liu K, et al. (2020) [15], who reported that elderly patients with COVID-19 disease are more likely to have critical illness than young and middle-aged groups. Moreover, Berenguer J, et al. (2020) [7], Yang J, et al. (2020) [16], and Richardson S, et al. (2020) [12], reported similar results. Elderly people are more susceptible to COVID-19 disease, which may be associated with a higher frequency of comorbidities and immune problems.

The transmission rate of COVID-19 is unknown, as various factors impact its transmission [9]. Our study revealed that 23.7% had contact with confirmed COVID-19 cases regarding exposure history, and 13.7% had a travel history outside Hail. Several studies showed a higher risk of COVID-19 infection in travelers, especially those who travel to endemic areas with COVID-19 [17,18].

In our study, DM, CKD, COPD, and cancer were the most common comorbidities. Overall, the deceased patients had more significant comorbidities than survivors. These results may suggest that age and comorbidities are risk factors for critical patients. Diseases such as HTN, DM, respiratory system disease, cardiovascular disease, and their susceptibility conditions may be linked to the pathogenesis of COVID-19 [14]. Chronic diseases share several standard features with infectious disorders, such as the pro-inflammatory state and the innate immune response [16]. These findings were consistent with the previous meta-analysis studies that reported similar data [7,9,12,15,16, and 19]. Although smoking history was presented among 43 (32.8%) patients, there are no significant differences between the deceased and survivors' patients. However, the COPD was significantly higher in the deceased group with an agreement to other COVID-19 studies found a correlation of COPD and COVID-19 infection and poor outcome in COPD cases [9]. Smoking is probably associated with the bad prognosis and adverse outcomes of COVID-19 [20].

The clinical features of COVID-19 infection are non-specific and variable among country reports [14]. The current study revealed that fever (95.4%), cough (80.9%), dyspnea (65.6%), body aches, and myalgia (35.9%) were the most frequent clinical presentations among COVID-19 patients, while sore throat (15.3%), headache (13.7%), runny nose (4.6%), diarrhea (6.9%) and loss of taste or smell (2.3%) were the least frequent ones. Our findings in agreement with Guan WJ, et al. (2020) [11], revealed that the most frequent COVID-19 presentations were fever and cough (88.7% and 67.8%, respectively). Although nausea and/or vomiting (5%) and diarrhea (3.8%) were reported, they were uncommon. Moreover, Chan JWF, et al. (2020) [21] and Wang D, et al. (2020) [14], agreed with our results. Furthermore, our data showed that dyspnea and headache were significantly increased in deceased COVID-19 patients. Uygun Ö, et al. (2020) [22], reported that headache is a diagnostic feature of COVID-19. Our data agreed with Zheng Z, et al. (2020) [23], who reported a significant positive association of shortness of breath/dyspnea with COVID-19 progression to severe illness and death. In addition, a meta-analysis study reported similar results and suggested dyspnea instead of fever as an indicator of poor outcome in COVID-19 patients [24]. Fever is a clinical feature of patients with COVID-19 on admission; in our study, there is a significant increase in the deceased group's temperature than that of the survivors' group. Some reports found that low temperature at the initial presentation is a marker of poor prognosis, and high temperature during COVID-19 infection was a significant indication of poor outcomes [25].

Our study reported a significant reduction in SBP in deceased patients than in survivors. In agreement with previous studies [19,26], it has been found that COVID-19 patients will have complications such as shock and acute myocardial injury, and the complications are higher in the deceased than in the survived group. The current study demonstrated significant increases in the deceased patients' heart rate compared with the survived group. Acute myocardial injury (MI) is one of the complications of the COVID-19 infection, which is associated with increased death risk. Tachycardia indicates the damage of myocardial energy supply. In addition to ARDS, systemic inflammation with cardiac dysfunction is the main cause of death from severe COVID-19 [27]. New or deteriorating heart failure or MI was less frequent in three patients (10.7%) of deceased patients. On the other hand, it has been found that Cardiac complications are common, and cardiac arrest occurs in about 3% of hospitalized patients with pneumonia [28].

The current study found that the RR of the deceased patients was significantly higher than that of the survival group, and oxygen saturation was significantly lower than that of the survival group that indicates lung damage. Earlier studies had found that the COVID-19 cell entry receptor is located mainly in the lungs, over half of the patients might develop dyspnea, and >10% might require ventilatory support. Tachypnea and hypoxia indicated lung injury, worsening of the disease, and death [29].

Our finding showed bilateral lung infiltrations in CXR in all deceased patients compared to 51.55% of the survivors. In survivors, CXR was normal in 13.6%of cases and unilateral lung infiltration in 35% of cases. Similar conclusions were reported in previous studies concomitant with CT chest reports analysis [27,30]. We noted that patients in the deceased group were vulnerable to multiple organ failure, especially respiratory failure, heart failure, acute kidney, and liver injury. No confirmed evidence of the COVID-19 infection on solid organs except lungs was detected in pathological analysis and autopsy [31].

In our study, we noticed that 29 patients (22.1) had respiratory failure and all patients in the deceased group had ARDS (100%) vs. one patient in the survived group who need invasive ventilator support, indicating a very low survival rate in ICU patients. Also, some previous studies showed similar results; careful consideration should be given to early diagnosis and treatment to prevent aggravation of critically ill patients [9,19, and 27]. We noticed that sepsis occurred in 26% of COVID-19 patients and 67.9% of deceased patients. Sepsis was a frequent complication due to COVID-19 infection, but further studies are needed to understand the pathogenesis of sepsis in COVID-19 infection as a viral infection can cause sepsis syndrome [19].

Our findings demonstrated that during hospital admission, 24 patients (18.3%) with COVID-19 patients developed AKI and 11 patients (39.3%) were in deceased patients. In contrast, AKI in hospitalized COVID-19 patients was common and is associated with high morbidity and mortality rate [32]. We documented ALI in 7 (5.3%) cases; six of them were in the deceased group. However, some studies reported that more than one-third of patients admitted COVID-19 infection had ALI but is most frequently mild. A severe course would be predicted among the 6.4% of patients with severe liver injury [33,34]. The clinical features of COVID-19 and previous beta-coronavirus (SARS-CoV and MERS-CoV) infections are similar [6].

Arabi YM, et al. (2018) [35], initiated a placebo-controlled trial of interferon beta-1b and Kaletra (lopinavir and ritonavir) among

patients with MERS infection with considerable clinical benefit in Saudi Arabia. During the time of our study, there is no established antiviral treatment for COVID-19. The combination of hydroxychloroquine (HCQ), Kaletra, ribavirin, and interferon beta-1b, and started in KK-HH to evaluate its efficiency and safety in hospitalized patients with COVID-19 infection. In our study, 61% of patients were given HCQ, 42% of patients used kaletra and ribavirin, and interferon beta-1b was used in 11.5% of patients. Systemic corticosteroids were given to 76 patients (58%). Of these 76 patients, 28 patients were in the deceased group. Systemic corticosteroids were commonly used to manage patients with severe illness by reducing inflammatory-induced lung injury but suppressing immune responses and pathogen clearance simultaneously [36]. Thus, corticosteroids should not be routinely used systemically, and further clinical trials to confirm its benefits according to WHO provisional guidance [37]. All patients received antibiotic treatment, including cephalosporins and quinolones.

Mechanical ventilation was the main supportive treatment for ICU patients, but the benefit was low because most patients had suffered multiple organs failure due to severe hypoxia before mechanical ventilation. So, for critical patients, early invasive mechanical ventilation treatment should be considered. The principal approach in the management of COVID-19 is to offer supportive treatment and symptomatic treatment and mechanical ventilation and vasopressors for critical patients [38].

Our laboratory data revealed an increase in WBC count and decreasing lymphocytes in the deceased group. Similarly, previous studies reported lymphocytopenia among most COVID-19 patients on admission [39,40]. Lymphopenia was a well-defined feature in a retrospective analysis of SARS-CoV in 2 patients in Hong Kong and Singapore and was associated with poor outcomes in ICU [41]. The high leukocyte count is frequent in critically ill patients as damaged cells induce innate inflammation in the lungs [42]. COVID-19 might mainly act on lymphocytes, especially T lymphocytes [43]. Additionally, lymphopenia and neutrophilia on admission are related to poor outcomes in patients with COVID-19. Thus, lymphocyte count may help as a clinical predictor of severity and prognosis [44,45]. We noted a significant decrease in hemoglobin level among the deceased patient more than the survived group. In agreement with our finding, the previous studies showed a significant decline in hemoglobin among severe COVID-19 cases, and anemia was an independent risk factor for COID-19 patients associated with severe illness [46]. Moreover, the platelet count was significantly reduced in deceased patients. This is in concordance with earlier studies [8,11]. Our research found that the deceased group had significant hyperglycemia than the patients in the survived group. In agreement with our findings, Chen J, et al. (2020) [47], reported that severe COVID-19 is associated with increased blood glucose and focuses on efficiently monitoring blood glucose to improve prognosis in COVID-19 infection. There were significant increases in AST, ALT, BUN, serum creatinine, and cardiac troponin I in dead COVID-19 patients than the survivors in the present study. These elevations may indicate viral myocarditis and cardiac injury from multiple organ failure due to sepsis and hypoxia. Similar results were described by other studies [48,49]. In the present study, the dead COVID-19 had significantly higher D-dimer and prolonged PTT than survivors. Similar findings were seen in other studies [5,10,37, and 47]. Regarding inflammatory markers, our data revealed significant elevation of ESR, CRP, ferritin, LDH, and CK among the deceased group compared with the survivors. Our findings were in agreement with several reports [14,15, and 19]. The elevation of inflammatory biomarkers in COVID-19 patients may indicate serious lung injury. Viral infection induces acute phase reactant production and provokes a severe immunological reaction in the host, identified as a cytokine storm, which is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction [41]. Inflammatory markers are used in establishing the diagnosis of infections and predict the disease prognosis. From the start of the COVID-19 pandemic, the inflammatory markers were widely researched and found to help anticipate the probability of disease aggravation of COVID-19 patients. CRP was found to be a relatively beneficial prognostic indicator for COVID-19 infection [19]. Henry BM, et al. (2020) [48], reported poor clinical outcomes for patients with COVID-19 infections with elevated LDH and considered LDH an important mortality marker.

In terms of the predictors of mortality in deceased patients with COVID-19, we found many symptoms, signs, and laboratory parameters to be independent predictors of death in these patients. However, after adjusting to the covariates, many predictors were insignificant (e.g., Old Age, DM, CKD, and anemia). Expectedly, patients with a high respiratory rate (>42 cycles/min) and low oxygen saturation (<89%) had extremely high odds for mortality. COPD also showed moderate odds for mortality in contradiction to other studies. In the Cleveland Clinic COVID-19 registry, the investigators found after adjustment for covariates, that the rates of hospitalization, ICU admissions, and invasive mechanical ventilation (AOR=1.36, 95% CI: 1.15, 1.60; AOR= 1.20, 95% CI: 1.02, 1.40; and AOR= 1.49, 95% CI: 1.28, 1.73) were higher in COPD patients, respectively. However, the risk of in-hospital mortality was not significantly different from the non-COPD population (AOR= 1.08, 95% CI: 0.81, 1.42) [50]. This is contradictory to our results and to results from another study by Guan WJ, et al. (2020) [51], who showed that COPD patients were 2.6 times more likely to die from COVID-19. In our study, the highest odds for mortality were associated with ALI with high AST and INR, showing moderate odds. Moreover, laboratory markers for inflammation (WBCs, ESR, CRP, D-DIMER) and shock (lactate, BUN, CK) were a significant predictor of mortality. This is in line with other studies reporting a "cytokine storm" and "multiorgan failure" as major causes of death in COVID19 patients [52-54].

This study has some limitations, including:

- Data of the present study were collected retrospectively with many potential biases, such as case ascertainment bias;
- We might have overestimated the importance of chronic disease at risk of hospital admission due to the substantial heterogeneity among the included patients;
- Our patients were from a single geographical area, treated within a single health system; factors correlated with poor outcomes might differ elsewhere.

In conclusion, among the included patients, the in-hospital mortality rate was 21.4%. Old age and male gender were associated with significant mortality. The independent predictors of COVID-19 mortality were COPD, SPO2<89, acute Liver Injury, leukocytosis, lymphopenia, and markers of inflammation (ESR, CRP, D- Dimer) and shock (lactate, and Creatine Kinase). Further studies are needed to assess definite mortality predictors in hospitalized COVID-19 patients to identify and guide the management of patients at risk.

Conflict of Interest

None.

Acknowledgment

None.

Funding Source

None.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382:727-733. https://doi.org/10.1056/nejmoa2001017
2. Velavan TP, Meyer CG (2020) The COVID-19 epidemic. Trop Med Int Health 25: 278-280. https://dx.doi.org/10.1111/tmi.13383
3. Wu YC, Chen CS, Chan YJ (2020) The outbreak of COVID-19: An overview. J Chin Med Assoc 83: 217-220. https://dx.doi.org/10.1097/JCMA.0000000000000270
4. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395: 507-513. https://doi.org/10.1016/S0140-6736(20)30211-7
5. Rivett L, Sridhar S, Sparkes D, Routledge M, Jones NK, et al. (2020) Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. Elife 9: e58728. https://doi.org/10.7554/eLife.58728
6. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395: 497-506. https://doi.org/10.1016/S0140-6736(20)30183-5
7. Berenguer J, Ryan P, Rodríguez-Baño J, Jarrín I, Carratalà J, et al. (2020) Characteristics and predictors of death among 4035 consecutively hospitalized patients with COVID-19 in Spain. Clin Microbiol Infect 26: 1525-1536. https://doi.org/10.1016/j.cmi.2020.07.024
8. Wallin GA (1854) Narrative of a Journey from Cairo to Medina and Mecca, by Suez, Arabá, Tawilá, al-Jauf, Jubbé, Háil, and Nejd, in 1845. J R Geogr Soc London 1: 115-207. https://doi.org/10.2307/3698106
9. Emami A, Javanmardi F, Pirbonyeh N, Akbari A (2020) Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. Arch Acad Emerg Med 8: e35.
10. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, et al. (2020) Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. BMJ 369: m1985. https://doi.org/10.1136/bmj.m1985
11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. (2020) Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 382: 1708-1720. https://doi.org/10.1056/NEJMoa2002032
12. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, et al. (2020) Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 10022: 1-8. https://doi.org/10.1001/jama.2020.6775
13. Zuk M, Stoehr AM (2010) Sex differences in susceptibility to infection: An evolutionary perspective. Sex hormones and immunity to infection. Springer, Heidelberg, Berlin. https://doi.org/10.1007/978-3-642-02155-8_1
14. Wang D, Hu B, Hu C, Zhu F, Liu X, et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 323: 1061-1069. https://doi.org/10.1001/jama.2020.1585
15. Liu K, Chen Y, Lin R, Han K (2020) Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect 80: e14-e18. https://doi.org/10.1016/j.jinf.2020.03.005
16. Yang J, Zheng Y, Gou X, Pu K, Chen Z, et al. (2020) Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: A systematic review and meta-analysis. Int J Infect Dis 94: 91-95. https://doi.org/10.1016/j.ijid.2020.03.017
17. Luo G, McHenry ML, Letterio JJ (2020) Estimating the prevalence and risk of COVID-19 among international travelers and evacuees of Wuhan through modeling and case reports. PLoS One 15: e0234955. https://doi.org/10.1371/journal.pone.0234955
18. Wei L, Sha Z, Wang Y, Zhang G, Jia H, et al. (2020) Willingness and beliefs associated with reporting travel history to high-risk coronavirus disease 2019 epidemic regions among the Chinese public: a cross-sectional study. BMC Public Health 20: 1164. https://doi.org/10.1186/s12889-020-09282-4
19. Zhou F, Yu T, Du R, Fan G, Liu Y, et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395: 1054-1062. https://doi.org/10.1016/S0140-6736(20)30566-3
20. Vardavas CI, Nikitara K (2020) COVID-19 and smoking: A systematic review of the evidence. Tob Induc Dis 18: 20. https://dx.doi.org/10.18332/tid/119324
21. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395: 514-523. https://doi.org/10.1016/S0140-6736(20)30154-9
22. Uygun Ö, Ertaş M, Ekizoğlu E, Bolay H, Özge A, et al. (2020) Headache characteristics in COVID-19 pandemic-a survey study. J Headache Pain 21: 121. https://doi.org/10.1186/s10194-020-01188-1
23. Zheng Z, Peng F, Xu B, Zhao J, Liu H, et al. (2020) Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 81: e16-e25. https://doi.org/10.1016/j.jinf.2020.04.021
24. Shi L, Wang Y, Wang Y, Duan G, Yang H (2020) Dyspnea rather than fever is a risk factor for predicting mortality in patients with COVID-19. J Infect 81: 647-679. https://doi.org/10.1016/j.jinf.2020.05.013
25. Tharakan S, Nomoto K, Miyashita S, Ishikawa K (2020) Body temperature correlates with mortality in COVID-19 patients. Crit Care 24: 298. https://doi.org/10.1186/s13054-020-03045-8
26. Cao J, Tu WJ, Cheng W, Yu L, Liu YK, et al. (2020) Clinical features and short-term outcomes of 102 patients with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis 71: 748-755. https://doi.org/10.1093/cid/ciaa243
27. Pan F, Yang L, Li Y, Liang B, Li L, et al. (2020) Factors associated with death outcome in patients with severe coronavirus disease-19 (COVID-19): a case-control study. Int J Med Sci 17: 1281-1292. https://dx.doi.org/10.7150/ijms.46614
28. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA (2013) Acute pneumonia and the cardiovascular system. Lancet 381: 496-505. https://doi.org/10.1016/S0140-6736(12)61266-5
29. Myers LC, Parodi SM, Escobar GJ, Liu VX (2020) Characteristics of hospitalized adults with COVID-19 in an integrated health care system in California. JAMA 323: 2195-2198. https://doi.org/10.1001/jama.2020.7202
30. Rousan LA, Elobeid E, Karrar M, Khader Y (2020) Chest x-ray findings and temporal lung changes in patients with COVID-19 pneumonia. BMC Pulm Med 20: 245. https://doi.org/10.1186/s12890-020-01286-5
31. Xu Z, Shi L, Wang Y, Zhang J, Huang L, et al. (2020) Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 8: 420-422. https://doi.org/10.1016/S2213-2600(20)30076-X
32. Zahid U, Ramachandran P, Spitalewitz S, Alasadi L, Chakraborti A, et al. (2020) Acute kidney injury in COVID-19 patients: an inner city hospital experience and policy implications. Am J Nephrol 51: 786-796. https://doi.org/10.1159/000511160
33. Fan Z, Chen L, Li J, Cheng X, Yang J, et al. (2020) Clinical features of COVID-19-related liver functional abnormality. Clin Gastroenterol Hepatol 18: 1561-1566. https://doi.org/10.1016/j.cgh.2020.04.002
34. Phipps MM, Barraza LH, LaSota ED, Sobieszczyk ME, Pereira MR, et al. (2020) Acute liver injury in COVID-19: prevalence and association with clinical outcomes in a large US cohort. Hepatology 72: 807-817. https://doi.org/10.1002/hep.31404
35. Arabi YM, Alothman A, Balkhy HH, Al-Dawood A, AlJohani S, et al. (2018) Treatment of Middle East Respiratory Syndrome with a combination of lopinavir-ritonavir and interferon-β1b (MIRACLE trial): study protocol for a randomized controlled trial. Trials 19: 81. https://doi.org/10.1186/s13063-017-2427-0
36. Arabi YM, Mandourah Y, Al-Hameed F, Sindi AA, Almekhlafi GA, et al. (2018) Corticosteroid therapy for critically ill patients with Middle East Respiratory Syndrome. Am J Respir Crit Care Med 197: 757-767. https://doi.org/10.1164/rccm.201706-1172OC
37. World Health Organization (2012) Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. Geneva, Switzerland.
38. National Institute for Health and Care (2020) COVID-19 rapid guideline: managing suspected or confirmed pneumonia in adults in the community. NICE Guidelines, United States.

39. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, et al. (2020) Hematologic parameters in patients with COVID-19 infection. Am J Hematol 95: e131-e134. https://doi.org/10.1002/ajh.25774

40. Chng WJ, Lai HC, Earnest A, Kuperan P (2005) Haematological parameters in severe acute respiratory syndrome. Clin Lab Haematol 27: 15-20. https://doi.org/10.1111/j.1365-2257.2004.00652.x

41. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R (2020) Features, evaluation and treatment coronavirus (COVID-19). StatPearls.

42. Shi Y, Wang Y, Shao C, Huang J, Gan J, et al. (2020) COVID-19 infection: the perspectives on immune responses. Cell Death Differ 27: 1451-1454. https://doi.org/10.1038/s41418-020-0530-3

43. Qian K, Deng Y, Tai Y, Peng J, Peng H, et al. (2020) Clinical characteristics of 2019 novel infected coronavirus pneumonia: a systemic review and meta-analysis. MedRxiv. https://doi.org/10.1101/2020.02.14.20021535

44. Henry BM, Cheruiyot I, Vikse J, Mutua V, Kipkorir V, et al. (2020) Lymphopenia and neutrophilia at admission predicts severity and mortality in patients with COVID-19: A meta-analysis. Acta Biomed 91: 1-16. https://dx.doi.org/10.23750/abm.v91i3.10217

45. Liu J, Li S, Liu J, Liang B, Wang X, et al. (2020) Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine 55: 102763. https://doi.org/10.1016/j.ebiom.2020.102763

46. Tao Z, Xu J, Chen W, Yang Z, Xu X, et al. (2020) Anemia is associated with severe illness in COVID-19: A retrospective cohort study. J Med Virol 93: 1478-1488. https://doi.org/10.1002/jmv.26444

47. Chen J, Wu C, Wang X, Yu J, Sun Z (2020) The impact of COVID-19 on blood glucose: a systematic review and meta-analysis. Front Endocrinol (Lausanne) 11: 574541. https://dx.doi.org/10.3389/fendo.2020.574541

48. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G (2020) Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 58: 1021-1028. https://doi.org/10.1515/cclm-2020-0369

49. Chen J, Fan H, Zhang L, Huang B, Zhu M, et al. (2020) Retrospective analysis of clinical features in 101 death cases with COVID-19. MedRxiv. https://doi.org/10.1101/2020.03.09.20033068

50. Attaway AA, Zein J, Hatipoğlu US (2020) SARS-CoV-2 infection in the COPD population is associated with increased healthcare utilization: An analysis of Cleveland clinic's COVID-19 registry. EClinicalMedicine 26: 100515. https://doi.org/10.1016/j.eclinm.2020.100515

51. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, et al. (2020) Comorbidity and its impact on 1590 patients with Covid-19 in China: A nationwide analysis. Eur Respir Soc 55: 2000547. https://doi.org/10.1183/13993003.00547-2020

52. Fajgenbaum DC, June CH (2020) Cytokine storm. N Engl J Med 383: 2255-2273. https://doi.org/10.1056/NEJMra2026131

53. Mokhtari T, Hassani F, Ghaffari N, Ebrahimi B, Yarahmadi A, et al. (2020) COVID-19 and multiorgan failure: A narrative review on potential mechanisms. J Mol Histol 51: 613-628. https://doi.org/10.1007/s10735-020-09915-3

54. Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and multiorgan response. Curr Probl Cardiol 45: 100618. https://doi.org/10.1016/j.cpcardiol.2020.100618