

## RESEARCH ARTICLE

# Epidemiological, clinical, and laboratory findings for patients of different age groups with confirmed coronavirus disease 2019 (COVID-19) in a hospital in Saudi Arabia

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## Abstract

### Background

Although the coronavirus disease 2019 (COVID-19) pandemic continues to rage worldwide, clinical and laboratory studies of this disease have been limited in many countries. We investigated the epidemiologic, clinical, and laboratory findings of COVID-19 infected patients to identify the effective indicators correlated with the disease.

### Methods

A retrospective study was conducted at King Abdullah Hospital in Bisha Province, Saudi Arabia, from March 20 to June 30, 2020. Patients of different age groups were confirmed as having COVID-19 infection using a real-time polymerase chain reaction. The demographic, clinical, and laboratory data of the patients were statistically analyzed.

### Results

Of the 132 patients, 85 were male and 47 were female, with a mean age of 50.9 years (SD  $\pm 16.7$ ). The patients were elderly ( $n = 29$ ) and adults ( $n = 103$ ). Of these, 54 (40.9%) had comorbidities, (25%) were admitted to the intensive care unit (ICU), and 12 (9.1%) died. On admission, the main clinical manifestations were fever (84.1%), cough (64.4%), shortness of breath (25%), chest pain (20.5%), and fatigue (18.2%). In all patients, increased neutrophils and decreased lymphocytes were observed. Patients' lactate dehydrogenase (LDH) was elevated. C-reactive protein (CRP) was elevated in 48.5%, D-dimer in 43.2%, and the erythrocyte sedimentation rate (ESR) in 40.9% of patients. The elderly showed higher neutrophil ( $p = 0.011$ ) and lower lymphocyte ( $p = 0.009$ ) counts than adults. Glucose, creatine kinase-MB, LDH, bilirubin, D-dimer, and ESR were significantly higher in the elderly than in

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the adults. The COVID-19 death group had a higher leucocyte count ( $p = 0.036$ ), and higher urea ( $p = 0.029$ ) and potassium ( $p = 0.022$ ) than the recovered group but had a lower hemoglobin concentration ( $p = 0.018$ ). A significant association was determined between COVID-19 death and the presence of cardiovascular disease ( $\chi^2(1) = 16.297$ ,  $p < 0.001$ ), hypertension ( $\chi^2(1) = 12.034$ ,  $p = 0.001$ ), renal failure ( $\chi^2(1) = 3.843$ ,  $p = 0.05$ ), old age ( $t(130) = 4.9$ ,  $p < 0.001$ ), and ICU admission ( $\chi^2(1) = 17.6(1)$ ,  $p < 0.001$ ).

## Conclusions

Investigating some of the laboratory and clinical parameters could help assess the disease progression, risk of mortality, and follow up patients who could progress to a fatal condition.

## Introduction

The novel coronavirus designated as 2019-nCoV is a human pathogen discovered in China at the end of 2019 during an outbreak of endemic pneumonia of unknown etiology [1, 2]. The World Health Organization (WHO) named this new coronavirus SARS-CoV-2, and the disease coronavirus disease 2019 (COVID-19) [2]. The disease continues to spread in more than 200 countries worldwide, with a high rate of infection and mortality, creating a significant dilemma for global health [1, 3].

The COVID-19 infection is represented by a spectrum of clinical severity. From no symptoms or mild upper respiratory tract symptoms [4–6], the disease can develop to severe pneumonia characterized by fever, cough, fatigue, dyspnea, bilateral pulmonary infiltrates, and acute respiratory injury [4]. The clinical characteristics and severity of COVID-19 have been described as similar to other coronaviruses, such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) [3]. Patients with severe illness can develop acute respiratory distress syndrome (ARDS), which requires extended care in an intensive care unit [6, 7]. Recent studies have confirmed that critically ill patients develop severe complications such as septic shock, severe metabolic acidosis, coagulopathy, thrombocytopenia, arrhythmias, and multiple organ dysfunction syndrome [5, 8, 9].

In Saudi Arabia, the first confirmed case of COVID-19 was recorded on March 2, 2020, and the number of discovered cases is increasing [10]. By September 27, 2020, the Saudi Ministry of Health had reported a cumulative total of 332,790 cases and 4,655 deaths confirmed in Saudi Arabia [11]. Such a large number of cases highlights the importance of analyzing the characteristics of patients confirmed to have the disease [3]. Recent studies have noted that the clinical and laboratory features of the disease are variable between populations because of their distinct demographic features, comorbidities, and immune system responses [8, 12]. However, testing the epidemiological, clinical, and laboratory elements correlated with COVID-19 infections is important for determining high-risk groups, mapping the disease, and designing appropriate management [8]. To date, multiple studies have described the disease among various population groups, but these have been mainly in China [4, 7, 12, 13]. Published data concerning the epidemiological, clinical, and laboratory findings of the disease in Saudi Arabia are limited [3, 8, 14]. This study investigated the potential role of the epidemiological, clinical, and laboratory findings of COVID-19 infected patients of different ages to identify the effective indicators associated with the disease.

## Methodology

### Study design and setting

A retrospective single-center study was conducted at King Abdullah Hospital (KAH), Bisha Province, Saudi Arabia. This hospital is a referral hospital with nearly 400 beds. It covers various specialties, thus serving various patient groups and most of the population in different areas in Bisha Province and surrounding villages [15]. KAH is the only hospital that admits COVID-19 patients in Bisha Province and the surrounding rural areas.

### Patients and procedures

Patients having COVID-19 infection who were admitted to KAH between March 20 and June 30, 2020 were enrolled in this study. We categorized patients into two groups, namely adults (15 to 64 years), and elderly (65 years or older). Patients who were less than 15 year old were excluded from the study due to insufficient clinical and laboratory data. All patients were confirmed as having the virus by positive SARS-CoV-2 nucleic acid results using a real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay on nasopharyngeal swab specimens. The RT-PCR test for COVID-19 was validated and processed at the Aseer Regional Hospital, Aseer region, Saudi Arabia. The tests were reported as positive or negative findings and available online within 24 h. The results were extracted from the Health Electronic Surveillance Network (HESN) database, a national electronic surveillance platform, Ministry of Health, Saudi Arabia.

### Collection of clinical and laboratory data

Data on the demographic characteristics, clinical manifestations, and laboratory findings were obtained from patients' medical records and local health authorities, and were entered into data collection form on admission. We also collected laboratory test results, including results for complete blood count, glucose levels, coagulation tests, D-dimer levels, erythrocyte sedimentation rate (ESR), renal and liver function tests, electrolytes, C-reactive protein (CRP), lactate dehydrogenase (LDH), creatine kinase (CK), and CK-MB.

### Ethical clearance

This study was reviewed and approved by the Research Ethics Local Committee at the College of Medicine, University of Bisha (UBCOM/ H-06-BH-087 (05/03)). The data were collected in an anonymous format, without violating the personal privacy of the patients. The study was carried out as part of the response by the University of Bisha to investigate the COVID-19 outbreak.

### Statistical analysis

Data were entered and analyzed using the software Statistical Package for Social Sciences (SPSS version 22) (Armonk, NY: IBM Corp.). Descriptive statistics were calculated to present the baseline demographic data and clinical symptoms in terms of proportion and frequency. Normally distributed continuous data were presented as mean  $\pm$  standard deviation (SD), and were compared using independent group t-tests. Non-normal distributed continuous variables were examined by the Mann-Whitney U test and expressed as the median and interquartile ranges (IQR). Non-parametric Kruskal-Wallis rank sum was applied for pairwise and multiple comparisons between the groups, and was presented as the median and IQR. Categorical variables were compared using the chi-squared test and displayed as numbers and proportions. All p-values of  $<0.05$  were considered statistically significant.

## Results

One hundred thirty-seven confirmed cases of COVID-19 were admitted to the King Abdullah Hospital during the period from March 18, 2020, to June 30, 2020. The average length of a hospital stay was four days (IQR, 3–7 days). The total number of admitted cases per month was six in March and four in April, which increased 28 in May and 94 in June. Of the 132 patients, 85 (64.4%) were male and 47 (35.6%) were female, with a mean age of 50.9 years (SD±16.7). One hundred and three (78%) of the patients were adults and 29 (22%) patients were elderly. Most of the patients (72.7%) were Saudi. One hundred and three patients (78%) had direct contact with infected individuals, and 29 (22%) had a history of travel outside the country.

## Clinical presentation

[Table 1](#) outlines the main clinical manifestations associated with the disease. On admission, the most common clinical manifestation was fever (84.1%), followed by cough (64.4%), shortness of breath (25%), chest pain (20.5%), and fatigue (18.2). Fifty-four (40.9%) of the patients

**Table 1. Baseline characteristic of patients with COVID-19 infection.**

Characteristic	n(%)
Age group	
16 to 64	103 (78.0)
65 and above	29 (22.0)
Gender	
Male	85 (64.4)
Female	47 (35.6)
Nationality	
Saudi	96 (72.7)
Non-Saudi	36 (27.3)
Symptoms	
Fever	111 (84.1)
Cough	85 (64.4)
Shortness of breath	33 (25)
Chest pain	27 (20.5)
Fatigue	24 (18.2)
Headache	22 (16.7)
Sore throat	13 (9.8)
Nausea and vomiting	9 (6.8)
Abdominal pain	8 (6.1)
Congested nose	6 (4.5)
Diarrhea	5 (3.8)
Muscle pain	4 (3.0)
Comorbidity	54 (40.9)
Diabetes mellitus	37 (28.0)
Renal failure	19 (14.4)
Hypertension	14 (10.2)
Liver diseases	5 (3.8)
Cardiovascular diseases	5 (3.8)
Respiratory diseases	2 (1.5)
Mortality rate	12 (9.1)
No. of cases transferred to intensive care unit	33 (25.0)

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had chronic disease, including diabetes mellitus, renal failure, hypertension, liver disease, cardiovascular disease, and respiratory disease. Thirty-three (25%) of the cases were admitted to the ICU. The mortality rate of the admitted cases was 9.1% (12/132).

Of the 12 deceased patients, 7 were females, and 5 were males. Nine (75%) of the deceased were elderly (age  $\geq 65$  years), 2 (16.7%) were adults (age 45 to 65 years), and one (8.3%) adult (age 15 to 44 years). Seven (58.3%) out of the 12 cases exhibited different types of underlying medical conditions. Hypertension was the most frequent chronic condition found in the deceased (n = 5), followed by diabetes mellitus (n = 4), chronic kidney disease (n = 4), and cardiovascular disease (n = 3). Half (n = 6) of the patients exhibited  $\geq 2$  comorbidities. [S1 Fig](#) shows the numbers and the frequency of comorbidities among both genders.

## Laboratory results

The results of the laboratory parameters obtained at the time of patient admission are displayed in [Table 2](#). The complete blood count results of all patients were recorded as average values and showed slightly increased neutrophil and decreased lymphocyte counts. Overall, the average blood biochemistry parameters were normal, but elevated levels were detected for LDH (276 UL, normal values = 81–234 U/L). Regarding the inflammatory biomarkers, the mean value of D-dimer of all COVID-19 patients was 1.1 (SD, 1.26) mg/L. D-dimer at level of more than 0.5 mg/L reported as increased values, which was seen in 43.6% of the patients. While CRP was increased in 48.5% of the patients; and ESR was increased in 40.9% of patients.

**Comparison of laboratory parameters by age group.** [Table 2](#) compares the laboratory findings of the two age groups of adults and the elderly. Neutrophil counts were significantly higher in the elderly group (median = 7.31, IQR [6.76–8.18]) than in adult group (median = 6.65, IQR [5.9–7.61]). Lymphocytes were significantly higher in the adult (median = 2.39, IQR [1.66–3.03]) than in elderly group (median = 1.96, IQR [1.415–2.30]). Platelet counts were significantly lower in the elderly than in adult patients ( $p = 0.014$ ). There were no significant differences in other blood count parameters between the two age groups.

In terms of blood biochemistry results, glucose, CK-MB, LDH, and bilirubin were significantly higher in the elderly than in the adults ([Table 2](#)). Significant differences ( $p < 0.001$ ) in creatinine levels were determined between the two aged groups, with the highest level in the elderly group (median = 103, IQR [80–139.5]). There were no significant differences in alanine transaminase (ALT), aspartate aminotransferase (AST), albumin, CK, and potassium levels among the two groups ([Table 2](#)).

As shown in [Table 2](#), the number of patients with increased D-dimer and ESR was significantly higher in the elderly group compared with the adult group ([D-dimer: 65.5% vs. 36.9%;  $p = 0.006$ ], [ESR: 62.1% vs. 35%;  $p = 0.009$ ]). The number of patients with increased CRP levels did not significantly differ between the elderly and adult groups (58.6% vs. 45.6%;  $p = 0.216$ ).

## Factors associated with COVID-19 death

In [Table 3](#), the analysis of several factors in relation to COVID-19 death is shown. There was a statistically significant association between COVID-19 death and ICU admission ( $\chi^2(1) = 17.6$ ,  $p < 0.001$ ), cardiovascular disease ( $\chi^2(1) = 16.297$ ,  $p < 0.001$ ), hypertension ( $\chi^2(1) = 12.034$ ,  $p = 0.001$ ), and renal failure ( $\chi^2(1) = 3.843$ ,  $p = 0.05$ ). Moreover, COVID-19 death was significantly increased ( $t(130) = 4.9$ ,  $p < 0.001$ ) in the elderly group (mean = 50.9, SD [16.9]) compared with the adult group (mean = 47.2, SD [17.1]) (mean = 48.9, SD [15.2]). However, there was no significant effect for sex ( $\chi^2(1) = 2.974$ ,  $p = 0.085$ ), although men (n = 85) were more likely to be infected by the disease than women (n = 47).

**Table 2. Laboratory findings for patients of different age groups with confirmed COVID-19.**

Parameter	Median (IQR)			P value
	Total	Adults	Elderly	
	(n = 132)	(n = 103)	(n = 29)	
TLC (4–11) x10 <sup>9</sup> /L	6.6 (4.8–9.1)	6.3 (4.7–9.1)	7.6(5.36–10)	0.146
Neutrophil (2.0–7.0) G/L	6.78 (6.0–7.61)	6.65 (5.9–7.61)	7.31(6.76–8.18)	0.011
Lymphocyte (1.1–3.3) G/L	2.25 (1.65–2.93)	2.39 (1.66–3.03)	1.96(1.41–2.30)	0.009
Monocyte (0.3–0.9) G/L	0.76 (0.50–0.98)	0.8 (0.5–0.95)	0.6(0.33–0.1)	0.084
Eosinophil (0.0–0.5) G/L	0.03 (0.0–0.15)	0.03 (0.0–0.13)	0.02(0.0–0.23)	0.933
Basophil (0.0–0.3) G/L	0.4 (0.3–0.6)	0.4 (0.3–0.6)	0.4(0.3–0.7)	0.415
Hemoglobin (12–16) g/dl	13.7 (11.8–15.1)	13.7 (11.9–15.1)	12.6(11.6–14.9)	0.267
Platelets (130–400) x10 <sup>9</sup>	227.0 (178.0–303.5)	231 (184–314)	196 (164–244)	0.014
PT (9.0–14.0) second	11.3 (10.9–12.2)	11.3 (10.9–12.2)	11.8(10.8–12)	0.817
INR	1.0 (0.9–1.0)	1 (0.9–1.1)	1(0.9–1.0)	0.63
Glucose (3.9–11) mmol/L	6.7 (5.6–10.7)	6.2 (5.4–7.9)	8.7(6.45–15.65)	0.003
Urea (1.7–8.3) mmol/L	4.6 (3.4–6.2)	4.2 (3.3–5.5)	6.4(4.25–12.35)	<0.001
Creatinine (15–115) μmol/L	83.0 (68.3–104.8)	77 (67–98)	103(80–139.5)	0.001
Albumin (34–50) g/L	33.0 (29.9–36.0)	33 (30–37)	33(28.75–35.75)	0.415
ALT (0.0–41) U/L	30.5 (20.0–49.8)	34 (20–51)	29(20–49)	0.777
AST (0.0–38) U/L	34.0 (21.0–55.0)	30 (18–55)	41(27–61.5)	0.076
CKMB (0–25) U/L	18.0 (14.0–24.0)	17 (14–23)	23(16.5–29.5)	0.035
CK (26–192) U/L	118.0 (60.5–244.8)	104 (60–227)	166 (73–317.5)	0.168
LDH (81–234) U/L	276.0 (169.0–345.0)	260 (167–342)	322 (207–448.5)	0.024
Na <sup>+</sup> (135–145) mmol/L	135.0 (132.0–138.0)	136 (133–138)	134 (131–138.5)	0.313
K <sup>+</sup> (3.5–5.0) mmol/L	4.0 (3.7–4.4)	3.98 (3.6–4.3)	4.1(3.74–4.95)	0.109
Bilirubin (0.0–18.1) μmol/L	6.1 (4.8–10.8)	6.3 (4.7–9.1)	9.4(5.1–12.3)	0.043
CRP, mg/L				0.216
Increased, n(%)	64/132 (48.5)	47/103 (45.6)	17/29 (58.6)	
D-Dimer, mg/L				
Increased, n(%)	57/132 (43.2)	38/103 (36.9)	19/29 (65.5)	0.006
ESR, mm/h				
Increased n(%)	54/132 (40.9)	36/103 (35)	18/29 (62.1)	0.009

ALT alanine transaminase, AST aspartate aminotransferase, CK creatine kinase, CRP C-reactive protein, ESR erythrocyte sedimentation rate, INR international, IQR interquartile range, K<sup>+</sup> potassium normalized ratio, LDH lactate dehydrogenase, Na<sup>+</sup> sodium, PT prothrombin time, TLC total leucocyte count.

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### Laboratory findings associated with COVID-19 death

Compared with the recovered group, the COVID-19 death group had significantly higher total leucocyte count (median = 8.78, IQR [5.73–13.50] vs. median = 6.4, IQR [4.7–8.5];  $p = 0.036$ ), urea (median = 7.05, IQR [3.90–12.93] vs. median = 4.5, IQR [3.43.3–5.9];  $p = 0.029$ ), and potassium (median = 4.5, IQR [3.96–4.90] vs. median = 3.9, IQR [3.6–4.3];  $p = 0.022$ ). In contrast, decreased levels of hemoglobin (median = 11.75, IQR [10.90–13.20] vs. median = 13.7, IQR [11.9–15.2];  $p = 0.017$ ) were reported in the COVID-19 death group compared with the recovered group. There were no statistical differences in the results of other tested laboratory parameters between the recovered and death groups (Table 4).

Table 3. Factors associated with COVID-19 death.

Variable	Total number (n = 132)	Improved (n = 120)	No of death (%)	df	P value
Gender				2.974 (1)	0.085
Male	85	80	5 (5.9)		
Female	47	40	7 (14.9)		
Nationality				2.186 (1) 2.387	0.122
Saudi	96	85	11 (11.5)		
Non-Saudi	36	35	1 (2.8)		
ICU admission				17.6 (1)	<0.001
Yes	33	24	9 (27.3)		
No	99	96	3 (3)		
Hypertension					0.001
Yes	15	10	5 (33.3)	12.034 (1)	
No	117	110	7 (6.0)		
Renal failure				3.843 (1)	0.05
Yes	19	15	4 (21.1)		
No	113	105	8 (7.1)		
Diabetes mellitus				0.184 (1)	0.668
Yes	37	33	4 (10.8)		
No	95	87	8 (8.1)		
Liver diseases				0.520 (1)	0.471
Yes	5	5	0		
No	127	115	12 (9.4)		
Cardiovascular disease				16.297 (1)	<0.001
Yes	5	2	3 (60)		
No	127	118	9 (7.1)		
Respiratory diseases				0.203 (1)	0.652
Yes	2	2	0		
No	130	118	12 (100)		
Length of hospital stay, median (IQR)		4 (3–7)	4.5 (3–7)		0.795
Age, (Mean±SD)	50.9±16.7	(48.9±15.2)	(71.7±17.0)	4.9 (130)	<0.001

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## Treatment

Detailed medical therapies initiated for COVID-19 patients are presented in S1 Table. Besides supportive therapies, three main types of medications were used for the management of COVID-19 infection, including antiviral drugs, antibiotics, and antimalarial treatments. Of the total number of patients, 87 (65.9%) were received antiviral therapies in monotherapy (48 with favipiravir, 22 with oseltamivir, and 17 with lopinavir/ritonavir). The antiviral drugs were utilized in 26 (78.7%) patients admitted to ICU and in 8 (66.7%) non-survivor patients. Anti-malarial drug (hydroxychloroquine) was utilized in 19 (14.4%) patients, and 2 of them died. Most patients (127; 96.2%) received antibiotics either as a single agent or combination therapy. The selection of antibiotic agent was based on the patient clinical conditions and the judgment of the treating physician. The most commonly utilized antibiotics were fluoroquinolones (81; 61.4%) (levofloxacin or moxifloxacin or ciprofloxacin) followed by azithromycin (50; 37.9%) and cephalosporins (33; 25.0%) (ceftriaxone or cefuroxime). Most of ICU patients (23; 69.7%)

**Table 4. Laboratory investigation associated with COVID-19 death.**

Parameter	Improved	Dead	<i>P</i> value
<b>Hematology and coagulation, median (IQR)</b>			
TLC, 10 <sup>9</sup> /L	6.4 (4.7–8.5)	8.78 (5.73–13.50)	0.036
Neutrophil, G/L	6.76 (6.0–7.57)	7.45 (6.82–8.14)	0.084
Lymphocyte, G/L	2.3 (1.65–2.96)	1.84 (1.48–2.16)	0.089
Monocyte, G/L	0.77 (0.51–0.98)	0.53 (0.32–0.91)	0.091
Eosinophil, G/L	0.03 (0.0–0.15)	0.02 (0.0–0.08)	0.465
Basophil, G/L	0.04 (0.03–0.06)	0.02 (0.01–0.05)	0.019
Hemoglobin, g/dl	13.7 (11.9–15.2)	11.75 (10.90–13.20)	0.017
Platelets count, x10 <sup>9</sup>	229 (178–308)	198.5 (151.00–289.50)	0.417
PT, second	11.3 (11.0–12.2)	11.35 (10.58–11.98)	0.385
INR	1.0 (0.9–1.1)	0.95 (0.90–1.00)	0.698
<b>Blood biochemistry, median (IQR)</b>			
Glucose, mmol/L	6.5 (5.6–9.3)	9.75 (5.68–15.78)	0.182
Urea, mmol/L	4.5 (3.4–5.9)	7.05 (3.90–12.93)	0.029
Creatinine, μmol/L	83 (68.3–102.8)	100 (69.50–135.50)	0.261
Albumin, g/L	33 (30.0–36.0)	32.3 (24.50–38.60)	0.496
ALT, U/L	34.0 (20.0–51.0)	27 (14.50–38.25)	0.232
AST, U/L	33.5 (20.0–55.0)	41 (29.25–60.75)	0.28
CK-MB, U/L	18 (14.0–24.0)	20.5 (1.18–32.00)	0.242
CK, U/L	118 (62.0–244.8)	155 (52.75–240.75)	0.887
LDH, U/L	275 (169–345)	321 (161.50–357.00)	0.918
Na, mmol/L	135 (132–138)	135.5 (132.50–139.75)	0.62
K, mmol/L	3.9 (3.6–4.3)	4.5 (3.96–4.90)	0.022
Bilirubin, μmol/L	6.1 (4.9–10.8)	5.65 (3.60–11.58)	0.447
<b>Inflammatory biomarkers, n(%)</b>			
CRP, mg/L			0.294
Normal	68	5/12 (41.7)	
Increased	57	7/12 (58.3)	
D-dimer, mg/L			0.065
Normal	76	4/12 (33.3)	
Increased	49	8/12 (6.7)	
ESR, mm/h			0.160
Normal	78	5/12 (41.7)	
Increased	47	7/12 (58.3)	

ALT alanine transaminase, AST aspartate aminotransferase, CK creatine kinase, CRP C-reactive protein, ESR erythrocyte sedimentation rate, INR international, K<sup>+</sup> potassium normalized ratio, IQR interquartile range, LDH lactate dehydrogenase, Na<sup>+</sup> sodium, PT prothrombin time, TLC total leucocyte count

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and non-survivors (8; 66.7%) received fluoroquinolones. Six (50%) of the non-survivors and 12 (36.4%) of ICU patients received cephalosporins.

Regarding the supportive care treatments, thromboprophylaxis therapy was administered to 74 (56.1%) patients. Most patients (n = 62) received enoxaparin, 7 patients received heparin, and 5 patients received apixaban. The thromboembolism treatment was not administered to patients with a current history of gastrointestinal bleeding, or a short duration of hospital stay. Thirty-four (25.8%) of our patients received oxygen treatment (21 with invasive ventilation and 13 with non-invasive ventilation). Supplemental oxygen was utilized in 60.6% of ICU



patients and 50% of non-survivors. Twenty-nine patients received corticosteroids (19 with prednisolone and 10 with dexamethasone). Corticosteroids were most likely given to the patients who require supplemental oxygen, including those requiring invasive and non-invasive ventilation.

## Discussion

In this study, we described the epidemiology, clinical characteristics, and laboratory parameters of 137 confirmed patients with COVID-19 in Bisha, Saudi Arabia. We found that COVID-19 frequently infected the middle-aged group. This is in agreement with previous reports that showed the middle-aged, from 40 to 60 years, were the most commonly infected group [16–19]. However, the virus can infect individuals of all age groups [17, 18]. The study reported a greater number of men than women as having the infection, which is similar to the findings of other studies [19–21]. A study conducted among 56 elderly patients found that more men than women were infected by 2019-nCoV [13]. A single-arm meta-analysis showed that the men made up a larger percentage of the gender distribution of COVID-19 patients at 60% (95% CI [0.54, 0.65]) [20]. Previous studies have documented more men than women to be infected with other coronavirus infections, such as in SARS-CoV [22] and MERS-CoV [23]. The decrease in women's susceptibility to coronavirus infections could be attributed to sex hormones and an X chromosome, which play an essential role in innate and adaptive immunity [19, 20].

Our findings revealed that fever, cough, and shortness of breath were the most frequent symptoms in COVID-19 patients, which is in agreement with many previous studies [13, 24–26]. Research evidence suggests that the disease's complete clinical characteristics are nonspecific and are not yet clear, as the associated symptoms range from mild to severe, with several cases resulting in death [11, 27]. However, it is unclear whether the viral load affects the clinical presentation [18]. It is well known that the clinical manifestations in symptomatic patients begin to present with mild symptoms in less than 1 week, and that patients tend to recover within 1 week [14, 27]. Some patients may progress to severe disease with dyspnea, which may be accompanied by pneumonia in the second or third weeks of the disease [9, 27, 28]. Severe cases have been found to develop to progressive respiratory failure due to alveolar damage from the virus, leading to death [14, 27].

Regarding the hematological parameters, an estimation of white blood counts is essential to predicting the outcomes of COVID-19 infection [8]. We found normal leucocyte counts in our results, with a decreased level of lymphocytes and an upper limit of neutrophil counts. Similarly, Jin et al. showed that in the early stage of the disease, the total number of leucocytes in peripheral blood was normal or decreased, and the lymphocyte count was decreased [26]. Recent reports have also found increased neutrophil counts and decreased lymphocyte counts associated with COVID-19 [29, 30]. Lymphocytopenia could explain the effect of SARS-CoV-2 on T lymphocytes, mainly on CD4+ T cells and CD8+ T cells, resulting in a decrease in lymphocyte numbers and IFN- $\gamma$  production [19, 30]. It is well known that SARS-CoV-2 spreads through the respiratory mucosa and invades other cells, induces a series of immune responses, and causes changes in peripheral white blood cells, including lymphocytes [19]. Studies suggest that a substantial decrease in the total number of lymphocytes indicates that coronaviruses disrupt many immune cells and suppress cellular immune function [31, 32].

In comparing hematological findings, we detected significantly higher neutrophil levels among elderly patients compared with adult patients. Similar findings have been reported by others, where older patients with COVID-19 infections have shown high neutrophil counts and decreased lymphocytes [13, 29]. The elevated neutrophil counts in this study could be

explained by the fact that elderly 2019-nCoV infected patients are more susceptible to bacterial infection [13, 25]. This study also found that lymphocyte counts were significantly lower in elderly than in adult patients. In a retrospective study compared the clinical features of COVID-19 in elderly patients with young and middle-aged patients, Liu et al. found that the proportion of lymphocytes in the elderly group was significantly lower than that in the young and middle-aged group ( $p < 0.001$ ) [13]. The changes in the muscles that aid respiration, and the anatomical changes in the lungs associated with an older age may lead to physiological changes in the respiratory system, poor airway clearance and reduced lung reserve, and defense barrier mechanisms [33].

In terms of blood biochemical findings, we also found that glucose, creatinine, and urea were significantly higher in older patients with COVID-19 infection than in adults. In contrast, studies have shown that there was no significant difference in serum creatinine when the elderly were compared with young and middle-aged patients [13]. We showed that 40% of the patients had various comorbid conditions, which might have explained the increased creatinine and glucose levels in the older adults in this study. Likewise, a recent study indicated that COVID-19 patients with severe conditions had high blood urea and creatinine levels, and that their lymphocyte counts continued to decrease [25]. In our results, the LDH level was elevated in the two age groups, and indicated an adverse clinical outcome. Elevated LDH has been found to be an independent risk factor for severe/critical COVID-19 in patients [7]. Research data suggest that SARS-CoV-2 may damage liver and myocardium tissues, lead to elevated levels of AST, CK, and myoglobin to various degrees, and increased troponin in critical patients [9]. Tsui et al. showed that LDH levels reflect tissue necrosis related to immune hyperactivity in SARS, and thus relate to poor outcome [34]. Therefore, the monitoring of LDH levels and other cardiac and liver enzymes could help predict severe COVID-19 in patients [12].

Determining the levels of D-dimer, CRP, ESR, and other inflammatory biomarkers is essential to detecting bacterial infection in the lungs, and may help preliminarily evaluate patients' immune status [26]. We found that most COVID-19 patients had elevated ESR rates, and over 40% of the patients presented increased CRP and D-dimer levels. Likewise, studies have documented that an increased D-dimer concentration is a common feature of COVID-19 infections, especially for severe patients [9, 25, 26]. However, the elderly are more likely to develop a severe disease [21]. Our findings revealed significantly higher levels of ESR and D-dimer in the elderly than in the adult group, while there were no significant differences in CRP levels between the two groups. A recent study found that the CRP level in elderly patients was significantly higher than that in young and middle-aged groups [13].

Our findings revealed that many patients infected by SARS-CoV-2 were older men and had chronic underlying diseases. This is in agreement with a previous report, in which COVID-19 patients were reported to have comorbid conditions [4, 19]. In addition, research data show that patients  $\geq 60$  years old are at higher risk than children, who are less likely to have an infection, or who show mild to asymptomatic infection [28]. The increased risk of developing severe COVID-19 complications in older people with comorbid conditions have been well documented in the literature [19]. In multivariate analysis of 487 COVID-19 patients including 49 severe cases, Chi et al. noted that elder age (OR 1.06 [95% CI 1.03–1.08],  $p < 0.001$ ), male (OR 3.68 [95% CI 1.75–7.75],  $p = 0.001$ ), and presence of hypertension (OR 2.71 [95% CI 1.32–5.59],  $p = 0.007$ ) are independently associated with severe disease at admission [4]. Chen et al. [19] suggested that 2019-nCoV is more likely to infect older adult men with chronic comorbidities as a result of the weaker immune functions of these patients [19]. A study indicated that COVID-19 infection progresses rapidly to acute respiratory distress syndrome, septic shock, metabolic acidosis, coagulation dysfunction, and leads to death in older patients and those with comorbid conditions [25]. Therefore, identifying host risk factors associated with

severe COVID-19 infections may help in designing specific strategies to prevent and treat the disease [4].

We found that 25% of the patients were admitted to the ICU. This proportion was much higher than the 4.7% reported in a multi-center retrospective study that included 1519 cases from all regions of Saudi Arabia [8]. The mortality rate of COVID-19 in our study was 9.1%, which was higher than the 3.4% reported in the literature [25]. The overall fatality rate of the disease as found by others was in the range of 3% to 14% [35]. The high mortality rate and ICU admission observed in this study could be explained by the fact that the study selected only confirmed cases that were admitted to our hospital. Therefore, a further survey with a larger sample size could show some differences. In comparing the death rate of COVID-19 with other coronaviruses, the available data indicate that COVID-19 infection results in a lower mortality rate than that reported for SARS (9.60%) and MERS (34.4%) [36]. Therefore, extensive studies of the pathogenic and virulence mechanisms of SARS-CoV, SARS-CoV-2, and MERS-CoV are needed to explain these variations.

We found that the mortality rate of COVID-19 infection was quite high among the elderly and those admitted to the ICU, which resembled previous findings [13, 29]. However, patients in the ICU were more likely to receive mechanical ventilation, surgical interventions, and prolonged treatment, which might have increased the death rate [29]. In addition, the study also revealed that hypertension, renal failure, and cardiovascular disease increased the risk of death in COVID-19 cases. This agrees with previous reports, in which hypertension, coronary heart disease, and diabetes were found to be risk factors that resulted in death [12, 27, 29, 36]. Research evidence indicates that the elderly and those with chronic underlying diseases develop severe and fatal respiratory failure because of alveolar damage from the virus [17, 19, 21].

## Limitations

Our study has several limitations: First, the sample size was relatively small, and may not fully reflect the characteristics of the disease for these aged groups. Therefore, a large sample size could give a more comprehensive understanding of 2019-nCoV. Second, the study findings might have been biased by reporting only confirmed cases in a single hospital center. Further studies that include suspected and undiagnosed cases may show some differences. Third, we statistically analyzed the laboratory findings based on a comparison of means, median, and proportions between different age groups that were not subdivided into groups of patients with individual comorbid conditions. Finally, the study assessed the epidemiological, laboratory, and clinical characteristics of COVID-19 on admission of the patients; more detailed information from other laboratory tests and clinical outcomes were unavailable at the time of analysis.

## Conclusions

In summary, this study revealed the epidemiological, clinical, and laboratory findings of patients of different age groups confirmed to have COVID-19. On admission, patients were most likely to present with mild symptoms of fever, cough, shortness of breath, and chest pain. Increased LDH, CRP, ESR, and D-dimer levels were common laboratory findings on patient admission. However, glucose, CK-MB, LDH, bilirubin, D-dimer, and ESR levels were significantly higher in the elderly than in adult patients. We found an increased disease mortality rate, which may be attributed to the high percentage of patients with various comorbidities. This study revealed that older age, ICU admission, cardiovascular disease, hypertension, and renal failure were risk factors for death. Increased levels of leucocytes, potassium, and urea,

and decreased hemoglobin concentration were frequent laboratory findings associated with death. The common symptoms found in this study may help in identifying potential severe COVID-19 patients. Moreover, some routine laboratory findings could help assess disease progression and manage patients who could develop critical conditions and be at risk of mortality. These findings should be confirmed in future studies coupled with testing other suitable clinical and laboratory indicators for evaluating disease severity and outcomes.

## Supporting information

**S1 Fig. Frequency of comorbidities among deceased patients (n = 12) with confirmed COVID-19 infection.**

(TIF)

**S1 Table. Medications and supportive therapies for patients (n = 132) with COVID-19 infection.**

(DOCX)

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