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### Analysis of the Clinical Characteristics of COVID-19 Patient Severity Amongst Saudi Hospital Admission in 2020

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#### ABSTRACT

**Background and aims:** Coronavirus Disease 2019 (COVID-19), the infection caused by the SARS-CoV-2 virus, is associated with variable clinical symptoms ranging from asymptomatic to severe manifestations that lead to increased mortality. Some of these abnormalities are linked to hematologic, inflammatory, biochemical and immune biomarkers, in cases with severe forms of the illness compared to mild systemic disease. However, such associations have not been studied in detail in Saudi Arabia. This study was conducted to evaluate these clinical indices in a Saudi population admitted to hospital in Makkah during 2020 with a positive diagnosis of COVID-19, as possible risk factors for COVID-19 related fatality.

**Materials and methods:** Demographic and biochemical data related to type of admission, hematological indices, liver and renal functions, markers of inflammation and blood gases were collected at the time of patient admission. The variables were then compared between both groups to determine potential risk factors that contribute to COVID-19 fatality.

**Results:** A total of 315 patients with confirmed COVID-19 infection by PCR and complete final status (recovered or dead) were identified and included in the study. By additional analysis, mean age was significantly higher in deceased patients compared with those who recovered from infection. Moreover, death from COVID-19 infection was significantly more common in patients admitted to ICU compared with ward admission. Patients admitted to ICU had a substantially greater risk of dying from COVID-19 infection (46-fold) compared with ward admission. Contrariwise, higher mean O<sub>2</sub>sat was associated with significantly lower odds of death.

**Conclusions:** Males and non-Saudi residents were more susceptible to acquiring infection during the first wave of COVID-19. Although liver and renal biochemical parameters, haematological indices, and respiratory functions were significantly altered with COVID-19 infection and more pronounced in deceased patients, only ICU admission and low O<sub>2</sub> pressure showed higher risks of death from the infection.

#### 1. Introduction

In December 2019, a novel coronavirus, presently known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), developed in Wuhan, China (Huang *et al.*, 2019, Al-Mulla *et al.*, 2021). To date, the infection has spread quickly all over the world and was announced a pandemic by the World Health Organization in March 11, 2020. With the number of cases as of now surpassing 100 million, and more than two million fatalities, the virus is considered a serious problem in the world [1, 2]. Coronavirus Disease 2019 (COVID-19), the infection caused by the virus, has a profoundly variable clinical introduction, extending from asymptomatic to severe manifestations leading to increased mortality. The COVID-19 symptoms include malaise, fever, cough, myalgia, dyspnea, cerebral infarction, headache and loss of taste or scent. Most patients encounter mild symptoms, in spite of the fact that a few may experience serious complications, such as acute respiratory distress syndrome (ARDS), hypercoagulation, multiorgan failure and septic shock, which can inevitably lead to death [3-6]. However, the reasons for the variability in disease signs and symptoms are not completely understood.

Furthermore, younger age cases appear to have a milder clinical course [7], with poorer prognosis in geriatric and male gender cases. Currently, certain medical conditions, including cardiovascular diseases, chronic kidney disease hypertension, chronic obstructive pulmonary disease and diabetes, are associated with worsening COVID-19 prognosis [8-12]. Indeed, people with diabetes mellitus (DM) are more prone to be infected and are at a greater risk of death and severe complications from COVID-19. And remarkably, there was a parallel trend of increased risk for Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS) diseases caused by the related beta-coronaviruses, in people with DM [13].

On March the 9th, 2020, the Saudi Ministry of Health had recorded four new patients with COVID-19. However, this figure had increased to 3,717 cases of the disease within a month, with the total number of the active cases standing at 33,515 on June 10, 2020, whilst critical cases were 1,693 between the total active cases [14]. Regarding the foremost newly published Diagnosis and Management Program of 2019 New Coronavirus Pneumonia [12], COVID-19 patients are separated into 3 groups, mild, moderate and severe. Consequentially,

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from laboratory blood analysis, hematological parameters, including lymphopenia, white blood cell (WBC), C-reactive protein (CRP), and biochemical parameters, including creatine kinase (CK), LDH and troponin were found to be related with increased COVID-19 severity [15, 16]. Additionally, numerous research studies have described the clinical features and laboratory variations related to COVID-19 patients [17-19]. Furthermore, total number of COVID-19 cases are increasing considerably, and admission in intensive care units (ICUs) has developed an important challenge for countries and governments [20]. The disease caused by SARS-CoV-2 infection can also cause serious respiratory disease, which may advance to clinically severe stages, demanding ICU admission and ventilator care [17, 21]. A severe form of the illness has been linked with abnormalities associated with hematological, inflammatory, biochemical and immune biomarkers, compared to groups with mild systemic disease [4, 17, 19, 21-24]. Moreover, there is lack of available data within the Kingdom of Saudi Arabia, especially amongst hospitalized patients, on how these clinical indices may affect disease burden. To this end, this study aimed to investigate the biochemical profiles, haematological indices, liver and renal functions, markers of inflammation and blood gases, among COVID-19 patients admitted to hospital in the Makkah region, who had either recovered or deceased, to determine any association with COVID-19 fatality.

## 2. Patients and methods

### Study design and data collection

This was a retrospective cohort study. All patients with confirmed COVID-19 infection by polymerase chain reaction (PCR) during June, August and October 2020 were recruited from Alawi Tunki hospital in Makkah. The clinical date at the day of admission was collected for those patients with a listed final status, as either recovered or deceased, at the time of discharge. Patients transferred to a different health facility, or their unclear final status were excluded from the study.

In addition to demographic data, the biochemical data related to the type of admission, haematological indices, liver and renal functions, a marker of inflammation and blood gases were collected at the time of patient admission. The main outcome was recovery or death from COVID-19 infection, and the patients were categorised as recovered or deceased groups. The variables were then compared between both groups to determine the potential risk factors that contribute to COVID-19 fatality.

### Statistical analysis

Version 25 of the Statistical Package for the Social Sciences (SPSS; NY, USA) for data analysis. Ordinal and non-continuous variables were analysed to measure frequency, and the results are shown as numbers and percentages and by cross-tabulation followed by the Chi-square ( $\chi^2$ ) test. We also assessed the normality and homogeneity of continuous data by the Kolmogorov and Smirnov, and the Levene tests, respectively. Student's t-test or Mann-Whitney u test were applied to compare between both study groups according to data normality. The results of continuous data are expressed either as mean  $\pm$  standard deviation (SD) or median with the interquartile range (IQR: 25<sup>th</sup> – 75<sup>th</sup> percentiles) according to data normality. Binary logistic regression was done to identify the demographic and biochemical factors associated with death from COVID-19 infection. Statistical significance was considered when P value was < 0.05.

### Ethical approval

This study is part of larger multicentre study involving the Western region of Saudi Arabia, and ethical approval was obtained from the Internal Review Board of Security Forces Hospital Makkah (SFHM) (SFHM; # 0432-280621) in Makkah.

## 3. Results

### Demographic characteristics of COVID-19 patients

A total of 315 patients with confirmed COVID-19 infection by PCR alongside a complete final status (recovered or dead) were identified and included in the study. The overall mean age of the 315 patients was  $43.2 \pm 12.9$  years. The numbers of cases were 108 (34.3%) in June, 104 (33%) in August, and 103 (32.7%) in October, and the rates were equal during the three months ( $P = 0.9$ ). However, the frequencies of males ( $n = 239$ ; 75.9%) and non-Saudis ( $n = 176$ ;

55.9%) were significantly higher compared with female ( $P < 0.0001$ ) and Saudi ( $P = 0.04$ ) patients. While most of the patients were admitted to Medical ward ( $n = 203$ ; 64.4%), the remainder were admitted to the intensive care unit (ICU) ( $n = 112$ ; 35.6%). By additional analysis, the mean of age was significantly higher in the deceased patients compared with those who recovered from the infection (Table 1). Moreover, death from COVID-19 infection was significantly more common in those patients admitted to ICU compared with ward admission (Table 1). However, there was no significant difference between the recovered and deceased group in relation to gender, nationality, month of diagnosis of having a history of diabetes mellitus (Table 1).

**Table 1** The frequency of demographic characteristics of the study participants ( $n = 315$ ) according to demise.

Parameter	COVID-19 positive cases ( $n = 315$ ; 100%)		P value
	Recovered ( $n = 284$ ; 90.2%)	Deceased ( $n = 31$ ; 9.8%)	
Mean $\pm$ SD of Age (year)	42.3 $\pm$ 12.9	50.9 $\pm$ 10.5	$P < 0.0001$
Month of infection			0.19
June	93 (29.5%)	15 (4.8%)	
August	95 (30.2%)	9 (2.8%)	
October	96 (30.5%)	7 (2.2%)	
Gender			0.27
Male	218 (69.2%)	21 (6.6%)	
Female	66 (21%)	10 (3.2%)	
Nationality			0.3
Saudi	128 (40.7%)	11 (3.5%)	
Non-Saudi	156 (49.5%)	20 (6.3%)	
Admission			$P < 0.0001$
Ward	202 (64.1%)	1 (0.3%)	
ICU	82 (26.1%)	30 (9.5%)	
History of diabetes mellitus			0.2
No	244 (77.5%)	24 (7.6%)	
Yes	40 (12.7%)	7 (2.2%)	

### Laboratory biochemical parameters

#### Haematological indices

As shown in Table 2, the deceased group had significantly lower red blood cells (RBCs) count, haemoglobin (Hb) concentrations, haematocrit value, mean corpuscular volume (MCV), and mean corpuscular haemoglobin (MCH) than the recovered group. The remaining RBCs indices and serum ferritin levels were, however, comparable between both groups (Table 2). Whilst the platelet count was also significantly lower in the deceased group, there were no significant differences between both study groups in the mean platelet volume (MPV), pro-thrombin time (PT), partial thromboplastin time (PTT), and international normalised ratio (INR).

Moreover, the total numbers of WBCs and basophils were similar between the recovered and deceased groups, whilst the neutrophil count was significantly higher in the latter group (Table 2). In contrast, the numbers of lymphocytes, monocytes and eosinophils were markedly higher in the recovered group than the deceased group at the time of admission (Table 2).

**Table 2** The mean ( $\pm$ SD) and median (IQR) of haematological indices at admission according to demise in the study participants (n = 315).

Parameter	COVID-19 positive cases (n = 315; 100%)		P value
	Recovered (n = 284; 90.2%)	Deceased (n = 31; 9.8%)	
Median (IQR) of serum ferritin ( $\mu$ g/L)	759 (327.3 – 1593.5)	759.1 (308.67 – 1327.0)	0.9
Mean $\pm$ SD of RBCs count ( $10^6/\mu$ L)	4.4 $\pm$ 0.9	3.6 $\pm$ 0.9	< 0.0001
Mean $\pm$ SD of Hb (g/dL)	12.1 $\pm$ 2.3	10.3 $\pm$ 2.5	< 0.0001
Median (IQR) of haematocrit value (%)	37.15 (30.75 – 40.6)	31.6 (25.1 – 35.0)	< 0.0001
Mean $\pm$ SD of MCV (fL)	82.7 $\pm$ 7.4	85.6 $\pm$ 7.5	0.04
Mean $\pm$ SD of MCH (pg)	28.2 $\pm$ 2.7	29.8 $\pm$ 2.7	0.005
Mean $\pm$ SD of MCHC (g/dL)	33.6 $\pm$ 1.9	33.2 $\pm$ 1.7	0.2
Median (IQR) of platelets count ( $10^3/\mu$ L)	269.5 (199.25 – 359)	221 (137 – 300)	0.004
Mean $\pm$ SD of MPV (fL)	10.4 $\pm$ 1.7	10.7 $\pm$ 1.8	0.4
Mean $\pm$ SD of PT (sec)	12 $\pm$ 2.4	12.2 $\pm$ 1.5	0.6
Mean $\pm$ SD of PTT (sec)	33.1 $\pm$ 9.8	33.9 $\pm$ 6.8	0.6
Mean $\pm$ SD of INR	1.02 $\pm$ 0.2	1.05 $\pm$ 0.2	0.4
Median (IQR) of WBCs count ( $10^6/\mu$ L)	8.35 (6.25 – 10.98)	7.8 (6.15 – 12.6)	0.9
Mean $\pm$ SD of neutrophil count ( $10^3/\mu$ L)	76.02 $\pm$ 14.2	83.02 $\pm$ 10.7	0.008
Median (IQR) of lymphocyte count ( $10^3/\mu$ L)	14.15 (6.9 – 22.4)	8.7 (4.6 – 16)	0.02
Median (IQR) of monocyte count ( $10^3/\mu$ L)	5.6 (3.6 – 8.6)	4.1 (3.1 – 6.7)	0.03
Median (IQR) of eosinophil count ( $10^3/\mu$ L)	0.1 (0.0 – 0.8)	0.0 (0.0 – 0.4)	0.01
Median (IQR) of basophil count ( $10^3/\mu$ L)	0.3 (0.1 – 0.5)	0.2 (0.1 – 0.3)	0.07

**Markers of systemic inflammation and liver function tests**

Regarding the systemic inflammatory markers, the erythrocyte sedimentation rate (ESR) and serum concentrations of lactate dehydrogenase were equal between both study groups (Table 3).

While the serum levels of total and direct bilirubin alongside alkaline phosphatase enzyme were substantially elevated in the deceased group, there was no significant difference between both groups in the serum amounts of alanine transferase (ALT) and aspartate aminotransferase (AST) enzymes. In contrast, the levels of serum total protein and albumin were markedly higher in the recovered group (Table 3).

**Table 3** The mean ( $\pm$ SD) and median (IQR) of markers of systemic inflammation and liver function parameters at admission according to demise in the study participants (n = 315).

	Parameter	COVID-19 positive cases (n = 315; 100%)		P value
		Recovered (n = 284; 90.2%)	Deceased (n = 31; 9.8%)	
Inflammation	Median (IQR) of ESR (mm/hour)	45 (10 – 86)	30 (10 – 70)	0.5
	Mean $\pm$ SD of lactate dehydrogenase (U/L)	366.5 $\pm$ 168.7	318.2 $\pm$ 124.9	0.1
Liver functions	Median (IQR) of total bilirubin (mg/dL)	8.04 (5.8 – 13.1)	10.7 (7.7 – 15.6)	0.08
	Median (IQR) of direct bilirubin (mg/dL)	2.77 (1.7 – 4.6)	4 (2.9 – 7.1)	< 0.0001
	Median (IQR) of ALP (U/L)	72 (58 – 96.75)	100 (69 – 175)	0.002
	Median (IQR) of ALT (U/L)	37.5 (25 – 59)	49 (26 – 87)	0.1
	Median (IQR) of AST (U/L)	41.5 (28 – 58)	40 (29 – 74)	0.6
	Median (IQR) of total protein (g/L)	70 (62 – 76)	66 (54.5 – 71)	0.01
	Median (IQR) of albumin (g/L)	25 (21 – 29)	22 (18 – 25)	0.02

P<0.05 statistically significant: results in bold font

**Serum electrolytes and renal biochemical parameters**

The serum concentrations of sodium and chloride were significantly higher in the deceased, whereas as potassium was equal, compared with the recovered group (Table 4). Additionally, both serum creatinine and blood urea nitrogen (BUN) were also substantially higher in the deceased group relative to the recovered group (Table 4).

**Table 4** The mean ( $\pm$ SD) and median (IQR) of serum electrolytes and renal function parameters at admission according to demise in the study participants (n = 315).

	Parameter	COVID-19 positive cases (n = 315; 100%)		P value
		Recovered (n = 284; 90.2%)	Deceased (n = 31; 9.8%)	
Electrolytes	Mean $\pm$ SD of sodium (mmol/L)	137.4 $\pm$ 6.8	140.6 $\pm$ 4.8	0.009
	Mean $\pm$ SD of potassium (mmol/L)	3.86 $\pm$ 0.6	3.97 $\pm$ 0.8	0.4
	Mean $\pm$ SD of chloride (mmol/L)	102.7 $\pm$ 7	105.8 $\pm$ 5.9	0.02
Renal functions	Median (IQR) of BUN (mmol/L)	5.6 (3.7 – 7.7)	8.5 (6.1 – 12.4)	< 0.0001
	Median (IQR) of creatinine ( $\mu$ mol/L)	75.4 (59.4 – 91.3)	84.6 (62.3 – 102.2)	0.03

P<0.05 statistically significant: results in bold font

**Blood gases**

The deceased group had significantly lower levels of arterial oxygen saturation (O<sub>2</sub>sat) and oxygen pressure (pO<sub>2</sub>) that concurred with increased carbon dioxide pressure (pCO<sub>2</sub>) and blood pH (Table 5). However, the levels of blood HCO<sub>3</sub> were unaffected.

**Risk factors associated with death from COVID-19 patients**

The multivariate analysis revealed that patients admitted to ICU had a substantially greater risk of dying from COVID-19 infection (46-fold) compared with ward admission (Table 6). In contrast, higher O<sub>2</sub>sat was associated with significantly lower odds of death (0.962). All the remaining demographic and biochemical parameters did not correlate with death from COVID-19 (Table 5).

**Table 5** The mean ( $\pm$ SD) and median (IQR) of blood gases at admission according to demise in the study participants (n = 315).

Parameter	COVID-19 positive cases (n = 315; 100%)		P value
	Alive (n = 284; 90.2%)	Deceased (n = 31; 9.8%)	
Median (IQR) of sO <sub>2</sub> (%)	90.2 (78.4 – 97.2)	64 (43.9 – 82)	< 0.0001
Median (IQR) of pO <sub>2</sub> (KPa)	8 (5.9 – 10.3)	6.2 (4.8 – 8.3)	0.005
Median (IQR) of pCO <sub>2</sub> (KPa)	5.3 (4.3 – 6.5)	3.2 (2.8 – 4.5)	< 0.0001
Mean $\pm$ SD of HCO <sub>3</sub> (mEq/L)	22.7 $\pm$ 4.1	23.4 $\pm$ 5.6	0.3
Mean $\pm$ SD of pH	7.36 $\pm$ 0.09	7.4 $\pm$ 0.06	0.02

P<0.05 statistically significant: results in bold font

**Table 6** Predictors of death from COVID-19 infection by binary logistic regression analysis presenting odds ratios and confidence intervals, in the total study participants (n = 315).

Predictors	Death from COVID-19 infection	
	Odds ratio (95%CI)	P Value
Admission Ward	Ref.	0.002
ICU	46.14 (4.02 - 528.6)	
Age (Year)	1.018 (0.975 - 1.062)	NS
RBCs count ( $10^6/\mu\text{L}$ )	0.42 (0.00016 - 102.94)	NS
Hb (g/dL)	1.184 (0.298 - 4.709)	NS
Haematocrit value (%)	1.243 (0.427 - 3.622)	NS
MCH (pg)	1.018 (0.797 - 1.300)	NS
MCV (fL)	0.806 (0.517 - 1.256)	NS
PLT count ( $10^3/\mu\text{L}$ )	0.996 (0.991 - 1.002)	NS
Neutrophil count ( $10^3/\mu\text{L}$ )	1.246 (0.751 - 2.068)	NS
Lymphocyte count ( $10^3/\mu\text{L}$ )	1.228 (0.743 - 2.032)	NS
Monocyte count ( $10^3/\mu\text{L}$ )	1.284 (0.744 - 2.225)	NS
Eosinophil count ( $10^3/\mu\text{L}$ )	0.849 (0.300 - 2.402)	NS
Total bilirubin (mg/dL)	1.067 (0.929 - 1.227)	NS
Direct bilirubin (mg/dL)	0.918 (0.712 - 1.183)	NS
ALP (U/L)	1.006 (0.996 - 1.015)	NS
Total protein (g/L)	0.996 (0.712 - 1.183)	NS
Albumin (g/L)	1.039 (0.944 - 1.143)	NS
Sodium (mmol/L)	1.048 (0.869 - 1.265)	NS
Chloride (mmol/L)	1.005 (0.823 - 1.227)	NS
BUN (mmol/L)	1.142 (0.945 - 1.381)	NS
Creatinine ( $\mu\text{mol/L}$ )	0.988 (0.969 - 1.006)	NS
$s\text{O}_2$ (%)	0.997 (0.990 - 1.005)	NS
$p\text{O}_2$ (KPa)	0.962 (0.931 - 0.994)	0.02
$p\text{CO}_2$ (KPa)	0.990 (0.975 - 1.005)	NS
pH	4.154 (0.003 - 5583.733)	NS

NS = Non-significant

P&lt;0.05 statistically significant: results in bold font

#### 4. Discussion

Herein, we retrospectively reviewed the rate of death in 315 patients with PCR-confirmed COVID-19 infection admitted to a single centre in Makkah city during the early wave of the pandemic. Additionally, we also measured the potential demographic factors alongside the laboratory parameters at the time of presentation that were associated with the risk of dying from this highly transmissible infection.

Following the WHO official declaration in March 2020 that COVID-19 is a pandemic, there were 43,766,712 confirmed positive cases and 1,163,459 deaths (2.7%) worldwide by the end of October [25]. In Kingdom of Saudi Arabia (KSA), the infection rate was maximal during June 2020, followed by a gradual decrease and was lowest in October 2020 resulting in 346,047 cumulative cases and 5,348 (1.6%) total deaths [25, 26]. Moreover, a large retrospective study, which included 240,474 cases across the different regions of the KSA, has also reported that COVID-19 infection was more common in males, most of the patients were non-Saudi, and the highest case fatality rates (CFR) were in Jeddah (2.6%) and Makkah (2.16%) relative to the other cities, and death was more common in elders [27]. Other national reports have similarly shown that men and non-Saudis had higher rates of infection, ICU admission occurred in 12-25% of the patients, and elders had a higher risk of dying from the infection [28-30]. Furthermore, the risk of dying from COVID-19 infection increased significantly in patients admitted to ICU [28-32].

Our results revealed that males (75.9%) and non-Saudi residents of KSA (55.9%) were predominant. Additionally, mortality rates were markedly higher in the patients admitted to ICU and deceased patients had significantly higher age compared with those who recovered from the infection. Moreover, the risk of death from COVID-19 increased 46-fold with ICU admission. The present findings support the epidemiological results reported by many of the above-mentioned national reports [27-30].

However, the frequency of cases was equal between the three months (June, August, and October of 2020) study period. Additionally, ICU admission was more prevalent in this study (35.6%) compared with international [31, 32] and national studies [28-30] reported during the same period. The rate of death from COVID-19 infection in the present study was also relatively higher (9.8%) than the WHO and Saudi CDC reports [25, 26].

A possible explanation for the discrepancies between our findings and earlier data could be related to the small sample size included in the current report. Moreover, we only included patients from a single private centre that acted as an auxiliary support facility for the Ministry of Health (MOH) regional hospitals to increase hospitalisation capacity during the pandemic [33-35]. We were also unable to include many of the admitted patients during the study period since they were transferred to different hospitals during their illness and prior to reaching a final clinical outcome (recovery vs. death). Hence, future studies should either obtain the data from the Saudi MOH registry and/or focus on major governmental hospitals to achieve a better follow-up of cases. Additionally, a multicentre approach could be more precise in revealing the prevalence of death from COVID-19, since ours and several earlier single-centre reports demonstrated higher mortality rates than those reported by multicentre studies [28-30].

Prior studies from KSA [29, 36-38] and other countries [39-41] revealed higher rates of anaemia in patients with COVID-19. Furthermore, the abnormal RBCs indices were more pronounced in patients admitted to ICU and/or those who died from COVID-19 infection. The researchers have also reported significant decreases in platelets (PLTs) and lymphocyte counts during infection and the numbers correlated negatively with the severity of COVID-19 [29, 36-41]. While no association between the haematological indices and the risk of dying from COVID-19 infection were reported [29, 38], others showed that anaemia, thrombocytopenia and lymphocytopenia increased the odds of death in their patients [30, 36, 37, 42, 43]. Moreover, numerous reports also disclosed significantly abnormal liver and renal function parameters [29, 36-38, 40, 41]. However, results related to an increased risk of death with the parameters of interest are inconsistent between the studies.

Herein, there were aberrant haematological indices depicted by low RBCs counts, haematocrit value, Hb concentrations, MCV and MCH alongside low PLTs counts and lymphocytopenia in the deceased group. Our findings also showed marked elevations in ALP enzyme, bilirubin, BUN, and creatinine together with decreases in total protein and albumin the deceased group. Nevertheless, none of the haematological parameters increased the odds of death by multivariate analysis, which could possibly be due to small numbers of patients included in our report. Hence, future studies with larger numbers of patients are still needed to accurately calculate the associations between the haematological and biochemical parameters with the severity of COVID-19 infection.

COVID-19 mainly affects the respiratory system, and hyperventilation, hypoxaemia and hypercapnia are common findings and associate directly with the severity of the infection and clinical outcomes [28, 30, 38, 39]. In agreement, the present data demonstrated significant decreases in  $\text{O}_2$  pressure and saturation that concurred with declines in  $p\text{CO}_2$  and alkalosis in the deceased group. Additionally, the logistical regression analysis revealed a significantly increased risk of death with low  $\text{O}_2$  pressure. Our findings suggest the development of type-2 respiratory failure, which is a serious common manifestation of COVID-19 infection, is a major independent risk factor associated with increased infection severity and fatality [44-47].

#### Limitations

This report has several drawbacks, including the small numbers of cases in addition to missing many variables related to the socioeconomic status, treatment protocols and status of co-morbidities (e.g., cardiovascular and renal diseases, etc.). Furthermore, the patients' data were obtained from a single research site and a multicentre strategy could have reflected the factual death rates and the independent risk factors associated with the severity and fatality of COVID-19 more precisely. Moreover, collecting the clinical, radiological, and biochemical findings during the full duration of hospitalisation could have more accurately elucidated the course of COVID-19 infection in Saudi Arabia.

#### Future work

We, therefore, suggest to conduct forthcoming multicentre studies to precisely reveal the case fatality rate and complications of COVID-19 infection in KSA, especially after the observed surge in the numbers of cases during the recent weeks [26]. Additionally, data

related to mechanical ventilation, chronic diseases, and socioeconomic status should be detailed in future studies. The roles of the different types of vaccines in preventing viral transmission as well as limiting the severity of COVID-19 is needed for establishing highly effective infection control and public health policies against this highly transmissible viral infection.

## 5. Conclusions

Males and non-Saudi residents of KSA appeared to be more susceptible for acquiring infection during the first wave of COVID-19 disease. Although liver and renal biochemical parameters, haematological indices, and respiratory functions were significantly altered with COVID-19 infection and more pronounced in the deceased patients, only ICU admission and low O<sub>2</sub> pressure showed higher risks of death from the infection. Nevertheless, additional multicentre studies with larger numbers of patients and more stringent strategies to follow-up the cases are needed to precisely identify the risk factors that could augment the severity and fatality of COVID-19 infection.

## References

- [1] Dong, E., H. Du, and L. Gardner, *An interactive web-based dashboard to track COVID-19 in real time*. Lancet Infect Dis, 2020. **20**(5): p. 533-534.
- [2] Al-Shammari, A.A., et al., *The Impact of Strict Public Health Measures on COVID-19 Transmission in Developing Countries: The Case of Kuwait*. Front Public Health, 2021. **9**: p. 757419.
- [3] Lai, C.C., et al., *Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths*. J Microbiol Immunol Infect, 2020. **53**(3): p. 404-412.
- [4] Wan, S., et al., *Clinical features and treatment of COVID-19 patients in northeast Chongqing*. J Med Virol, 2020. **92**(7): p. 797-806.
- [5] Wang, D., et al., *Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China*. Jama, 2020. **323**(11): p. 1061-1069.
- [6] Alshukry, A., et al., *Clinical characteristics of coronavirus disease 2019 (COVID-19) patients in Kuwait*. PLoS One, 2020. **15**(11): p. e0242768.
- [7] Lu, X., et al., *SARS-CoV-2 Infection in Children*. N Engl J Med, 2020. **382**(17): p. 1663-1665.
- [8] Al-Mulla, F., et al., *ACE2 and FURIN variants are potential predictors of SARS-CoV-2 outcome: A time to implement precision medicine against COVID-19*. Heliyon, 2021. **7**(2): p. e06133.
- [9] Ali, H., et al., *Outcomes of COVID-19: Disparities by ethnicity*. Infect Genet Evol, 2021. **87**: p. 104639.
- [10] Yang, J., et al., *Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis*. Int J Infect Dis, 2020. **94**: p. 91-95.
- [11] Zheng, Z., et al., *Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis*. J Infect, 2020. **81**(2): p. e16-e25.
- [12] Alahmad, B., et al., *Fasting Blood Glucose and COVID-19 Severity: Nonlinearity Matters*. Diabetes Care, 2020. **43**(12): p. 3113-3116.
- [13] Guan, W.J., et al., *Clinical Characteristics of Coronavirus Disease 2019 in China*. N Engl J Med, 2020. **382**(18): p. 1708-1720.
- [14] MOH, *The Kingdom of Saudi Arabia's Experience in Health Preparedness and Response to COVID-19 Pandemic.*, M.o. Health, Editor. 2020: Kingdom of Saudi Arabia.
- [15] *Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)*. Chin Med J (Engl), 2020. **133**(9): p. 1087-1095.
- [16] Du, R.H., et al., *Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2*. Eur Respir J, 2020. **56**(3).
- [17] Skevaki, C., et al., *Laboratory characteristics of patients infected with the novel SARS-CoV-2 virus*. J Infect, 2020. **81**(2): p. 205-212.
- [18] Fan, B.E., et al., *Hematologic parameters in patients with COVID-19 infection*. Am J Hematol, 2020. **95**(6): p. E131-e134.
- [19] Ponti, G., et al., *Biomarkers associated with COVID-19 disease progression*. Crit Rev Clin Lab Sci, 2020. **57**(6): p. 389-399.
- [20] Velavan, T.P. and C.G. Meyer, *Mild versus severe COVID-19: Laboratory markers*. Int J Infect Dis, 2020. **95**: p. 304-307.
- [21] Chen, G., et al., *Clinical and immunological features of severe and moderate coronavirus disease 2019*. J Clin Invest, 2020. **130**(5): p. 2620-2629.
- [22] Wu, F., et al., *A new coronavirus associated with human respiratory disease in China*. Nature, 2020. **579**(7798): p. 265-269.
- [23] Zhang, J.J., et al., *Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China*. Allergy, 2020. **75**(7): p. 1730-1741.
- [24] Du, R.H., et al., *Hospitalization and Critical Care of 109 Decedents with COVID-19 Pneumonia in Wuhan, China*. Ann Am Thorac Soc, 2020. **17**(7): p. 839-846.
- [25] WHO. *Situation Report No. 166 - Kingdom of Saudi Arabia. Coronavirus Disease 2019 (COVID-19) Situation Report 2020* [cited 2021 13/05]; Available from: [http://www.emro.who.int/images/stories/saudi\\_arabia/saudi-arabia-covid-sit-rep-166-2020-10-29.pdf?ua=1](http://www.emro.who.int/images/stories/saudi_arabia/saudi-arabia-covid-sit-rep-166-2020-10-29.pdf?ua=1).
- [26] SCDC. *(COVID-19) Disease Interactive Dashboard*. 2020 [cited 2021 13/05]; Available from: <https://covid19.cdc.gov.sa/daily-updates/>.
- [27] Awwad, F.A., M.A. Mohamoud, and M.R. Abonazel, *Estimating COVID-19 cases in Makkah region of Saudi Arabia: Space-time ARIMA modeling*. PLoS One, 2021. **16**(4): p. e0250149.
- [28] Khan, A.A., et al., *Survival and Estimation of Direct Medical Costs of Hospitalized COVID-19 Patients in the Kingdom of Saudi Arabia*. Int J Environ Res Public Health, 2020. **17**(20).
- [29] Ibrahim, M.E., et al., *Epidemiological, clinical, and laboratory findings for patients of different age groups with confirmed coronavirus disease 2019 (COVID-19) in a hospital in Saudi Arabia*. PLoS One, 2021. **16**(4): p. e0250955.
- [30] Alwafi, H., et al., *Predictors of Length of Hospital Stay, Mortality, and Outcomes Among Hospitalised COVID-19 Patients in Saudi Arabia: A Cross-Sectional Study*. J Multidiscip Healthc, 2021. **14**: p. 839-852.
- [31] Zhou, F., et al., *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study*. Lancet, 2020. **395**(10229): p. 1054-1062.
- [32] Salje, H., et al., *Estimating the burden of SARS-CoV-2 in France*. Science, 2020. **369**(6500): p. 208-211.
- [33] MOH. *The Kingdom of Saudi Arabia's Experience in Health Preparedness and Response to COVID-19 Pandemic*. 2020 [cited 2021 13/05]; Available from: <https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Documents/COVID-19-NATIONAL.pdf>.
- [34] Alqahtani, F., et al., *Bed Surge Capacity in Saudi Hospitals during COVID-19 Pandemic*. Disaster Med Public Health Prep, 2021: p. 1-25.
- [35] Aziz, S., et al., *Managing ICU surge during the COVID-19 crisis: rapid guidelines*. Intensive Care Med, 2020. **46**(7): p. 1303-1325.
- [36] Algassim, A.A., et al., *Prognostic significance of hemoglobin level and autoimmune hemolytic anemia in SARS-CoV-2 infection*. Ann Hematol, 2021. **100**(1): p. 37-43.
- [37] Ghaith, M.M., et al., *Potential Predictors of Poor Prognosis among Severe COVID-19 Patients: A Single-Center Study*. Can J Infect Dis Med Microbiol, 2021. **2021**: p. 6656092.
- [38] Almalki, Z.S., et al., *Clinical Characteristics and Outcomes Among COVID-19 Hospitalized Patients with Chronic Conditions: A Retrospective Single-Center Study*. J Multidiscip Healthc, 2020. **13**: p. 1089-1097.
- [39] Briguglio, M., et al., *Clinical Characteristics of Severe COVID-19 Patients Admitted to an Intensive Care Unit in Lombardy During the Italian Pandemic*. Front Med (Lausanne), 2021. **8**: p. 582896.
- [40] Lu, W., et al., *Survival analysis and risk factors in COVID-19 patients*. Disaster Med Public Health Prep, 2021: p. 1-15.

- [41] Ghazanfari, T., et al., *Interpretation of Hematological, Biochemical, and Immunological Findings of COVID-19 Disease: Biomarkers Associated with Severity and Mortality*. Iran J Allergy Asthma Immunol, 2021. **20**(1): p. 46-66.
- [42] Faghih Dinevari, M., et al., *Anemia predicts poor outcomes of COVID-19 in hospitalized patients: a prospective study in Iran*. BMC Infect Dis, 2021. **21**(1): p. 170.
- [43] Lanini, S., et al., *COVID-19 disease-Temporal analyses of complete blood count parameters over course of illness, and relationship to patient demographics and management outcomes in survivors and non-survivors: A longitudinal descriptive cohort study*. PLoS One, 2020. **15**(12): p. e0244129.
- [44] Leone, P.M., et al., *Ventilatory Support in Patients with COVID-19*. Adv Exp Med Biol, 2021. **1318**: p. 469-483.
- [45] Kofod, L.M., et al., *COVID-19 and acute respiratory failure treated with CPAP*. Eur Clin Respir J, 2021. **8**(1): p. 1910191.
- [46] Mejía, F., et al., *Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru*. PLoS One, 2020. **15**(12): p. e0244171.
- [47] Zhu, J., et al., *Clinical characteristics of 3062 COVID-19 patients: A meta-analysis*. J Med Virol, 2020. **92**(10): p. 1902-1914.