Clinical Characteristics, Outcomes and Prognostic Factors for Critical Illness in Hospitalized COVID-19 Patients in Saudi Arabia: A Retrospective Cohort Study

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Background: A good understanding of the possible risk factors for coronavirus disease 19 (COVID-19) severity could help clinicians in identifying patients who need prioritized treatment to prevent disease progression and adverse outcome. In the present study, we aimed to correlate clinical and laboratory characteristics of hospitalized COVID-19 patients to disease outcome in Saudi Arabia.

Materials and Methods: The present study included 199 COVID-19 patients admitted to King Fahd Specialist Hospital, Buraydah, Qassim, Saudi Arabia, from April to December 2020. Patients were followed-up until discharge either for recovery or death. Demographic data, clinical data and laboratory results were retrieved from electronic patient records.

Results: Critical COVID-19 cases showed higher mean of age and higher prevalence of co-morbid conditions. Fifty-five patients died during the observation period. Risk factors for in hospital death for COVID 19 patients were leukocytosis (OR 1.89, 95% CI 1.008–3.548, p = 0.081), lymphocytopenia (OR 2.152, 95% CI 1.079–4.295, p = 0.020), neutrophilia (OR 1.839, 95% CI 0.951–3.55, p = 0.047), thrombocytopenia (OR 2.152, 95% CI 0.852–5.430, p = 0.085), liver injury (OR 2.689, 95% CI 1.373–4.944, p = 0.003), acute kidney injury (OR 1.248, 95% CI 0.631–2.467 p = 0.319), pancreatic injury (OR 1.973, 95% CI 0.939–4.144, p = 0.056) and high D dimer (OR 2.635, 95% CI 0.747–9.287, p = 0.047), thrombocytopenia (OR 2.152, 95% CI 0.852–5.430, p = 0.085), liver injury (OR 2.689, 95% CI 1.373–4.944, p = 0.003), acute kidney injury (OR 1.248, 95% CI 0.631–2.467 p = 0.319), pancreatic injury (OR 1.973, 95% CI 0.939–4.144, p = 0.056) and high D dimer (OR 2.635, 95% CI 0.747–9.287, p = 0.091).

Conclusion: Clinical and laboratory data of COVID-19 patients may help understanding the pathogenesis of the disease and subsequently improve of the outcome of patients by determination of the associated risk factors and recognition of high risk group who are more liable for complications and in hospital death. The present study put an eye on some parameters (laboratory and clinical) that should be alarming signs that the patient is at high risk bad prognosis.

Keywords: clinical, outcomes, prognosis, COVID-19, Saudi Arabia

Introduction
Coronavirus Disease 2019 (COVID-19) is a newly described viral disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).1 First few cases of COVID-19 were reported, in December 2019, in City of Wuhan, China. The World Health Organization (WHO) announced COVID-19 a pandemic in 11th March 2020.2 The pandemic then became a global concern due to high transmissibility of the virus and its fatality rate.1
COVID-19 patients may remain asymptomatic or present with mild, moderate, or severe symptoms, primarily respiratory symptoms. Fever and cough were reported as the predominant symptoms, and over 90% of patients present with more than one symptom. However, only a small number of COVID-19 patients progress to severe acute respiratory distress syndrome and those patients are at higher risk of acute hypoxemic respiratory failure and death. The mortality rate ranges from 1% to 10% depending on patients’ clinical presentations and availability of medical resources in different countries. Although any individual can present with severe COVID-19, it is more common in elderly individuals or in patients with underlying chronic diseases. Chronic diseases that associated with severe cases of COVID-19 and increased mortality include cardiovascular diseases, diabetes mellitus, hypertension, chronic lung diseases, cancer, chronic kidney diseases and obesity.

Patients with severe COVID-19 may experience respiratory failure, shock, disseminated coagulopathy, and multiple-organ failure requiring admission to the intensive care unit (ICU). A good understanding of the possible risk factors for COVID-19 severity could help clinicians in identifying patients who need prioritized treatment to prevent disease progression and adverse outcome. Risk factors may include demographic factors, such as age. It was found that patients with age ≥50 years confirmed with SARS-CoV-2 infection were associated with 3.45- and 15.4-folds significantly increased risk of SARS-CoV-2 test positivity and mortality as compared to patients with age <50 years. Moreover, sex and ethnicity, diet and lifestyle habits, underlying diseases, complications and laboratory findings were reported to be a significant predicting factors for the severity and prognosis of COVID-19. Many studies have reported predictive models using various risk factors to identify high-risk patients and silent mutations that may develop severe COVID-19.

Understanding pathological laboratory findings can also be used as guide strategies to find a new treatment or vaccine. Several studies have correlated laboratory findings in COVID-19 patients to disease severity. These laboratory findings included elevated Total Leukocyte Count (TLC), Lactate Dehydrogenase (LDH), Alanine Transaminase (ALT), Aspartate Transaminase (AST), total bilirubin, prothrombin time (PT), D-dimer test, serum ferritin, C-reactive protein, cardiac troponin and procalcitonin (PCT), as well as reduced lymphocytes and serum albumin.

Although, several studies had been conducted in Saudi Arabia illustrating the clinical characteristics of Saudi COVID-19 patients in different localities, no studies were conducted in Qassim province. We believe that identifying factors that associate with COVID-19 disease severity could help in early identification of patients at high risk of developing severe COVID-19 and could guide better disease prevention measures to reduce mortality. In the present study, we aimed to correlate demographic, clinical and laboratory characteristics of hospitalized COVID-19 patients with disease severity, prognosis and outcomes in Buraydah, Qassim province, Saudi Arabia.

**Materials and Methods**

**Patients Included in the Study**

The present study is an observational retrospective study. It was carried out at King Fahd Specialist Hospital, Buraydah, Qassim, Kingdom of Saudi Arabia. All patients with COVID-19 who were admitted to the hospital from April to December 2020 and presented with symptoms suggestive of COVID-19 infection such as fever, cough, sore throat, headache, fatigue, muscle pain, and dyspnea were included in the study. COVID-19 was confirmed by SARS-CoV-2 Real Time reverse transcription-polymerase chain reaction (Real-Time RT-PCR) (LabGunTM COVID-19 RT-PCR Kit, LabGenomics Co., Ltd.) assay performed on nasopharyngeal swabs. Patients were observed until recovery or death. Demographic characteristics including age, gender, comorbidities (diabetes mellitus, hypertension, chronic pulmonary diseases, malignancy, cardiovascular disease and chronic liver disease) and laboratory investigations including white blood cells, platelets, and red blood cells (RBCs) counts; hemoglobin; serum levels of urea, creatinine, lactate dehydrogenase, albumin, total protein, amylase, D-dimer and C-reactive protein; and prothrombin time, were retrieved from electronic patient records.

Patients in the present study were classified according to the current Chinese guidelines into three groups: moderate, severe, and critically ill patients. Patients with fever, cough, and pneumonia were considered moderate cases. Patients who had at least one of the following criteria: (i) respiratory rate >30/min, (ii) oxygen saturation ≤93%, (iii) PaO2/FiO2 ratio ≤300 mmHg, or (iv) signs of progression of pulmonary infiltration >50% in 24–48h were considered severe COVID-19 patients. However, critically ill COVID-19 patients were patients who showed one of the following: (i)
respiratory failure demand mechanical ventilation, (ii) shock, or (iii) occurrence of multi-organ failure requiring management in intensive care units (ICUs).45

Definitions
Leukocytosis was defined as a white blood cells count of more than 10,000 per cubic millimeter, while leukopenia is a condition of low white blood cells count (less than 4000 per cubic millimeter).12,20,37,46 On the other hand, lymphocytopenia was defined as a condition with low count of lymphocytes (less or more than 1500 per cubic millimeter).47 Thrombocytopenia was defined as a platelet count of less than 150,000 per cubic millimeter.47 Finally, neutrophilia was defined as a neutrophil count of more than 6000 per cubic millimeter.6

Statistical Analysis
Data analysis was carried out using the IBM SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean ± standard deviation. Categorical data were expressed as numbers and percentages. Comparison of two independent groups was performed using the independent sample t test or the chi-squared test, for continuous and categorical variables, respectively. Binary logistic regression analysis to measure risk estimation of mortality from COVID-19 was used. Ninety-five percent confidence intervals (95% CI) of odds ratio (OR) was used as common measure to assess relative risk. Significance was set at P < 0.01. For survival analysis, univariant analysis was done using Kaplan–Meier analysis. Correlation studies were performed using Spearman’s test.

Results
Baseline Characteristics
The current study included 199 patients who tested positive for COVID-19 and were admitted to the hospital between April and December 2020. Age of participants ranged from 18 to 101 years old (Mean ± SD was 65.02±17.11). Male patients made up the majority of the participants (59.3%). Diabetes and hypertension were the two most frequent co-morbidities. Fever was the most common presenting symptom. The majority (90.6%) of critically ill patients admitted to the ICU required mechanical ventilation. Patients were followed up on for 7 to 66 days after they were discharged (either for recovery or death).

Critical patients showed statistically significant higher mean of age, higher prevalence of co-morbid conditions (particularly diabetes mellitus and cardiovascular disorders), and higher incidence of dyspnea when compared to non-critical cases. Critical cases had higher levels of D dimer (P < 0.01), ALT (P < 0.01), serum amylase (P < 0.01), and lactate dehydrogenase (P < 0.01). Serum albumin levels, on the other hand, were found to be significantly lower (statistically significant, P < 0.01) (Table 1).

Moreover, critical patients showed a higher mean neutrophil count, a lower mean lymphocyte count, a lower mean platelet count, and a lower haemoglobin percentage (Table 1). Analysis of haematological parameters including leukocytosis, lymphopenia, neutrophilia, thrombocytopenia and high level of D dimer showed high prevalence of those conditions among male COID-19 patients with no statistical significance, Tables 2 and 3.

ICU Admission
Sixty patients representing 30.2% were admitted to the ICU during the observation period. The majority of them had diabetes (20%), whereas chronic cardiac diseases and cerebrovascular diseases had the same prevalence among hospitalized COVID-19 patients (16.7% with statistical significance). Patients admitted to the ICU had higher mean of age. Hematological abnormalities were reported in higher rates in ICU patients when compared to non ICU patients as following: leukocytosis (51.7% vs 48.2%), Neutrophilia (65% vs 56.1%), lymphocytopenia (68.3% vs 59.7%) and thrombocytopenia (13.3% vs 6.5). In addition, ICU patients had higher mean levels of D dimer (statistically significant, P value <0. 005), AST (statistically significant, P value <0. 002), ALT (statistically significant, P value <0. 001), serum amylase (statistically significant, P value <0. 001), lactate dehydrogenase (statistically significant, P value <0. 006), ALP, CRP, and serum ferritin, Table 4 and Figure 1.
| Variable                        | Critical COVID-19 (n=53) | Non-Critical COVID-19 (n=146) | P value |
|--------------------------------|--------------------------|-------------------------------|---------|
| Age (years)                    | 73.09 (47–93)            | 62.1 (18–101)                 | 0.001*  |
| Male patients (n/%)            | 26 (47.2)                | 92 (61.4)                     | 0.126   |
| **Comorbid diseases**          |                          |                               | 0.009   |
| Diabetes (N/%)                 | 11 (20)                  | 18 (12.3)                     |         |
| Hypertension (N/%)             | 7 (13.2)                 | 10 (6.8)                      |         |
| Cardiac diseases (N/%)         | 9 (16.9)                 | 21 (14.4)                     |         |
| Cerebrovascular disorder (N/%) | 8 (15.1)                 | 10 (6.8)                      |         |
| Chronic respiratory disease (N/%) | 2 (3.8)             | 7 (4.8)                       |         |
| Chronic kidney disease (N/%)   | 2 (3.8)                  | 16 (10.9)                     |         |
| Malignancy (N/%)               | 2 (3.8)                  | 5 (3.4)                       |         |
| **Clinical presentation**      |                          |                               | 0.098   |
| Fever (N/%)                    | 16 (30.2)                | 42 (28.7)                     |         |
| Cough (N/%)                    | 12 (22.6)                | 38 (26.03)                    |         |
| Sore throat (N/%)              | 2 (3.8)                  | 7 (4.8)                       |         |
| Shortness of breath (N/%)      | 14 (26.4)                | 71 (48.6)                     |         |
| **ICU admission**              |                          |                               | 0.000*  |
| Yes (N/%)                      | 5 (9.4)                  | 134 (91.8)                    |         |
| NO (N/%)                       | 48 (90.6)                | 12 (8.2)                      |         |
| **Laboratory data**            |                          |                               |         |
| WBCs (4–10 10^3/uL)            | 11.06 (2.7–27.5)         | 10.4 (2.3–29.4)               | 0.481   |
| Lymphocytes (1–3 10^3/uL)      | 1.34 (0.3–6.8)           | 1.64 (0.2–12.2)               | 0.163   |
| Neutrophils (1.8–7.7 10^3/uL) | 8.9 (1.8–23.4)           | 7.7 (1–26.5)                  | 0.185   |
| Platelets (150–410 10^3/uL)    | 269.5 (71–788)           | 299.8 (53–1047)               | 0.207   |
| Hemoglobin (11–16 g/dL)        | 11.9 (3.4–16.3)          | 12.3 (6.9–17.2)               | 0.336   |
| RBCs (4–6 10^6/uL)             | 4.25 (2.0–5.5)           | 4.4 (3–6)                     | 0.242   |
| PT                             | 14.7 (10.7–25.8)         | 14 (10.1–45.1)                | 0.209   |
| D dimer (0–0.5 mg/L)           | 5.7 (0.5–35)             | 2.7 (0.2–35)                  | 0.006*  |
| Total protein (64–86 G/L)      | 68.6 (51.2–87.6)         | 67.5 (52–89)                  | 0.447   |
| Serum albumin (34–35G/L)       | 31.7 (18.6–44.8)         | 34.4 (16–50)                  | 0.001*  |
| AST (5–41 U/l)                 | 165.9 (12–4933)          | 37.4 (8–102)                  | 0.024*  |
| ALT (5–41 U/l)                 | 99.89 (6–1825)           | 31.2 (2–167)                  | 0.002*  |
| ALP (50–140 U/l)               | 117.2 (44–471)           | 103.1 (4–430)                 | 0.219   |

(Continued)
Table 1 (Continued).

| Variable                        | Critical COVID-19 (n=53) | Non-Critical COVID-19 (n=146) | P value |
|---------------------------------|--------------------------|--------------------------------|---------|
| Serum creatinine (44–116/umol/L)| 124.8 (38–1080)          | 109.6 (44–974)                 | 0.405   |
| Serum Urea (2.76–8.07 mmol/L)   | 9.4 (2.9–40)             | 8.8 (1.8–41.7)                 | 0.671   |
| Lactate dehydrogenase (100–190 U/L) | 360.93±182.5            | 349.1 (90–959)                 | 0.003*  |
| Sodium (135–145 mmol/L)         | 137.28 (123–149)         | 137.2 (132–152)                | 0.856   |
| Amylase (28–100 U/L)            | 117.9 (4–801)            | 66.18 (10–279)                 | 0.001*  |
| CRP (0–3.3 mg/L)                | 90.3 (3–173)             | 76.6 (4–199)                   | 0.690   |
| ESR                             | 46.43 (11–105)           | 68.7 (16–115)                  | 0.220   |

Hospital stay

| Number of days                   | 20.5 (7–73)              | 20.04±13.1                     | 0.973   |

Outcome

| Living (N/%)                     | 16 (30.2)                | 128 (87.4)                     | 0.001*  |
| Dead (N/%)                       | 37 (69.1)                | 18 (12.6)                      | 0.001*  |

Note: *Indicates statistical significance.

Table 2 Showing the Distribution of Leukocytosis, Lymphopenia and Neutrophilia in Relation to Gender of Covid 19 Patients in the Present Study

| Gender | Leukocytosis | Lymphopenia | Neutrophilia |
|--------|--------------|-------------|--------------|
|        | Yes | No  | Yes | No  | Yes | No  |
| Female | 31  | 49  | 50  | 30  | 46  | 34  |
| Male   | 48  | 71  | 74  | 45  | 71  | 48  |
| Total  | 79  | 120 | 124 | 75  | 117 | 82  |
| P value| 0.470 | 0.542 | 0.437 |

Table 3 Showing the Distribution of Thrombocytopenia and D Dimer Level in Relation to Gender of Covid 19 Patients in the Present Study

| Gender | Thrombocytopenia | D Dimer |
|--------|-----------------|---------|
|        | Yes | No  | High | Normal |
|        | No  | No  | No   | No     |
| Female | 6   | 74  | 72   | 8      |
| Male   | 15  | 104 | 105  | 14     |
| Total  | 21  | 178 | 177  | 22     |
| P value| 0.181 | 0.470 |
### Table 4 Showing the Demographic Clinical and Laboratory Data of ICU Patients versus Non ICU Cases

| Variable                          | Non ICU (n=139) | ICU (n=60) | P value |
|-----------------------------------|-----------------|------------|---------|
| **Clinical characteristics**      |                 |            |         |
| Age (years)                       | 62.07±18.27     | 71.83±15.2 | 0.001*  |
| Male patients (n/%)               | 89(64.02)       | 30(50)     | 0.064   |
| Diabetes (N/%)                    | 17(12.2)        | 12(20)     |         |
| Hypertension (N/%)                | 10(7.2)         | 7(11.7)    |         |
| Cardiac diseases (N/%)            | 20 (14.4)       | 10(16.7)   |         |
| Cerebrovascular disorder (N/%)    | 8(5.8)          | 10(16.7)   |         |
| Chronic respiratory disease (N/%) | 4(2.9)          | 3(5)       |         |
| Chronic kidney disease (N/%)      | 14 (10.1)       | 4 (6.6)    |         |
| Malignancy (N/%)                  | 5(3.6)          | 2(3.3)     |         |
| **Clinical presentation**         |                 |            |         |
| Fever (N/%)                       | 55(39.6)        | 28(46.7)   | 0.258   |
| Cough (N%)                        | 32(23)          | 7(11.7)    |         |
| Sore throat (N/%)                 | 7(5)            | 5(8.3)     |         |
| Shortness of breath (N/%)         | 45(32.4)        | 20(33.3)   |         |
| **Severity of COVID 19**          |                 |            |         |
| Moderate (N/%)                    | 12(8.6)         | 7(11.7)    | 0.000   |
| Severe (N%)                       | 122(87.8)       | 5(8.3)     |         |
| Critical (N%)                     | 5(3.6)          | 48(80)     |         |
| **Laboratory data**               |                 |            |         |
| CRP (0–3.3 mg/L)                  | 69.7± 24.3      | 90.3± 32.1 | 0.706   |
| Ferritin                          | 339.2± 190      | 522.6± 328 |         |
| D dimer (0–0.5 mg/L)              | 2.84±5.9364     | 5.16±8.4147| 0.005   |
| <0.5                              | 15              | 6          |         |
| >1                                | 124             | 54         |         |
| WBCs (4–10 10^3/uL)               | 10.56± 5.8      | 10.62±5.5  | 0.865   |
| <4                                | 4               | 5          |         |
| 4–10                              | 68              | 24         |         |
| >10                               | 67              | 31         |         |
| Lymphocytes (1–3 10^3/uL)         | 1.66±1.4        | 1.3±0.9868 | 0.246   |
| <1.500                            | 83              | 41         |         |
| >1.500                            | 56              | 19         |         |

(Continued)
Table 4 (Continued).

| Variable                        | Non ICU (n=139) | ICU (n=60) | P value |
|---------------------------------|-----------------|------------|---------|
| Neutrophils (1.8–7.7 10^3/uL)   | 7.86±5.3        | 8.39±5.1   | 0.729   |
| <6                              | 61              | 21         |         |
| >6                              | 78              | 39         |         |
| Platelets (150–410 10^3/uL)     | 302.4±159.2     | 266.9±121.6| 0.279   |
| <150                            | 13              | 8          |         |
| >150                            | 126             | 52         |         |
| Hemoglobin (11–16 g/dL)         | 12.3±2.4319     | 11.8±2.4   | 0.421   |
| <11                             | 43              | 19         |         |
| >11                             | 96              | 41         |         |
| PT                              | 14.1±4.1        | 14.5±3.1   | 0.971   |
| <12                             | 38              | 9          |         |
| >12                             | 101             | 51         |         |
| AST (5–41 U/l)                  | 37.2±26.57      | 150.4±673.813| 0.002* |
| <40                             | 89              | 28         |         |
| >40                             | 50              | 32         |         |
| ALT (5–41 U/l)                  | 31.3±26.1       | 91.9±293.8 | 0.001* |
| <40                             | 105             | 43         |         |
| >40                             | 34              | 17         |         |
| ALP (50–140 U/l)                | 101.4±62.6      | 119.6±87.005| 0.107  |
| <140                            | 113             | 47         |         |
| >140                            | 26              | 13         |         |
| Serum creatinine (44–116/umol/L)| 113.4±124.5     | 114.2±85.5 | 0.784   |
| <116                            | 106             | 44         |         |
| >116                            | 33              | 16         |         |
| Lactate dehydrogenase (100–190 U/L)| 352.6±160.5 | 538.9±887.633| 0.006* |
| <245                            | 38              | 7          |         |
| >245                            | 101             | 53         |         |
| Serum albumin (34–35G/L)        | 34.7±6.21       | 30.97±5.233| 0.193   |
| <35                             | 77              | 37         |         |
| >35                             | 62              | 23         |         |
| Total protein (64–86 G/L)       | 68.6±8.4        | 67.5±9.7   | 0.115   |
| <64                             | 37              | 25         |         |
| >64                             | 102             | 35         |         |

(Continued)
Mortality

Patients in the present study were followed up until discharge (either due to recovery or death). Fifty-five patients representing (27.6%) died during the observation period. Non survivors were on average older than survivors. They also had higher levels of D dimer, AST, ALT, ALP, serum amylase and lactate dehydrogenase.

We performed binary logistic regression analysis to measure risk estimation of mortality from COVID-19 for different laboratory parameters. Risk factors for death in the present study were admission to the ICU (OR 10.7, 95% CI 5.2–22.04, \( p = 0.001 \)), leukocytosis (OR 1.6445, 95% CI 0.325–1.114, \( p = 0.081 \)), lymphocytopenia (OR 2.152, 95% CI 1.079–4.295, \( p = 0.020 \)), Neutrophilia (OR 1.739, 95% CI 0.279–1.113, \( p = 0.067 \)), thrombocytopenia (OR 2.152, 95% CI 0.852–5.430, \( p = 0.085 \)), liver injury (diagnosed by high AST or high ALT levels) (OR 2.689, 95% CI 1.267–4.50, \( p = 0.005 \)), acute kidney injury (OR 1.248, 95% CI 0.574–1.584 \( p = 0.424 \)), pancreatic injury (OR 1.875, 95% CI 0.255–1.115, \( p = 0.071 \)), high D dimer (OR 4.048, 95% CI 0.56–1.099, \( p = 0.036 \)), Table 5.

We found a moderate correlation between leucocyte count and absolute neutrophil count (\( r = 0.988** \), \( P=0.001^* \)) (Table 6). In addition, fair correlation is observed between leucocyte count and absolute lymphocytes and RBCs and ferritin. Other correlations can be seen in Table 6.

A Kaplan–Meier analysis of the effect of different laboratory parameters on case fatality in hospitalized patients with COVID-19 showed that leukocytosis, lymphocytopenia, neutrophilia, thrombocytopenia, liver injury (diagnosed by high AST or high ALT levels), acute kidney injury, pancreatic injury and high D dimer, associated with an increased risk of death (P-value < 0.05 for all variables). Figure 2A and B.

Discussion

Within months of emergence from Wuhan, China, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of (COVID-19)-aggressively spreads across the globe, causing a devastating human illness. While the search for effective treatments continues and vaccines have commenced early implementation, it is necessary that recent data – from diverse populations on the disease epidemiology, clinical presentation, and population-specific characteristics influencing COVID-19 prevention, treatment, and vaccine strategies – to be available.
Figure 1  Violin plot showing demographic and laboratory parameters in strong association with ICU admission in COVID-19 patients.
Table 5 Comparison Between of Living and Dead COVID-19 Patients Regarding Clinical and Laboratory Data

| Variable                        | Survivors (n=144) | Non Survivors (n=55) | P value |
|---------------------------------|-------------------|----------------------|---------|
| **Clinical characteristics**    |                   |                      |         |
| Age (years)                     | 61.62±17.721      | 73.91±15.454         | 0.000*  |
| Male patients (n/%)             | 94(65.3)          | 25(45.5)             | 0.032*  |
| Diabetes (N/%)                  | 18(12.5)          | 16(29.1)             |         |
| Hypertension (N/%)              | 7(4.9)            | 7(12.7)              |         |
| Cardiac diseases (N/%)          | 21(14.6)          | 8(14.5)              |         |
| Cerebrovascular disorder (N/%)  | 9(6.3)            | 8(14.5)              |         |
| Chronic respiratory disease (N/%)| 4(2.8)           | 1(1.8)               |         |
| Chronic kidney disease (N/%)    | 15(10.4)          | 3(5.5)               |         |
| Malignancy (N/%)                | 3(2.1)            | 4(7.3)               |         |
| **Clinical presentation**       |                   |                      |         |
| Fever (N/%)                     | 41(28.5)          | 15(27.3)             | 0.140   |
| Cough (N/%)                     | 34(23.6)          | 15(27.3)             |         |
| Sore throat (N/%)               | 8(5.5)            | 4(7.3)               |         |
| Shortness of breath (N/%)       | 60(41.7)          | 31(56.4)             |         |
| **Severity of COVID 19**        |                   |                      |         |
| Moderate (N/%)                  | 17(11.8)          | 2(3.6)               | 0.000*  |
| Severe (N/%)                    | 111(77.1)         | 16(29.1)             |         |
| Critical (N/%)                  | 16(11.1)          | 37(67.3)             |         |
| **ICU admission**               |                   |                      |         |
| Yes (N%)                        | 19(13.2)          | 34(61.8)             | 0.000*  |
| NO (N%)                         | 125(86.8)         | 21(38.2)             |         |
| **Laboratory data**             |                   |                      |         |
| CRP (0–3.3 mg/L)                | 74.7±24.3         | 85.5±32.1            | 0.690   |
| Ferritin                        | 315±190           | 511.4±328            |         |
| D dimer (0–0.5 mg/L)            | 3.075±6.4090      | 4.773±7.7971         |         |
| <0.5                            | 19                | 2                    | 0.121   |
| >1                              | 125               | 53                   |         |
| WBCs (4–10 10^3/uL)             | 10.221±5.65       | 11.530±6.0308        |         |
| <4                              | 5                 | 4                    | 0.153   |
| 4–10                            | 73                | 19                   |         |
| >10                             | 66                | 32                   |         |

(Continued)
Table 5 (Continued).

| Variable                          | Survivors (n=144) | Non Survivors (n=55) | P value |
|-----------------------------------|-------------------|----------------------|---------|
| Lymphocytes (1–3 10^3/uL)         | 1.703±1.48        | 1.217±7124           |         |
| <1.500                            | 83                | 41                   | 0.021*  |
| ≥1.500                            | 61                | 14                   |         |
| Neutrophils (1.8–7.7 10^3/uL)     | 7.490±5.08        | 9.429±5.6213         |         |
| <6                                | 65                | 17                   | 0.020*  |
| ≥6                                | 79                | 38                   |         |
| Platelets (150–410 10^3/uL)       | 303.01±160.7      | 262.29±110.997       |         |
| <150                              | 12                | 9                    | 0.086   |
| ≥150                              | 132               | 46                   |         |
| Hemoglobin (11–16 g/dL)           | 12.304±2.44       | 11.887±2.3896        |         |
| <11                               | 43                | 19                   | 0.280   |
| ≥11                               | 101               | 36                   |         |
| RBCs (4–6 10^6/uL)                | 4.396±0.84        | 4.277±0.6500         | 0.343   |
| PT                                | 14.03±4.04        | 14.67±3.0055         |         |
| <12                               | 40                | 7                    | 0.290   |
| ≥12                               | 104               | 48                   |         |
| AST (5–41 U/l)                    | 38.10±26.57       | 159.47±673.813       |         |
| <40                               | 93                | 24                   | 0.032*  |
| ≥40                               | 51                | 31                   |         |
| ALT (5–41 U/l)                    | 31.37±27.05       | 97.15±293.8          |         |
| <40                               | 109               | 39                   | 0.008*  |
| ≥40                               | 35                | 16                   |         |
| ALP (50–140 U/l)                  | 98.75±58.8        | 128.18±94.005        |         |
| <140                              | 119               | 41                   | 0.009*  |
| ≥140                              | 25                | 14                   |         |
| Serum creatinine (44–116 umol/L)  | 109.78±95.2       | 123.84±153.140       |         |
| <111                              | 108               | 38                   | 0.438   |
| ≥111                              | 36                | 17                   |         |
| Lactate dehydrogenase (100–190 U/L)| 360.93±182.5    | 533.89±917.6         |         |
| <245                              | 111               | 39                   | 0.032*  |
| ≥245                              | 33                | 16                   |         |

(Continued)
The present retrospective study reported the clinical characteristics of hospitalized COVID-19 patients in Buraidah, Saudi Arabia. The mean age was higher among critical than mild cases. Similar age distribution among COVID-19 patients has been reported by previous studies.\textsuperscript{49,50}

High prevalence of COVID-19 infections among elderly patients may be attributed to reduced immunity associating aging as a result of by biological changes in the immune system leading to increased susceptibility to respiratory infections and a high prevalence of associated comorbidities (mainly diabetes and hypertension and respiratory viral infection particularly influenza virus).\textsuperscript{52–57} Regarding gender, infection was more prevalent among males, which is in agreement with previous studies on COVID 19 patients.\textsuperscript{57,58} Male sex has been previously reported as a risk factor for

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
Variable & Survivors (n=144) & Non Survivors (n=55) & P value \\
\hline
Serum albumin (34–35G/L) & 34.75±6.21 & 30.97±5.233 & \\
<35 & 37 & 8 & 0. 000* \\
>35 & 137 & 47 & \\
Total protein (64–86 G/L) & 69.23±9.15 & 65.95±7.656 & \\
<64 & 39 & 23 & 0. 020* \\
>64 & 105 & 32 & \\
Sodium (135–145 mmol/L) & 138.01±6.15 & 135.87±7.157 & \\
<135 & 38 & 23 & 0. 037* \\
135–150 & 102 & 32 & \\
<150 & 2 & 0 & \\
Amylase (28–100 U/L) & 66.99±51.23 & 112.76±149.743 & \\
<100 & 123 & 40 & 0. 002* \\
>100 & 23 & 15 & \\
Hospital stay & & & & \\
Number of days & 20.5(7–73) & 20.04±13.1 & 0.973 \\
Outcome & & & & \\
Living (N/%) & 16(30.2) & 111(87.4) & 0.001* \\
Dead (N/%) & 37(69.1) & 16(12.6) & 0.001* \\
\hline
\end{tabular}
\caption{Correlation Between Hematological Parameters in Hospitalized COVID-19 Non Survivors}
\end{table}

\textbf{Note:} *Indicates statistical significance.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
Variables & \textit{r} & \textit{p} value & Remarks \\
\hline
Leukocytes and Absolute lymphocytes & −0.154 & 0.261 & Fair correlation \\
Leukocytes and Neutrophils & 0.988** & <0.001* & Strong correlation \\
Leukocytes and RBCs & −0.238 & 0.084 & Fair correlation \\
\hline
\end{tabular}
\caption{Correlation Between Hematological Parameters in Hospitalized COVID-19 Non Survivors}
\end{table}

The present retrospective study reported the clinical characteristics of hospitalized COVID-19 patients in Buraidah, Saudi Arabia. The mean age was higher among critical than mild cases. Similar age distribution among COVID 19 patients has been reported by previous studies.\textsuperscript{49,50} High prevalence of COVID-19 infections among elderly patients may be attributed to reduced immunity associating aging as a result of by biological changes in the immune system leading to increased susceptibility to respiratory infections and a high prevalence of associated comorbidities (mainly diabetes and hypertension and respiratory viral infection particularly influenza virus).\textsuperscript{52–57} Regarding gender, infection was more prevalent among males, which is in agreement with previous studies on COVID 19 patients.\textsuperscript{57,58} Male sex has been previously reported as a risk factor for
Figure 2 Continue.
**Figure 2** (A) Kaplan–Meier curve in patients with confirmed COVID-19 patients. The composite endpoint was death. (B) Kaplan–Meier curve in patients with confirmed COVID-19 patients. The composite endpoint was death.
high incidence of infections.\textsuperscript{59,60} A large body of research attributed female advantage in COVID-19 to higher numbers of CD4+ T cells more CD8+ T cell cytotoxic activity, and increased B cell production of immunoglobulin compared to males.\textsuperscript{59,60} In addition to the higher production of type 1 interferon (IFN), a potent anti-viral cytokine, upon toll-like receptor 7 sensing of viral RNA than males.\textsuperscript{60,61}

The majority of patients in the current study had comorbid diseases. Diabetes, cardiovascular and cerebrovascular disorders, and hypertension were the most prevalent. According to previous studies, people with comorbidities were more likely to have a severe illness and experience associated death.\textsuperscript{63–70} In agreement with our findings, diabetes, cardiovascular diseases and hypertension were more frequently observed in critical COVID-19 cases.\textsuperscript{70} On the other hand, cytokine storm by overproduction of pro-inflammatory cytokines including IL-6 and TNF-\(\alpha\) has been associated with bad prognosis in patients with no associated comorbidities.\textsuperscript{71,72}

Concerning haematological parameters, higher rates of neutrophilia, leukocytosis, lymphocytopenia and thrombocytopenia were reported among critical cases in comparison to other patients’ categories. Similar results have been reported in several studies.\textsuperscript{12,74–80} While, the precise pathology of hematological abnormalities in COVID-19 patients is still not fully clear, several studies had discussed the underlying mechanisms of abnormal hematological parameters in COVID-19 patients and its correlation with bad outcome. Leukocytosis and neutrophilia were explained as inflammatory response and were reported to have a significant association with the disease severity and bad outcome.\textsuperscript{80} On the other hand, lymphopenia has been postulated to be caused by the generation of excessive pro-inflammatory cytokines during COVID-19 infection, which induce robust lymphocyte apoptosis.\textsuperscript{50,81} Finally, thrombocytopenia in COVID-19 patients have been assumed to be multifactorial. In SARS, it was suggested that the viral infection together with mechanical ventilation cause endothelial damage triggering platelet activation, aggregation and thrombosis in the lung, causing vast platelet consumption. Moreover, virus-induced alteration of the pulmonary capillary bed may lead to deranged platelet defragmentation. Coronaviruses can potentially infect bone marrow cells directly, causing improper hematopoiesis or initiating an auto-immune reaction against blood cells.\textsuperscript{83–85} It also has been suggested that a low grade disseminated intravascular coagulation (DIC) consistently associate SARS and may propagate a low platelet count in.\textsuperscript{50,85,86}

Higher mean levels of D-dimer were observed among critical COVID-19 cases in the present work, which are in agreement with the findings of previous studies.\textsuperscript{87} D-dimer is the product of degradation of fibrin and is elevated in hypercoagulable condition which is a well-documented state in Patients with COVID-19. Elevated D-dimer in previous studies was associated with high susceptibility of severe disease, ICU admission and in hospital death of COVID 19 patients.\textsuperscript{88,89}

Our findings showed higher mean of liver function among critical patients in comparison with other cases. Abnormally high levels of AST and ALT were associated with high probability of patients in ICU and in hospital death. These findings are supported by previous studies which demonstrated that abnormalities of liver function, especially elevation of AST were significantly associated with COVID-19 severity and mortality.\textsuperscript{47,90,91}

It is postulated that ACE receptors are found abundantly in the kidneys, so we assessed the concentration of serum Creatinine in COVID-19 patients. We recognized that Critical cases had higher concentrations of serum Creatinine than others. It was also associated with high incidence of ICU admission and mortality as reported in previous studies.\textsuperscript{92}

 Patients in the present study were observed till discharge either for recovery or death, we reported a hospital case fatality rate of 27.6%. However, this is unlikely to reflect the true fatality rate of the disease, as out-patients and those with missing data were excluded. Different rates have been reported from different localities in Saudi Arabia as Riyadh (4.27%),\textsuperscript{93} Mecca (2.7%),\textsuperscript{94} Jazan (19%).\textsuperscript{95} Moreover, variable rates were reported worldwide. Higher rates of mortality were observed in European and American countries. Among the European region, the highest mortality was observed in Italy (53.4%),\textsuperscript{96} followed by Spain (30.5%).\textsuperscript{97} In USA, the case fatality rate was also high (39%).\textsuperscript{98} Compared to European and American countries, the case fatality rate was low in Asian countries. The mortality rate among COVID-19 patients in Bangladesh was 10%\textsuperscript{99} followed by Iran and Kuwait 8.06% and 1.73%, respectively.\textsuperscript{5,100} Among the Asian region, higher mortality rates were found in China (61.5%) and South Korea (75%).\textsuperscript{101,102} Different rates of mortality reported from different countries may be attributed to different sample size, different characters of studied patients including the age, gender and different laboratory findings.

In the present study, we identified several risk factors that may associate in-hospital death of COVID 19 patients. These factors included ICU admission, leukocytosis, lymphocytopenia, neutrophilia, thrombocytopenia, liver injury...
(diagnosed by high AST or high ALT levels), acute kidney injury, pancreatic injury and high D dimer. Similar risk factors were identified by several studies from different population worldwide.\textsuperscript{12,31,32,48,68,80}

**Conclusion**

We believe that up to date data (epidemiological, clinical and laboratory) of COVID-19 patients from different population may help understanding the pathogenesis of the disease and subsequently improvement of the outcome of patients by determination of the associated risk factors and recognition of high risk group who are more liable for complications and in hospital death. The present study put an eye on some parameters (laboratory and clinical) that – when associate COVID-19 disease – should be alarming signs that the patient is at high risk bad prognosis. We identified several factors as risk factors for mortality in Covid-19 patients such as ICU were at higher risk of death, leukocytosis, lymphocytopenia, neutrophilia, thrombocytopenia, liver injury, acute kidney injury, pancreatic injury and high D dimer. The occurrence of these conditions has been explained by the attachment of the virus to the human angiotensin converting enzyme 2 (ACE2) receptor in most tissues including kidneys, heart, intestine and lungs causing more severe manifestations.\textsuperscript{103}

**Ethics Statement**

The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the local ethics committee and the Scientific Research Platform of the Ministry of Health of the kingdom of Saudi Arabia (Protocol code 479604-1442). Informed consent was waived since this was a retrospective study without patient identifiers.

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**Disclosure**

The authors report no conflicts of interest in relation to this work.

**References**

1. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. *Glob Heal Res Policy*. 2020;5(1):6. doi:10.1186/s41256-020-00135-6
2. Johnson M. Wuhan 2019 Novel Coronavirus - 2019-nCoV. *Mater Methods*. 2020;10(JANUARY):1–5. doi:10.13070/mm.en.10.2867
3. Kimball A, Hatfield KM, Arons M, et al. Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility - King County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(13):377–381. doi:10.15585/mmwr.mm6913e1
4. Hoehl S, Rabenau H, Berger A, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. *N Engl J Med*. 2020;382(13):1278–1280. doi:10.1056/NEJMct2001899
5. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med*. 2020;382(22):2081–2089. doi:10.1056/NEJMoa2008457
6. Alsharrah D, Alhaddad F, Alyaseen M, et al. Clinical characteristics of pediatric SARS-CoV-2 infection and coronavirus disease 2019 (COVID-19) in Kuwait. *J Med Virol*. 2021;93(5):3246–3250. doi:10.1002/jmv.26684
7. Al-Shamsi HO, Coomes EA, Aldhaheri K, Afrawi S. Serial screening for COVID-19 in asymptomatic patients receiving anticancer therapy in the United Arab Emirates. *JAMA Oncol*. 2021;7(1):129–131. doi:10.1001/jamaoncol.2020.5745
8. Al-Qahtani M, AlAli S, AbdulRahman A, Salman Alsayyad A, Otoom S, Atkin SL. The prevalence of asymptomatic and symptomatic COVID-19 in a cohort of quarantined subjects. *Int J Infect Dis IJID off Publ Int Soc Infect Dis*. 2021;102:285–288. doi:10.1016/j.ijid.2020.10.091
9. Almazeedi S, Al-Youha S, Jamal MH, et al. Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait. *EclinicalMedicine*. 2020;24:100448. doi:10.1016/j.eclinm.2020.100448
10. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020;8(4):420–422. doi:10.1016/S2213-2600(20)30076-X
11. Gibson PG, Qin L, Puaah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. *Med J Aust*. 2020;213(2):54–56.e1. doi:10.5694/mja2.50674
12. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5
13. Ranney ML, Griffin V, Jha AK. Critical supply shortages - the need for ventilators and personal protective equipment during the Covid-19 pandemic. *N Engl J Med*. 2020;382(18):e41. doi:10.1056/NEJMp2006141.

14. Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. *N Engl J Med*. 2020;382(21):2049–2055. doi:10.1056/NEJMs2005114.

15. Djelifski D, Munawwarah S, Nurulita A, Ilyas M, Tabri NA, Lihawa N. Comorbidities and mortality in COVID-19 patients. *Gac Sanit*. 2021;35 Suppl 2:S530–S532. doi:10.1016/gacsan.2021.10.085.

16. Shaikh FS, Aldhaferi N, Baker A, et al. Comorbidities and risk factors for severe outcomes in COVID-19 patients in Saudi Arabia: a retrospective cohort study. *J Multidiscip Heathc. Sci*. 2021;14(2):2169–2183. doi:10.2147/JMDHS.S37884.

17. Zhang H, Cao YY, Tan G, et al. Clinical, radiological, and laboratory characteristics and risk factors for severity and mortality of 289 hospitalized COVID-19 patients. *Allergy*. 2021;76(2):533–550. doi:10.1111/all.14496.

18. Sokolowska M, Lukasz M, Ageche I, et al. Immunology of COVID-19: mechanisms, clinical outcome, diagnoses, and perspectives-A report of the European Academy of Allergy and Clinical Immunology (EAACI). *Allergy*. 2020;75(10):2445–2476. doi:10.1111/all.14462.

19. Wolff D, Nee S, Hickey NS, Marschilok M. Risk factors for Covid-19 severity and fatality: a structured literature review. *Infection*. 2021;49(1):1–28. doi:10.1007/s00134-020-01509-1.

20. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA - J Am Med Assoc*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585.

21. Li R, Tian J, Yang F, et al. Clinical characteristics of 225 patients with COVID-19 in a tertiary Hospital near Wuhan, China. *J Infect Public Health*. 2021;14(4):214–238. doi:10.2991/jegh.k.200806.002.

22. Feng Y, Ling Y, Bai T, et al. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med*. 2020;201(11):1380–1388. doi:10.1164/rccm.202002-0445OC.

23. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020;323(16):1574–1581. doi:10.1001/jama.2020.5394.

24. Ebinge JE, Achamallah N, Ji H, et al. Pre-existing traits associated with Covid-19 illness severity. *PLoS One*. 2020;15(7):1–16. doi:10.1371/journal.pone.0236240.

25. Zhang J, Wang X, Jia X, et al. The laboratory tests and host immunity of COVID-19 patients with different severity of illness. *Kidney Int*. 2020;98(1):209–218. doi:10.1016/j.kint.2020.05.006.

26. Huang G, Kovalic AJ, Graber CJ. Prognostic value of leukocytosis and lymphopenia for coronavirus disease severity. *Front Radiat Ther Oncol*. 2020;55(5):102763. doi:10.1016/j.berm.2020.102763.

27. Li R, Tian J, Yang F, et al. Clinical characteristics of 225 patients with COVID-19 in a tertiary Hospital near Wuhan, China. *J Clin Virol* (Pan Am Soc Clin Virol). 2020;76(2):510–532. doi:10.1016/j.jcv.2020.104363.

28. Du H, Dong X, Zhang JJ, et al. Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status. *Front Immunol*. 2020;11:128. doi:10.3389/fimmu.2020.001427.

29. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *Thorax*. 2020;75(7):1813–1815. doi:10.1111/all.14327.

30. Wang D, Hu B, Hu C, et al. Clinical characteristics of patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J*. 2020;55(5):2000524. doi:10.1183/13993003.00524-2020.

31. Aleanizy FS, Alqahtani FY, Alanazi MS, et al. Clinical characteristics and risk factors of patients with severe COVID-19 in Riyadh, Saudi Arabia: a retrospective cohort study. *J Infect Public Health*. 2021;14(4):437–443. doi:10.2991/jegh.k.200806.002.

32. Almutair A, Alhumaid S, Alhuqbani WN, et al. Clinical, epidemiological, and laboratory characteristics of mild-to-moderate COVID-19 patients in Saudi Arabia: an observational cohort study. *Eur J Med Res*. 2020;25(1):61. doi:10.1186/s40001-020-00462-x.

33. Al-Mahdawi M, Al-Omari M, Al-Swaise H. Clinical characteristics and outcome of COVID-19 patients with severe COVID-19 in Riyadh, Saudi Arabia: a retrospective study. *J Infect Public Health*. 2021;14(9):1133–1138. doi:10.1016/j.jiph.2021.07.014.

34. Almahemi AA, Khan AA, Elganaiany A, et al. Epidemiological and clinical features of COVID-19 patients in Saudi Arabia. *J Infect Public Health*. 2021;14(4):437–443. doi:10.2991/jegh.k.200806.002.

35. Alsofayan YM, Althunayyan SM, Khan AA, Hakawi AM, Assiri AM. Clinical characteristics of COVID-19 patients in Saudi Arabia: a retrospective descriptive cross-sectional study. *Front Public Heal*. 2020;8:593256. doi:10.3389/fpubh.2020.593256.

36. AlJishi JM, Alhajaj AH, Alkhubbaz FL, et al. Clinical characteristics of asymptomatic and symptomatic COVID-19 patients in the Eastern Province of Saudi Arabia. *J Infect Public Health*. 2021;14(1):1–11. doi:10.1016/j.jiph.2021.11.002.

37. Alenazi FS, Aqalany AY, Al-Raisi NS, et al. Clinical characteristics and risk factors of patients with severe COVID-19 in Riyadh, Saudi Arabia: a retrospective study. *J Infect Public Health*. 2021;14(9):1133–1138. doi:10.1016/j.jiph.2021.07.014.

38. Almahdawi M, Almahmoud S, Alhumaidi WN, et al. Clinical, epidemiological, and laboratory characteristics of COVID-19 patients in Saudi Arabia: an observational cohort study. *Eur J Med Res*. 2020;25(1):61. doi:10.1186/s40001-020-00462-x.

39. Yen Y, Yang Y, Wang F, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. *BMJ Open Diabetes Res Care*. 2020;8(1):e001345. doi:10.1136/bmjdrd-2020-001343.
52. Franceschi C, Bonafè M, Valensin S, et al. Inflamm-aging. An evolutionary perspective on immunosenescence. *Annu Rev Acld Sci.* 2000;908:244–254. doi:10.1001/0005-1762.2000.06651x

53. Fuentes E, Fuentes M, Alarcon M, Palomo I. Immune system dysfunction in the elderly. *An Acad Bras Cienc.* 2017;89(1):285–299. doi:10.1161/0005-1762.20160487

54. Fulop T, Larbi A, Dupuis G, et al. Immunosenescence and inflamm-aging as two sides of the same coin: friends or foes? *PLoS Pathog.* 2020;16(4):1–13. doi:10.1371/journal.ppat.1008520

55. Meng Y, Wu P, Lu W, et al. Sex-specific clinical characteristics and prognosis of coronavirus disease-19 infection in Wuhan, China: a retrospective study. *Lancet.* 2020;395(10229):1054–1062. doi:10.1016/S1474-6632(20)30566-3

56. Liu X, Zhang R, He G. Hematological findings in coronavirus disease 2019: indications of progression of disease. *Ann Hematol.* 2020;99(7):1421–1428. doi:10.1007/s00277-020-04103-5

57. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019. *in China N Engl J Med.* 2020;382(18):1708–1720. doi:10.1056/nejmoa2002032

58. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021;19(3):141–154. doi:10.1038/s41579-020-00459-7

59. Liu K, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Clin Med J.* 2020;133(9). Available from: https://journals.lww.com/cmj/FullText/2020/05050/Clinical_characteristics_of_novel_coronavirus-A.aspx

60. Zhou F, Yu T, Du R, 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):1054–1062. doi:10.1016/S1474-6632(20)30566-3

61. Dong Y, Hou W, Hu Y, et al. Clinical characteristics, in-hospital outcomes, and predictors of mortality for 128 COVID-19 patients in Wuhan, China: a retrospective cohort study. *Front Med.* 2020;14(9):713–716. doi:10.2217/bmm-2020-0201

62. Alguwaihes AM, Al-Sofiani ME, Megdad M, et al. Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: a single-centre retrospective study. *Diabetes Metab Syndr.* 2020;14(3):247–250. doi:10.1016/j.dsx.2020.03.013

63. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol.* 2020;17(9):543–558. doi:10.1038/s41569-020-0413-9

64. Tsiygoulis G, Palaiodimou L, Zand R, et al. COVID-19 and cerebrovascular diseases: a comprehensive overview. *Ther Adv Neurol Disord.* 2020;13:1756286420978004. doi:10.1177/1756286420978004

65. Tsivgoulis G, Palaiodimou L, Zand R, et al. COVID-19 and cerebrovascular diseases: a systematic review and perspectives for clinicians. *Front Neurol.* 2020;11:574694. doi:10.3389/fneur.2020.574694

66. Sanyaolu A, Okorie C, Shokunbi O, et al. The impact of COVID-19 disease on platelets and coagulation. *Biol Proced Online.* 2020;22:1–14. doi:10.2217/bmo-2020-0143

67. Fraiman P, Godeiro Junior C, Moro E, Cavallieri F, Zedde M. COVID-19 and cerebrovascular diseases: a systematic review and perspectives for stroke management. *Front Neurol.* 2020;11:574694. doi:10.3389/fneur.2020.574694

68. Ejaz H, Alsharni A, Zafar A, et al. COVID-19 and comorbidities: deleterious impact on infected patients. *J Infect Public Health.* 2020;13(12):1833–1839. doi:10.1016/j.jiph.2020.07.014

69. Savoia C, Volpe M, Kuretz R. Hypertension, a moving target in COVID-19: current views and perspectives. *Circ Res.* 2021;128(7):1062–1079. doi:10.1161/CIRCRESAHA.121.318054

70. Ilapu N, Licastro N, Provenzano M, Andreucci M, de Franciscis S, Serra R. Cardiovascular disease as a biomarker for an increased risk of COVID-19 infection and related poor prognosis. *Biomark Med.* 2020;14(9):713–716. doi:10.2217/bmm-2020-0201

71. Grimmel RF. The effects of sulfur amino acid intake on immune function in humans. *J Nutr.* 2006;136(8Suppl):1660S–1665S. doi:10.1093/jn/136.6.1660S

72. Zolfgahari Emanehe R, Nosrati H, Eftekhar M, Falak R, Khoshmirmafi A. Expansion of single cell transcriptomics data of SARS-CoV infection in human bronchial epithelial cells to COVID-19. *Biol Proced Online.* 2020;22:16. doi:10.2217/bmo-2020-00127-3

73. Borges L, Putin-Curi TC, Curi R, Hatanaka E. COVID-19 and neutrophils: the relationship between hyperinflammation and neutrophil extracellular traps. *Mediators Inflamm.* 2020;2020:8829674. doi:10.1155/2020/8829674

74. Mei H, Luo L, Hu Y. Thrombocytopenia and thrombosis in hospitalized patients with COVID-19. *J Hematol Oncol.* 2020;13(1):161. doi:10.1186/s11604-020-01003-z

75. Selim S. Leukocyte count in COVID-19: an important consideration. *Egypt J Bronchol.* 2020;14(1):4–5. doi:10.1186/s43168-020-00045-8

76. Tavakolpour S, Rakhshaneshroo T, Wei EX, Rashidian M. Lymphopenia during the COVID-19 infection: what it shows and what can be learned. *Immunol Lett.* 2020;225:31–32. doi:10.1016/j.imlet.2020.06.013

77. Lee J, Park SS, Kim TY, Lee DG, Kim DW. Lymphopenia as a biological predictor of outcomes in COVID-19 patients: a nationwide cohort study. *Cancers.* 2021;13(3):471. doi:10.3390/cancers13030471

78. Wool GD, Miller JL. The impact of COVID-19 disease on platelets and coagulation. *Pathobiology.* 2021;88(1):15–27. doi:10.1159/000512007

79. Reusch N, De Domenico E, Bonaguro L, et al. Neutrophils in COVID-19. *Front Immunol.* 2021;12:652470. doi:10.3389/fimmu.2021.652470
80. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parameters in patients with COVID-19 infection. Am J Hematol. 2020;95(6):E131–E134. doi:10.1002/ajh.25774
81. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care. 2020;8(1):1–10. doi:10.1186/s40560-020-00453-4
82. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033–1034. doi:10.1016/S0140-6736(20)30628-0
83. Prieto-Pérez L, Fortes J, Soto C, et al. Histiocytic hyperplasia with hemophagocytosis and acute alveolar damage in COVID-19 infection. Mod Pathol. 2020;33(11):2139–2146. doi:10.1038/s41379-020-0613-1
84. Harris CK, Hung YP, Nielsen GP, Stone JR, Ferry JA. Bone marrow and peripheral blood findings in patients infected by SARS-CoV-2. Am J Clin Pathol. 2021;155(5):627–637. doi:10.1093/ajcp/aqaa274
85. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846–848. doi:10.1007/s00134-020-05991-x
86. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475–481. doi:10.1016/S2213-2600(20)30079-5
87. Chen X, Zhu B, Hong W, et al. Associations of clinical characteristics and treatment regimens with the duration of viral RNA shedding in patients with COVID-19. Int J Infect Dis IJID off Publ Int Soc Infect Dis. 2020;98:252–260. doi:10.1016/j.ijid.2020.06.091
88. Yu Y, Xu D, Fu S, et al. Patients with COVID-19 in 19 ICUs in Wuhan, China: a cross-sectional study. Crit Care. 2020;24(1):1–10. doi:10.1186/s13054-020-02939-x
89. Han MS, Choi EH, Chang SH, Jin BL, Lee EJ, Kim BN. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. JAMA Pediatr. 2020;175:73–80.
90. Parohan M, Yaghoubi S, Seraji A. Liver injury is associated with severe coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of retrospective studies. Hepatol Res. 2020;50(8):924–935. doi:10.1111/hepr.13510
91. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020;21:100331. doi:10.1016/j.eclinm.2020.100331
92. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97(5):829–838. doi:10.1016/j.kint.2020.03.005
93. Abokhamra SI, Abazid RM, Aldossari MA, et al. Clinical characteristics and in-hospital mortality of COVID-19 adult patients in Saudi Arabia. Saudi Med J. 2020;41(11):1217 LP-1226. doi:10.15537/smj.2020.11.25495
94. Shabrawishi M, Al-Gethamy MM, Naser AY, et al. Clinical, radiological and therapeutic characteristics of patients with COVID-19 in Saudi Arabia. PLoS One. 2020;15(8):e0237130. doi:10.1371/journal.pone.0237130
95. Hakami A, Badedi M, Elsidid M, et al. Clinical characteristics and early outcomes of hospitalized COVID-19 patients with end-stage kidney disease in Saudi Arabia. Int J Gen Med. 2021;14:4837–4845. doi:10.2147/IJGM.S327186
96. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med. 2020;180(10):1345–1355. doi:10.1001/jamainternmed.2020.3539
97. Goicoechea M, Sánchez Cámara LA, Macias N, et al. COVID-19: clinical course and outcomes of 36 hemodialysis patients in Spain. Kidney Int. 2020;98(1):27–34. doi:10.1016/j.kint.2020.04.031
98. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020;395(10239):1763–1770. doi:10.1016/S0140-6736(20)31189-2
99. Mowla SGM, Azad KAK, Kabir A, et al. Clinical profile of 100 confirmed COVID-19 patients admitted in Dhaka medical college hospital, Dhaka, Bangladesh. J Bangladesh Coll Physicians Surg. 2020;29–36. doi:10.3329/jbpcs.v38i0.47445
100. Nikpouraghdam M, Jalali Farahani A, Alshiri G, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in Iran: a single center study. J Clin Virol off Publ Pan Am Soc Clin Virol. 2020;127:10378. doi:10.1016/j.jcv.2020.104378
101. Xu J, Yang X, Yang L, et al. Clinical course and predictors of 60-day mortality in 239 critically ill patients with COVID-19: a multicenter retrospective study from Wuhan, China. Crit Care. 2020;24(1):394. doi:10.1186/s13054-020-03098-9
102. Hwang JM, Kim JH, Park JS, Chang MC, Park D. Neurological diseases as mortality predictive factors for patients with COVID-19: a retrospective cohort study. Neurol Sci. 2020;41(9):2317–2324. doi:10.1007/s10072-020-04541-z
103. Zolfaghari Emameh R, Falak R, Bahreiini E. Application of system biology to explore the association of nephrilsyn, angiotensin-converting enzyme 2 (ACE2), and Carbonic Anhydrase (CA) in pathogenesis of SARS-CoV-2. Biol Proced Online. 2020;22:11. doi:10.1186/s12575-020-00124-6

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