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ORIGINAL RESEARCH

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, $p = 0.091$).

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]

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COVID-19 patients may remain asymptomatic[3–9] or present with mild, moderate, or severe symptoms, primarily respiratory symptoms.[10] 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.[11,12] The mortality rate ranges from 1% to 10% depending on patients' clinical presentations and availability of medical resources in different countries.[13,14] Although any individual can present with severe COVID-19, it is more common in elderly individuals or in patients with underlying chronic diseases.[13,14] 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.[15,16]

Patients with severe COVID-19 may experience respiratory failure, shock, disseminated coagulopathy, and multiple-organ failure requiring admission to the intensive care unit (ICU).[17] 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.[18] Risk factors may include demographic factors, such as age.[19,20] 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.[21–23] Moreover, sex and ethnicity,[24,25] diet and lifestyle habits,[26,27] underlying diseases,[28,29] complications[30,31] and laboratory findings[32,33] 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.[34,35]

Understanding pathological laboratory findings can also be used as guide strategies to find a new treatment or vaccine.[36] 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.[37]

Although, several studies had been conducted in Saudi Arabia illustrating the clinical characteristics of Saudi COVID-19 patients in different localities,[38–42,44,45] 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). Table 1.

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.

Table 1 Showing Demographic, Clinical and Laboratory Data of Hospitalized COVID-19 Patients

Variable	Critical COVID-19 (n=53)	Non-Critical COVID-19 (n=146)	P value
Clinical characteristics			
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			
Diabetes (N/%)	11(20)	18(12.3)	0.009
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			
Fever (N/%)	16(30.2)	42(28.7)	0.098
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			
Yes (N/%)	5(9.4)	134(91.8)	0.000*
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)	76.66(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
	No	No	No	No	No	No
Female Male	31 48	49 71	50 74	30 45	46 71	34 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 Male	6 15	74 104	72 105	8 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)	2.844± 5.9364	5.16± 8.4147	0. 005
<0.5	15	6	
>1	124	54	
WBCs (4–10 10^3/uL)	10.563± 5.8	10.628±5.5	0. 865
<4	4	5	
4–10	68	24	
>10	67	31	
Lymphocytes (1–3 10^3/uL)	1.668±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)	7.866±5.3	8.397±5.1	0. 729
<6	61	21	
>6	78	39	
Platelets (150–410 10^3/uL)	302.4±159.2	266.90±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)	34.75±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*)

Table 4 (Continued).

Variable	Non ICU (n=139)	ICU (n=60)	P value
Sodium (135–145 mmol/L)	137.01±6.4	136.87±6.7	0. 900
<135	41	20	
135–150	96	40	
<150	2	10	
Amylase (28–100 U/L)	68.5+51.23	105.3±149.7	0. 001*
<100	120	41	
>100	19	19	
Hospital stay			
Admission (days)	20.5(7–73)	20.04±13.1	0.973
Outcome			
Living (N/%)	119(30.2)	25(87.4)	0.001*
Dead (N/%)	20(69.1)	35(12.6)	0.001*

Note: *Indicates statistical significance.

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.[48] 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.[48]

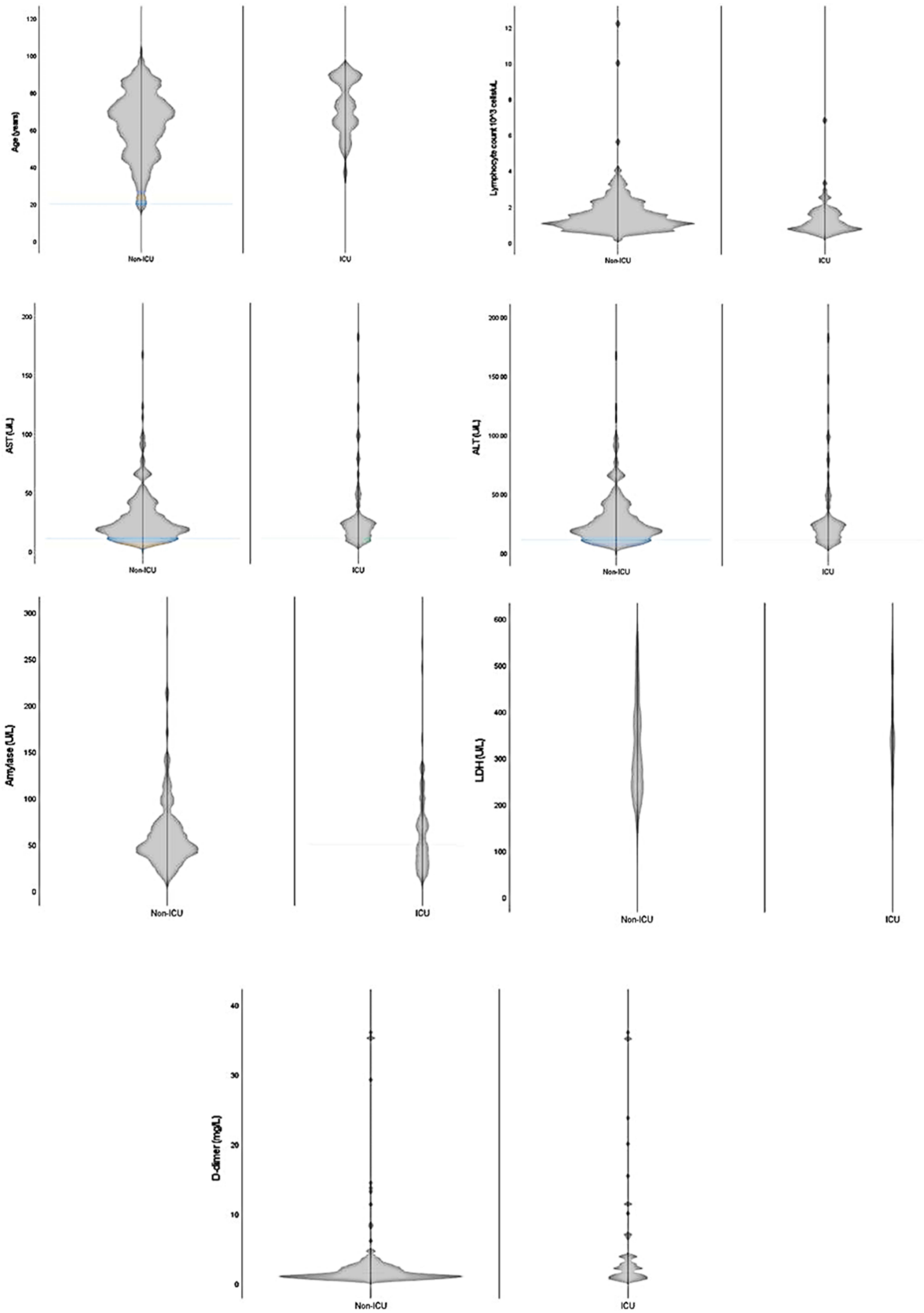

Figure 1 Violin plot showing demographic and laboratory parameters in strong association with ICU admission in COVID-19 patients.

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
Ferrittin	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	14.036±4.04	14.673±3.0055	
<12	40	7	0. 290
>12	104	48	
AST (5–41 U/)	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*)

Table 5 (Continued).

Variable	Survivors (n=144)	Non Survivors (n=55)	P value
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*

Note: *Indicates statistical significance.

Table 6 Correlation Between Hematological Parameters in Hospitalized COVID-19 Non Survivors

Variables	*r*	*p* value	Remarks
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

Notes: *p<0.05, **Strong correlation.

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.[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).[52–57] Regarding gender, infection was more prevalent among males, which is in agreement with previous studies on COVID 19 patients.[57,58] Male sex has been previously reported as a risk factor for

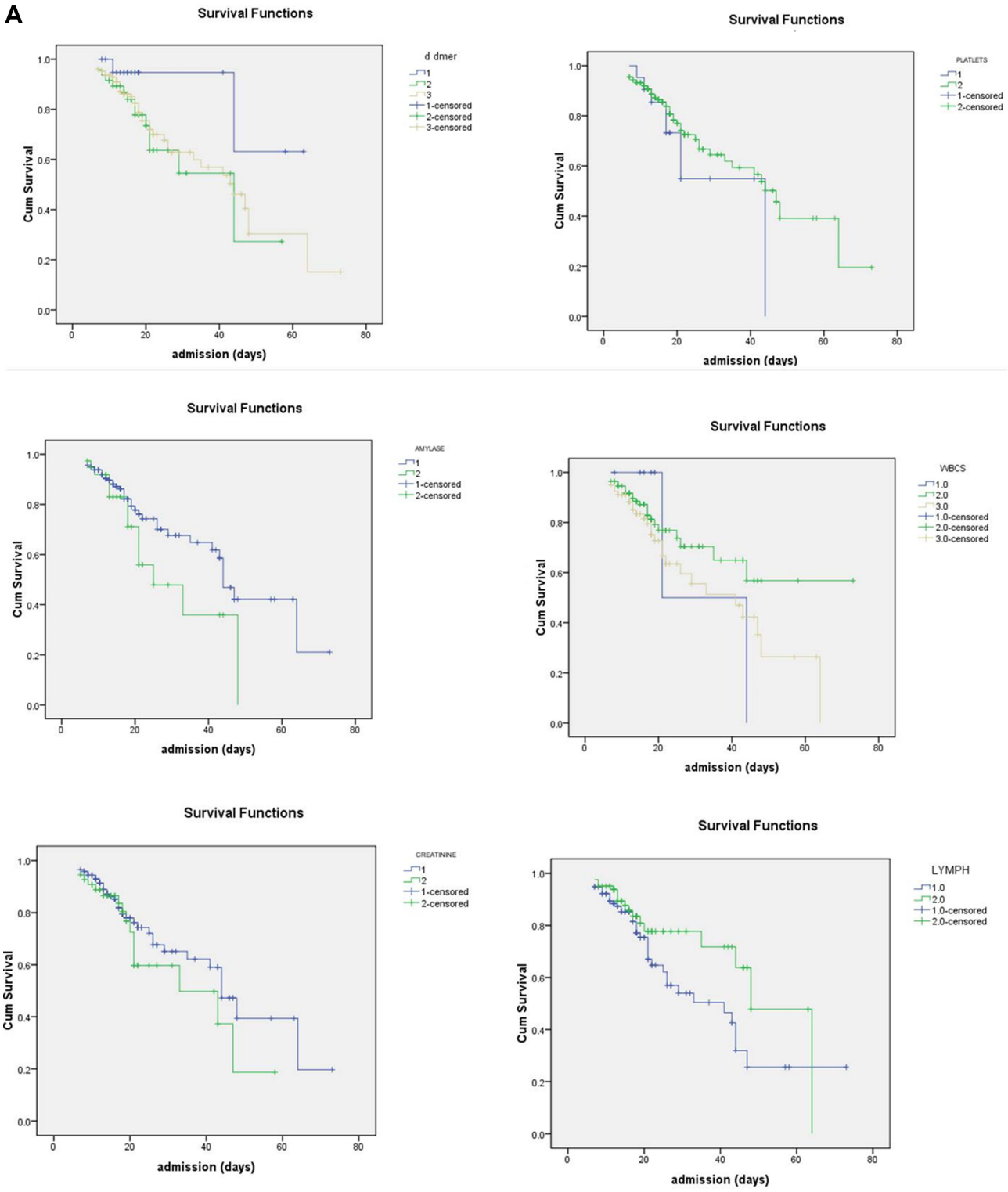

Figure 2 Continue.

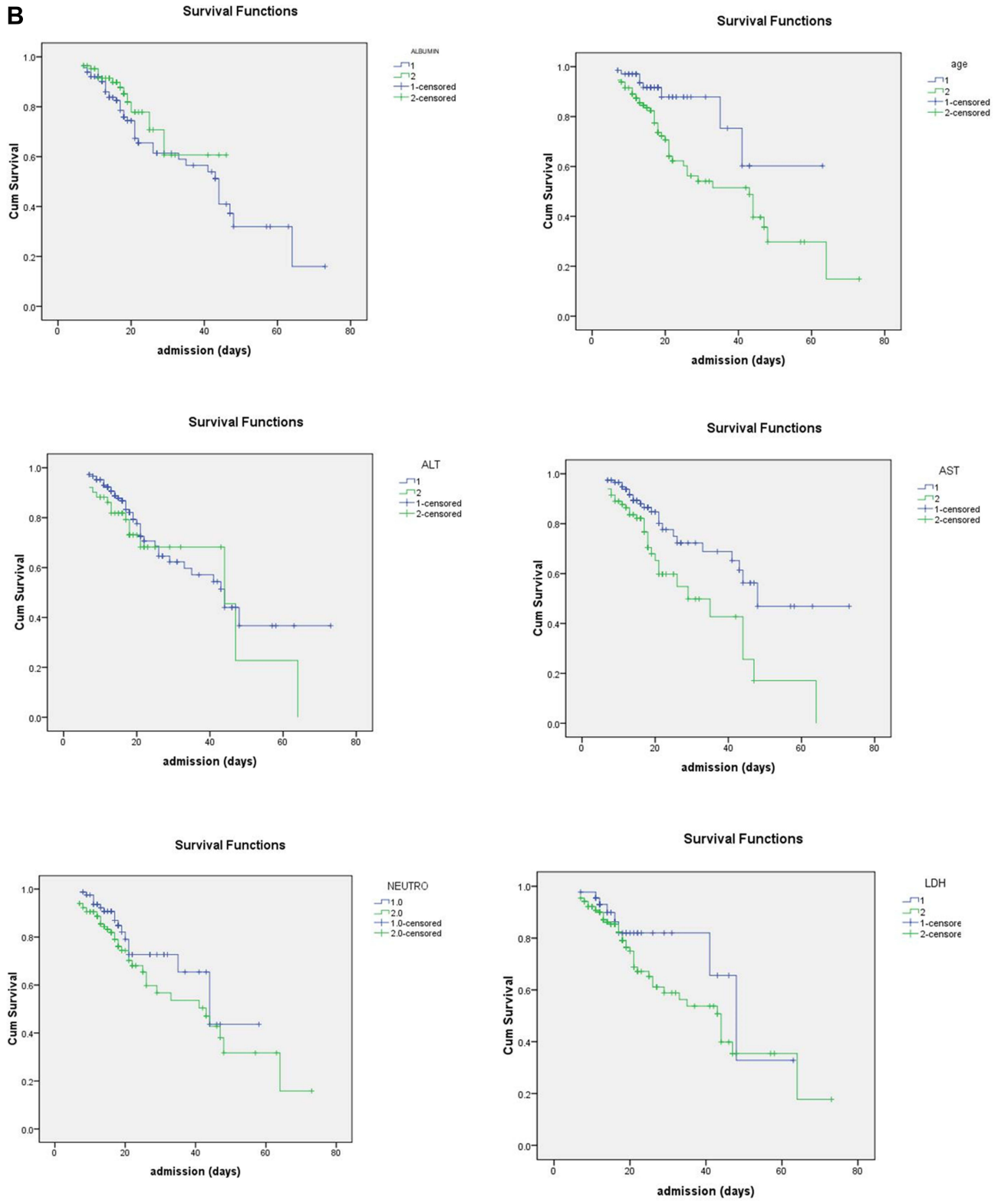

Figure 2 (**A**) Kaplan–Meier curve in patients with confirmed COVID-19 patients. The composite endpoint was death. (**B**) Kaplan–Meier curve in patients with confirmed COVID-19 patients. The composite endpoint was death.

high incidence of infections.[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.[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.[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.[63–70] In agreement with our findings, diabetes, cardiovascular diseases and hypertension were more frequently observed in critical COVID 19 cases.[70] On the other hand, cytokine storm by overproduction of proinflammatory cytokines including IL-6 and TNF-α has been associated with bad prognosis in patients with no associated comorbidities.[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.[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.[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.[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.[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.[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.[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.[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.[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.[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%),[93] Mecca (2.7%),[94] Jazan (19%).[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%),[96] followed by Spain (30.5%).[97] In USA, the case fatality rate was also high (39%).[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%[99] followed by Iran and Kuwait 8.06% and 1.73%, respectively.[9,100] Among the Asian region, higher mortality rates were found in China (61.5%) and South Korea (75%).[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.[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.[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.

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