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EPIDEMIOLOGICAL, CLINICAL, AND LABORATORY FINDINGS IN COVID-19 POSITIVE PATIENTS IN HOSPITALS OF QUETTA, PAKISTAN: A RETROSPECTIVE MULTI-CENTERD STUDY

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Abstract
The coronavirus disease 2019 (COVID-19) is a respiratory disease caused by SARS-CoV-2 in humans and animals. This study aimed to find out socio-demographic factors, epidemiology, clinical characteristics, and laboratory findings in COVID-19 diseased patients. Data was collected on a predesigned questionnaire from COVID-19-positive patients admitted to hospitals. Blood samples were collected for hematology, and serum biochemical analysis.
A total of 199 COVID-19-positive patients were enrolled, among which 145 (72.86%) were from the Quetta division. High prevalence was observed in the age group 51-75 years. Amidst total, 127(63.8%) males and 72(36.2%) were female patients including 78(39.2%) smokers. Forty-nine 49(24.6%) hospitalized patients were critical, 52(26.1%) moderate and 98(49%) with mild health issues. Patients diagnosed with comorbidities like diabetes, chronic respiratory disease, and cardiovascular disease. The total death rate was 33(16.58%). Patients presented general symptoms and infrequent symptoms of diarrhea, chest distress, breath shortness, and vomiting.
Increased count of leucocytes and neutrophils and lower count of erythrocytes, hemoglobin, platelets, and lymphocytes were measured in critical patients. Higher level of C-reactive protein, D-dimer, urea, and creatinine, was measured in critical patients. Impairments in hematological parameters such as biochemical profiles predict disease severity in patients and serve as indicators for the prognosis and severity of COVID-19.

Key word: covid-19; clinical features; epidemiology; hematological; sars-cov-2.

- **Introduction:**

Coronavirus disease-19 (COVID-19) is a novel viral infectious disease determined in December 2019 in a Chinese province, Wuhan. The infection is caused by a novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (Huang et al. 2020) The COVID-19-positive patients had previously visited a local market of Huanan Seafood and the transmission was considered to be associated with Huanan Seafood market and causes SARS-CoV-2 transmission from animals to humans(Li et al., 2020). However, later it was known that it spread more rapidly from human-to-human .

Earlier the lungs were considered the target organ for infection, however, the presence of angiotensin-converting enzyme 2 (ACE2) receptors in other body organs made them susceptible to SARSCoV-2 infection The novel coronavirus damages the body organs by binding to the epithelial cell receptors of the lungs, intestines, blood vessels, and kidneys by the ACE2 receptor(Yang et al.,2020). Pneumonia is the most prevalent clinical characteristic of COVID-19 infection including fever, cough, myalgia, and exhaustion (Huang et al., 2020).

Studies have determined that age, gender, and comorbidities increase the severity of the disease and men are more vulnerable to COVID-19 disease than women(Chen N et al.,2020). It was shown that comorbid medical conditions in COVID-19 patients were observed over the age of 65 years(Onder G et al.,2020). The common comorbidities include hypertension, diabetes, cardiovascular disease(Yang J et al.,2020) and respiratory disease and high frequency is realized among active smokers(Guan et al., 2020). Hematological abnormalities in COVID-19-positive patients are a major cause of disease progression, severity, and mortality. Thrombocytopenia, abnormal coagulation profile, and lymphopenia are associated with disease progression, severity, and risk of mortality(Lillicarp, D et al.,2020).

Other frequent abnormalities in COVID positive patients include C-reactive protein (CRP) and D-dimer(Feng, P et al., 2019). The electrolyte imbalance is also observed in COVID-19 patients(Guan et al., 2020). In meta-analysis lower concentrations of electrolytes that is sodium, calcium and potassium were determined to cause the severity of the disease(Lippi, G et al., 2020). The purpose of the study is to reveal the epidemiological, clinical characteristics and laboratory findings in COVID-19-positive patients admitted to hospitals. The association between the epidemiological, and clinical markers including laboratory investigations will help in finding the transmission pattern, alteration in blood cells as diagnostic markers, and associated physiological and biochemical factors.

- **Materials and methods**

2.1. ***Study design:***A retrospective, multi-centered study was conducted on epidemiological and clinical features and laboratory findings of the COVID-19 positive patients admitted at Fatima Jinnah institute of chest disease and Sheikh Khalifa bin Zayed hospital, Quettafor a period of 7 months (Sep 2020 to March 2021).

2.2. ***Study population:*** A total of 199 COVID-19-positive patients were enrolled in this study.

2.3. ***Data collection:***Data was collected on predesigned proforma and kept confidential. Positive patients were earlier confirmed for SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR) using samples from the upper respiratory tract. Data from different epidemiological parameters, and clinical and laboratory findings were considered. Blood samples were collected for hematological profile and serum biochemistry investigations such as CRP, D-Dimer, LDL, HDL, cholesterol, urea and creatinine, and serum electrolytes.

2.4. ***Ethical approval****:* The study was established after approval from the ethical review committee, at the center for advanced studies in vaccinology and biotechnology (CASVAB), University of Balochistan, Quetta Pakistan.

2.5. ***Statistical analysis:***Descriptive analysis of the variables was expressed as mean or percent (%). All the statistical analyses were performed by using the SPSS program. Statistically significant values of $p<0.05$ was considered.

Results

3.1 ***Epidemiological characteristics*****:** In this study, a total of 199 COVID-19-positive patients were enrolled, among which 127(63.8%) were male, and 72(36.2%) were females.

The highest number of 88(44.2%) infected patients were from the age group 51-75Y, followed by 63(31.7%) patients from the age group 26-50Y and 30(15.07%) patients were from the age group 1-25Y. Interestingly, the lowest infected age group 76-100Y, where containing only 18(9.04%) individuals infected with COVID-19 disease. Remarkably, the higher percentage of 145(72.86%) of infected patients were from the Quetta division, followed by Zhob 17(8.54%), Sibi 15(7.53%), Kalat 16(8%) and Makran 7(3.51%). The data further showed that 18 (9.04%) patients were health workers, while 181(90.95%) were non-health workers. The highest rate of COVID-19 infection was realized in Pashtoon 84(42.2%) community, followed by Baloch 58(29.1%), Punjabi 41 (20.6%), Hazara 9 (4.5%) and others 7 (3.5%) (Table 1).

Table 1. Epidemiological parameters of COVID-19 patients

Characterization		Frequency	Percent
(Age years)			
1-25		30	15.07
26-50		63	31.65
51-75		88	44.2
76-100		18	9.04
Gender			
Male		127	63.8
Female		72	36.2
Region	Makran division	7	3.51
	Kalat division	16	8.00
	Sibi division	15	7.53
	Zhob division	17	8.54
	Quetta division	145	72.86
	Others	7	3.5
Ethnic group	Hazara	9	4.5
	Punjabi	41	20.6
	Baloch	58	29.1
	Pashtoon	84	42.2
Employment status	Health worker	18	9.04
	Non-health worker	181	90.95

3.2 ***Clinical features:*** Clinical features were grouped into mild, moderate, and critical based on health conditions. The asymptomatic or patients with few symptoms were placed in the mild group, while symptomatic cases were placed in moderate and critical groups. Data analysis showed that 49(24.6%) patients were critical, 52(26.1%) were moderate and 98(49%) were determined with mild health problems. Most of the patients (36.68%) had a fever and a temperature between 37.3oC to 38oC. Furthermore, 58(29.14%) patients had high temperature (38.1oC-39.0oC), where most of the cases 23(46.9%) were critical. Of the patients with high temperature >39oC were 32(16.08%), among which 14(28.57%) were critical, 10(19.23%) were moderately sick and 8 (8.16%) were of mild cases.

A total of 135(67.83%) patients had coughs, among which mild, moderate, and critical patients were 68(69.38%), 30(57.69%), and 37(75.51%), respectively. Chest distress was present in 76(38.19%) patients, among which the highest number 33(67.34%) belong to a critical group. Of patients which had shortness of breath 96(48.2%), among which the highest number 35(71.42%) of patients were critically ill. Intensive ventilation was provided to 48(24.12%) patients, among which 30(61.22%) patients were critical and 14(26.92%) were moderately sick.

Headache, myalgia, and anorexia were reported in 95(47.73%), 153(76.9%), and 152(76.38%) were present in overall 199 patients, respectively, however, these features were higher in critical patients. Vomiting and diarrhea were comparatively low and only 40(20.10%) and 68(34.17%) had vomiting and diarrhea, respectively (Table 2). Patients with clinical symptoms of fatigue were 108(54.27%) and nasal congestion was realized in 66 (33.16%) patients. Fifty-five, 55(27.63%) patients were admitted to the intensive care unit (ICU), of which 34(69.38%) were in critical condition. A total of 33(16.58%) patients died, among which 21(42.85%) were critically ill (Table 2).

Table 2. Clinical features of COVID-19 positive patients

Clinical signs and symptoms	Mild n=98 (%)	Moderate n=52 (%)	Critical n=49 (%)	Total n=199 (%)
Fever				
37.3-38°C	38(38.77)	21(40.38)	14(28.57)	73(36.68)
38.1-39°C	20(20.40)	15(28.84)	23(46.9)	58(29.14)
>39°C	8(8.16)	10(19.23)	14(28.57)	32(16.08)
Cough	68(69.38)	30(57.69)	37(75.51)	135(67.83)
Chest distress	18(18.36)	25(48.07)	33(67.34)	76(38.19)
Breath shortness	34(34.69)	27(51.92)	35(71.42)	96(48.24)
Invasive ventilation	4(4.08)	14(26.92)	30(61.22)	48(24.12)
Headache	28(28.57)	32(61.53)	35(71.42)	95(47.73)
Myalgia	72(73.46)	38(73.07)	42(85.71)	152(76.38)
Vomiting	12(12.24)	13(25)	15(30.61)	40(20.1)
Diarrhea	33(33.67)	16(30.76)	19(38.77)	68(34.17)
Anorexia	73(74.48)	38(73.07)	41(83.67)	152(76.38)
Nasal congestion	34(34.69)	15(28.84)	17(34.69)	66(33.16)
Nausea	38(38.77)	24(46.15)	30(61.22)	92(46.23)
Unconsciousness	11(11.22)	19(36.53)	33(67.34)	63(31.65)
Fatigue	48(48.97)	28(53.84)	32(65.30)	108(54.27)
Admission to ICU	3(3.06)	18(34.61)	34(69.38	55(27.63)

Clinical outcomes				
Recovered	96(97.95)	42(80.76)	28(57.14)	166(83.41)
Died	2(2.04)	10(19.23)	21(42.85)	33(16.58)

3.3 ***Chest tomography of the patients****:* Sixty-five 65(32.66%) positive patients were investigated by computerized tomography (CT) scan, among which 27 (41.53%) had unilateral, 16 (24.61%) had a bilateral lung infection, 9 (13.84%) had ground glass opacities, 8(12.3%) had subpleural lesions, and 5(7.69%) had tiny nodules. Twelve (n=12) patients with a unilateral lung infection were critical and 10 patients fell in moderate infection. However, 8 patients were critical and 6 were fall into moderate groups in bilateral lung infection. In-ground glass opacities 7 patients were critical (Table 3).

Table 3. Chest computed tomography of COVID-19 patients

Chest computed tomography	Mild n=98	Moderate n=52	Critical n=49	Total n=199
Unilateral	5	10	12	27
Bilateral	2	6	8	16
Ground glass opacities	1	1	7	9
Sub pleural lesion	2	2	4	8
Tiny nodules	1	2	2	5

3.4. ***Smoking status:*** Data showed, 78 (39.2 %) patients were smokers and 121(60.8%) were non-smokers (60.8%). The health condition of the smokers was poor than nonsmokers, and the majority of smokers were placed on mechanical ventilation. Invasive ventilation was provided to 25 (32.05%) patients, whereas in non-smokers 23% of patients were placed on ventilation. The death ratio among smokers was 17.94%, which was less (15.7%) in non-smokers (Table 4).

Table 4. Smoking status of COVID-9 positive patients

	Frequency (%)	Invasive ventilation	Survivor	Died	Death (%)
Smoker	78 (39.2)	25	64	14	17.94
Non-smoker	121 (60.8)	23	102	19	15.70
Total	199 (100.0)	48	154	33	16.58

3.5. ***Comorbidities:*** Results showed 118(59.29%) COVID-19-positive patients had no associated disease. Patients with comorbidities were in pattern of, diabetic 45(22.61%), chronic respiratory disease 24(12.06%), cardiovascular disease 8(4.02%), and chronic kidney disease were 4(2.01%). Patients had also underlying comorbidities such as 5(11.11%) patients having diabetes and chronic respiratory disease, 4(8.88%) had diabetes with cardiovascular disease, and 1(2.22%) patient had diabetes with chronic kidney disease (Table 5).

Table. 5 Comorbidities associated with COVID-19 disease

Disease		Numbers (%)		
COVID-19 without comorbidities		118 (59.29)		
	Disease	**Numbers (%)**	**Diabetes + Comorbidities**	**Numbers (%)**
COVID-19 with Comorbidities	Diabetes	45 (22.61)	Diabetes	35 (77.77)
			Diabetes + CVD	4 (8.88)
			Diabetes + Respiratory disease	5 (11.11)
			Diabetes + Kidney disease	1 (2.22)
	Respiratory disease	24 (12.06)		
	CVD	8 (4.02)		
	Kidney disease	4 (2.01)		
Total: 199				

3.6. ***Effect on the hematological parameter in COVID-19 positive patients*****:** A significant difference was realized in the blood physiological parameters of COVID-19-positive patients. Variations were realized in total leucocyte count, lymphocyte, and neutrophils. Patients with critical conditions had higher values of white blood cells (12.28±0.61), and a lower count of lymphocytes (11.59±0.52) was measured. However, in contrast, an increased neutrophil count of 79.28±0.72 was realized. It was noted that the value of erythrocytes (RBC 4.3±0.23) and hemoglobin (HGB 7.52±0.52) was significantly decreased in patients with critical conditions. whereas no significant difference was observed in the indices of RBCs except MCH. Depletion in the count of platelets (184.58±13.11) was observed in patients with critical health status compared to mild and moderate groups. A significant effect was seen on PCT (1.79±0.65) in critical patients as compared to other groups' distribution. Furthermore, no significant effect was realized in the value of MPV, and PDW in all three groups of critical, mild, and moderate patients as shown in (Table 6).

Table 6. Comparative analysis of hematological parameters of COVID-19 positive patients in mild, moderate and critical groups

Hematological parameter	Mild (n=98)	Moderate (n=52)	Critical (n=49)	P value <0.05
White blood cell(10^9/L)	8.65±0.30	9.71±0.56	12.28±0.61	0.005
Lymphocyte (%)	19.23±0.65	15.73±0.69	11.59±0.52	0.002
Monocyte(%)	10.86±0.43	9.83±0.46	8.61±0.51	0.004
Neutrophil (%)	69.08±0.88	73.12±1.00	79.28±0.72	0.001
Eosinophil(%)	0.98±0.08	0.72±0.09	0.85±0.11	0.12
Basophils(%)	0.09±0.03	0.02±0.01	0.04±0.02	0.06
Hemoglobin (g/L)	9.35±0.32	9.13±0.45	7.52±0.52	0.003
Red blood cell (10^{12}/L)	5.29±0.15	4.74±0.21	4.3±0.23	0.002
Hematocrit (HCT) (%)	33.98±0.99	32.41±1.7	30.8±1.66	0.24
Mean corpuscular volume (MCV) (fL)	80.12±1.45	77.52±2.25	76.37±2.72	0.35
Mean corpuscular hemoglobin (MCH) (pg)	30.54±0.37	28.71±0.92	29.23±1.11	0.17
Mean corpuscular hemoglobin	33.60±0.3	34.08±0.31	32.43±0.58	0.005

concentration(MCHC) (g/dL)				
Platelets 10^9/L	255.28±8.14	226.1±11.95	184.58±13.11	0.001
Platelet crit (PCT) (%)	0.35±0.02	0.81±0.32	1.79±0.65	0.005
Mean platelet volume (MPV) (Fl)	7.96±0.16	7.67±0.21	7.83±0.28	0.60
Platelet distribution width (PDW) (fL)	13.21±0.33	13.12±0.44	12.46±0.69	0.50

P<0.05 showing significant level. P>0.05 Showing non-significant result

3.7. ***Effect of COVID-19 infection on the biochemical profile:*** The critical patients were realized to have a significant increase in C-reactive protein (CRP) (24.27±2.33), D-dimer (168.92±8.3), and LDH (175.10±21.70) in critical patients as compared to mild and moderate patients. However, a non-significant effect was seen on serum ferritin and ALT (Table 7). Troponin which shows damage to the heart muscle was significantly (0.05±0.02) higher in critical patients, however, the non-significant effect of creatine kinase (CK) was realized. Furthermore, a significant effect was seen in sugar level, urea, and creatinine, while no significant difference was observed for uric acid value. Significantly, higher cholesterol (218.8±8.22) and low HDL (39.67±0.75) were measured in critical patients. No effect was seen on LDL and triglyceride (Table 7).

Table 7. Effect on serum profile of COVID-19 positive patients in mild, moderate and critical groups

Serum Parameter	Mild (n=98)	Moderate (n=52)	Critical (n=49)	P value <0.05
C-reactive protein(CRP) (mg/L)	11.29±0.8	17.1±1.91	24.27±2.33	0.002
D-dimer (ng/L)	143.49±3.71	142.15±4.09	168.92±8.3	0.004
Serum ferritin (ng/mL)	212.05±5.84	174.79±8.24	197.43±11.96	0.008
Alanine amino transaminase (ALT) (U/L)	30.47±0.74	30.73±1.11	34.71±1.44	0.006
Lactate dehydrogenase (LDH) (U/L)	93.88±7	129.46±14.67	175.10±21.70	0.001
Creatine kinase (CK) (U/L)	79.00±5.81	79.10±8.36	79.88±8.19	0.987
Troponin (ng/mL)	0.01±.00	0.03±.01	0.05±.02	0.001
Glucose fasting (mg%)	115.11±2.88	123.73±5.49	139.51±7.5	0.001
Uric acid (mg%)	0.79±0.02	0.97±0.07	1.13±0.1	0.099
Urea (mg%)	40.35±0.78	45.48±2.03	48.75±2.49	0.003
Creatinine (mg%)	0.79±0.02	0.97±0.07	1.13±0.1	0.001
Low-density lipoprotein(LDL) (mg%)	150.57±3.68	146.77±2.8	157.38±2.89	0.253
High density lipoprotein(HDL) (mg%)	51.42±0.77	43.80±0.80	39.67±0.75	0.003
Cholesterol (mg%)	174.26±4.2	201.08±5.94	218.8±8.22	0.002
Triglyceride (mg%)	202.27±4.81	202±5.16	213.02±5.87	0.406

P<0.05 showing significant level. P>0.05 showing non-significant result.

3.8. ***Effect on serum electrolytes:*** A significant difference was realized in the electrolytes of COVID-19 patients. Results showed that critical patients had a significantly lower value of potassium (3.62±0.15), sodium (102.98±2.33), chloride (91.53±1.67), calcium (6.45±0.22), and bicarbonate (15.88±0.61) as compare to mild and moderate patients (Table 8).

Table 8. Serum electrolytes of COVID-19 positive patients

Serum Electrolytes	Mild (n=98)	Moderate (n=52)	Critical (n=49)	P value <0.05
Potassium [K^+] (meq/L)	4.66±0.09	3.72±0.11	3.62±0.15	0.001
Sodium [Na^+] (meq/L)	134.31±0.83	119.00±1.78	102.98±2.33	0.003
Chloride [Cl^-] (meq/L)	100.81±0.53	98.10±0.91	91.53±1.67	0.001
Calcium [Ca+] (mg/dl)	8.47±0.09	7.62±0.10	6.45±0.22	0.003
Bicarbonate [HCO3] (meq/L)	24.13±0.34	20.90±0.54	15.88±0.61	0.001

P<0.05 showing significant levels. P>0.05 Showing non-significant result

- **Discussion**

Our study described epidemiology, clinical characteristics, and correlation of laboratory investigations regarding COVID-19-positive patients of Balochistan province, which was affected by different waves of COVID-19 disease. During this study, we identified different epidemiological parameters, clinical features, and associated factors identified in SARS-CoV-2 infected patients. The frequency of COVID-19-positive cases in the age group of 51-75 years was higher than in younger age groups showing that the adult age group was more prone to acquire the infection. This advocate that a considerable country's population comprises young adults, showing strong immunity against disease (Ahmad et al. 2021). These findings were also in agreement with the previous study, where patients of ≥ 50 years were more vulnerable to COVID-19 disease(Jakhmola et al., 2021). Furthermore, including old age other factors such as weakened immune system, and underlying morbidities are the risk factors associated with COVID-19 infection(Mehra et al., 2020).

Interestingly, the frequency of COVID-19-positive cases was 1.76 times greater in males compared to females. The possible reason which is also reported in other studies that men are more exposed to COVID-19 due to changes in daily routine activities. The men population in this study was mostly employed, exposed publicly more, or in close contact putting them at higher risk to acquire COVID-19 infection than females(Stelzig et al., 2020). This advocate that individuals with more public exposure are at higher risk of acquiring the disease. In addition, men mostly have the habit of smoking and alcohol consumption compared to women and this behavior makes men more susceptible to acquiring infection (Raimondi et al. 2021). Furthermore, biological and environmental factors, sex steroids and higher levels of estrogen, which has immune-stimulatory roles in women are supposed to be the cause of low incident rate in females .

In a previous study among 252 critical care unit admitted patients in the United Kingdom (UK), 66.8% were White, 15.2% were Asian, 9.9% were Black and 8.1% were from other ethnic groups(Gov.uk 2019).

The current study revealed that Pashtoon and Baloch ethnic groups were more affected than other communities. The reason for which high population community in the region, the trend of the joint family system including poor housing ventilation and weak socioeconomic status is considered. According to our results, the local transmission of the virus is determined in Quetta, which is the most populated city of the province of Balochistan, where human-to-human transmission of the disease is considered. Social distancing is always encouraged to avoid the dissemination of the disease in the area(Dalton

et al., 2020).

The occupational risk of acquiring COVID-19 infection was not uniform. In non-health workers like drivers, daily wagers, transporters, shopkeepers, barbers, police, driver, and district administrators were at higher risk of acquiring infection. As these individuals were continuously exposed and in contact with the public had a higher risk of acquiring COVID-19 infection.While the teachers, students, and housewives were at less risk, and the possible reason for this due to the educational institute was closed and the teachers and students were likely in less risk of acquiring the disease. This is also in line with the study of (Magnusson et al. 2021)

Interestingly, a very less number of 18 (9.04%) health workers were infected with COVID-19 infection, which shows that the standard operating procedure (SOPs) were followed and prevented the disease while treating patients in hospitals and health care centers. However, in contrast, in the early days of the disease, considerable numbers of healthcare workers were infected by COVID-19 in China(Chen T et al., 2021) and a study showed that 23 healthcare workers died revealing the risk, that health workers have while dealing with infectious diseases(Ing EB et al., 2020).

Amidst the clinical features cough and fever are the most common symptoms, which shows the organism's response to various infectious diseases(Plaza, J et al., 2016). It was reported that 81.3% of COVID-19 patients had fever(Xie et al., 2021) and 76% had cough (Huang et al. 2020) which was considered the second most common clinical manifestation(da Rosa Mesquita et al., 2021). Our study showed clinical presentations of anorexia, diarrhea, and chest distress including dyspnea, headache, and myalgia, vomiting, nausea in all three categories of the study. However, the severity of the clinical parameters was higher in critical patients.

The Angiotensin-converting enzyme 2 (ACE2), the cellular receptor for SARS-CoV-2 is widely distributed in different cell organs including the gastrointestinal tract (GIT)(Hikmat et al., 2020). This indicates that cell types in the GIT are potentially susceptible to SARS-CoV-2 infection and the study corresponds that diarrhea is associated with COVID-19 infection. The clinical symptoms of dyspnea, headache, and myalgia, vomiting, nausea was also reported previously(Murat et al., 2021; Asghar et al., 2020).

Smoking damages the upper respiratory tract and decreases the pulmonary immune system which results in increased severity of the disease(Baur et al., 2013). It is associated with the progression of COVID-19 and is considered a high-risk factor in facilitating COVID-19 disease compared to non-smoker(Patanavanich et al., 2020). In our study, we reported that the severity and death ratio is higher in smokers. Furthermore, it was determined that COVID-19-positive patients with respiratory disease or asthma had critical health conditions(Chen N et al., 2020).

In this study, diabetes showed adverse effects on COVID-19-positive patients followed by respiratory and cardiovascular disease (CVD), respectively. Previously, it was determined that 57.7% COVID-19 positive patients had one or more comorbidities(Bajgain et al., 2021). The long-term effect of elevated blood sugars results in a weakened immune system, with a possible link to ACE2 expressions in cardiac tissues(Ma RCW et al., 2020). Patients with renal disease and those on dialysis were reported to have increased mortality when infected with SARS-CoV-2 virus(Alberic et al., 2020). The ACE2 expression in kidney cells is a unique target for SARS-CoV-2 causing tubular and glomerular damage (Diao et al., 2020).

Moreover, the mortality rate (16.58%) was measured in our study with the highest mortality (42.85%) in critically ill patients. Various studies previously reported mortality percentages in the double digits of 22% to 23%(Ciceri et al., 2020) and determined that a higher degree of inflammation is triggered in critical patients(Henry BM et al., 2020).

Our study revealed a significant effect on hematological parameters. An increased count of leukocytes and neutrophils was realized in critical patients as compared to

moderate and mild groups. However, a significant decrease in lymphocytes was observed. It was determined that leukocytosis and lymphopenia are associated with C-reactive protein(Javanian et al., 2020). The lymphopenia can be used as a diagnostic marker in COVID-19 infection(Zhao et al., 2019). Similarly, we observed a lower count of RBCs and hemoglobin concentration, which was also reported elsewhere(Wang C et al., 2020). The low count of RBCs may arise due to the immune damage that leads to the suppression of the bone marrow, resulting in the gradual increase of anemia, however, no significant effect was seen on the indices of erythrocytes in COVID-19-infected patients.

The decrease in hemoglobin concentration is associated with the severity of the diseaseas, as the concentration of HGB was severe in critical groups of this study. Platelets are important for homeostasis and also play a key role in defense mechanisms in inflammatory conditions (Shahri et al., 2021).

In this study, thrombocytopenia occurred in severe COVID-19 infection. A previous study also reported thrombocytopenia in COVID-19-positive patients and was considered a diagnostic biomarker and severity of the disease(Yang X et al., 2020). The SARSCoV-2 has an impact on megakaryocytic maturation and increases platelet aggregation, which led platelet consumption in the microcirculation of damaged lung tissue. Additionally, the novel coronavirus inhibits erythropoiesis in the bone marrow which consequently causes thrombocytopenia by reducing platelet production(Ulrich et al., 2020).

In our study, an increased level of C-reactive protein (CRP) was reported in critical patients, which showed statistically significant results between the groups, and this corresponds to previous studies(Erol et al., 2021; Huyut et al., 2022), where patients who died from COVID-19 infection had higher CRP levels(Ardestani et al., 2021). In addition, the level of D-dimer was significantly higher in critical patients as compared to the mild and moderate groups. This is also reported in other research studies (Dubey et al., 2021; Guan et al., 2020).

The enzyme lactate dehydrogenase (LDH) level was significantly higher in critical patients. This is also in line with previous research(Erol et al., 2021), which showed an increase in LDH enzymes and indicates that liver dysfunction occurs in COVID-19 disease. Cardiac troponin is a marker of heart muscle damage and was significantly higher in critical patients, which indicates the risk of tissue death, organ failure, or heart attack in patients with COVID-19 disease. An increase in the neutrophil count is associated with elevated troponin levels including an increased risk of acute respiratory syndrome(Terpos et al., 2020). This correlates to our results of an increase in neutrophilic leukocytosis and troponin level. Urea and creatinine were significantly higher in the critical patients compared to the mild and moderate groups which indicates that impairment in kidney function develops in COVID-19 infection. Previous studies also have obtained a similar pattern of results (Mertoglu et al., 2021).

Furthermore, the COVID-19 infection showed a significant effect on cholesterol and high-density lipoprotein (HDL) in critically ill patients when compared to mild and moderate groups of patients. Previous studies advocate our results that patients with COVID-19 infection had significantly decreased levels of cholesterol and HDL(Hu et al., 2020). In this study, we report the depletion of electrolytes in critical patients. This study is in line with previous studies(De Carvalho et al., 2021), which also showed that low serum concentration of electrolytes is measured in severe cases of COVID-19-infected patients(Chen D et al., 2020; Tezcan et al., 2020). In conclusion, the characteristics of the biochemical and hematological laboratory parameters in COVID-19 patients were determined, and obtained different indicators regarding the severity of the disease. The findings will provide important evidence for better diagnosis and treatment of COVID-19 patients in order to improve clinical outcomes.

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- **References**

1. Henry, B. M., Benoit, S. W., de Oliveira, M. H. S., Hsieh, W. C., Benoit, J., Ballout, R. A., ... & Lippi, G. (2020). Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): a pooled analysis and review. Clinical biochemistry, 81, 1-8.

2. Ulrich H, Pillat MM. CD147 as a target for COVID-19 treatment: suggested effects of azithromycin and stem cell engagement. Stem Cell Rev and Rep. 2020; 16:434-440. https://doi.org/10.1007/s1201 5-020
09976-7.

3. Yang X, Yang Q, Wang Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. J Thromb Haemost. 2020; 18: 1469-1472. https://doi.org/10.1111/jth.14848.

4. Karimi Shahri, M., Niazkar, H. R., & Rad, F. (2021). COVID-19 and hematology findings based on the current evidences: A puzzle with many missing pieces. International journal of laboratory hematology, 43(2), 160-168.

5. Javanian M, Bayani M, Shokri M, et al. Clinical and laboratory findings from patients with COVID-19 pneumonia in Babol North of Iran: a retrospective cohort study. Rom J Intern Med. 2020;58(3):161- 167.
https://doi.org/10.2478/rjim-2020-0013.

6. Asghar MS, Kazmi SJH, Khan NA, Akram M, Khan SA, Rasheed U, et al. Clinical profiles, characteristics, and outcomes of the first 100 admitted COVID-19 patients in Pakistan: a single-center retrospective study in a tertiary care Hospital of Karachi. Cureus. (2020) 12:c34. doi: 10.7759/cureus.c34.

7. Chen T, Li G, Liu H, Wan W, Zheng H, Chen C. Clinical characteristics of 132 healthcare worker cases with
COVID-19: a retrospective study from a single center in Wuhan, China. J Med Virol. (2021) 93:1631–8. doi: 10.1002/jmv.26511.

8. Ing EB, Xu QA, Salimi A, Torun N. Physician deaths from corona virus (COVID-19) disease. Occup Med. (2020) 70:370–4. doi: 10.1093/occmed/kqaa088.

9. Dalton CB, Corbett SJ, Katelaris AL. Pre-emptive low cost social distancing and enhanced hygiene implemented before local COVID-19 transmission could decrease the number and severity of cases. Med J Austral. (2020) 212:1–10. doi: 10.2139/ssrn.3549276.

10. Ahmad, M., Beg, B. M., Majeed, A., Areej, S., Riffat, S., Rasheed, M. A., ... & Hafeez, M. A. (2021). Epidemiological and clinical characteristics of covid-19: A retrospective multi-center study in pakistan. Frontiers in Public Health, 9, 644199.

11.Yu, W. B., Tang, G. D., Zhang, L., & Corlett, R. T. (2020). Decoding the evolution and transmissions of the novel pneumonia coronavirus (SARS-CoV-2/HCoV-19) using whole genomic data. Zoological
research, 41(3), 247.

12. Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., ... & Feng, Z. (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England journal of medicine.

13. Bauer CMT, Morissette MC, Stämpfli MR. The influence of cigarette smoking on viral infections:translating bench science to impact COPD pathogenesis and acute exacerbations of COPD clinically. Chest. 2013;143(1):196–206.

14. Zhao Q, Meng M, Kumar R, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a systemic review and meta-analysis. Int J Infect Dis. 2020;96:131-135 https:// doi.org/10.1016/j.ijid.2020.04.086

15. Wang, G., Wu, C., Zhang, Q., Wu, F., Yu, B., Lv, J., ... & Zhong, Y. (2020, May). C-reactive protein level may predict the risk of COVID-19 aggravation. In Open forum infectious diseases

(Vol. 7, No. 5, p. ofaa153). US: Oxford University Press.
16. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020; 95: 834-847. https://doi.org/10.1002/ajh.25829
17.Hu, X., Chen, D., Wu, L., He, G., & Ye, W. (2020). Declined serum high density lipoprotein cholesterol is associated with the severity of COVID-19 infection. Clinica Chimica Acta, 510, 105-110.
18. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cheng, Z. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet, 395(10223), 497-506.
19. Onder, G., Rezza, G., & Brusaferro, S. (2020). Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. Jama, 323(18), 1775-1776.
20. Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., ... & Zhou, Y. (2020). Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International journal of infectious diseases.
21.Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Zhong, N. S. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine, 382(18), 1708
1720.
22. Raimondi, F., Novelli, L., Ghirardi, A., Russo, F. M., Pellegrini, D., Biza, R., ... & Di Marco, F. (2021). Covid19 and gender: lower rate but same mortality of severe disease in women—an observational study. BMC pulmonary medicine, 21(1), 1-11.
23. Stelzig KE, Canepa-Escaro F, Schiliro M, Berdnikovs S, Prakash YS, Chiarella SE. Estrogen regulates the expression of SARS-CoV-2 receptor ACE2 in differentiated airway epithelial cells. Am J Physiol Lung Cell Mol Physiol. 2020;318(6):L1280–L1.
24. Mehra, M. R., Desai, S. S., Kuy, S., Henry, T. D., & Patel, A. N. (2020). Cardiovascular disease, drug therapy, and mortality in Covid-19. New England Journal of Medicine, 382(25), e102.
25. Jakhmola, S., Baral, B., & Jha, H. C. (2021). A comparative analysis of COVID-19 outbreak on age groups and both the sexes of population from India and other countries. The Journal of Infection in Developing Countries, 15(03), 333-341.
26. Magnusson, K., Nygard, K. M., Methi, F., Vold, L., & Telle, K. E. (2021). Occupational risk of COVID-19 in the 1st vs 2nd wave of infection. medRxiv, 2020-10.
Gov.uk.Population of England and Wales. 2019. https://www.ethnicity-facts-figures.service.gov.uk/ukpopulation-by-ethnicity/national-and-regional-populations/population-of-england-andwales/latest(Accessed May 14, 2019).
27. Patanavanich, R., & Glantz, S. A. (2020). Smoking is associated with COVID-19 progression: a meta analysis. Nicotine and Tobacco Research, 22(9), 1653-1656.
28. Xie, J., Wang, Q., Xu, Y., Zhang, T., Chen, L., Zuo, X., ... & Song, Y. (2021). Clinical characteristics, laboratory abnormalities and CT findings of COVID-19 patients and risk factors of severe disease: a systematic review and meta-analysis. Ann Palliat Med, 1928-1949.
29. Plaza, J. J. G., Hulak, N., Zhumadilov, Z., & Akilzhanova, A. (2016). Fever as an important resource for infectious diseases research. Intractable & rare diseases research, 5(2), 97-102.
30. da Rosa Mesquita, R., Francelino Silva Junior, L. C., Santos Santana, F. M., Farias de Oliveira, T., Campos Alcântara, R., Monteiro Arnozo, G., ... & Freire de Souza, C. D. (2021). Clinical manifestations of COVID-19 in the general population: systematic review. Wiener klinische Wochenschrift, 133(7), 377-382.
31. Alizadehsani, R., Alizadeh Sani, Z., Behjati, M., Roshanzamir, Z., Hussain, S., Abedini, N., ... & Islam, S. M. S. (2021). Risk factors prediction, clinical outcomes, and mortality in COVID-19 patients. Journal of medical virology, 93(4), 2307-2320.
32. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507-513

33. Hikmet F, Méar L, Edvinsson Å, Micke P, Uhlén M, Lindskog C. The protein expression profile of ACE2 in human tissues. Mol Syst Biol 2020; 16: e9610.
34. Zhao, C., Bai, Y., Wang, C., Zhong, Y., Lu, N., Tian, L., ... & Jin, R. (2021). Risk factors related to the severity of COVID-19 in Wuhan. International journal of medical sciences, 18(1), 120.
35. Murat, S., Dogruoz Karatekin, B., Icagasioglu, A., Ulasoglu, C., İçten, S., & Incealtin, O. (2021). Clinical presentations of pain in patients with COVID-19 infection. Irish Journal of Medical Science (1971), 190(3), 913-917.
36. Bajgain, K. T., Badal, S., Bajgain, B. B., & Santana, M. J. (2021). Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. American journal of infection control, 49(2), 238-246.
37. Ma RCW, Holt RIG. COVID-19 and diabetes. Diabet Med. 2020; 37:72.
Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17:259–260.
38. Diao B, Feng Z, Wang C, Wang H, Liu L, Wang Cet al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. medRxiv. 2020.
39. Alberici F, Delbarba E, Manenti C et al. Management of patients on dialysis and with kidney transplant during SARS-COV-2 (COVID-19) pandemic in Brescia, Italy. Kidney Int Rep 2020: 5(5): 580– 585.
40. Aveyard, P., Gao, M., Lindson, N., Hartmann-Boyce, J., Watkinson, P., Young, D., ... & Hippisley-Cox, J. (2021). Association between pre-existing respiratory disease and its treatment, and severe COVID-39: a population cohort study. The lancet Respiratory medicine.
41. Ciceri, F., Castagna, A., Rovere-Querini, P., De Cobelli, F., Ruggeri, A., Galli, L., ... & Zangrillo, A. (2020). Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clinical immunology, 217, 10809.
42. Lillicrap, D. (2020). Disseminated intravascular coagulation in patients with 2019-nCoV pneumonia. Journal of Thrombosis and Haemostasis, 18(4), 786.
43. Feng, P., Tianhe, Y., Peng, S., Shan, G., Bo, L., Lingli, L., ... & Jiazheng, W. (2019). Hesketh Richard L. Yang Lian, Zheng Chuansheng. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease, 715-721.
44. Lippi, G., South, A. M., & Henry, B. M. (2020). Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). Annals of clinical biochemistry, 57(3), 262-265.
45. De Carvalho, H., Richard, M. C., Chouihed, T., Goffinet, N., Le Bastard, Q., Freund, Y., ... & Montassier, E. (2021). Electrolyte imbalance in COVID-19 patients admitted to the Emergency Department: a case control study. Internal and Emergency Medicine, 16(7), 1945-1950.
46. Wang, C., Deng, R., Gou, L., Fu, Z., Zhang, X., Shao, F., ... & Li, C. (2020). Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters. Annals of translational medicine, 8(9).
47. Erol, A. T., Aşar, S., BİLGİN, B. Ö., ÇUKUROVA, Z., & SABAZ, S. (2021). Risk factors for 28-day mortality among COVID-19 patients in an intensive care unit of a tertiary care center in Istanbul. Bakırköy Tıp Dergisi, 17(1), 100-107.
48. Mertoglu, C., Huyut, M. T., Arslan, Y., Ceylan, Y., & Coban, T. A. (2021). How do routine laboratory tests change in coronavirus disease 2019?. Scandinavian Journal of Clinical and Laboratory Investigation, 81(1), 24-33.
49. Huyut, M. T., Huyut, Z., İlkbahar, F., & Mertoğlu, C. (2022). What is the impact and efficacy of routine immunological, biochemical and hematological biomarkers as predictors of COVID-19 mortality?. International Immunopharmacology, 105, 108542.
50. Ardestani, A., & Azizi, Z. (2021). Targeting glucose metabolism for treatment of COVID-19. Signal Transduction and Targeted Therapy, 6(1), 1-2.
51. Chen D, Li X, Song Q, Hu C, Su F, Dai J (2020) Hypokalemia and clinical implication in patients with coronavirus disease 2019 (COVID-19)
52. Dubey, D. B., Mishra, S., Reddy, H. D., Rizvi, A., & Ali, W. (2021). Hematological and serum

biochemistry parameters as a prognostic indicator of severally ill versus mild Covid-19 patients: A study from tertiary hospital in North India. Clinical Epidemiology and Global Health, 12, 100806.

53. Tezcan, M. E., Gokce, G. D., Sen, N., Kaymak, N. Z., & Ozer, R. S. (2020). Baseline electrolyte abnormalities would be related to poor prognosis in hospitalized coronavirus disease 2019 patients. New Microbes and New Infections, 37, 100753.

54. Hamming, I., et al., Tissue distribution of ACE2 protien, the functional receptors for SARS coronavirus. A first step in understanding SARS pathogenesis. The journal of pathology, 2004. 203(2): p. 631-637.