

Paraclinical Characteristics of Fatal and Recovered COVID-19 Cases: a Retrospective Study

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ABSTRACT

Introduction: COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). It is a potentially deadly disease with grave consequences for public and global health. This study compared laboratory indices in recovered and fatal COVID-19 cases. **Methods:** In this descriptive-analytical cross-sectional study, sampling was conducted using the total count method, and the data was collected from the Borujerd Health Network's Disease Management Center database. From February 20, 2020, to July 21, 2020, 380 patients with positive PCR tests were included. The extracted data was exported into Stata-14 software. To analyze descriptive objectives, mean, percentage, standard deviation, Chi-squared test, and t-test were used. **Results:** Out of 380 positive COVID-19 cases, 300 patients recovered, and 80 lost their life. More than half of the recovered and fatal cases were men (55.16%). The highest mortality rate belonged to $80 \leq$ years (27.5%). Among fatal cases, 38.75% had no underlying disease, and the most common underlying diseases were diabetes (27.5%), chronic hypertension (18.75%), and malignancy (7.5%). Comparison of laboratory indices revealed a significant difference in the mean LHD, Na, K, BUN, BS, PT, AST, ALT, ALP, and ALP Hb between recovered and fatal cases ($P < 0.05$). **Conclusion:** This finding can help determine patients' prognoses and adjust the treatment approach. Further studies on paraclinical characteristics will shed further light on the pathogenesis of COVID-19 and appropriate treatment measures.

INTRODUCTION

Coronaviruses are a large family of viruses and a subfamily of Coronaviridae with an animal origin, belonging to the order Nidovirales and the genus Coronavirus. They include various causative agents ranging from the common cold virus to severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and COVID-19. In late December 2019, unexplained cases of pneumonia emerged in Wuhan, China. On January 12, 2020, the World Health Organization (WHO) used the temporary label of New Coronavirus-2019 for the new causative virus, and on January 30, 2020, declared the New Coronavirus-2019 epidemic as a public health emergency [1]. COVID-19 is presumed to be transmitted through droplets, close contact, aerosols, and possibly fecal-oral route.

Asymptomatic patients can spread the virus during the incubation period. According to studies, the symptoms of this infectious disease include dry cough, chills, sore throat with shortness of breath with or without fever, and acute respiratory infection syndrome [2].

Coronavirus spread rapidly from China to other countries, including Japan, South Korea, Thailand, Vietnam, Malaysia, Singapore, Nepal, Cambodia, Philippines, Russia, UAE, Australia, Canada, USA, and Europe (France, Germany, Italy, England, Finland, and Sweden) [3]. On February 19, 2020, two confirmed COVID-19 cases were reported in Qom, Iran, and shortly afterward, this contagious disease spread to 31 provinces across the country. With the spread of the disease globally, extensive research has been undertaken, with the

results showing that vulnerable people, including the elderly with underlying diseases, are at more risk of the fatal disease. Some studies have also found that hypertension, diabetes, cardiovascular disease, and immunodeficiency are strongly associated with COVID-19 infection [4]. Also, various studies have shown that age could be an essential factor in predicting the prognosis of the disease so that children and adolescents are the least likely to be infected with COVID-19, and even if they do, they will contract a mild type of disease with no severe side effects [5, 6].

The most critical challenge facing humanity in controlling and managing this emerging disease is its unknown nature, i.e., causing virus characteristics, transmission routes, vulnerable individuals, signs and symptoms, and preventive, diagnostic, and therapeutic methods. Hence, studies on the transmission routes, treatment, and etiology of the disease and its clinical and paraclinical characteristics can effectively monitor the spread of this pandemic. The present study compares paraclinical characteristics in recovered and fatal cases of COVID-19 in Borujerd city, Lorestan province, west of Iran.

MATERIAL AND METHODS

Data collection. In this descriptive, analytical, cross-sectional study, the sampling was performed using the total count method. The study population comprised all suspected COVID-19 cases with a diagnostic test referring to the 16-hour screening centers and Ayatollah Borujerd Hospital in Borujerd, Iran, from February 20 to July 21, 2020. The data was obtained from Borujerd Health Network's Disease Management Center portal. This system contains patients' demographic information, clinical status, underlying diseases, admission to the ICU or homecare, epidemiological data, contact information, laboratory data, diagnostic test results, and treatment outcomes (discharge/death). The data registered in this system was extracted in compliance with ethical issues

ensuring confidentiality, i.e., the anonymity of subjects. Finally, 400 patients with a positive PCR test were included in the study. The Ethics Committee of Lorestan University of Medical Sciences approved this project (Code No.: IR.LUMS.REC.1399.051).

Inclusion and exclusion criteria. All patients who tested positive for PCR were eligible for inclusion in the study without any age or sex restrictions. The patients with incomplete recorded data in the system were excluded. Individuals diagnosed as suspected or probable cases with diagnostic tests but negative PCR were also excluded from the study.

Statistical analysis. The extracted data was exported to the Stata-14 software. For the analysis of data, mean (standard deviation), frequency (percentage), Chi-Square, and t-test were used. A significance level of 0.05 was considered in this study.

RESULTS

Out of 387 COVID-19 cases, seven were excluded from the study due to incomplete information, and 380 positive cases were finally included. More than half of the recovered and fatal cases were male (55.16%). More than 80% of patients (recovered and fatal) lived in urban areas and less than 20% in rural areas. About 8% and 10% of cases in the recovered and fatal groups had a history of drug abuse, respectively. CT scan of lung results revealed abnormalities in more than 90% of recovered and fatal cases indicative of lung involvement. Blood type A was the most abundant blood type in the recovered (33.88%) and fatal (46.43%) cases. About 37.67% of patients in the recovered group had an underlying disease, while more than half the cases (61.25%) had underlying diseases in the fatal group. The results showed no significant difference between recovered and fatal groups in terms of gender, place of residence, history of substance abuse, and blood type ($P>0.05$). At the same time, there was a statistically significant difference between underlying diseases in the two groups (Table 1).

Table 1. Comparison of demographic variables in recovered and fatal cases of COVID-19 disease

Variables		Recovered cases (No.=300)	Fatal cases (No.=80)	Chi-2	P-value
Sex	Male	163(54.33)	44(55)	0.01	0.9851
	Female	137(45.67)	36(45)		
Place of resident	City	242(80.67)	65(81.25)	0.01	0.9792
	Village	58(19.33)	15(18.75)		
History of drug abuse	No	276(92)	72(90)	0.32	0.5561
	Yes	24(8)	8(10)		
Blood type	A	41(33.88)	13(46.43)	3.7	0.2982
	B	33(27.27)	5(17.86)		
	AB	9(7.44)	4(14.29)		
	O	38(31.4)	6(21.43)		
Chest X-ray	Abnormal	275(94.83)	71(95.95)	0.15	0.6653
	Normal	15(5.17)	3(4.05)		
Underlying disease	No	187(62.33)	31(38.75)	14.3	0.0001
	Yes	113(37.67)	49(61.25)		

According to the results, the highest death rate associated with COVID-19 disease belonged to the age

group > 80 years (27.5%), and in the age group under 10 and 20-29 years, no fatal COVID-19 case was reported (Fig. 1).

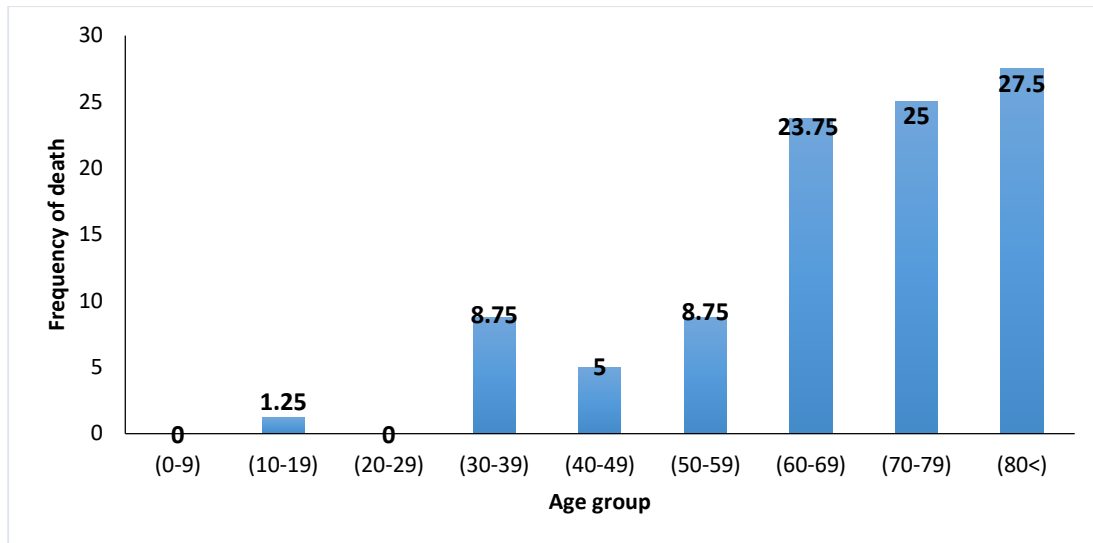


Fig. 1. Distribution of COVID-19 mortality by age groups

Concerning the history of underlying disease, our analysis showed that in the fatal cases group, 38.75% had no an underlying disease, and the most common underlying diseases were diabetes (5 27.2%), chronic

hypertension (18.75%), and malignancy (7.5%) (Fig. 2). In the recovered COVID-19 group, 67.33% had no underlying disease, and diabetes (13.67%) and chronic hypertension (10.33%) were the most prevalent ones (Fig. 3).

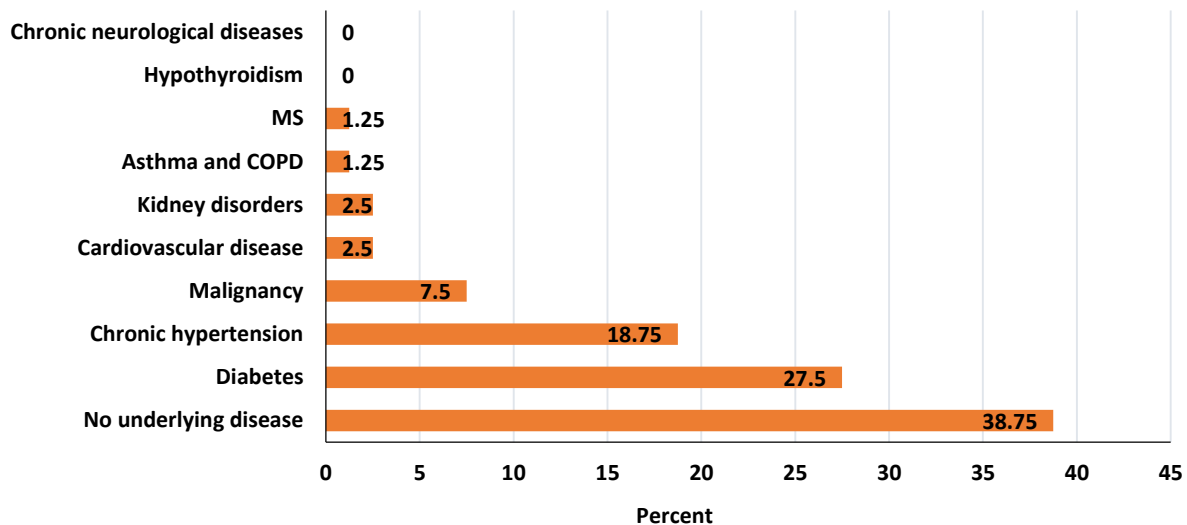


Fig. 2. Distribution of underlying diseases in fatal cases of COVID-19.

A comparison of paraclinical characteristics in recovered and fatal COVID-19 disease cases revealed a statistically significant difference between the mean LHD, Na, K, BUN, BS, PT, AST, ALT, ALP, and Hb in recovered and cases ($P < 0.05$). However, other paraclinical indices, i.e., the mean PCK, Cr, Mg, Ca, and PLT, exhibited no significant difference in the recovered and fatal cases ($P > 0.05$) (Table 2).

DISCUSSION

According to our study, the highest death rate associated with COVID-19 belonged to the age group above 80 years (27.5%). A new study indicated that COVID-19 predominantly affects middle-aged and older adults [7]. In line with this study, most of the patients in our study were middle-aged and elderly. A study on 199 patients found that the mean age for the fatal SARS cases was 52 years [8]. One possible explanation for this result may be that pulmonary aging is associated with impaired lung cells and frequent structural and functional changes

in the respiratory tract, undermining lung function [9]. Elderly patients are at higher risk of developing acute respiratory distress syndrome (ARDS) [10].

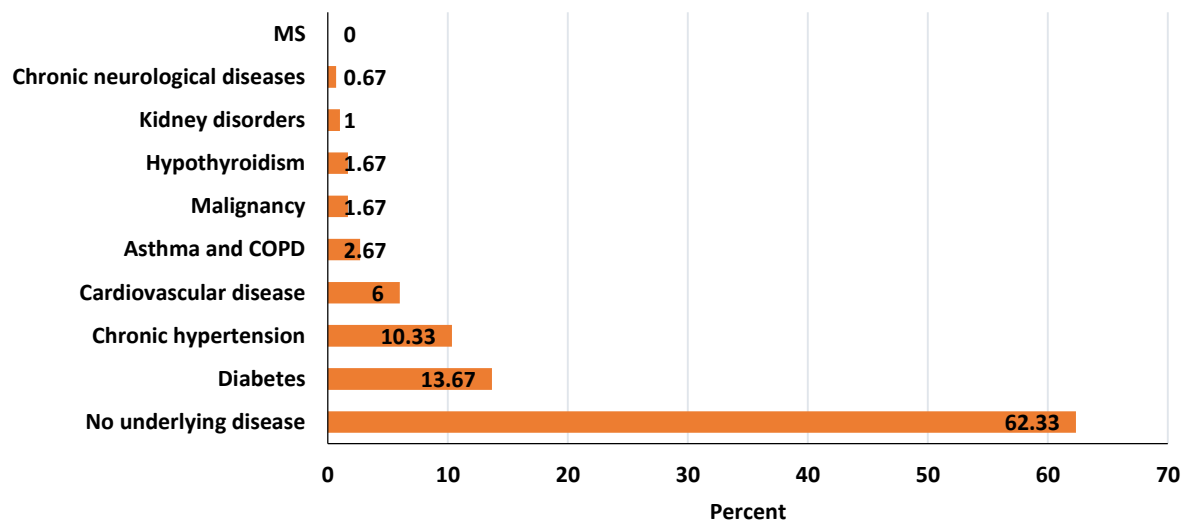


Fig. 3. Distribution of underlying diseases in patients recovering from COVID-19.

Table 2. Paraclinical indices in recovered and fatal COVID-19 cases.

Paraclinical indices	Mean \pm SD		T-test	P-value
	Recovered	Deaths		
PCK	251 \pm 143.9	224 \pm 167.1	0.34	0.321
LHD	689 \pm 235.5	1208 \pm 203.5	-3.17	0.023
Na	136.7 \pm 3.4	135.7 \pm 3.7	2.09	0.012
K	4.06 \pm 0.4	4.2 \pm 0.5	-2.94	0.013
BUN	41.48 \pm 30.0	61.19 \pm 50.9	-5.26	0.001
Cr	1.47 \pm 1.04	1.69 \pm 0.9	-1.53	0.325
BS	135.5 \pm 91.2	198.6 \pm 105.9	-3.79	0.011
PT	12.9 \pm 1.5	14.1 \pm 3.9	-2.98	0.019
AST	46.09 \pm 65.6	464.4 \pm 119.2	-2.33	0.021
ALT	34.11 \pm 34.8	494.1 \pm 149.7	-2.05	0.021
ALP	187.04 \pm 89.7	301.7 \pm 233.5	-2.7	0.023
Mg	2.2 \pm 0.3	2.1 \pm 0.2	0.6	0.351
Ca	9.1 \pm 0.5	8.9 \pm 1.08	1.12	0.235
PLT	193.2 \pm 76.2	199.7 \pm 80.8	-0.6	0.558
Hb	13.7 \pm 1.7	13.2 \pm 2.2	1.9	0.013

The results of our study showed that in the fatal group, more than half of the cases (61.25%) had an underlying disease, with diabetes (27.5%), chronic hypertension (18.75%), and malignancy (7.5%) being the most common underlying diseases. In the study of Deng *et al.* (2020), most patients in the fatal group had underlying diseases, especially hypertension, lung disease, and heart disease [11], consistent with our findings. Diabetes is assumed to increase the risk of infection and possibly delay recovery from infectious diseases. Deng *et al.* (2020) reported no significant difference between the mortality and recovery rate in diabetes patients, which is inconsistent with our findings [11]. Recent studies have also demonstrated that diabetes is not significantly associated with the onset, progression, and prognosis of ARDS [12, 13].

Hematologic changes frequently occur in SARS-CoV-2 virus infections and other infectious diseases. Laboratory abnormalities, especially hematological changes, allow assessing the status of SARS-CoV-2 infection. The most common hematological changes are lymphocytopenia [14, 15], neutrophilia [16, 17], eosinopenia [18, 19], mild thrombocytopenia [15] and to a less degree thrombocytosis [14, 20]. Leukocyte count may be normal or display a decreasing or increasing trend [21-23]. According to a meta-analysis, leukocytosis, lymphopenia, and thrombocytopenia were linked with higher severity and even fatality in COVID-19 cases [24]. As the disease progresses, hematological changes become more pronounced, with a significant decrease in lymphocyte counts, more evident in fatal cases than recovered cases [23]. Our study revealed that ALT, AST, and creatinine levels in the fatal cases were higher than in

recovered cases, consistent with the study of Deng *et al.* (2020) [11]. Previous studies have also shown elevated transaminases in patients with MERS and SARS [23, 25]. A recent study found that elderly patients infected with COVID-19 have higher CRP levels [7]. In addition, CRP is a significant predictor of disease severity in SARS [23, 26]. Hematological changes may predict the patient's clinical outcome [27].

Various studies suggest that lymphocytopenia is the most common alteration among all hematological abnormalities from patients' admission to death [7, 28, 29]. Among data obtained from a complete blood count is the ratio of parameters, the interpretation of which is of utmost clinical value [11, 30]. A possible explanation for the dramatic reduction in lymphocyte count may include (a) direct infection of these cells, which leads to lysis by SARS-CoV-2, (b) possible lymphocyte apoptosis induced by the production of large cytokines, (c) atrophy of lymphoid organs such as the spleen, impaired lymphocyte circulation, and (d) lymphocyte proliferation inhibitions by lactic acidosis, which is more evident in cancer patients [27].

Platelet morphology also exhibits abnormalities in the platelet count, which may indicate a severe myelopoietic disorder in patients with acute symptomatic COVID-19. This disorder may be related to the cytokines storm, which appears with the progression of COVID-19 pneumonia [31-33].

Other laboratory abnormalities included increased erythrocyte sedimentation rate (ESR), elevated lactic dehydrogenase (LDH), and CRP levels, in addition to changes in heart, kidney, and liver function, to mention a few [1]. In Wuhan, China, a survey on epidemiological, clinical, laboratory, and radiological features and treatment and clinical outcomes of 41 infected SARS-CoV-2 patients showed a decline in leukocyte levels and lymphopenia with lower lymphocyte counts in patients admitted to the ICU compared to patients not admitted to this ward [21].

According to Jin *et al.* (2020) [1], it is necessary to monitor patients with absolute low lymphocyte count or a dramatic reduction in CD4 and CD8 T cell counts. Hence, re-evaluating the hematological changes after three days is recommended [1]. Analysis of 1099 admitted COVID-19 patients data in 552 hospitals from 30 provinces in China showed that 83.2% had lymphopenia, 36.2% thrombocytopenia, and 33.7% leukopenia, the majority with elevated CRP [34]. Also, In a retrospective cohort study, lymphopenia was reported in 40% of these patients [23].

Leukocytosis, increased LDH, ALT, serum ferritin, creatine kinase (CK), and creatinine were associated with COVID-19 mortality. The lymphocyte number is significantly higher in the recovered cases than in the fatal cases [35]. In both survivors and non-survivors groups,

LDH elevates at the outset of COVID-19 but drops from day 13 in the survivors [35, 36].

A retrospective study on 138 SARS-CoV-2 patients in Zhongnan Hospital, Wuhan University, China, compared the laboratory characteristics of patients admitted to the ICU with those admitted to other wards and revealed several significant indices such as higher leukocyte, neutrophil counts, D-Dimer, CK, urea, creatinine, troponin, prolactin, LDH, AST ALT levels as well as total bilirubin in the first group [37]. In addition, most patients displayed lymphopenia during the admission, which tended to deteriorate progressively in the deceased patients [22, 23].

Considering blood clotting in the most severe COVID-19 cases, the thrombin generation assay (TGA) test can be helpful because it can assess both phenotypes, i.e., hyperactivity and impaired coagulation [38, 39]. Further studies should explore thrombin generation potential (CAT method) relative to the coagulation coefficient described in COVID-19 patients. Eilinghaus *et al.* (2020) reported an association between blood types ABO with susceptibility to COVID-19. They concluded that blood type "O" was associated with a lower risk of infection by SARS-CoV-2 than other types, while blood type A was linked to a higher risk of the disease [40]. Our results showed no significant difference between recovered and fatal cases concerning blood groups, which can be attributed to the small sample size in our study, as this relationship may gain significance with larger sample sizes.

Our study revealed noticeable hematologic changes in recovered and fatal cases of COVID-19 disease. Available data suggest that several hematological parameters may alter throughout SARS-CoV-2 infection, some of which may be important for future studies as predictors of adverse clinical outcomes, such as ICU admission or even death. Therefore, further investigations on other blood and biochemical abnormalities during SARS-CoV-2 infection are essential to shedding light on the pathogenesis of COVID-19 and clinical monitoring of treatment. Some patients who may have developed the disease but were not referred to medical centers or undergone laboratory tests to confirm their disease were excluded from the study. That is why we only studied individuals referred to medical centers and who had undergone diagnostic tests.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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