

ORIGINAL PAPER
INFECTIOUS DISEASES

Evaluation of epidemiology, clinical features, prognosis, diagnosis and treatment outcomes of patients with COVID-19 in West Azerbaijan Province

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Abstract

Background: COVID-19 is considered a widespread concern in global public health. Diagnoses of COVID-19 in some cases are necessary because of severe prognosis. In this study, epidemiologies, clinical and demographic characteristics of patients with COVID-19 were studied in Taleghani Hospital, Urmia, Iran.

Methods: This descriptive-analytical cross-sectional study was carried out on 215 patients with COVID-19 during March and April 2020. Approved COVID-19 case was considered as a person with a positive respiratory sample performed by at least one of two RT-PCR methods or genetic sequencing. ANOVA repeated measure, independent t-test and logistic regression were done. A $P < .05$ was considered significant.

Results: The mean age of patients was 50.93 ± 17.92 years. Regarding gender, there were 91 females (42.3%) and 124 males (57.7%). The mean hospital stay, the temperature at admission, and onset of symptoms were 4.91 ± 3.68 days, $37.40 \pm 0.96^\circ\text{C}$ and 5.88 ± 4.80 days, respectively. Close contact with suspected people was found in 10.2% of patients. Additionally, 44 patients (20.5%) were smokers. Shortness of breath and cough were found in 62.8% and 49.3% of patients. Diabetes mellitus and hypertension were the most common comorbidities of patients. Regarding lung involvement, 33 patients (33%) were normal, most of the patients ($n = 71$) had 5%-25% involvement in their lung and a minority of patients ($n = 13$) had a severe condition of 50%-75% lung involvement. The association between smoking and mortality was tested using chi-square showing no significant difference ($X^2: 2.959$, $P = .085$). There was no significant difference between AST, ALT, ALP, total, direct Bilirubin, lung involvement and suffering from fever ($P > .05$). High Spo2 can increase the chance of recovery by 24% with each unit reduction. Kidney involvement increases the chance of death by about 80% (95% CI: 0.104-0.013). The odds ratio of spo2 for recovery of COVID-19 was 1.24 (95% CI: 1.014-1.528; $P = .037$). Kaletra with odds ratio of 31.960 had the most highest effect on recovery following COVID-19 ($P = .043$).

Conclusion: COVID-19 involves different organs of the body with different severity. In the meantime, smoking was not a risk factor for the virus or associated with severe manifestations of the disease. Patients with high creatinine and CPK, pulmonary involvement above 25%, and hypoxemia had a higher mortality rate. Increase of Spo₂ by 1% can improve the patients by 24%. The results indicated that Kaletra had the most highest effect on improvement following COVID-19.

1 | INTRODUCTION

Coronavirus disease (COVID-19) is caused by SARS-COV2, and is considered a causative agent of a potentially deadly disease resulted widespread concern in global public health. Coronavirus is one of the largest pathogens that mainly target the human respiratory tract. Previous coronavirus outbreaks have included severe acute respiratory syndrome (SARS) -CoV and Middle East Respiratory Syndrome (MERS) -CoV, which have long been known to be very threatening to public health. In late December 2019, a number of patients were admitted to hospitals whose initial diagnosis was pneumonia with unknown cause. These patients were associated with a wholesale market for seafood and wet animals in Wuhan, Hubei Province, China.^{1,2} Preliminary reports predicted the launch of a potential COVID-19 epidemic, based on estimates of the number of reproductions for the COVID-19, which was calculated more than 1 (ranging from 2.24 to 3.58).³ On February 19, 2019, 66 402 COVID-19 infections have been confirmed in China. This number of infections has exceeded the prevalence of severe acute respiratory syndrome in China. Epidemiological studies of primary cases of COVID-19 showed that many cases were exposed to the seafood market in Wuhan, China.⁴ A study by Wang et al showed that from 10 January to 24 January, 2019, the number of people infected with the new Coronavirus-2019 infection in China increased 31.4 times. They estimated the mortality rate for COVID-19 to be 2.84% based on the number of patients. The researchers also found that the male-to-female mortality ratio was 3.25 to 1, the median age of death was 75 years, the median time from the first symptoms to death was 14 days, and the median time from the initial symptoms to death in people aged 70 years and older (11.5 days) was shorter than people under 70 years (20 days). These findings suggest that the disease may progress more rapidly in elderly than in young people especially in metropolis.^{5,6} COVID-19 can cause multi-organ failure threatening the health of patients including lung and kidney involvement.⁷⁻¹¹ Nowadays there is no specific drug to treat COVID-19 patients because of the complexity of the SARS-COV2.^{12,13}

A study by Li et al reported that the mean age of 425 patients infected with COVID-19 was 59 years, of which 56% were men. The mean incubation period was 2.5 days, and almost half of the adult patients were 60 years and older. In the early stages, the number of infected patients doubled every 7.4 days. The production rate of transmission (R₀) of the disease from the infected person was 2.2. The incubation period for COVID-19 is thought to be 14 days after

exposure, with most cases occurring approximately 4 to 5 days after exposure.¹⁴ Diagnoses of coronavirus infections in most cases are unnecessary because most patients have mild or moderate syndrome with a good prognosis. However, it may be required to identify an etiological factor in epidemiological studies, especially during the epidemic. Since the new COVID-19 has not been found in humans before, no specific vaccine or treatment has been provided. The number of cases is rapidly increasing. Therefore, it is important to diagnose all suspected cases as soon as possible and to isolate them quickly for cutting off the source of infection. Conventional diagnostic testing methods, such as assessment to detect antiviral antibodies or viral antigens, have been clinically developed and used. New diagnostic solutions, including PCR-RT and microscopic-based measurements, may be effective in monitoring epidemiological measures, along with preventive measures. COVID-19 nucleic acids can be detected in samples such as nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood and faeces.^{15,16} Clinical symptoms and graphic findings provide an acceptable diagnosis. In a study, 1099 cases of the new coronavirus infection were reported. They found that fever (78.9%) and cough (67.7%) were the most common symptoms, and diarrhoea (3.7%) and vomiting (5%) were rare. Abnormalities in CT images of the chest were observed in 96% of patients infected with COVID-19, and in 82.1% of them lymphopenia was recorded.¹⁷ In addition to pulmonary involvement, COVID-19 could target other organs, including coagulation disorders in patients who died, compared with patients who survived.¹⁸ Neurological manifestations in 36.4% and liver involvement in 14.3%-58% of patients with COVID-19 have been reported.^{19,20} Acute kidney injury (AKI) risk has been reported to be 28% and at the time of hospitalisation 10% of patients have an increase in creatinine accompanied by proteinuria (60%) and urinary incontinence (48%). Also, AKI can be considered as a prognostic factor in the mortality of patients with COVID-19, in which the mortality is 5.3 times higher in patients with AKI.²¹

There are several new medical treatments that are used in COVID-19 patients, and The United States Food and Drug Administration (FDA) has given permission to give some drugs in emergency conditions for such a situation, but the only drug with FDA approval is remdesivir,²² other antivirals such as favipiravir, mulnopiravir (mk-4482), lopinavir, ritonavir is used too, among them favipiravir can be helpful specially during virmic phase of covid -19 by blocking the Replication of virus genetic material²³⁻²⁵; dexamethasone and corticosteroids are helpful in severe

COVID-19 patients requiring supplementary oxygen but its effect is not proved in earlier stage of disease with mild disease²⁶; recombinant ACE-2 that can prevent COVID-19 virus entering inside the cells, but up to now there is not any trial in animals or human, but there are some on-going clinical trials²⁷; convalescent plasma and monoclonal antibodies in such a way that sing plasma of recovered patients from COVID-19 or monoclonal antibodies are also be helpful in treating course for COVID-19 patients but, large RCT is undergoing for better evaluation of the this technique effect²⁸; interfrons: inhaled form of interferon called SNG001 lowers the risk of severe COVID-19 in infected patients in a small clinical trial²⁹ and also blood filtration that can omit harmful cytokines from blood in the patients with severe COVID-19 patients to end organ damage caused by cytokines.³⁰

Given the emergence of this coronavirus disease, and the World Health Organization's announcement of a pandemic in February 2020, further studies are needed to identify the symptoms of the disease, prognosis, graphical and paraclinical findings for a definitive diagnosis. In this study, clinical and demographic characteristics of patients with COVID-19 were studied in Taleghani Hospital, Urmia, Iran.

2 | METHODS

The present study was a descriptive-analytical cross-sectional that has been performed on 215 patients with COVID-19 during March and April 2020 in Taleghani Hospital, Urmia, West Azerbaijan, Iran. After receiving the approval of the ethics committee from Urmia University of Medical Sciences, this study was performed on the existing files. In this case, the existing scans of the patient with COVID-19 were evaluated and the variables of age, gender, body mass index, comorbidities, symptoms, liver profile, lipid profile, haemoglobin, platelet, WBC, lymphocyte, neutrophil, C-reaction protein (CRP), Polymerase chain reaction (PCR), Creatine phosphokinase (CPK), creatinine, urea, potassium, magnesium, sodium and medications were recorded. The sampling method in this study was census (all patients in March and April). Unreadable files were removed from the study. Clinical features of suspected cases were considered to have at least two criteria of the following conditions: fever and/or respiratory symptoms; radiographic evidence of pneumonia and low or normal white blood cell counts or low lymphocyte levels. Also, epidemiological history was at least one criterion of the following conditions: travel history to epidemic areas within 14 days of the onset of symptoms; a history of contact with a patient with fever or respiratory symptoms in the epidemic areas within 14 days of the onset of symptoms; a history of close contact with approved COVID-19. With a strict definition, all cases that met the criteria of clinical characteristics but do not comply with epidemiological history was considered as suspicious cases. Approved COVID-19 case was considered as a person with a positive respiratory sample performed by at least one of two Reverse transcription polymerase chain reaction (RT-PCR) methods or genetic sequencing. After entering the required

information, the data were provided to the statistical analyst to be analysed based on the studied objectives.

2.1 | Ethical issues

This research was performed according to the Declaration of Helsinki. Informed written consent was obtained from the patients, and the study was approved by the Ethics Committee of Urmia University of Medical Sciences (ethical code: IR.UMSU.REC.1399.017) available at <https://ethics.research.ac.ir/ProposalCertificateEn.php?id=126928&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true>.

2.2 | Statistical analysis

After entering the required data from the patient's records, the data were analysed using SPSS version 18. Besides, descriptive data for continuous variables and qualitative statistics were used as bar charts and tables. Mean difference tests (independent t-test) and ANOVA repeated measure was used to compare the patients as well as logistic regression was applied to predict the factors affecting the mortality of COVID-19. Logistic regression gives us Odds Ratio (OR), a measure of association between exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure.

3 | RESULTS

The mean age of patients was 50.93 ± 17.92 years. Regarding gender, there were 91 females (42.3) and 124 males (57.7). The mean hospital stay, the temperature at admission, and onset of symptoms were 4.91 ± 3.68 days, $37.40 \pm 0.96^\circ\text{C}$, and 5.88 ± 4.80 days, respectively. Close contact with suspected people was found in 10.2% of patients. Additionally, 44 patients (20.5) were smokers. Paraclinical characteristics of patients with COVID-19 were presented by the mean and standard deviation. Also, hemodynamic and respiratory features of patients with COVID-19 were presented by the mean and standard deviation (Table 1). Creatinine at admission, on the first day and the third day significantly declined (Table 2). Repeated measure analysis showed a decreasing trend after admission between two groups of cured patients and died patients (Figure 1). Also, there is another analysis on the creatinine level in three points by gender (Table 3 and Figure 2).

Common symptoms, comorbidities, lung and renal involvements were investigated and reported as frequency and percent. Shortness of breath and cough were found in 62.8% and 49.3% of patients. Diabetes mellitus and hypertension were the most common comorbidities of patients, in which 18.1% and 20.5% reported, respectively. Regarding lung involvement, 33 patients (33%) were normal, most of

Variables	Minimum	Maximum	Mean	SD
WBC (10 ⁹ /L)	1400.00	131 000.00	10 079.24	14 235.73
NEUT (%)	8.00	100.00	71.63	14.82
LYMPH (%)	1.50	80.00	22.42	13.07
HB (g/dL)	5.00	21.00	13.96	2.22
Platelet (10 ⁹ /L)	75.00	760.00	227.88	105.75
CRP (mg/L)	1.00	2.00	1.64	0.47
ESR (mm/h)	0.90	215.00	35.12	34.39
CPK (U/L)	2.40	1081.00	163.18	192.77
LDH (U/L)	5.20	3173.00	527.22	402.56
ALP (U/L)	11.00	1633.00	190.46	150.91
ALT (U/L)	11.00	2435.00	51.61	196.28
AST (U/L)	11.00	4892.00	88.82	475.62
BILIT (mg/dL)	0.20	6.20	0.84	0.94
BILID (mg/dL)	0.10	2.90	0.31	0.41
Spo2 (%)	55.00	99.00	91.01	7.40
Respiratory rate (bpm)	3.00	32.00	19.68	3.89
SBP (mm Hg)	85.00	180.00	116.55	13.63
DBP (mm Hg)	50.00	110.00	75.41	9.03

TABLE 1 Clinical and paraclinical characteristic of patients with COVID-19

Variable	Expired	Mean	SD	F	P value
Creatinine at admission (mg/dL)	Yes	3.39	3.98	4.833	.039
	No	1.60	0.62		
Creatinine at first day (mg/dL)	Yes	3.12	3.46		
	No	1.28	0.54		
Creatinine at third day (mg/dL)	Yes	2.72	1.95		
	No	1.14	0.50		

TABLE 2 Comparison of creatinine levels between two groups of cured patients and died patients

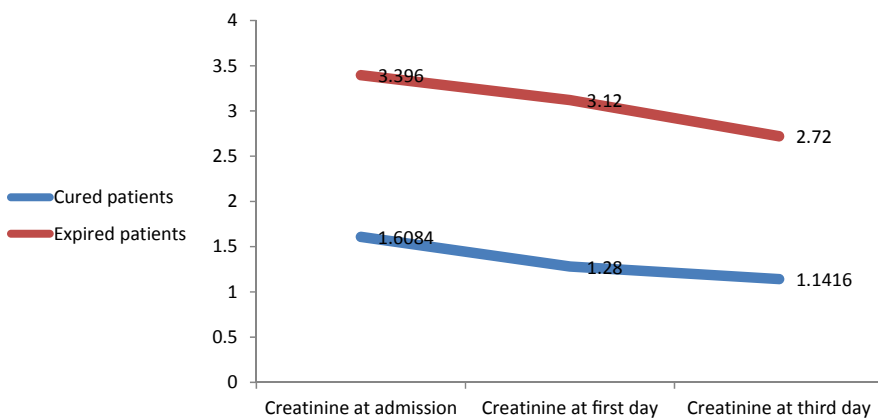
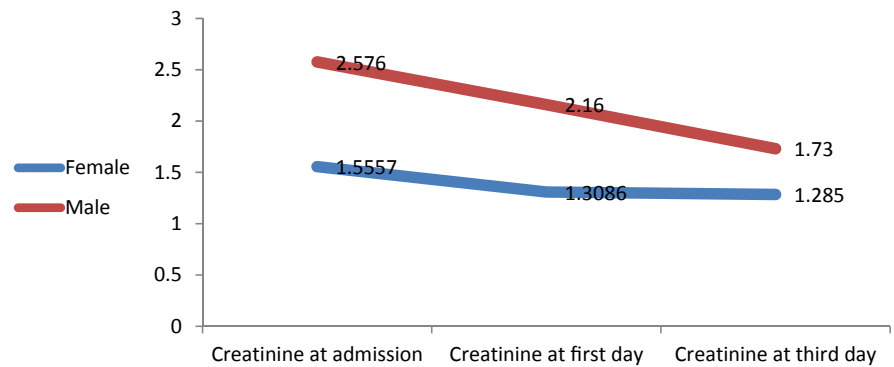


FIGURE 1 Comparison of creatinine levels between two groups of cured patients and died patients

TABLE 3 Comparison of creatinine levels between two groups of men and women patients

Variable	Gender	Mean	Std. Deviation	F	P value
Creatinine at admission (mg/dL)	Female	1.55	0.59	7.350	.013
	Male	2.57	2.83		
Creatinine at first day (mg/dL)	Female	1.30	0.59		
	Male	2.16	2.53		
Creatinine at third day (mg/dL)	Female	1.28	0.59		
	Male	1.73	1.63		

FIGURE 2 Comparison of creatinine levels between two groups of men and women patients

the patients ($n = 71$) had 5%-25% involvement in their lung and a minority of patients ($n = 13$) had a severe condition of 50%-75% lung involvement. Additionally, 32 patients (14.9%) had creatinine more than 1.5 mg/dL (Table 4).

Regarding liver profile, 88.4% of patients had ALP more than 115 U/L; 12% of patients had ALT more than 56 U/L; 23.2% of patients had AST more than 40 U/L; 95.9% of patients had LDH more than 222 U/L. Platelet count in 17.3% of patients was below 150 000 per μ L; ESR above 20 mm/h was observed in 58.7% of patients. Total bilirubin among 9% was high and 91% had normal range (0.2-1.2 mg/dL). Direct bilirubin among 8% was high and 92% had normal range (0-0.4 mg/dL). In overall, nine patients received IVIG and two of nine patients died (22.2%). Among 19 patients who passed away, 15 patients were hospitalised in ICU, so a total of 175 patients (81.4%) had no history of hospitalisation in ICU (Table 5). The association between smoking and mortality was tested using chi-square showing no significant difference ($X^2:2.959$, $P = .085$). There was no significant difference between AST, ALT, ALP, total, direct Bilirubin, lung involvement and suffering from fever ($P > .05$) (Table 6).

To prevent estimation bias, variables with a significance level less than of 0.2 were entered in the logistic model. Link function was logit with significant fitting ($P < .05$) and large goodness of fit ($P > .05$). In the binary logistic regression model, high Spo2 can increase the chance of recovery by 24% with each unit reduction. Kidney involvement increases the chance of death by about 80% (95% CI: 0.104-0.013). The odds ratio of spo2 for recovery of COVID-19 was 1.24 (95% CI: 1.014-1.528; $P = .037$) (Table 7).

4 | DISCUSSION

In our study, the creatinine levels of the patients with COVID-19 decreased during hospitalisation, 18 patients who were admitted to the ICU had a creatinine level above 1.5 mg/dL, and 12 patients who died had a high creatinine level, according to a systematic review, 193 patients had high creatinine levels at the time of hospitalisation in 10% of patients, and 22% of patients experienced an increase in creatinine levels within 5 days of hospitalisation.³¹ In various studies, an increase in creatinine in patients with COVID-19 has been reported from 0.5% to 19%.³² Huang et al found that 98% of patients with COVID-19 had fever, of which 78% had a temperature above 38°C. They observed 76% of patients with cough, 44% of patients with fatigue and myalgia and 55% of patients with dyspnoea. In addition, the patients had sputum expectoration (28%), headache (8%), hemoptysis (5%) and diarrhoea (3%). Laboratory tests showed that 25% of infected patients had leukopenia and 64% had lymphopenia. Aspartate aminotransferase levels are elevated in 37% of patients. Myocarditis was diagnosed in 12% of patients, and very sensitive troponin I levels was significantly increased in these patients. Abnormalities in chest CT images were observed in 100% of patients. Grinding glass-like and consolidation were found in 37% of the lungs on both sides of infected patients.³³

Zhao et al stated ACE2 as a receptor for the COVID-19. In the normal human lung, ACE2 is expressed in type 2 and 1 alveolar epithelial cells, of which 83% of type 2 alveolar cells express ACE2. Men have higher levels of ACE2 in their alveolar cells than women. Asians have higher levels of ACE2 expression in their alveolar cells

TABLE 4 The frequency of symptoms, comorbidity, renal and lung involvements in patients with COVID-19

Symptoms	Frequency	Percent
Shivering	33	15.3
Lethargy	3	1.4
Pharyngitis	10	4.7
Shortness of breath	135	62.8
Cough	106	49.3
Dry cough	33	15.3
Diarrhoea	25	11.6
Myalgia	58	27
Weakness	45	20.9
Lung involvement		
Normal	33	16.1
Less than 5%	64	31.2
5%-25%	71	34.6
25%-50%	24	11.7
50%-75%	13	6.3
Comorbidity		
Asthma	19	8.8
Heart disease	11	5.1
Rheumatism	4	1.9
DM	39	18.1
HTN	44	20.5
Autoimmune disease	2	0.9
Lupus	1	5
Renal involvement		
Positive	32	14.9
Negative	183	85.1

than in white and African-American populations. Connection of new coronavirus-2019 to ACE2 increases the expression of ACE2, which can lead to damage to alveolar cells. Injury to alveolar cells can in turn cause a series of systemic reactions and even death. They also confirmed that Asian men were more prone to COVID-19.³⁴ Studies to find acceptable medication is ongoing and many drug are tested in clinical trials such as bromhexine effect on COVID-19.³⁵ A review of Rahmat et al on the new coronavirus included a total of 50 studies. According to the World Health Organization, it is necessary to examine all people with acute respiratory diseases with a history of travel to Saudi Arabia or countries with epidemics of this new virus.^{36,37} These results show the importance of knowledge about the epidemiological aspect of this disease. Guan et al reported 1099 cases of the new coronavirus infection. They found that fever (78.9%) and cough (67.7%) were the most common symptoms. Diarrhoea (3.7%) and vomiting (5%) were rare. Abnormalities in CT images of the chest were observed in 96% of the patients infected with the new Coronavirus-2019, and lymphocytes were recorded in 82.1% of them.¹⁷ In the study of Besharat et al in Tehran, the clinical and demographic characteristics of patients who died following COVID-19

TABLE 5 Abnormality of paraclinical tests in patients with COVID-19

Abnormality		Frequency	Percent
ALP (U/L)	Yes	114	88.4
	No	15	11.6
ALT (U/L)	Yes	20	12.0
	No	147	88.0
AST (U/L)	Yes	39	23.2
	No	129	76.8
LDH (U/L)	Yes	165	95.9
	No	7	4.1
Platelet ($10^9/L$)	Yes	35	17.3
	No	167	82.7
ESR (mm/h)	Yes	98	58.7
	No	69	41.3
Direct bilirubin (mg/dL)	Yes	9	8.0
	No	103	92.0
Total bilirubin (mg/dL)	Yes	10	9.0
	No	101	91.0
Fever ($^{\circ}C$)	Yes	92	43.6
	No	119	56.4

TABLE 6 Association of paraclinical abnormality and lung involvement with fever in patients with COVID-19

Abnormality		Fever		X^2, P value
		Yes	N	
AST (U/L)	Yes	14	24	0.927, .336
	No	58	69	
ALT (U/L)	Yes	7	13	0.733, .392
	No	65	79	
ALP (U/L)	Yes	50	62	0.689, .406
	No	5	10	
Total bilirubin (mg/dL)	Yes	2	8	1.772, .183
	No	42	59	
Direct bilirubin (mg/dL)	Yes	2	7	1.195, .274
	No	42	61	
Lung involvement (%)	Normal	13	20	1.797, .773
	Less than 5%	26	36	
	5%-25%	35	34	
	25%-50%	11	13	
	50%-75%	5	8	

development were consistent with this study.³⁸ In this study, we showed that COVID-19 can involve multiple organs such as liver and kidney. Samimi Ardestani et al³⁹, showed that olfactory dysfunction is one of the other complications following COVID-19 and about 86% of the patients were recovered from olfactory dysfunction approximately a month after the onset of olfactory dysfunction.

TABLE 7 Logistic regression to predict the binary outcome (recovery following COVID-19)

Variable	B	SE	Wald	P value	Odds ratio	95% CI	
						Lower	Upper
Spo2 (%)	0.219	0.105	4.365	0.037	1.244	1.014	1.528
HB (g/dL)	-0.094	0.244	0.148	0.700	0.910	0.564	1.470
Age (y)	0.006	0.038	0.024	0.877	1.006	0.934	1.083
Positive chest-X ray	1.747	2.065	0.716	0.398	5.736	0.100	328.26
Positive HRCT	-0.335	2.269	0.022	0.883	0.715	0.008	61.062
LDH (U/L)	-0.002	0.001	3.387	0.066	0.998	0.996	1.000
ICU	1.472	1.248	1.391	0.238	4.358	0.377	50.338
Kaletra	3.464	1.713	4.090	0.043	31.960	1.113	917.83
Neut (%)	-0.121	0.167	0.524	0.469	0.886	0.639	1.230
Lymph (%)	-0.075	0.186	0.163	0.686	0.928	0.644	1.336
Cough	0.154	1.097	0.020	0.888	1.166	0.136	10.024
Kidney involvement	-2.262	1.045	4.682	0.030	0.104	0.013	0.808
Lung involvement	-0.347	0.419	0.687	0.407	0.707	0.311	1.606

5 | CONCLUSION

COVID-19, like other viral diseases, can involve different organs of the body with different severity. In the meantime, it has a lot in common with other viral diseases and there are some common points. Its differences include its high infectivity. Also, in this study, smoking was not a risk factor for the virus or associated with severe manifestations of the disease. Early lymphopenia and high CRP disease were common manifestations of the disease, but in this study a significant number of patients were at first without lymphopenia and CRP high. The patients who were worse at the onset of symptoms had worse prognosis than patients with mild symptoms. The main symptoms of the patients were fever and cough and most of the patients with fever had a low-grade one. It is important to note that patients should be hospitalised until the improvement of the severe symptoms and treatment should be continued on an outpatient basis at home. This study revealed that at the time of referral, creatinine, CPK, pulmonary involvement above 25%, and hypoxemia had a higher mortality rate. Also, increase of Spo2 can improve the patients following COVID-19. The results indicated that Kaletra had the highest effect on recovery following COVID-19.

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How to cite this article: Gharebaghi N, Farshid S, Boroofeh B, et al. Evaluation of epidemiology, clinical features, prognosis, diagnosis and treatment outcomes of patients with COVID-19 in West Azerbaijan Province. *Int J Clin Pract.* 2021;75:e14108. <https://doi.org/10.1111/ijcp.14108>