

Risk factors, clinical, and laboratory characteristics of patients with a diagnosis of COVID-19



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Abstract

Objective: An outbreak of coronavirus disease 2019 (COVID-19) occurred in late 2019. A better understanding of this disease will help us in preventing and managing it. This study evaluated the risk factors and clinical and laboratory characteristics of patients admitted to Shahid Sadoughi hospital in Yazd with a diagnosis of COVID-19.

Methods: This cross-sectional study was conducted on patients with the diagnosis of COVID-19 admitted to Shahid Sadoughi hospital in Yazd in May 2020, Iran. Patients' clinical information, including their symptoms at admission, history of smoking or drug/ alcohol abuse, history of Td (tetanus, diphtheria) vaccine, radiographic/computed tomography (CT) scan findings, and blood oxygen saturation, was recorded. The patients were also asked about their previous history of diabetes, hypertension, autoimmune disorder, and cancer or history of diseases in heart, lung, liver, and thyroid. Laboratory findings, height, weight and body mass index of the patients were also recorded. Statistical analyses were performed using SPSS 21.

Results: The mean age of 86 patients enrolled in the study was 61.40±17.37 years, of which 56 (65.11%) had mild pulmonary involvement and 30 (34.89%) had severe pulmonary involvement, according to CT scan results. Also, 26 (30.2%) of all patients had diabetes and about 30 (36%) had high blood pressure, but current smokers (6%) were rare. In patients with severe pulmonary involvement, the level of neutrophil, creatinine, and lactate dehydrogenase (LDH) was higher than patients with mild pulmonary involvement. Out of 56 patients with mild pulmonary involvement, 47 patients had a history of Td vaccination in the last 5 years. Only one patient in the severe group had a history of Td vaccination.

Conclusion: A lower percentage of blood lymphocytes as well as higher levels of neutrophils, creatinine, and LDH were observed in patients with severe pulmonary involvement. Numerous factors, especially more prominent laboratory abnormalities, determine the severity of the disease, and a better understanding of these factors can help physicians know the severity of the disease and its prognosis. These findings help us to further clarify the characteristics of COVID-19. Also, the effect of Td vaccine should be investigated in future studies.

Keywords: Infection, Radiology, COVID-19, SARS-CoV-2, Risk factor, Prevention and control

Introduction

There are so many different acute and chronic diseases in the world. The world is currently experiencing the third major epidemic of coronavirus (CoV). The new CoV epidemic began in late 2019 in Wuhan, China, originally called nCoV-19, and was renamed COVID-19 on February 2020 by the World Health Organization (WHO). Previous CoV epidemics included severe acute respiratory syndrome (SARS) -CoV, which occurred in

China in 2002, and Middle East respiratory syndrome (MERS) -CoV, which began in 2012 in the Middle East. All of these epidemics probably began with the transmission of the virus from animals to humans. The leading cause of death is usually acute atypical pneumonia (1-7).

COVID-19 infects human respiratory epithelial cells probably through interaction between the S protein virus and angiotensin-converting enzyme 2 (ACE2) on the cell. Therefore, COVID-19 has a strong ability to infect



humans. Although the first outbreak was probably through animal-to-human transmission, it was discovered that COVID-19 transmits quickly from human to human. The number of cases infected with COVID-19 is increasing rapidly. As of September 2020, more than 32 000 000 cases of COVID-19 infection have been reported in China and in other parts of the world with a mortality rate of about 2 percent (1,2,5-7).

Clinical signs in COVID-19-infected patients include respiratory tract involvement with fever, dry cough, myalgia, fatigue, shortness of breath, and manifestations similar to those of the other two diseases: SARS and MERS (1,7-12). Comorbidities, dyspnea, chest pain, cough, increased white blood cells, older age, and increased C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) were risk factors for severe/critical COVID-19 pneumonia (10-14).

Although most of the patients are thought to have a favorable prognosis, some patients with chronic illnesses will have poor prognosis. Patients with an acute condition may develop shortness of breath and hypoxia shortly after the onset of the disease, which may quickly lead to acute respiratory distress syndrome and organ failure. At present, no treatment or vaccine has been recorded for the disease, although researchers are working on this area (1,7-12).

This infectious disease has many effects on human life, especially from economic and social perspectives, so it is necessary to find ways to reduce the risk of infection and death due to COVID-19. Given the above, as well as easy transmission from person to person, and the possibility of re-infection in different countries in the coming autumn and winter, this disease should be well known. The aim of this study was to evaluate the risk factors and clinical and laboratory characteristics of patients admitted to Shahid Sadoughi hospital in Yazd with a diagnosis of COVID-19.

Methods

In this cross-sectional study, demographic, clinical, and laboratory information of patients admitted to Shahid Sadoughi hospital in Yazd (an educational hospital, which is a tertiary center) due to COVID-19 in May and June 2020, Iran, were reviewed. Yazd Shahid Sadoughi hospital is the largest educational hospital in Yazd province and during the pandemic period, it was the main center for COVID-19 patients. Yazd is one of the 20 largest cities in Iran.

In this study, patients with confirmed diagnoses of COVID-19 according to a positive RT-PCR and/or typical chest computed tomography (CT) findings were included based on the standard protocol. In order to gather patients' data, we designed a checklist. Items in this checklist were discussed in a group of medicine specialists. Demographic, clinical, laboratory, and patient management data were recorded. Clinical information including patient symptoms at admission (cough, fever,

shortness of breath, fatigue, myalgia, diarrhea, any kind of recent sleep problems, abdominal pain, loss of sense of smell or taste), smoking/drugs/alcohol, history of the last Td vaccine in the last 5 years (diphtheria and tetanus), medications used, radiographic/CT scan findings, and patients' blood oxygen saturation were recorded. The patient was also asked about his previous history of diabetes, hypertension, autoimmune disorder, and cancer or history of diseases in heart, lung, liver, and thyroid. Height, weight, and body mass index were also measured based on standard protocols. CT scan findings were reviewed by a radiologist and an emergency medicine specialist (with at least five years of experience).

Lab findings including white blood cell count (WBC), neutrophil count, lymphocyte count, hemoglobin, platelet count, creatinine, blood urea nitrogen (BUN), Aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), blood sugar (BS), lactate dehydrogenase (LDH), CRP, and ESR were recorded.

The patients were classified into two groups of not severe and severe based on lung computed tomography scan. All patients had undergone 64-slice scanner, low dose protocol, without contrast, and non-contrast lung computed tomography scan in supine position during end-inspiration. Chest CT images were interpreted by an expert radiologist with 12 years of experience. The patterns of lung involvement were categorized and the extent of the lung involvement was assessed using a scoring system: not severe involvement: < 50% and severe involvement: > 50% (13,14). In fact, the scores for each specific zone of both lungs were summed up to calculate the total involvement score. Scores for each specific segment of both lungs were considered to calculate bilateral pulmonary involvement (13,14).

Quantitative variables were expressed as mean and SD and qualitative variables were expressed as counts (percent). Kolmogorov-Smirnov test was used to assess the normality of data. Chi-square test was applied to compare the distribution of categorical variables. We applied independent samples *t* test to evaluate means of quantitative variables. Mann-Whitney non-parametric test was the alternative one when the assumptions of normality were not met. Statistical analyses were performed, using SPSS software version 21 (Armonk, NY: IBM Corp.). *P* values < 0.05 (two-tailed) were considered as statistically significant.

Results

A total of 86 patients were included in the study and were divided into two groups with severe or mild pulmonary involvement for analysis. The mean age of patients was 61.40 ± 17.37 years, of which 40 (48.2%) were male and 46 (51.8%) were female. Thirty patients had severe pulmonary involvement. Of the 86 patients included in the study, 27 patients were over 75 years of age (Figure 1).

The mean age of patients in both groups with severe pulmonary involvement and mild involvement were 64.45 ± 17.49 and 59.76 ± 17.25 years ($P=0.24$), respectively. Two (6.7%) patients with severe pulmonary involvement were current smoker, and four (7%) patients with mild pulmonary involvement reported cigarette smoking (Table 1).

Totally, 26 (30.2%) out of 86 patients had a history of diabetes; of these, 16 (33.3%) patients were with mild pulmonary involvement and 10 (28.6%) with severe pulmonary involvement ($P=0.6$). Compared to mild involvement, there was no significant difference in the history of diabetes and blood pressure (Table 1).

In patients with mild pulmonary involvement, 22 (39.3%) patients had fever, but in the group with severe pulmonary involvement, only 5 (16.7%) patients had fever, which was statistically significant ($P=0.03$). The most prevalent comorbidities included hypertension (36%), diabetes (30.2%), respiratory system disease (8.1%), and cardiovascular disease (17.4%).

Out of 56 patients with mild pulmonary involvement, 47 patients had a history of Td vaccination in the last 5 years. In fact, the other 9 patients did not know about the history of the vaccine in the last 5 years. Only one patient in severe group had a history of Td vaccination in recent five years (The information of 3 patients is missing in this group) (Table 1).

The mean of oxygen saturation in patients with severe involvement was significantly lower than patients with mild involvement (89.31 ± 6.48 , 94.49 ± 2.98 , $P<0.001$, respectively) (Table 1). The mean percentage of lymphocytes in patients with severe pulmonary involvement was 17.50 ± 9.62 , and in patients with mild pulmonary involvement was 26.72 ± 17.23 , which was significantly different ($P=0.014$; Table 2).

Discussion

COVID-19 is currently the seventh member of the

Coronaviridae family (1- 4). The study of clinical, laboratory, and imaging characteristics of patients with COVID-19 improves our understanding of patients' conditions and enhances the process of clinical management. The aim of this study was to evaluate the risk factors and clinical and laboratory characteristics of patients admitted to Shahid Sadoughi hospital in Yazd with the diagnosis of COVID-19. The results of this study showed that most of the hospitalized patients were over 50 years of age. In patients with severe pulmonary involvement, neutrophils, creatinine, and LDH were higher than in patients with mild pulmonary involvement. Also, patients with severe pulmonary involvement were not different in terms of history of diabetes and blood pressure compared to mild ones.

In the present study, patients with severe pulmonary involvement had a higher mean age than the other group, but this was not statistically significant. In some studies (13-16), it was found that higher mean of age is associated with the severity of COVID-19, and it was noted that older people have a weaker immune system due to various causes. The study by Zhou et al (17) also showed that increased mortality was associated with higher mean of age. However, although the mean age of the group with severe pulmonary involvement was higher than mild, it should be noted that out of a total of 86 patients included in the study, 71 patients were over 50 years of age.

The results of the study by Mertz et al (16) on patients with COVID-19 showed that patients with chronic obstructive pulmonary disease, respiratory system disease, cardiovascular disease, and hypertension were at a higher risk of death. Shi et al (18) found that severe cases are elderly with a higher incidence of hypertension, diabetes, and cardiovascular diseases. The study by Wu et al (19) showed that higher mean of age and comorbidities increase the chances of death and develop acute respiratory distress syndrome in patients with COVID-19. However, in the present study, the underlying diseases were not significantly associated with the severity of pulmonary involvement in patients. Of course, the blood sugar of patients with severe pulmonary involvement was clinically higher than people with mild pulmonary involvement, but this finding could be due to the greater use of corticosteroids in patients with severe pulmonary involvement.

The results of the study by Shi et al (20) showed that in patients with COVID-19, leukocyte counts increase. Also, the levels of troponin I, creatine kinase, and NT-proBnp were significantly higher in patients with cardiac injury. These markers are among the most useful and well-known markers of organ damage. In the present study, the levels of LDH, creatinine, and white blood cells were higher in patients with severe pulmonary involvement. These findings were in line with other studies, but inflammatory markers such as CRP and ESR were not different between

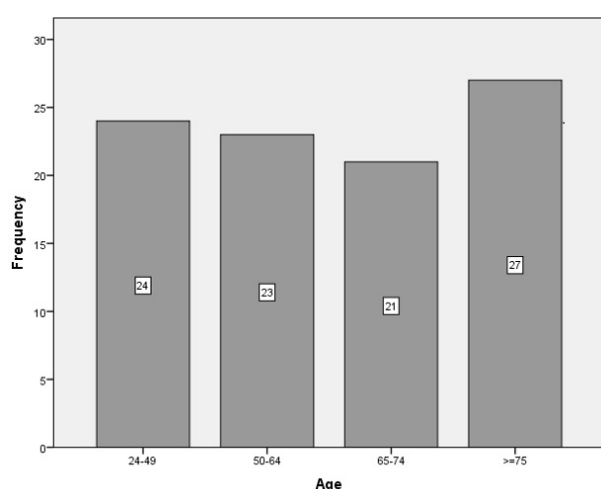


Figure 1. Distribution of age groups among COVID-19 patients.

Table 1. COVID-19 patient's characteristics across lung involvement severity

Variables	Lung involvement		Total	P value
	Sever (n=30)	Not severe (n=56)		
Age, Mean \pm SD	64.45 \pm 17.49	59.76 \pm 17.25	61.40 \pm 17.37	0.24 ^a
Length of hospital stay, Mean \pm SD	10.51 \pm 5.2	7.42 \pm 4.8	8.92 \pm 5.02	0.03 ^a
Body mass index, Mean \pm SD	25.31 \pm 2.76	25.44 \pm 4.32	25.40 \pm 3.79	0.91 ^a
Male, No. (%)	13 (46.4%)	27 (49.1%)	40 (48.2%)	0.82 ^b
Current Smoker, No. (%)	2 (6.7%)	4 (7.1%)	6 (7%)	1 ^c
Current drug use, No. (%)	0 (0%)	2 (3.6%)	2 (2.3%)	0.54 ^c
Current alcoholic drinker, No. (%)	0 (0%)	0 (0%)	0 (0%)	-
Td vaccine (in recent 5 years), No. (%)	1 (3.33%)	47 (83.92%)	48 (55.81%)	<0.001 ^c
Clinical manifestation, No. (%)				
Cough	13 (43.3%)	35 (62.5%)	48 (55.8%)	0.09 ^b
Fever	5 (16.7%)	22 (39.3%)	27 (31.4%)	0.03^b
Dyspnea	20 (66.7%)	28 (50%)	48 (55.8%)	0.14 ^b
Fatigue	3 (10%)	10 (17.9%)	13 (15.1%)	0.53 ^c
Myalgia	4 (13.3%)	5 (8.9%)	9 (10.5%)	0.71 ^c
Diarrhea	1 (3.3%)	4 (7.1%)	5 (5.8%)	0.65 ^c
Sleep problems	1 (3.3%)	0 (0%)	1 (1.2%)	0.35 ^c
Stomachache	1 (3.3%)	3 (5.4%)	4 (4.7%)	1 ^c
Loss of taste	1 (3.3%)	0 (0%)	1 (1.2%)	0.35 ^c
Loss of smell	1 (3.3%)	1 (1.8%)	2 (2.3%)	1 ^c
Disease history, No. (%)				
Diabetes	16 (33.3%)	10 (28.6%)	26 (30.2%)	0.65 ^b
Hypertension	13 (43.3%)	18 (32.1%)	31 (36%)	0.30 ^b
Cancer	1 (3.3%)	1 (1.8%)	2 (2.3%)	1 ^c
Dyslipidemia	3 (10%)	3 (5.4%)	6 (7%)	0.42 ^c
CVD	5 (16.7%)	10 (17.9%)	15 (17.4%)	0.89 ^b
Respiratory system disease	2 (6.7%)	5 (8.9%)	7 (8.1%)	1 ^c
Liver disease	0	0	0	-
Thyroid disease	3 (10%)	3 (5.4%)	6 (7%)	0.42 ^c
Auto-immune disease	1 (3.3%)	0	1 (1.2%)	0.35 ^c
Oxygen saturation (SaO ₂), % (Mean \pm SD)	89.31 \pm 6.48	94.49 \pm 2.98	92.66 \pm 5.14	<0.001^d
ICU admission, No. (%)	21 (70)	11 (19.64)	33 (38.37)	<0.001^a

CVD: Cardiovascular disease, Td: Tetanus diphtheria, ICU: Intensive care unit.

^a Obtained from *t* test.

^b Obtained from chi-square test.

^c Obtained from Fisher exact test.

^d Obtained from Mann-Whitney U test.

the two groups.

In a study by Nabavi et al, (21) demographic, clinical, laboratory, and radiologic findings and disease severity in a population of inpatients with COVID-19 were collected. Two hundred patients with the mean age of 69.75 \pm 6.39 years were studied. Disease severity was significantly associated with age, comorbidities, respiratory rate, O₂ saturation, extent of CT involvement, and serum CRP ($P < 0.05$). Serum CRP levels were higher in patients with severe disease and can be used to predict severe cases in COVID-19 patients. In a study by Hodges et al (22), association between biomarkers and COVID-19

severity and mortality was evaluated. Of 1310 patients aged ≥ 18 years, in 39.2% of patients, CRP was significantly and severely elevated. Also, higher levels of leucocytes, procalcitonin, troponins, and D-dimer were associated with the severity of disease.

In the study conducted by Li et al (15), in the group of severe patients, compared to ordinary patients, shortness of breath and cough were significantly higher. They reported that CT scores of severe/critical patients, consolidation, linear opacities, crazy-paving pattern, and bronchial wall thickening were significantly higher in severe/critical patients than other patients. Decreased

Table 2. COVID-19 patient's laboratory-test across lung involvement severity

Laboratory findings	Lung involvement		Total	P value
	Sever (n = 30)	Not severe (n = 56)		
White blood cell count, 10 ⁹ /L	9.12±5.47	8.20±3.68	8.51±4.34	0.76 ^a
Neutrophil ratio, %	77.06±9.51	67.14±14.73	69.56±15.99	0.003^b
Lymphocytes ratio, %	17.50±9.62	26.72±17.23	23.79±15.21	0.014^a
Platelets, 10 ⁹ /L	218.93±71.24	219±98.47	218.97±89.09	0.37 ^a
Hemoglobin, g/dL	12.77±2.17	12.95±1.93	12.90±1.90	0.70 ^b
Creatinine	1.67±1.57	1.22±0.73	1.39±1.13	0.04^a
BUN	46.72±28.78	38.75±28.16	41.75±28.48	0.10 ^a
Blood sugar	144.18±59.41	127.73±42.47	133.68±49.28	0.55 ^a
ALT, U/L	33.67±31.80	23.71±18.83	27.03±24.15	0.35 ^a
AST, U/L	33.80±19.69	25.90±14.02	28.49±16.37	0.12 ^a
ALP	222.17±136.79	223.46±86.38	223.05±103.65	0.14 ^a
LDH	602.25±274.11	457.69±138.56	512.76±211.30	0.01^a

BUN: Blood urea nitrogen, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, LDH: lactate dehydrogenase

^a Obtained from Mann-Whitney U test.

^b Obtained from *t* test.

lymphocytes and increased systemic inflammation are risk factors for severe/critical COVID-19 pneumonia. The findings of the present study are in the same direction.

Moreover, in the study by Zhang et al (23), they concluded that there was no significant relationship between smoking and being infected with COVID-19. In the present study, there was no relationship between smoking and the severity of pulmonary involvement in patients with COVID-19. However, from a clinical point of view, in the group with mild involvement, the number of smokers was twice as many as in the group with severe lung involvement.

Evaluation of the symptoms of patients with COVID-19 in various studies showed that fever was the most common symptom in patients with COVID-19. Huang et al (11) also indicated that almost all patients had fever at the onset of symptoms. Cough was another common symptom in these patients (11, 17). Zhou et al (17), in a retrospective cohort study showed that the frequency of cough, fever, and fatigue did not differ significantly between the two groups of patients (survivor vs. non-survivor), and as a risk, it is not considered a mortality factor. In the present study, only the frequency of fever was significantly different between the two groups and other symptoms associated with the disease did not show any association with the severity of pulmonary involvement.

Also, in the present study, dyspnea was not significantly associated with the severity of pulmonary involvement. In another study, Li et al (15) reported that the incidence of chest pain and dyspnea was higher in severe/critical patients. Chest pain may be due to an inflammatory complication of the pleura. Dyspnea is associated with severe damage to the lung in patients. Fever, chest pain, and dyspnea may indicate that the immune system of patients with severe condition is very active. The onset

of these symptoms can help physicians determine the severity of the operation in clinical practice (15,17).

Furthermore, Zhou et al (17) highlighted that the level of lymphocytes in patients who were discharged from the hospital was significantly higher than patients who died. In fact, the results showed that decreased lymphocyte is a risk factor for severe/critical COVID-19 pneumonia. LDH and IL-6 also increase as the disease exacerbates. In some studies (23), the number of lymphocytes in patients with worse condition was significantly lower. However, the level of leukocytes in patients with severe condition was significantly higher than the other groups. In line with previous findings in this study, it was observed that the level of lymphocytes in patients with severe pulmonary involvement was significantly lower than the group with a better condition. Higher leukocyte counts may also be due to secondary bacterial infection. Decreased lymphocytes in critically-ill patients indicate that large numbers of immune cells are depleted and immune system function is inhibited. Decreased lymphocytes and increased systemic inflammation are risk factors that increase the deterioration of patients with COVID-19 (16-19).

Zhou et al (17) conducted a study to investigate the risk factors for mortality in patients with COVID-19. The results of laboratory studies showed that the level of lymphocytes in patients who were discharged from the hospital was significantly higher than patients who died. In fact, the results showed that low levels of lymphocytes are a risk factor for mortality. LDH and IL-6 were also associated with death. In COVID-19 patients, the number of lymphocytes in patients with worse condition was significantly lower. However, the level of leukocytes in patients with severe condition was significantly higher than the other group (23). In line with previous findings in this study, it was observed that the level of lymphocytes

in patients with severe pulmonary condition was significantly lower than the group with a better condition. Higher leukocyte counts may also be due to secondary bacterial infection. Decreased lymphocytes in critically-ill patients indicate that large numbers of immune cells are depleted and immune system function is inhibited.

Lymphocyte damage may be very important in clinical course of the disease and can be used as an important factor in assessing the severity of the disease. Elevated neutrophil counts in critically-ill patients may be related to cytokine storms caused by virus attack and secondary infections (12).

Regarding sleep problems, according to the clinical observations of the emergency medicine specialists, there are reports of sleep problems for patients with COVID-19 after being infected. In fact, clinical observations indicated that some patients with COVID-19 had problems such as insomnia and nightmares. This problem could occur for a number of reasons. Decreased blood oxygen saturation in patients is one of the most important reasons that can cause sleep problems. Also, when a patient develops cold symptoms, fear of COVID-19 and getting the virus can lead to problems such as sleep disturbances. For this reason, the theory was examined in this study that COVID-19 can cause some sleep problems, but only one person mentioned this problem in the study. Although clinically 3% of the group with severe pulmonary involvement had sleep problems, perhaps for various reasons, such as the small number of samples, this study was not able to evaluate the clinical observations of clinicians and provide strong evidence. From a clinical point of view, this needs further investigation.

All patients in this study had COVID-19 and there was no healthy person in the control group. Although there was no significant difference between the two groups in terms of comorbidity, 33.3% of patients with severe pulmonary involvement and 28.6% of patients with mild involvement had diabetes. Also, about 43.3% of the patients with severe pulmonary involvement and 32.1% of the patients with mild pulmonary involvement had hypertension. In fact, about 30% of all patients had diabetes and about 36% had high blood pressure, which is definitely higher than the normal population. Underlying diseases including blood pressure and diabetes can be considered as the risk factors for COVID-19.

According to clinical observations in Shahid Sadoughi hospital, most of the patients with severe complications due to COVID-19 had no history of Td vaccination. By the same token, children also seem to be better protected from COVID-19 than adults. But there is no robust evidence regarding effectiveness of Td against COVID-19. So, we hypothesized that Td vaccination might influence the severity of the disease in patients with COVID-19. Out of 56 patients with mild pulmonary involvement, 47 patients had a history of Td vaccination in the last 5 years;

but only one patient in severe pulmonary involvement had the history of Td vaccine.

Some possible explanations exist in this regard. First of all, vaccine injection can stimulate the immune system in human body and generate a scattered immunity against non-self antigens and also there could be a cross-protective immunity. The cellular and molecular mechanisms could be responsible for this phenomenon (24,25). Further studies need to be conducted in this field.

Limitations and suggestions

This study, like other studies, had some limitations. Data in this study were collected in one center. Also, due to the cross-sectional study design and patients' lack of follow-up, no information was collected from patients' outcomes such as death. Also, the presence of a group of healthy individuals, as a control group, could help to analyze the results better. Also, in some variables, missing data was our concern in analysis.

Conclusion

Patients with severe pulmonary involvement had higher neutrophil, creatinine, and LDH levels than patients with mild pulmonary involvement. In patients with severe pulmonary involvement, the percentage of lymphocytes and O₂ saturation was lower than the group with mild involvement. Patients with severe pulmonary involvement were no different in terms of history of diabetes and blood pressure compared to mild. These findings help us to further clarify the epidemiological, laboratory, and clinical characteristics of COVID-19. Also, the effect of Td vaccine should be investigated in future studies.

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Authors' contributions

AE: Conception and design, revising, final approval, agreement to be accountable for all aspects of the work. FSK: Concept, revising, data acquisition, analysis, final approval, agreement to be accountable for all aspects of the work. HM: Concept, drafting, final approval, agreement to be accountable for all aspects of the work. RH: Concept, drafting, analysis, interpretation, final approval, agreement to be accountable for all aspects of the work. FJ, ML and AZ: Concept, drafting, data acquisition, final approval, agreement to be accountable for all aspects of the work. EZ: Conception and design, drafting, data acquisition, final approval, agreement to be accountable for all aspects of the work.

Ethics issues

This research was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1399.125). All patients' information remained confidential and ethical issues related to human studies (according to the Helsinki Declaration) were considered. Personal protective

equipment was used according to national guidelines during this study.

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