

# Clinical characteristics and Mortality risk factors among COVID-19 patients in Qom–Iran; The results of a Retrospective Cohort study

**Ahmad Hormati**

Qom University of Medical Sciences and Health Services

**SeyedYaser Foroghi Ghomi**

Qom University of Medical Sciences and Health Services

**masoudreza sohrabi** (✉ [sohrab\\_r@yahoo.com](mailto:sohrab_r@yahoo.com))

Firoozgar Hospital <https://orcid.org/0000-0001-5688-2776>

**Ali Gholami**

Neyshabur University of Medical Sciences

**Saeede Jafari**

Qom University of Medical Sciences and Health Services

**Amir Jabbari**

Qom University of Medical Sciences and Health Services School of Medicine

**Reza AminNejad**

Qom University of Medical Sciences and Health Services School of Medicine

**Javad Khodadadi**

Qom University of Medical Sciences and Health Services

**Mansoureh shakeri**

Qom University of Medical Sciences and Health Services

**Alireza ShahHamzeh**

Qom University of Medical Sciences and Health Services

**Mahbobeh Afifian**

Qom University of Medical Sciences and Health Services

**Zohre Azad**

Qom University of Medical Sciences and Health Services School of Medicine

**Sajjad Ahmadpour**

Qom University of Medical Sciences and Health Services

**MohammadHadi Karbalai**

Iran University of Medical Sciences

**MohammadReza Babaei**

Iran University of Medical Sciences

**Parisa Karimzadeh**

Islamic Azad University

**SeyedKamal Eshagh Hosseini**

Qom University of Medical Sciences and Health Services

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## Research article

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# Abstract

## Background & Aim

Coronavirus 2019 (COVID-19) outbreak in the Middle East was initially reported in Qom-Iran. Clinical and epidemiologic and mortality risk factors details have not been already fully explained.

## Method

In a retrospective study, the hospitalized adult patients with laboratory diagnosed COVID-19 between February 25 to March 20, 2020 were enrolled. A checklist including demographic, clinical, laboratorial, imaging, and treatment data was completed for each of the participant. The data were extracted from electronic medical records. In case of lack of information, a member of the research team contacted them via phone. All the dead patients and the first one hundred survived patients with these criteria were enrolled in the study. Outcome defined as death or discharge of patients.

## Results

Of admitted patients, 200 patients who had been discharged or died were involved in this study. The majority of them were male (56%). The mean age of all patients was  $62.63 \pm 14.9$ . Co-morbidity was reported in 124 (62%) patients in which hypertension was the most common. The most frequent clinical presentations were dyspnea in 169 (84.5%), cough in 150 (75%), and fatigue/weakness in 123 (61.5%) patients. The main complications were respiratory failure and acute respiratory distress syndrome with prevalence of 143 (71.5%) and 105 (52.5%), accordingly. Multiple logistic models showed that decline of hemoglobin level (OR = 10.09), neutrophilia (OR = 3.48), high blood urea nitrogen (OR = 4.29),  $SpO_2 \leq 90\%$  (OR = 3.38), and presence of patchy consolidation (OR = 6.81) were associated with poor outcome.

## Conclusion

COVID-19 disease has multiple aspects. CT scan findings, complete blood count with differential, high blood urea nitrogen and  $SpO_2$  are related to mortality. Hence needs to pay serious attention during admitting and surveillance, particularly among elderly patients and who with preexisting morbidities.

## Highlights:

- COVID-19 has vast presentation that can associated with mortality
- We found increasing the risk of in-hospital mortality associated with decrease of hemoglobin value, lymphopenia  $<1.0 \times 10^9$ , neutrophilia  $>7.7 \times 10^9$  and  $SpO_2 < 90\text{mmhg}$  on admission.
- CT scan finding on admission has a predictive value to diagnose of sever status.
- Older age as well as presence of co-morbidity and quick SOFA , have a clinically impact on outcome of patients

- Assessment of Hemoglobin concentration also WBC differentiates, at beginning and during surveillance strongly recommend. These items can help physicians to predict the severity of disease.

Note:

1-The First two authors have same right as the first author

2- the authors number 3-11 have same right

## Introduction:

In January 2020 a new RNA virus of Beta coronavirus family was isolated that has been named the coronavirus disease-19 (COVID-19) and alerted this virus as a worldwide public health problem (1, 2). The data indicated that the main route of its transmission is the person-to-person spread. By advancing the knowledge, the other routs of transmission such as formit ,airborne , urine and animal-to-human were also taken into account (3-6). Wang et al, in a study on 1070 specimens of 205 patients, indicated that COVID-19 can be detected in respiratory specimens as well as fecal and blood samples with different concentration levels (7). Furthermore, it is proposed that virus could be distributed by asymptomatic patients, same as which was reported in Middle East Respiratory Syndrome (*MERS*) and **severe acute respiratory syndrome** (SARS) epidemic (8-10).

In about middle of February 2020 the breakout of COVID-19 in the Middle East was first announced in Qom –Iran. The city is almost located in the center of the country with significant industrial and religious centers, causes many travels from and to this city daily. Hence, along with increasing the number of infected patients in this city the disease rapidly has spread to the whole country.

The clinical manifestation may include a wide spectrum from asymptomatic infection to gastrointestinal symptoms , sever viral pneumonia, respiratory failure, and eventually death. Based on recent data the mortality rate can reach to 20% although the risk factors of mortality were different and may include elderly, preexisting morbidity and elevated sequential organ failure assessment (SOFA) score.

During the primary months of COVID-19 epidemic, because of the throng patients referred to the hospital, the crisis was developed. Hence diagnosis of patients was complicated due to the vast variety of presentations and severity of the disease. In fact, recently the data from different parts of world have been released. In this concern, there are a few reports from the Middle East region that has not covered all aspects of patients. Furthermore, we have tried to enroll patients with a complete medical record. According to our knowledge, this is one of the leading reports from Iran and Middle East including alive or death hospitalized COVID-19 patients.

## Method:

### Patient selection

This is a retrospective study including hospitalized adult patients between February 25 to March 20, 2020 in Shahid Beheshti referral hospital, Qom-Iran. This hospital is one of the designated hospitals for COVID-19. All the admitted adult patients with definite outcome in this period were considered. The patients who were diagnosed with the COVID-19 according to WHO guidelines were selected. Detection of the RNA of the virus was considered as the confirmed positive result. Also, other non-definite results were considered as highly suspected patients who did not enroll in our study. The outcome was defined as death (non-survivor) or discharge (survivor). All dead patients as well as the first one hundred living patients were enrolled in our study.

The criteria for discharge were the improvement of the general status and respiratory symptoms, absence of fever for at least 3 days, chest CT scan improvement in both lungs and at least one time throat-swab or nasal – swap samples negative for SARS-CoV-2 RNA assessment.

### **Data Acquisition:**

The data were obtained retrospectively from patient's medical records in the hospital who had been admitted due to COVID-19 infection. According to WHO recommendation, a questionnaire including demographic, anthropometric, clinical presentation, laboratorial, and imaging data was designed. It was filled up for each patient by 2 trained residence of internal medicine. In case of lack of data, a member of the team called him/her to complete the questionnaire. Regarding dead patients, the information was asked from one of the first-degree relatives. The filled-up questionnaire was approved by three experts. Two of them were professors of internal medicine and the third one was an epidemiologist.

### **Laboratorial Data:**

Obtaining the specimens, transferring to the central laboratory and also the lab safety issues were according to the WHO recommendations (WHO laboratory testing strategy recommendations for COVID-19: Interim guidance2020).

As a standard method, venous blood samples were obtained from each patient in the first day of admission. Complete blood count (CBC) with differential was measured ( by Sysmex K1000, Hamburg, Germany).Also the alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), uric acid (UA), blood urea nitrogen (BUN), creatinine, C-reactive protein (CRP), were measured by using the diagnostic kits from Pars Azmoon Company (Pars Azmoon Co., Tehran, Iran) .

COVID-19 one-step Real-time PCR was performed by the referred diagnostic laboratory, which was confirmed by the ministry of health based on universal protocols. A nasopharyngeal swab into viral transport media (VTM) used for commercial RNA extraction according to manufacturer's instructions.

All patients have undergone a standard high-resolution CT scan (HRCT) of chest. The results of the imagines were acquired via electronic reports of each patient.

### **Statistical analysis**

Mean (SD) and n (%) were presented for continuous and categorical variables, respectively. Independent t-test was applied to compare normally distributed data, while Mann-Whitney U test was used for non-normally distributed ones. Chi-square or Fisher's exact test was used to evaluate differences between survivors and non-survivors.

Univariate and multivariate (with backward method) logistic regression models were used to examine the association between different variables and in-hospital death related to COVID-19. Some variables were excluded from univariate analysis if they were self-reported, if they hadn't enough number of events, and if the association between them and death status were not significant. All the statistical analyses were done using STATA software version 15 and  $p < 0.05$  was considered as statistically significant.

## Results:

Totally 650 patients were admitted to the Shahid Beheshti general hospital, in the mentioned period. We have just selected the patients who were admitted and diagnosed with COVID19 with the confirmed outcomes. The patients without available key reports were excluded. Finally, we enrolled all non-survivor patients and one hundred survived patients in this study.

Table 1 reports the basic characteristics of patients. The mean age of survivors and none-survivors were  $58.9 \pm 14.1$  and  $66.4 \pm 14.8$  year old, respectively ( $P < 0.001$ ). The majority of them were male with 112 (56%) patients. The mean time of hospitalization was  $4.3 \pm 3$  days. Moreover, the mean time from the first symptoms until referral to the hospital and until death or discharge was  $6.5 \pm 4.3$  days and  $10.7 \pm 5.4$ , respectively. The history of contact with suspected patients was reported in 50 (25%) patients. There was no history of contact with wild animal or sea whole market.

Table 1  
Basic Characteristics of Patients according to outcome

Variable	Total (N = 200)	Survive (N = 100)	Non-survive (N = 100)	P- value
	n (%)	n (%)	n (%)	
Age				
Mean ± SD (year)	62.6 ± 14.9	58.9 ± 14.1	66.4 ± 14.8	< 0.001
< 40	13 (6.5)	9 (9)	4 (4)	0.009
40–59	70 (35)	43 (43)	27 (27)	
≥ 60	117 (58.5)	48 (48)	69 (69)	
Sex				
Male	112 (56)	55 (55)	57 (57)	0.776
Education level				
Illiterate	76 (38)	27 (27)	49 (49)	0.005
Under diploma or diploma	95(47.5)	55 (55)	40 (40)	
Academic	29 (14.5)	18 (18)	11 (11)	
BMI				
Mean ± SD	28.1 ± 4.9	27.5 ± 4.2	28.7 ± 5.4	0.100
≥30	58 (29)	25 (25)	33 (33)	0.213
Smoking	47 (23.5)	24 (24)	23 (23)	0.868
Opium use	31 (15.5)	17 (17)	14 (14)	0.558
Co-Morbidity <sup>a</sup>				
Any	124 (62)	52 (52)	72 (72)	0.004
Hypertension	82 (41)	29 (29)	53 (53)	0.001
Cardiovascular disease	45 (22.5)	16 (16)	29 (29)	0.028
Lung Disease	23 (11.5)	10 (10)	13 (13)	0.506
Diabetes	58 (29)	27 (27)	31 (31)	0.533
Renal Disease	16 (8)	4 (4)	12 (12)	0.037
Cancer	7 (3.5)	2 (2)	5 (5)	0.248

Variable	Total (N = 200)	Survive (N = 100)	Non-survive (N = 100)	P-value
	n (%)	n (%)	n (%)	
Number of days of hospitalization, Mean ± SD	4.3 ± 3.0	4.5 ± 2.5	4.2 ± 3.5	0.484
Number of days from first symptom to admission, Mean ± SD	6.5 ± 4.3	7.2 ± 4.2	5.8 ± 4.3	<b>0.016</b>
Number of days from first symptom to death or discharge, Mean ± SD	10.7 ± 5.4	11.7 ± 5.2	9.7 ± 5.4	<b>0.042</b>
<sup>a</sup> Co-Morbidity Any was considered positive if patient had at least one of the diseases such as blood pressure, heart				
<sup>b</sup> BMI (body mass index) was calculated by using the square of the height (kg/m <sup>2</sup> ) measurement				

Pre-existing morbidity was reported in 124 (62%) patients. The number of patients, survivors and non-survivors, stated with morbidity were 52 (52%) and 72 (72%) patients, respectively (P = 0.001). Hypertension and diabetes type 2 were the most common co-morbidities in these patients (Table 1).

The main clinical presentations were dyspnea in 169 (84.5%), coughing in 150 (75%) and fatigue/weakness in 123 (61.5%) patients (Table 2). Fever more than 38<sup>C</sup> was not common and was seen in 20 (10%) patients, although fever between 37.6<sup>c</sup> – 38<sup>C</sup> was reported in 93 (46%) patients.



Table 2  
Clinical presentation according to outcome at baseline

Variable	Total (N = 200) n (%)	Survive (N = 100) n (%)	Non-Survive (N = 100) n (%)	P-value
Body temperature				
≤ 38°C	180 (90.0)	85 (85)	95 (95)	<b>0.018</b>
> 38°C	20 (10.0)	15 (15)	5 (5)	
Sore Throat	102 (51)	53 (53)	49 (49)	0.572
Headache	47 (23.5)	32 (32)	15 (15)	<b>0.005</b>
Chest pain	59 (29.5)	21 (21)	38 (38)	<b>0.008</b>
Coughing	150 (75)	81 (81)	69 (69)	0.050
Coughing with Sputum <sup>a</sup>	59 (39.3)	43 (53.1)	16 (23.2)	<b>&lt; 0.001</b>
Fatigue/Weakness	123 (61.5)	58 (58)	65 (65)	0.309
Myalgia /Arthralgia	56 (28)	42 (42)	14 (14)	<b>&lt; 0.001</b>
Chills	78 (39)	36 (36)	42 (42)	0.384
Sweating	6 (3)	4 (4)	2 (2)	0.407
Shortness of Breath /Dyspnea	169 (84.5)	78 (78)	91 (91)	<b>0.011</b>
Dizziness	34 (17)	15 (15)	19 (19)	0.451
Nausea and Vomiting	45 (22.5)	16 (16)	29 (29)	<b>0.028</b>
Abdominal pain	36 (18)	17 (17)	19 (19)	0.713
Diarrhea	51 (25.5)	24 (24)	27 (27)	0.626
Respiratory rate				
<24	170(85.4)	86 (86)	84 (84.8)	0.818
≥24	29 (14.6)	14 (14)	15 (15.2)	
Pulse rate				
≤90	133(66.5)	76 (76)	57 (57)	<b>0.004</b>
>90	67 (33.5)	24 (24)	43 (43)	

Variable	Total (N = 200) n (%)	Survive (N = 100) n (%)	Non-Survive (N = 100) n (%)	P-value
CURB score				
0–1	99 (49.5)	82 (82)	17 (17)	< 0.001
2	42 (21)	14 (14)	28 (28)	
≥3	59 (29.5)	4 (4)	55 (55)	
Quick SOFA score (≥ 2)	24 (12)	6 (6)	18 (18)	0.009
CT scan Finding				
Patchy Consolidation	49 (24.5)	8 (8)	41 (41)	< 0.001
Ground Glass				
One side	4 (2)	3 (3)	1 (1)	< 0.001
Both sides	164 (82)	66 (66)	98 (98)	
Patchy Infiltration				
One side	8 (4)	5 (5)	3 (3)	0.004
Both sides	123 (61.5)	50 (50)	73 (73)	
<sup>a</sup> Was calculated among who had a history of coughing				

Based on the laboratorial data, it was observed that the mean WBC levels was  $8.3 \pm 5.9 \times 10^3/\mu\text{L}$  in all patients,  $6.7 \pm 3.1 \times 10^3/\mu\text{L}$  in survivor group, and  $9.9 \pm 7.5 \times 10^3/\mu\text{L}$  in non-survivor group ( $P = 0.001$ ). The lymphocyte count less than  $1 \times 10^3/\mu\text{L}$  was stated in 46 (46%) of survivor and 68 (68%) of non-survivor patients ( $P < 0.006$ ). Neutrophils count has been significantly different between the two groups ( $5.0 \pm 2.9$  vs.  $8.1 \pm 4.4$  count  $\times 10^3/\mu\text{L}$ ;  $P < 0.001$ ). Moreover, we have found the level of hemoglobin (Hb), blood urea nitrogen (BUN), creatinine, CRP, international normalized ratio (INR), SpO<sub>2</sub>, and pH was significantly different between survivor and non-survivor patients; however, no significant difference was observed for other laboratories data such as platelets, erythrocyte sedimentation rate (ESR), ALT, AST and ALP (Table 3).

Table 3  
Para Clinic Finding according to outcome

Variables (Normal range)	Total (N = 200) n (%)	Survive (N = 100) n (%)	Non Survive (N = 100) n (%)	P-value
<b>WBC (<math>4-9.5 \times 10^9/L</math>)</b>				
Mean $\pm$ SD	8.3 $\pm$ 5.9	6.7 $\pm$ 3.1	9.9 $\pm$ 7.4	<b>&lt; 0.001</b>
> 10.0	49 (24.5)	11 (11)	38 (38)	<b>&lt; 0.001</b>
4-10	129 (64.5)	75 (75)	54 (54)	
< 4.0	22 (11)	14 (14)	8 (8)	
<b>Neutrophil (<math>1.8-7.4 \times 10^9/L</math>)</b>				
Mean $\pm$ SD	6.50 $\pm$ 4.01	5.0 $\pm$ 2.9	8071.00 $\pm$ 4409.52	<b>&lt;0.001</b>
$\leq 7.7$	140 (70)	86 (86)	54 (54)	<b>&lt; 0.001</b>
> 7.7	60 (30)	14 (14)	46 (46)	
<b>Lymphocyte (<math>1.0-4.4 \times 10^9/L</math>)</b>				
Mean $\pm$ SD	1.2 $\pm$ 3.1	1.1 $\pm$ 4.3	1.3 $\pm$ 4.5	<b>&lt; 0.001</b>
$\geq 1.00$	86 (43.0)	54 (54)	32 (32)	<b>0.002</b>
< 1.00	114 (57.0)	46 (46)	68 (68)	
<b>Plat (<math>150-400 \times 10^9/L</math>)</b>				
Mean $\pm$ SD	195.62 $\pm$ 82.53	192.83 $\pm$ 75.44	198.40 $\pm$ 89.36	0.851
> 150000	143 (71.5)	72 (72)	71 (71)	0.971
100000-150000(N)	38 (19)	19 (19)	19 (19)	
< 100000	19 (9.5)	9 (9)	10 (10)	
<b>BUN (7-20 mg/dl)</b>				
Mean $\pm$ SD	25.36 $\pm$ 22.83	15.68 $\pm$ 7.94	35.04 $\pm$ 28.20	<b>&lt; 0.001</b>
< 20	111 (55.5)	79 (79)	32 (32)	<b>&lt; 0.001</b>
$\geq 20$	89 (44.5)	21 (21)	68 (68)	
<b>Creatinine (0.6-1.4 mg/dl)</b>				
Mean $\pm$ SD	1.59 $\pm$ 1.45	1.14 $\pm$ 0.28	2.04 $\pm$ 1.94	<b>&lt; 0.001</b>
< 1.3	107 (53.50)	71 (71)	36 (36)	<b>&lt; 0.001</b>

Variables (Normal range)	Total (N = 200) n (%)	Survive (N = 100) n (%)	Non Survive (N = 100) n (%)	P-value
$\geq 1.3$	93 (46.50)	29 (29)	64 (64)	
CRP (< 20 mg/L)				
Mean $\pm$ SD	43.64 $\pm$ 16.81	42.61 $\pm$ 19.45	44.83 $\pm$ 13.15	0.921
< 25	29 (15.68)	24 (24.24)	5 (5.81)	<b>0.001</b>
$\geq 25$	156 (84.32)	75 (75.76)	81 (94.19)	
INR (< 1.3)				
Mean $\pm$ SD	1.33 $\pm$ 0.53	1.25 $\pm$ 0.45	1.41 $\pm$ 0.60	<b>&lt; 0.001</b>
< 1.3	111 (69.81)	65 (82.28)	46 (57.50)	<b>0.001</b>
$\geq 1.3$	48 (30.19)	14 (17.72)	34 (42.50)	
ESR (< 20 mm/h)				
Mean $\pm$ SD	51.19 $\pm$ 32.81	47.34 $\pm$ 30.81	57.37 $\pm$ 35.21	0.118
< 20	28 (21.05)	20 (24.39)	8 (15.69)	0.231
$\geq 20$	105 (78.95)	62 (75.61)	43 (84.31)	
SPO <sub>2</sub> (> 93%)				
Mean $\pm$ SD	83.18 $\pm$ 12.76	89.09 $\pm$ 6.27	77.27 $\pm$ 14.74	<b>&lt; 0.001</b>
< 90	120 (60)	41 (41)	79 (79)	<b>&lt; 0.001</b>
$\geq 90$	80 (40)	59 (59)	21 (21)	
PH (7.36–7.44)				
Mean $\pm$ SD	7.37 $\pm$ 0.12	7.40 $\pm$ 0.12	7.35 $\pm$ 0.12	<b>0.001</b>
< 7.4	66 (49.62)	18 (33.96)	48 (60.00)	<b>0.003</b>
$\geq 7.4$	67 (50.38)	35 (66.04)	32 (40.00)	
CO <sub>2</sub> (36–44 mmHg)				
Mean $\pm$ SD	0.060	40.19 $\pm$ 10.96	39.32 $\pm$ 10.01	0.788
< 40	66 (49.62)	25 (47.17)	41 (51.25)	0.645
$\geq 40$	67 (50.38)	28 (52.83)	39 (48.75)	
HCO <sub>3</sub> (21–27 meq/L)				
Mean $\pm$ SD	23.02 $\pm$ 6.16	24.79 $\pm$ 5.68	21.85 $\pm$ 6.21	<b>0.020</b>

<b>Variables (Normal range)</b>	<b>Total (N = 200)</b>	<b>Survive (N = 100)</b>	<b>Non Survive (N = 100)</b>	<b>P-value</b>
	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>	
< 24	66 (49.62)	21 (39.62)	45 (56.25)	0.060
≥ 24	67 (50.38)	32 (60.38)	35 (43.75)	
Abbreviation: BUN: Blood urea nitrogen ;ESR: Erythrocyte sedimentation rate; INR: International normalized ration				

Regarding lung imaging evaluations, almost all patients had abnormal findings in the imaging. The main presentations were both side ground glass view and also both sides patchy infiltration that significantly more common among non-survivor group ( $P < 0.001$  and  $P = 0.004$  respectively) (Table 3).

Moreover, the frequent complications were respiratory failure, acute respiratory distress syndrome (ARDS), acute kidney injuries and acidosis with 143 (71.5%), 105 (52.5%), 67 (33.5%) and 48 (24%) cases. Additionally, coagulopathy was common in non-survived patients 40 (40%) (Table 4).

Table 4  
Complication of patients during hospitalization according to Outcome

<b>Variables</b>	<b>Total (N = 200)</b>	<b>Survive (N = 100)</b>	<b>Non Survive (N = 100)</b>	<b>P-value</b>
	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>	
Sepsis	35 (17.5)	2 (2)	33 (33)	< 0.001
Respiratory failure	143 (71.5)	43 (43)	100 (100)	< 0.001
ARDS	105 (52.5)	6 (6)	99 (99)	< 0.001
Septic shock	9 (4.5)	0 (0)	9 (9)	0.002
Coagulopathy	47 (23.5)	7 (7)	40 (40)	< 0.001
Acute Kidney injury	67 (33.5)	10 (10)	57 (57)	< 0.001
Acidosis	48 (24)	5 (5)	43 (43)	< 0.001

In the univariate analysis, we have observed that older patients had higher odds of death (Table 5). In addition, having hypertension, having CVD, WBC, neutrophil level, lymphocyte level, hemoglobin level, BUN, creatinine level, CRP, INR, pH level, SpO2 level, patchy consolidation, ground glass and patchy infiltration were also related to death (Table 5).

Table 5  
Related factors associated with in-hospital death

Variable		Univariate		Multivariate*	
		OR (95%CI)	P-value	OR (95%CI)	P-value
Gender	Male/Female	1.08 (0.62–1.89)	0.776	-	-
Age	-	1.03 (1.01–1.04)	< 0.001	-	-
Age	≥ 60 / <60	2.41 (1.35–4.29)	0.003	-	-
Age	≥ 50 / <50	2.38 (1.16–4.87)	0.017	-	-
BMI	-	1.05 (0.99–1.11)	0.099	-	-
Smoking	Ever/Never	0.94 (0.49–1.81)	0.868	-	-
Opium	Ever/Never	0.79 (0.36–1.71)	0.558	-	-
Hypertension	Yes/No	2.76 (1.53–4.94)	0.001	-	-
CVD	Yes/No	2.14 (1.07–4.26)	0.030	-	-
Lung Disease	Yes/No	1.34 (0.56–3.22)	0.507	-	-
Renal Disease	Yes/No	0.31 (0.04–1.99)	0.221	-	-
Diabetes	Yes/No	1.21 (0.65–2.23)	0.533	-	-
WBC	< 4 or > 10/4–10	2.55 (1.40–4.65)	0.002	-	-
Hb	< 10/≥10	8.64 (1.92–38.89)	0.005	10.09 (1.24–82.13)	0.031
Lymphocyte	< 1 / ≥1	2.49 (1.40–4.43)	0.002	-	-
Neutrophil	>7.7/≤7.7	5.23 (2.62–10.41)	< 0.001	3.48 (1.04–11.70)	0.043
Plat	100000–150000/<100000	0.9 (0.29–2.71)	0.851	-	-
	> 150000/<100000	0.88 (0.34–2.31)	0.807	-	-
BUN	≥ 20/<20	7.99 (4.22–15.14)	< 0.001	4.29 (1.49–12.30)	0.007
Cr	≥ 1.3/<1.3	4.35 (2.40–7.88)	< 0.001	-	-
CRP	≥ 25/<25	5.18 (1.88–14.28)	0.001	7.92 (0.88–71.21)	0.065
INR	≥ 1.3/<1.3	3.43 (1.65–7.10)	0.001	-	-

Variable		Univariate		Multivariate*	
ESR	≥ 20/<20	1.73 (0.69–4.29)	0.235	-	-
SPo2	≥ 90/<90	5.41 (2.89–10.11)	< 0.001	3.38 (1.08–25.29)	0.036
PH	≥ 7.4/< 7.4	2.91 (1.41–6.01)	0.004	-	-
Co2	≥ 40/<40	0.84 (0.42–1.70)	0.645	-	-
HCo3	≥ 24/<24	1.96 (0.96–3.96)	0.062	-	-
Patchy Consolidation	Yes/No	7.99 (3.50–18.23)	< 0.001	6.81 (1.83–25.29)	0.004
Ground Glass	Yes/No	44.47 (5.93–333.58)	< 0.001	-	-
Patchy Infiltration	Yes/No	2.59 (1.41–4.74)	0.002	-	-
Abbreviation: <i>BUN</i> : blood urea nitrogen					
* Backward elimination method was used to fit multivariate logistic regression model.					

In further analysis, two hundred patients with complete data for selected variables were included in the multiple logistic regression model (with backward method). We have observed that Hb level ( $\leq 10$ ), neutrophil count ( $> 7.7$ ), creatinine level ( $\geq 1.3$ ), SpO2 level ( $< 90$ ), and patchy consolidation were related to increased odds of death after adjustment for other variables (Table 5).

## Discussion:

The present study is one of the primary reports with a large number of COVID-19 patients in Iran. We have observed that Hb, neutrophil, BUN, SpO2, and patchy consolidation in the CT assessment at admission time are statistically related to mortality. Although other factors may effect on outcome (Table 5).

Interestingly, just one quarter of our study patients revealed a history of contact with suspected patients, which is comparable with the another finding (11). The virus transmission rout remains an important issue, which may play a major role in development of disease. Besides the common routs, nosocomial, fecal-oral, and aerosol transmission should be considered (12–14). Nosocomial transmission of the disease may occur mainly during the incubation period as well as close contact with patients with minimal symptoms (5, 15–17). Although the outbreak in China has been started via zoonotic transmission, in the city of Qom, the main rout of transmission seems to be person-to-person. None of our patients had a history of travel to China in the last two months before the outbreak and had a history of wild animal contact. All of our patients have inhabited in Qom too. Indeed, familial cluster was common in the city that close contact have happened. We should emphasize that transmission can be occurred by asymptomatic cases during incubation period even by potential routs such as saliva and urine (11, 18).

The important point is the need to use well protective techniques, isolation and laboratory assessment, particularly for the healthcare staff. Moreover, in present study we did not estimate the virus reproductive value but according to the contamination speed, it may be higher than the previous reported data. Earlier studies indicated that the reproductive value ( $R_0$ ) of COVID-19 was estimated to be between 2 and 3.5. It means that one infected patient could infect 2 to 3.5 individuals (17, 19, 20).

The gender distribution in our study shows that the male gender is prominent. Although there was no significant association between gender and the outcome. This is similar to the previous reports (21, 22). Furthermore, we have observed the association of mortality with increasing age, although it was not an independent risk factor for the mortality and lower than former study of China. In this context, previous studies verified that aging has a positive relation with mortality rate in MERS, SARS as well as COVID-19. It may be secondary to either severe pneumonia or its own associated morbidities during elderly (23) (2, 11). Recent report of CDC team for COVID-19, revealed that 80% of deaths are secondary to COVID-19 and it was among adults aged  $\geq 65$  years (24). In a pathophysiology view, studies on immune system in elderly patients disclosed the impaired T and B cell function. In fact, at older age the alteration of cytokines has a key role in the immune system function, as excess production of type 2 cytokines has been reported. Altogether, cytokines dysregulation could lead to defect control of viral infection and inflammatory responses (25, 26).

In present study, the main presentations were dyspnea and shortness of breath, cough, and fatigue/weakness. Bilateral opacities in CT scan assessments were particularly frequent in patients. Among them, bilateral consolidation associated significantly with risk of mortality. The relation between drop of SpO<sub>2</sub> level with poor outcome may work in this context. The CT scan imaging is one of the principal and rapid diagnosis in COVID-19 for initiation of treatment and follow-up in order to find the healing changes in lungs. It was stated that consolidation with ground glass feature in both lungs were more prominent, particularly in dead patients, which was similar to our findings (27–29). The mechanism of lung damage needs more studies. It may be due to direct invasion of virus or inflammatory cascade, altogether, there is a need for more studies in order to identify the exact imaging feature of the disease for prognosis estimation and improvement assessment.

Clinical presentations of our study patients have some differences with other studies (29, 30). We have found fever more than 38<sup>o</sup>C was not a common symptom. In this regard the 87 (43.5%) subjects were fibril patients. This fact may reduce the predictive value of fever during surveillance. Moreover, number of patients with gastrointestinal manifestations at the time of admission was low and not significant differences between survivor and non-survivor patients regarding liver biochemistries has been observed. However, recent studies indicated the close relationship of abnormal liver function tests with severity of COVID-19 (1, 2, 11) that is not compatible with our findings.

Since this disease is a new disaster, we don't have a lot of documents regarding its epidemiologic features and clinical course. Rodrigez et al, based on a meta-analysis, have reported that fever (88.7%), cough (57.6%) and dyspnea (45.6%) were the most prevalent clinical manifestations (31). These findings



have some differences with SARS or MERS observations but almost comparable with the previous reports of COVID-19 (32, 33). Furthermore, Borges do Nascimento et al. reported that lymphopenia ( $0.93 \times 10^3/\mu\text{L}$ , 95% CI  $0.83-1.03 \times 10^3/\mu\text{L}$ ,  $n = 464$ ), and abnormal CRP (33.72 mg/dL, 95% CI 21.54–45.91 mg/dL;  $n = 1637$ ) are the most common laboratories findings in the patients with COVID-19 (34).

Neutrophilia ( $> 7.7 \text{count}10^3/\mu\text{L}$ ) was common among our patients that significantly associated with mortality. This is also consistent with the previous studies as it was observed that patients increased blood neutrophil counts had severe symptoms (35–37). In severe cases lymphopenia has a great potential prognostic value and neutrophilia involved in inflammatory process. Wu et al in Wuhan revealed that the risk of ARDS significantly associated with neutrophilia, as well as aging and coagulation dysfunction (38). Furthermore, almost all of non-survivor patients suffered from ARDS. In addition, we have revealed a strong significance association between low Hb level and poor prognosis. In previous studies Hb value was found to be significantly lower in COVID-19 patients with severe disease than in those with milder forms. Hb level may reflect the severity of disease and probably involved in pathophysiology of organ failure on these patients and worse clinical outcome. Decline of Hb level could be secondary of inflammation process (1, 39). Therefore; regular assessment of CBC with differentiate at beginning and during patients' follow up, clinically would strongly recommended.

It is documented that patients with acute viral and bacterial pneumonia are at the risk of acute cardiac events during and after elimination of infection. Unfortunately, due to the outbreak emergency, patients were not regularly evaluated for cardiac enzymes or echocardiography. Hence, we did not have enough data regarding cardiac events. Among patients with COVID-19, many of them had underlying cardiovascular diseases and developed acute cardiac injury during the course of the illness (40). The mechanism has not been fully cleared but it can be due to neutrophils activity and inflammation process or direct invasion of pathogen (41, 42). Moreover, it is documented that preexisting coronary heart disease can be associated with acute cardiac events and eventually poor outcome in respiratory viral infection such as influenza (43, 44).

In conclusion, this is a large study among patients with definite outcome. In fact, COVID19 is a clinically complex virus that affects all the vital organs either via direct attack or inflammatory processes. Shortness of breath or dyspnea and cough were the common and valuable clinical manifestations. Low value of Hb, neutrophilia, and high BUN along with consolidation in CT scan images were risk factors of mortality that need to pay more attention during surveillance of patients.

## **Appendix 1: Definition**

*Fever was defined as the sublingual temperature more than 37.6 °C. Sepsis defined as a life-threatening organ dysfunction caused by a dysregulated host response to the infection and septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality, according to the Third International Consensus Definition for Sepsis and Septic Shock (45). Acute kidney injury was diagnosed based on the KDIGO clinical practice*

*guidelines (46). Acute respiratory distress syndrome (ARDS) was defined as reported by the Berlin Definition (47). Coagulopathy was defined as INR more than 1.3 or more than 3-second extension of prothrombin time (PT). Exposure history was defined as exposure to people with suspected or confirmed COVID-19. Due to emergency circumstances some lab tests were not available.*

## **Declarations**

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### **Conflict of Interest:**

There is no conflict of Interest

### **Ethic approval:**

The study protocol was approved by ethic committee of Qom university of medical Sciences ;ID:IR.QUMS.rec.1398.154

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