Clinical and paraclinical predictive factors for in-hospital mortality in adult patients with COVID-19

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Abstract

Background

Since December 2019, a type of coronavirus has emerged in Wuhan, China, which has become the focus of global attention due to an epidemic of pneumonia of unknown cause, called COVID-19. This study aimed to investigate the factors affecting in-hospital mortality of patients with COVID-19 hospitalized in one of the main hospital in central Iran.

Methods

This retrospective cross-sectional study (February 2019-May 2020) was conducted on patients with confirmed diagnosis COVID-19, who were admitted in Yazd Shahid Sadoughi Hospital, in middle of Iran. The patients with uncompleted or missed medical files were excluded from the study. Data were extracted from the patients' medical files and then analyzed. The patients were categorized as survivors and non-survivors groups, and they were compared.

Results

Totally, 573 patients were enrolled, that 356 (62.2%) were male. The mean $\pm$ SD of age was 56.29 ± 17.53 years, and 93 (16.23%) were died. All the complications were more in non-survivors. Intensive care unit (ICU) admission was in 20.5% of the patients which was more in non-survivors ($P < 0.001$). The results of multivariate logistic regression test showed that plural effusion in lung computed tomography (CT) scan ($OR = 0.055$, $P = 0.009$), white blood cell (WBC) ($OR = 1.417$, $P = 0.022$), serum albumin ($OR = 0.009$, $P < 0.001$), non-invasive mechanical ventilation ($OR = 34.315$, $P < 0.001$), and acute respiratory distress syndrome (ARDS) ($OR = 66.039$, $P = 0.001$) were achieved as the predictive factors for in-hospital mortality were the predictive factors for in-hospital mortality.

Conclusion

In-hospital mortality in patients with COVID-19 was about 16%. Plural effusion in lung CT scan, WBC, albumin, non-invasive mechanical ventilation, and ARDS were obtained as the predictive factors for in-hospital mortality.

Background

Since December 2019, a type of coronavirus has emerged in Wuhan, China, which has become the focus of global attention due to an epidemic of pneumonia of unknown cause, called COVID-19. According to statistics of the World Health Organization, in this pandemic, more than 110 million definitive cases of patients with COVID-19 were identified until February 22, 2021. Also, in Iran, until the same date, more than 1.5 million cases and about 60,000 deaths have been reported due to the virus (1).

Early diagnosis of this disease is very important because it affects the prognosis of patients. On the other hand, controlling risk factors and identifying high-risk individuals are considered essential (9). Given that different studies on different communities have reported scattered results on common clinical symptoms and paraclinical findings as well as factors affecting the severity and mortality, this study aimed to investigate the factors affecting in-hospital mortality of patients with COVID-19 hospitalized in one of the main hospital in central Iran.

Methods

This retrospective cross-sectional study (February 2019-May 2020) was conducted on patients' medical files with diagnosis COVID-19, who were admitted and hospitalized in Shahid Sadoughi Hospital, Yazd, Iran, one of the biggest teaching and referral hospital in middle of Iran. The inclusion criteria were all adult patients (> 18 years), with confirmed diagnosis of COVID-19 using polymerase chain reaction (PCR) test. The patients with uncompleted or missed medical files were excluded from the study.

After relevant coordination, the patients' medical files were extracted from the hospital's archives unit and assessed. Data were recorded in a data gathering form, which was designed by the researchers according to previous researches. It was consist of below parts: 1) patients' demographic information (age, gender, marital status, type of residence, education levels); 2) medical history and clinical findings at the time of admission; 3) laboratory findings; 4) computed tomography (CT) scan findings; 5) treatments; 6) complications; and 7) outcomes (discharge or in-hospital mortality).

All analyses were performed by SPSS version 16.0 for Windows. The Shapiro-Wilk t-test was used to test normal distribution of numerical variables. Independent sample *t* or Mann-Whitney tests was used for two-group comparisons of continuous variables. Chi-square and Fisher's exact tests were used for proportions. In the univariate logistic regression analysis, each variable was separately entered. Variables with a $P < 0.2$ from the univariate analysis were entered into the multivariate logistic regression analysis, using the Forward Stepwise methods to determine predictive factors for in-hospital mortality, and odds ratio (OR) were reported. It is noteworthy that despite the large number of variables studied in this survey, the variables were entered the regression model in cluster form (medical findings, laboratory findings, treatments, and complications); and finally, significant variables in each cluster were entered the final multivariate logistic regression model. Results were presented as mean $\pm$ standard deviation (SD) for continuous variables and were summarized in number (percentage) for categorical ones. Two-sided *P*-value less than 0.05 and confidence interval (CI) of 95% were considered to be statistically significant.

The current study was conducted in accordance with the Declaration of Helsinki, and it was approved by the vice-chancellor of research and technology, as well as the local ethics committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1399.028). To consider ethical issue, the collected data were not revealed to anyone, except for the researchers; hence, patients' names were kept confidential.

Results

Totally, 573 patients were enrolled, that 356 (62.2%) were male ($P < 0.001$). The mean $\pm$ SD of age was 56.29 ± 17.53 (range; 19–94) years, and 93 (16.23%) were died in the hospital ($P < 0.001$). The patients were categorized as two groups: survivors and non-survivors. The patients' demographics' characteristics were statistically similar in both groups

Hypertension (36.4%), diabetes mellitus (DM) (26.6%), and chronic heart disease (CHD) (12.8%) were the most common underlying disease, which were observed more in non-survivors ($P < 0.001$, $P < 0.001$ and $P = 0.001$, respectively). Cough (72.9%), fever (69.8%), dyspnea (61%) and myalgia (43%) were the most common clinical findings. The frequency of dyspnea and loss of consciousness were higher in non-survivors ($P < 0.001$ and $P < 0.001$)

The mean $\pm$ SD of pulse rate (PR) and respiratory rate (RR) were 86.99 ± 13.18 and 19.37 ± 5.89 respectively, which were higher in non-survivors ($P < 0.001$ and $P < 0.001$). Moreover, higher body temperature was recorded in them ($P < 0.001$). On the other hand, the peripheral O₂ saturation was lower in this group ($P < 0.001$). But, the frequency of Glasgow coma scale (GCS) of 15 was more in survivors ($P < 0.001$) (Table 1).

Table 1

Demographic characteristics and clinical features of patients with definitive diagnosis of COVID-19

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
Age (year) (mean $\pm$ SD)	56.29 $\pm$ 17.53	69.71 $\pm$ 14.36	53.45 $\pm$ 16.42	< 0.001*
Gender (%)	356 (62.6)	64 (68.8)	262 (61.8)	0.236
Male	213 (37.4)	29 (31.2)	162 (38.2)	
Female				
Marital status (%)	477 (96.0)	88 (97.8)	389 (95.6)	0.552
Married	20 (4.0)	2 (2.2)	18 (4.4)	
Single				
Place of residence (%)	404 (94.8)	85 (98.8)	319 (93.8)	0.096
Urban	22 (5.2)	1 (1.2)	21 (6.2)	
Rural				
Smoking (%)	6 (5.9)	0 (0)	6 (6.9)	0.588
Hookah consumption (%)	3 (3.2)	0 (0)	3 (3.6)	0.999
Drug abuse (%)	5 (5.0)	2 (12.5)	3 (3.6)	0.180
Suspicious contact (%)	15 (51.7)	1 (50.0)	14 (51.9)	0.999
Recent travel (%)	5 (26.3)	1 (33.3)	4 (25.0)	0.999
Type of travel (%)	7 (70.0)	2 (100)	5 (62.5)	0.999
Internal	3 (30.0)	0 (0)	3 (37.5)	
Abroad				

* Statistically significant; COPD: chronic obstructive pulmonary disease; GCS: Glasgow coma scale; HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
History of underlying diseases (%)	178 (34.6)	48 (53.3)	130 (30.6)	< 0.001*
Hypertension	137 (26.6)	39 (43.3)	98 (23.1)	< 0.001*
Diabetes mellitus	18 (3.5)	9 (10.0)	9 (2.1)	0.001*
COPD	14 (2.7)	3 (3.3)	11 (2.6)	0.001*
Asthma	3 (0.6)	0 (0)	3 (0.7)	0.720
Pregnancy	66 (12.8)	22 (24.4)	44 (10.4)	0.999
Chronic heart diseases	18 (3.5)	11 (12.2)	7 (1.6)	0.001*
Chronic kidney diseases	3 (0.6)	1 (1.1)	2 (0.5)	< 0.001*
Liver diseases	2 (0.4)	1 (1.1)	1 (0.2)	0.439
Hematologic diseases	5 (1.0)	2 (2.2)	3 (0.7)	0.319
Neurological diseases	11 (2.1)	10 (11.1)	1 (0.2)	0.212
Immunodeficiency diseases	12 (2.3)	7 (7.8)	5 (1.2)	< 0.001*
Cancer	7 (1.4)	5 (5.6)	2 (0.5)	0.001*
Receiving chemotherapy	0 (0)	0 (0)	0 (0)	0.001*
HIV/AIDS	7 (1.4)	2 (2.2)	5 (1.2)	0.002*
Corticosteroid use				- 0.353

* Statistically significant; COPD: chronic obstructive pulmonary disease; GCS: Glasgow coma scale; HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
Clinical signs and symptoms at the time of admission (%)	360 (69.8)	61 (67.8)	299 (70.2)	0.705
Fever	376 (72.9)	62 (68.9)	314 (73.7)	0.363
Cough	69 (13.4)	16 (17.8)	53 (12.4)	0.232
Sputum	29 (5.6)	6 (6.7)	23 (5.4)	0.802
Sore throat	222 (43.0)	31 (34.4)	191 (44.8)	0.079
	107 (20.7)	25 (27.8)	82 (19.2)	0.085
	102 (19.8)	11 (12.2)	91 (21.4)	0.057
	314 (61.0)	72 (80.0)	242 (56.9)	< 0.001*
	87 (16.9)	12 (13.3)	75 (17.6)	0.357
Myalgia	63 (12.2)	9 (10.0)	54 (12.7)	0.491
	42 (8.1)	6 (6.7)	36 (8.5)	0.676
Fatigue	22 (4.3)	4 (4.5)	18 (4.2)	0.999
Headache	52 (10.1)	9 (10.0)	43 (10.1)	0.999
Dyspnea	5 (1.0)	0 (0)	5 (1.2)	0.593
Nausea	0 (0)	0 (0)	0 (0)	-
Vomiting	15 (2.9)	12 (13.3)	3 (0.7)	< 0.001*
Diarrhea	2 (0.4)	1 (1.1)	1 (0.2)	0.319
Abdominal pain				
Anorexia				
Anosmia				
Loss of taste				
Loss of consciousness				
Seizure				

* Statistically significant; COPD: chronic obstructive pulmonary disease; GCS: Glasgow coma scale; HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
Vital signs at the time of admission (mean $\pm$ SD)	120.17 $\pm$ 15.53	120.93 $\pm$ 19.31	120.02 $\pm$ 14.64	0.677
Systolic blood pressure (mmHg)	75.74 $\pm$ 10.40	75.34 $\pm$ 11.86	75.82 $\pm$ 10.08	0.697
Diastolic blood pressure (mmHg)	86.99 $\pm$ 13.18	92.38 $\pm$ 17.17	85.87 $\pm$ 11.91	< 0.001*
Pulse rate (per minute)	19.37 $\pm$ 5.89	23.00 $\pm$ 8.58	18.62 $\pm$ 4.85	< 0.001*
Respiratory rate (per minute)	37.46 $\pm$ 1.86	37.80 $\pm$ 1.07	37.39 $\pm$ 1.97	0.058
Body temperature ($^{\circ}$ C)	90.91 $\pm$ 8.61	82.94 $\pm$ 15.00	92.56 $\pm$ 5.26	< 0.001*
Oxygen saturation (%)	14.91 $\pm$ 3.67	13.64 $\pm$ 2.71	15.18 $\pm$ 3.78	
GCS				

* Statistically significant; COPD: chronic obstructive pulmonary disease; GCS: Glasgow coma scale; HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
Vital signs at the time of admission in categories (%)	139 (27.5)	70 (79.5)	69 (16.5)	< 0.001*
Systolic blood pressure ≤ 100 mmHg	41 (8.1)	24 (27.3)	17 (4.1)	< 0.001*
Pulse rate ≤ 60 per minute	243 (47.8)	75 (85.2)	168 (40.0)	< 0.001*
Pulse rate ≥ 90 per minute	196 (38.7)	83 (94.3)	113 (27.0)	< 0.001*
Respiratory rate ≥ 20 per minute	149 (49.8)	17 (70.8)	132 (48.0)	< 0.001*
Body temperature ≥ 37.8°C (under 60 years)	144 (58.8)	55 (76.4)	89 (51.4)	< 0.001*
Body temperature ≥ 37.5°C (over 60 years)	131 (25.7)	74 (84.1)	57 (13.5)	0.129
Oxygen saturation (%)	178 (34.8)	78 (88.6)	100 (23.6)	< 0.001*
≤ 85	264 (51.6)	58 (65.9)	206 (48.6)	< 0.001*
85–89	463 (90.6)	51 (58.6)	412 (97.2)	< 0.001*
90–92	491 (95.5)	66 (75.0)	425 (99.8)	< 0.001*
≥93	79 (15.4)	72 (81.8)	7 (1.6)	0.003*
GCS				< 0.001*
15				< 0.001*
>15				< 0.001*
* Statistically significant; COPD: chronic obstructive pulmonary disease; GCS: Glasgow coma scale; HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome				

Generally, bilateral lung infiltration (90.5%), peripheral pulmonary lobes involvement (65.3%), Ground-glass opacification/opacity (GGO) (45%), and air bronchogram (43%) were the most common lung CT scan findings. Mixed GGO/consolidation (P = 0.002), air bronchogram (P < 0.001), bilateral lung infiltration (P = 0.039), mixed central/peripheral pulmonary lobes involvement (P < 0.001), lymphadenopathy (LAP) ((P < 0.001), crazy paving (P < 0.001) and septal thickening were observed more in non-survivors. Nonetheless, consolidation (P = 0.018) and peripheral pulmonary lobes involvement (P < 0.001) were more in survivors (Table 2).

Table 2
Paraclinical findings of patients with definitive diagnosis of COVID-19

Variables	Total (n = 573)	Non-survivors (n = 93)	Survivors (n = 426)	P-value
Lung CT scan findings (%)	179 (45.0)	25 (36.8)	130 (46.4)	0.174
GGO	44 (11.1)	2 (2.9)	38 (13.6)	0.018*
Consolidation	171 (43.0)	41 (60.3)	108 (38.6)	0.002*
Mixed GGO/consolidation	56 (14.1)	22 (32.4)	26 (9.3)	< 0.001*
Air Bronchogram	34 (8.5)	2 (2.9)	28 (10.0)	0.088
Infiltration	360 (90.5)	66 (97.1)	248 (88.6)	0.039*
Unilateral	3 (0.8)	0 (0)	2 (0.7)	0.999
Bilateral	260 (65.3)	28 (41.2)	200 (71.4)	< 0.001*
Pulmonary lobe involvement	131 (32.9)	40 (58.8)	74 (26.4)	< 0.001*
Central	37 (9.3)	14 (20.6)	20 (7.1)	0.002*
Environmental	6 (1.5)	1 (1.5)	4 (1.4)	0.999
Central and peripheral composition	72 (18.1)	30 (44.1)	35 (12.5)	< 0.001*
Lymphadenopathy	72 (18.1)	30 (44.1)	35 (12.5)	< 0.001*
Nodules	27 (6.8)	7 (10.3)	18 (6.4)	0.294
Crazy paving	11 (2.7)	0 (0)	7 (2.5)	< 0.001*
Septal thickening	43 (10.6)	2 (3.0)	32 (11.3)	
Pleural effusion	145 (35.9)	9 (13.4)	118 (41.7)	
Severity of pulmonary involvement	149 (36.9)	35 (52.2)	97 (34.3)	
Normal	56 (13.9)	21 (31.3)	29 (10.2)	
Minimal				
Mild				
Moderate				
Severe				
Laboratory findings (mean ± SD)	6.60 ± 6.29	10.71 ± 14.12	5.84 ± 2.28	0.002*
* Statistically significant; ALT: alanine transaminase; ALKP: alkaline phosphatase; AST: aspartate transaminase; BUN: Blood urea nitrogen; CPK: creatine phosphokinase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GGO: Ground-glass opacification/opacity; INR: international normalized ratio; SD: standard deviation; WBC: white blood cell				

Variables	Total (n = 573)	Non-survivors (n = 93)	Survivors (n = 426)	P-value
WBC (10 ⁹ /L)	13.85 ± 6.04	12.86 ± 2.26	14.14 ± 6.86	0.087
	177.34 ± 67.01	177.75 ± 70.45	177.45 ± 65.59	0.970
	22.24 ± 11.34	14.72 ± 13.72	23.86 ± 10.12	< 0.001*
	143.01 ± 78.30	172.33 ± 88.35	129.81 ± 68.86	< 0.001*
	32.55 ± 26.10	54.85 ± 48.70	27.54 ± 14.51	< 0.001*
	1.51 ± 4.46	1.80 ± 1.35	1.48 ± 5.11	0.553
Hemoglobin (g/dL)	200.80 ± 329.47	338.47 ± 545.62	166.94 ± 248.42	0.021
Platelet (10 ⁹ /L)				< 0.001*
Lymphocyte (10 ² /μL)	530.65 ± 282.76	760.05 ± 510.24	484.29 ± 191.58	0.001*
Blood sugar (mg/dL)	39.27 ± 37.05	55.18 ± 48.22	34.92 ± 30.91	0.284
BUN (mg/dL)	33.39 ± 32.92	37.58 ± 42.08	32.0 ± 30.08	0.168
Serum creatinine (mg/dL)	197.32 ± 178.28	249.45 ± 375.91	185.56 ± 76.29	0.329
CPK (mcg/L)			1.21 ± 1.62	0.180
LDH (U/L)	1.31 ± 1.76	1.68 ± 2.26	0.40 ± 1.10	< 0.001*
AST (U/L)	0.48 ± 1.21	0.78 ± 1.67	137.31 ± 3.51	0.004*
ALT (U/L)	136.82 ± 3.80	135.25 ± 4.54	4.00 ± 0.44	< 0.001*
ALKP (IU/L)	4.05 ± 0.50	4.23 ± 0.68	8.33 ± 0.59	0.034*
Bilirubin total (mg/dL)	8.21 ± 0.64	7.84 ± 0.66	3.58 ± 0.66	0.467
Bilirubin direct (mg/dL)	3.66 ± 0.96	4.00 ± 1.53	1.88 ± 0.42	< 0.001*
Serum sodium (mEq/L)	1.88 ± 0.96	1.92 ± 0.38	3.98 ± 0.48	0.259
Serum potassium (mEq/L)	3.78 ± 0.58	3.27 ± 0.51	1.28 ± 0.34	< 0.001*
Calcium (mg/dL)	1.31 ± 0.32	1.34 ± 0.29	46.44 ± 28.64	0.028*
Phosphor (mg/dL)	50.01 ± 30.19	67.92 ± 30.93	102 (27.3)	0.999
Magnesium (mg/dL)	126 (25.4)	14 (18.4)	35 (9.4)	0.034*
Serum albumin (g/dL)	43 (8.7)	5 (6.6)	76 (20.3)	0.952
INR	113 (22.7)	25 (32.9)	123 (32.9)	0.012*
	159 (32.0)	19 (25.0)		

* Statistically significant; ALT: alanine transaminase; ALKP: alkaline phosphatase; AST: aspartate transaminase; BUN: Blood urea nitrogen; CPK: creatine phosphokinase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GGO: Ground-glass opacification/opacity; INR: international normalized ratio; SD: standard deviation; WBC: white blood cell

Variables	Total (n = 573)	Non-survivors (n = 93)	Survivors (n = 426)	P-value
ESR	56 (11.3)	13 (17.1)	38 (10.2)	
CRP			1 (0.8)	
Negative			132 (99.2)	
Poor positive			7.40 ± 0.12	
+ 1			37.16 ± 10.68	
+ 2			24.31 ± 6.98	
+3	2 (1.1)	0 (0)		
Troponin	184 (98.9)	34 (100.0)		
Positive	7.37 ± 0.11	7.35 ± 0.10		
Negative	37.25 ± 9.55	37.29 ± 9.30		
PH	22.25 ± 5.40	20.99 ± 4.23		
PCO2				
HCO3				
* Statistically significant; ALT: alanine transaminase; ALKP: alkaline phosphatase; AST: aspartate transaminase; BUN: Blood urea nitrogen; CPK: creatine phosphokinase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GGO: Ground-glass opacification/opacity; INR: international normalized ratio; SD: standard deviation; WBC: white blood cell				

The laboratory findings are also shown in Table 2. The mean ± SD of white blood cell (WBC) (P = 0.002), blood sugar (P < 0.001), urea (P < 0.001), lactate dehydrogenase (LDH) (P < 0.001), AST (P = 0.001), serum potassium (P = 0.004), phosphor (P = 0.034), erythrocyte sedimentation rate (ESR) (P < 0.001) were statistically higher in non-survivors. On the other hand, the mean ± SD of lymphocyte (P < 0.001), serum sodium (P = 0.004), calcium (P < 0.001), and serum albumin (P < 0.001) were higher in survivors.

Most frequent administrated treatment were lopinavir/ritonavir (Kaletra) (91.8%), hydroxychloroquine (88.7%), and oseltamivir (73%), respectively. In non-survivors vitamin D3 (P < 0.001), levofloxacin (tavanex) (P < 0.001), corticosteroids (P < 0.001), non-invasive mechanical ventilation (P < 0.001), invasive mechanical ventilation (P < 0.001), and renal replacement therapy (RRT) were more administered (P < 0.001). But, administration of hydroxychloroquine was more in survivors (P = 0.028) (Table 3).

Table 3
Treatments in patients with definitive diagnosis of COVID-19

Variables	Total (n = 573)	Non-survivors (n = 93)	Survivors (n = 426)	P-value
Hydroxychloroquine	456 (88.7)	72 (81.8)	384 (90.1)	0.028*
Kalletra	471 (91.8)	79 (89.8)	392 (92.2)	0.520
Oseltamivir	374 (73.0)	59 (67.0)	315 (74.3)	0.187
Vitamin D3	300 (58.6)	46 (52.9)	254 (59.8)	0.282
Antibiotics	176 (34.4)	57 (64.8)	119 (28.1)	< 0.001*
Meropenem	157 (30.7)	62 (70.5)	95 (22.5)	< 0.001*
Ceftriaxone	83 (16.2)	18 (20.5)	65 (15.4)	0.266
Tavanex	87 (17.0)	19 (21.6)	68 (16.1)	0.214
Corticosteroids	104 (20.3)	54 (61.4)	50 (11.8)	< 0.001*
Noninvasive mechanical ventilation	43 (8.4)	32 (36.4)	11 (2.6)	< 0.001*
Invasive mechanical ventilation	71 (13.8)	70 (79.5)	1 (0.2)	< 0.001*
Renal replacement therapy	17 (3.3)	16 (18.4)	1 (0.2)	< 0.001*
* Statistically significant				

As was shown in Table 4, respiratory failure (15.1%), sepsis (13.1%), and acidosis (9.2%) were the most common complications, totally. All the complications were more in non-survivors. Intensive care unit (ICU) admission was in 20.5% of the patients which was more in non-survivors ($P < 0.001$). The mean $\pm$ SD of hospitalization was 6.79 ± 4.98 days, which was more in non-survivors ($P < 0.001$). But, the duration of ICU admission was similar in both groups ($P = 0.201$).

Table 4
Complications and outcomes in patients with definitive diagnosis of COVID-19

Variables	Total (n = 573)	Non- survivors (n = 93)	Survivors (n = 426)	P- value
Complications (%)	67 (13.1)	60 (69.0)	7 (1.7)	< 0.001*
Sepsis	35 (6.8)	35 (40.2)	0 (0)	< 0.001*
Septic shock	77 (15.1)	73 (83.9)	4 (0.9)	< 0.001*
Respiratory failure		39 (45.3)	1 (0.2)	< 0.001*
ARDS		4 (4.7)	0 (0)	
Heart failure		38 (44.2)	9 (2.1)	
Acidosis		19 (22.1)	1 (0.2)	
Coagulopathy		31 (36.0)	1 (0.2)	
AKI		3 (3.5)	0 (0)	
Acute heart injury	40 (7.8)	7 (8.1)	0 (0)	< 0.001*
Secondary infection	4 (0.8)			0.001*
	47 (9.2)			< 0.001*
	20 (3.9)			< 0.001*
	32 (6.3)			< 0.001*
	3 (0.6)			0.005*
	7 (1.4)			< 0.001*

* Statistically significant; AKI: Acute kidney injury; ARDS: acute respiratory distress syndrome; SD: standard deviation

Variables	Total (n = 573)	Non-survivors (n = 93)	Survivors (n = 426)	P-value
Outcomes	27 (5.2)	10 (11.1)	17 (4.0)	0.015*
Hospital readmission (%)	103 (20.5)	79 (91.9)	24 (5.8)	< 0.001*
Admission to the intensive care unit (%)	6.79 ± 4.98	10.68 ± 7.91	5.97 ± 3.62	< 0.001*
Duration of hospitalization (days) (mean ± SD)	7.84 ± 7.25	8.36 ± 7.78	6.22 ± 5.11	0.201
Duration of hospitalization in the intensive care unit (days) (mean ± SD)	13.02 ± 6.26	15.68 ± 8.00	12.52 ± 5.76	0.003*
Time between onset of clinical symptoms and outcome (days) (mean ± SD)	10.10 ± 5.24	9.90 ± 5.12	11.00 ± 5.97	0.533
Duration between the onset of clinical symptoms and admission to the intensive care unit (day) (mean ± SD)	7.11 ± 4.27	6.42 ± 3.58	7.22 ± 4.36	0.310
Duration between onset of fever and hospital admission (days) (mean ± SD)	6.69 ± 4.04	6.26 ± 3.57	6.77 ± 4.12	0.463
Duration between cough onset and hospital admission (days) (mean ± SD)	6.25 ± 4.58	6.38 ± 4.89	6.22 ± 4.52	0.847
Duration between the onset of dyspnea and hospital admission (days) (mean ± SD)	12.34 ± 4.11	12.20 ± 4.38	13.25 ± 1.71	0.644
Time between onset of symptoms and onset of corticosteroid treatment (days) (mean ± SD)	* Statistically significant; AKI: Acute kidney injury; ARDS: acute respiratory distress syndrome; SD: standard deviation			

The results of multivariate logistic regression test in each cluster was shown in Table 5. Plural effusion in lung CT scan (OR = 0.055, P = 0.009), WBC (OR = 1.417, P = 0.022), albumin (OR = 0.009, P < 0.001), non-invasive mechanical ventilation (OR = 34.315, P < 0.001), and acute respiratory distress syndrome (ARDS) (OR = 66.039, P = 0.001) were achieved as the predictive factors for in-hospital mortality (Table 6).

Table 5

Results of multivariate logistic regression test in each category (medical findings, paraclinical findings, treatments, and complications)

Variables		B	Standard error	P-value	OR	95% CI for odds ratio	
						Lower	Upper
Medical findings	Age	0.043	0.011	< 0.001*	1.044	1.022	1.067
	Diabetes mellitus	0.711	0.325	0.029*	2.036	1.077	3.846
	Chemotherapy	2.579	0.933	0.006*	13.181	2.118	82.040
	Dyspnea	0.703	0.354	0.047*	2.020	1.010	4.042
	Respiratory rate	0.120	0.040	0.003*	1.128	1.043	1.220
	GCS	0.677	0.677	0.011*	0.177	0.047	0.667
	O ₂ saturation	0.024	0.024	0.002*	.930	0.887	0.974
Paraclinical findings	Plural effusion	-5.378	1.975	0.006*	0.005	0.001	0.222
	WBC	0.492	0.168	0.003*	1.635	1.177	2.271
	Albumin	-4.069	1.026	< 0.001*	0.017	0.002	0.128
Treatments	Hydroxychloroquine	-1.235	0.349	< 0.001*	0.291	0.147	0.576
	Antibiotics	0.716	0.288	0.013*	2.046	1.164	3.596
	Non-invasive mechanical ventilation	2.101	0.422	< 0.001*	8.174	3.577	18.677
	Corticosteroids	1.629	.303	< 0.001*	5.101	2.816	9.239
Complications	Respiratory failure	3.759	0.730	< 0.001*	42.923	10.263	179.510
	ARDS	4.156	1.376	0.003*	63.788	4.304	945.380
	AKI	4.345	1.328	0.001*	77.056	5.711	1039.743
	ICU admission	2.853	0.727	< 0.001*	17.346	4.175	72.070
	Readmission	2.337	0.915	0.011*	10.346	1.720	62.223
* Statistically significant; ARDS: acute respiratory distress syndrome; AKI: Acute kidney injury; CI: confidence interval; GCS: Glasgow coma scale; ICU: intensive care unit; OR: odds ratio; WBC: white blood cell							

Table 6

Results of multivariate logistic regression test to determine the predictive factors for in-hospital mortality

Variables	B	Standard error	P-value	OR	95% CI for odds ratio	
					Lower	Upper
Plural effusion	-2.901	1.237	0.019*	0.055	0.005	0.621
WBC	0.349	0.153	0.022*	1.417	1.051	1.911
Albumin	-4.688	1.208	< 0.001*	0.009	0.001	0.098
Non-invasive mechanical ventilation	3.536	0.799	< 0.001*	34.315	7.172	164.178
ARDS	4.190	1.274	0.001*	66.039	5.437	802.171
* Statistically significant; ARDS: acute respiratory distress syndrome; CI: confidence interval; OR: odds ratio; WBC: white blood cell						

The comparison of confirmed COVID-19 patients in regards of ICU and regular wards' admissions was shown in supplementary Table 1.

Discussion

The current study investigated the factors affecting in-hospital mortality of patients with COVID-19 hospitalized in one of the main teaching hospital in central Iran. The results showed that the mean $\pm$ SD of age was 17.53 ± 56.29 years, and about 60% of inpatients were male. In line with our findings, in a study by Chen et al., the mean age of inpatients was reported as 55 years, of which 67% were male (10). In another study by Wu et al., the highest mortality rate was reported in older men with underlying disease (3). During a systematic review and a meta-analysis, Li et al. epidemiologically investigated clinical features, risk factors, and treatment outcomes in patients with COVID-19. The results showed that the mean age of all patients with COVID-19 was 46.7 years, of which 51.8% were male (11).

In the present study, 93 patients (16.23%) died in the hospital. The mean $\pm$ SD of age of these patients was 14.36 ± 69.71 years. However, the results showed that age, gender, marital status, place of residence, cigarette, hookah, and drug use, recent travel history, and the history of contact with the suspect person were not different between survivors and non-survivors. In a study conducted in China, Wei et al. showed that the mean age of individuals who died from COVID-19 was 51 years, and most of them were elderly men (12). In a study by Zhou et al., the mean age of individuals who died from COVID-19 was reported as 69 years, which was significantly higher than the survived group, and most of the deceased patients were male (2). In a study by Tang et al., this rate was obtained 64 years which was significantly higher than the discharged group (13).

The most common underlying diseases in patients with COVID-19 in the present study were hypertension (36.4%), DM (26.6%), and CHD (12.8%), respectively, all of which were observed in non-survivors. Chen et al.

also reported that 51% of patients with a definitive diagnosis of COVID-19 had an underlying disease (10). Similarly, Liang et al. showed that 40% of patients with COVID-19 had an underlying disease, including cardiovascular, pulmonary, and cerebrovascular diseases, as well as DM and cancer, respectively (14). In another study performed by Zou et al., 51.59% of individuals had an underlying disease, including hypertension, cardiovascular diseases, DM, chronic respiratory disease, or cancer (15). In another study, the most common clinical manifestations of COVID-19 were reported as fever, cough, and fatigue (16). In Zhang et al.'s study, gastrointestinal symptoms, hypertension, and DM were reported as the main underlying diseases in these patients (17).

The present study showed that the most common clinical symptoms in patients were cough, fever, shortness of breath, and myalgia. Shortness of breath and loss of consciousness were significantly more common in non-survivors. Previous similar studies have shown that the most common symptoms observed in patients with COVID-19 were fever and chills, shortness of breath, cough, myalgia, weakness, lethargy, and gastrointestinal symptoms such as nausea, vomiting, and diarrhea (6, 10, 15). Common symptoms in patients with COVID-19 were reported by Wei et al. as fever and cough (12). Zou et al. stated that the most common symptom present in patients included fever, cough, shortness of breath, hemoptysis, and diarrhea, respectively (15). In a meta-analysis, Cao et al. showed that the most prevalent clinical manifestations in patients with COVID-19 were fever, cough, shortness of breath, myalgia or fatigue, and respiratory distress (18).

The mean $\pm$ SD of PR and RR per minute in this study were significantly higher in non-survivors. On the other hand, the percentage of O₂ saturation in non-survivors was lower. GCS of 15 was more common in survived patients. In a study by Liu et al., the means of heart rate and RR per minute were 24 and 94, respectively (19). A RR > 24 per minute was reported 29% in Chen et al.'s study, which was significantly higher in deceased patients (63% versus 16%). Also, a heart rate > 125 beats per minute was observed in only 1% of patients. Fever was recorded in 94% of patients and it was similar in survivors and non-survivors (10).

In the present study, the most findings of lung CT scan were bilateral infiltration (90.5%), peripheral lobes involvement (65.3%), GGO (45%), and air bronchogram (43%), generally. In non-survivors, mixed GGO/consolidation, air bronchogram, bilateral infiltration, mixed central-peripheral lobe involvement, LAP, crazy paving, and septal thickening were observed, but consolidation and peripheral lobe involvement were significantly higher in survivors. Chen et al. found that pulmonary involvement was mostly as bilateral pneumonia followed by GGO lesions (10). Francone et al. showed that the most common view observed on CT scan (less than 7 days from the onset of symptoms) was the GGO; and after 7 days, crazy paving, consolidation, and fibrosis were the most common views, respectively (20). In a study by Huang et al., 98% had bilateral lung involvement, and in general GGO was more common (6). Cao et al. mentioned the main findings of imaging as bilateral pneumonia and GGO (18). Salehi et al. stated that one of the known features of COVID-19 in patients' early lung CT scans is GGO with peripheral or posterior distribution, mainly in the lower lobes and less in the middle lobe. Septal thickening, bronchiectasis, pleural thickening, and subpleural involvement are some of the less prevalent findings that are mainly seen in the later stages of the disease. Pleural effusions, pericardial effusions, lymphadenopathy, cavitation, halo symptoms, and

pneumothorax are very rare but may be seen as the disease progresses. Imaging patterns related to clinical improvement usually occur after 2 weeks of illness and include the gradual removal of opacities and the decrease in the number of lesions and involved lobes (21).

In this study, the means $\pm$ SD of WBC, blood sugar, urea, LDH, aspartate transaminase (AST), serum potassium, phosphorus, and ESR were higher in non-survivors, but the mean $\pm$ SD of lymphocytes, serum potassium, calcium, and albumin were higher in survivors. In Huang et al.'s study, laboratory features in patients with COVID-19 included leukopenia (25%), lymphopenia (25%), and increased AST (37%) (6). Zhang et al. also found that prothrombin and D-dimer levels were higher in patients with ICU than (17). In a meta-analysis, Lippi et al. reported that in almost all patients with COVID-19 (99%), the troponin level increased to the maximum normal range. In addition, troponin levels highly increased in patients with severe infection than those with milder disease; and it could predict the likelihood of heart damage and disease progression toward worse clinical signs, and protective cardiac treatments may be helpful in these patients (23). In another systematic review and meta-analysis, it was reported that out of 4,663 patients, the most common laboratory finding related to COVID-19 was C-reactive protein (CRP), followed by decreased albumin, increased ESR, decreased eosinophil, increased interleukin 6, decreased lymphocyte count, and finally increased LDH, respectively. Their meta-analytic findings on 1905 patients also showed that the increased CRP and LDH levels, as well as decreased lymphocyte in the patients' blood samples, would be significantly associated with increased disease severity and mortality (25).

Our findings demonstrated that the most treatments performed were Kaletra, hydroxychloroquine, and oseltamivir, respectively. In non-survivors, vitamin D3, antibiotics, tavanex, corticosteroids, non-invasive mechanical ventilation, invasive mechanical ventilation, and RRT were further used. However, hydroxychloroquine was more administered to survivors. Zhou et al. stated antibiotics and corticosteroids as the most commonly used treatments (2). Moreover, Chen et al. mentioned the most commonly used treatments for patients as antiviral drugs, oxygen therapy, and antibiotics, but found no evidence of their effectiveness (10). Various treatments have been suggested for patients over time, which the reason for the observed differences may be due to the increased knowledge and experience of physicians regarding drugs effectiveness in the treatment of COVID-19 and its complications.

The most common complications observed in our studied patients included respiratory failure, sepsis, and acidosis, respectively. All complications were more common in non-survivors. Zhou et al. mentioned sepsis, respiratory failure, ARDS, and heart failure as the most common complications, all of which were significantly higher in non-survivors. The results regarding the difference between the onset of symptoms and the onset of complications in our study were similar to the obtained results by Zhou et al.'s (2). In Chen et al.'s study, ARDS was observed in 17% of patients, which was the most common complication (10).

Hospital readmission was observed in 5.2% of patients in the present study, which was higher in non-survivors. ICU admission was observed in 20.5% of patients, which was higher in non-survivors. In Zhou et al.'s study, 26% of patients were admitted to the ICU, which was significantly higher in non-survivors (2). Also, in our study, the mean of hospital stay were higher in patients with in-hospital mortality, but it was lower in deceased patients in Zhou et al.'s study. However, similar to their results (2), the duration of ICU

admission in patients of both groups was not significantly different in the present research. Also, in line with their results, the means of the time between the onset of clinical symptoms and outcome were more common in non-survivors (2).

The results of the present study showed that 76.7% of patients with ICU admission died, which was significantly higher than survivors. In the study by Auld et al., the mortality rate of patients with ICU admission was reported as 33.9%, which was lower than the result obtained in the present study. This rate was reported as 52–62% in other similar studies (28). Another study in the United States found that 50–67% of patients with ICU admission died (29).

The results of this study showed that plural effusion in lung CT scan, WBC, albumin, non-invasive mechanical ventilation, and ARDS were the predictive factors for in-hospital mortality in patients with COVID-19. Wang et al. found that CRP could be a valuable marker for predicting the likelihood of exacerbation of the disease in adult patients with non-severe COVID-19 (24). By examining the clinical findings of 82,719 patients with coronavirus that resulted in the treatment of 4632 patients who died, Deng et al. considered old age and male gender as risk factors for mortality. It was also observed that the time from the onset of symptoms to the treatment center, the time from the onset of symptoms to laboratory confirmation of COVID-19, and the duration of onset of symptoms to the patients' hospitalization of were directly related to higher mortality (30).

The retrospective nature of the study, lack of recording all data accurately, and lack of follow-up of discharged patients were among the limitations of this study. On the other hand, the high sample size of patients and the study of various factors were among the strengths of this study. Using the results of the current study can be effective in physicians' clinical decisions and also policy makers. However, performing multicenter and prospective studies with larger sample sizes and assessing other factors, especially the effect of vaccination, as well as the drug doses and their complications, can be valuable.

Conclusions

This study showed that most inpatients were male. In-hospital mortality was obtained at about 16% and ICU admission was observed in about 20% of patients with COVID-19. Plural effusion in lung CT scan, WBC, albumin, non-invasive mechanical ventilation, and ARDS were obtained as predictive factors for in-hospital mortality in these patients.

Abbreviations

ARDS

acute respiratory distress syndrome

AKI

Acute kidney injury

ALT

alanine transaminase

ALKP
alkaline phosphatase
AST
aspartate transaminase
BUN
Blood urea nitrogen
CHD
chronic heart disease
COPD
chronic obstructive pulmonary disease
CRP
C-reactive protein
CPK
creatine phosphokinase
CT scan
computed tomography scan
DM
diabetes mellitus
ESR
erythrocyte sedimentation rate
GCS
Glasgow coma scale
GGO
Ground-glass opacification/opacity
HIV/AIDS
human immunodeficiency virus/ acquired immunodeficiency syndrome
LAP
lymphadenopathy
LDH
lactate dehydrogenase
ICU
intensive care unit
INR
international normalized ratio
OR
odds ratio
PCR
polymerase chain reaction
PR
pulse rate
RR

respiratory rate
RRT
renal replacement therapy
SD
standard deviation
WBC
white blood cell

Declarations

Ethics approval and consent to participate

The current study was approved by Shahid Sadoughi University of Medical Sciences (grant No. 7745), as well as the local Ethic Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1399.028).

This was a retrospective cross-sectional study, which was conducted on patients' medical files. So informed consent was not required for this survey. To consider ethical issue, the collected data were not revealed to anyone, except for the researchers; hence, patients' names were kept confidential.

Consent for publication

Not applicable

Availability of data and materials

The data are available on logical request.

Competing interests

The authors have no conflicts of interest to declare for this study.

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Authors' contributions

SAM and RSM contributed to supervision, conception, design, acquisition of data, and writing up the manuscript. RSM, FN, SP, AG, HP, KA, RSM contributed to search literature and related studies. RSM, FN, SP, AG, HP, KA, ASY contributed to data acquisition. RSM and RSM contributed to data analysis. All authors contributed to write the first draft of the manuscript, reviewed and edited it. All authors approved the final version of the manuscript.

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