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

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Research

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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 hospitals 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 ± 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.

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 ± 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 ± 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 ± 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).
| Variables                    | Total (n = 573) | Non-survivors (n = 93) | Survivors (n = 426) | P-value |
|------------------------------|-----------------|------------------------|---------------------|---------|
| Age (year) (mean ± SD)       | 56.29 ± 17.53   | 69.71 ± 14.36          | 53.45 ± 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                      | 477 (96.0)      | 88 (97.8)              | 389 (95.6)          |         |
| Single                       | 20 (4.0)        | 2 (2.2)                | 18 (4.4)            |         |
| Place of residence (%)       | 404 (94.8)      | 85 (98.8)              | 319 (93.8)          | 0.096   |
| Urban                        | 404 (94.8)      | 85 (98.8)              | 319 (93.8)          |         |
| Rural                        | 22 (5.2)        | 1 (1.2)                | 21 (6.2)            |         |
| 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 (%)** |                |                        |                     |               |
| Hypertension                   | 178 (34.6)     | 48 (53.3)              | 130 (30.6)          | < 0.001*      |
| Diabetes mellitus              | 137 (26.6)     | 39 (43.3)              | 98 (23.1)           | < 0.001*      |
| COPD                           | 18 (3.5)       | 9 (10.0)               | 9 (2.1)             | 0.001*        |
| Asthma                         | 14 (2.7)       | 3 (3.3)                | 11 (2.6)            | 0.001*        |
| Pregnancy                      | 3 (0.6)        | 0 (0)                  | 3 (0.7)             | 0.720         |
| Chronic heart diseases         | 66 (12.8)      | 22 (24.4)              | 44 (10.4)           | 0.999         |
| Chronic kidney 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 (%) |                |                        |                     |         |
| Fever                                         | 360 (69.8)     | 61 (67.8)              | 299 (70.2)          | 0.705   |
| Cough                                         | 376 (72.9)     | 62 (68.9)              | 314 (73.7)          | 0.363   |
| Sputum                                        | 69 (13.4)      | 16 (17.8)              | 53 (12.4)           | 0.232   |
| Sore throat                                   | 29 (5.6)       | 6 (6.7)                | 23 (5.4)            | 0.802   |
| Myalgia                                       | 222 (43.0)     | 31 (34.4)              | 191 (44.8)          | 0.079   |
| Sore throat                                   | 107 (20.7)     | 25 (27.8)              | 82 (19.2)           | 0.085   |
| Fatigue                                       | 102 (19.8)     | 11 (12.2)              | 91 (21.4)           | 0.057   |
| Headache                                      | 314 (61.0)     | 72 (80.0)              | 242 (56.9)          | < 0.001*|
| Dyspnea                                       | 87 (16.9)      | 12 (13.3)              | 75 (17.6)           | 0.357   |
| Nausea                                        | 63 (12.2)      | 9 (10.0)               | 54 (12.7)           | 0.491   |
| Nausea                                        | 42 (8.1)       | 6 (6.7)                | 36 (8.5)            | 0.676   |
| Headache                                      | 22 (4.3)       | 4 (4.5)                | 18 (4.2)            | 0.999   |
| Headache                                      | 52 (10.1)      | 9 (10.0)               | 43 (10.1)           | 0.999   |
| Nausea                                        | 5 (1.0)        | 0 (0)                  | 5 (1.2)             | 0.593   |
| Vomiting                                      | 0 (0)          | 0 (0)                  | 0 (0)               | -       |
| Diarrhea                                      | 15 (2.9)       | 12 (13.3)              | 3 (0.7)             | < 0.001*|
| Abdominal pain                                | 2 (0.4)        | 1 (1.1)                | 1 (0.2)             | 0.001*  |
| Anorexia                                      |                |                        |                     | 0.319   |
| 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 ± SD)** |                |                        |                     |         |
| Systolic blood pressure (mmHg)                | 120.17 ± 15.53 | 120.93 ± 19.31         | 120.02 ± 14.64      | 0.677   |
| Diastolic blood pressure (mmHg)               | 75.74 ± 10.40  | 75.34 ± 11.86          | 75.82 ± 10.08       | 0.697   |
| Pulse rate (per minute)                       | 86.99 ± 13.18  | 92.38 ± 17.17          | 85.87 ± 11.91       | < 0.001*|
| Respiratory rate (per minute)                 | 19.37 ± 5.89   | 23.00 ± 8.58           | 18.62 ± 4.85        | 0.058   |
| Body temperature (°C)                         | 37.46 ± 1.86   | 37.80 ± 1.07           | 37.39 ± 1.97        | < 0.001*|
| Oxygen saturation (%)                          | 90.91 ± 8.61   | 82.94 ± 15.00          | 92.56 ± 5.26        | < 0.001*|
| GCS                                           | 14.91 ± 3.67   | 13.64 ± 2.71           | 15.18 ± 3.78        |         |

*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 (%)** | | | | |
| Systolic blood pressure ≤ 100 mmHg | 139 (27.5) | 70 (79.5) | 69 (16.5) | < 0.001* |
| Pulse rate ≤ 60 per minute | 41 (8.1) | 24 (27.3) | 17 (4.1) | < 0.001* |
| Pulse rate ≥ 90 per minute | 243 (47.8) | 75 (85.2) | 168 (40.0) | < 0.001* |
| Respiratory rate ≥ 20 per minute | 196 (38.7) | 83 (94.3) | 113 (27.0) | < 0.001* |
| Body temperature ≥ 37.8°C (under 60 years) | 131 (25.7) | 74 (84.1) | 57 (13.5) | 0.129 |
| Body temperature ≥ 37.5°C (over 60 years) | 144 (58.8) | 55 (76.4) | 89 (51.4) | 0.001* |
| 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 | | | | |
| 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).
| Variables                              | Total (n = 573) | Non-survivors (n = 93) | Survivors (n = 426) | P-value |
|----------------------------------------|-----------------|------------------------|---------------------|---------|
| **Lung CT scan findings (%)**          |                 |                        |                     |         |
| GGO                                    | 179 (45.0)      | 25 (36.8)              | 130 (46.4)          | 0.174   |
| Consolidation                          | 34 (8.5)        | 2 (2.9)                | 32 (7.5)            | 0.154   |
| Mixed GGO/consolidation                | 34 (8.5)        | 2 (2.9)                | 32 (7.5)            | 0.154   |
| Air Bronchogram                        | 34 (8.5)        | 2 (2.9)                | 32 (7.5)            | 0.154   |
| Infiltration                           | 360 (90.5)      | 66 (97.1)              | 248 (88.6)          | 0.039   |
| Unilateral                             | 3 (0.8)         | 0 (0)                  | 2 (0.7)             | 0.999   |
| Bilateral                              | 30 (7.8)        | 3 (4.2)                | 27 (6.3)            | 0.134   |
| Central lobe involvement               | 131 (32.9)      | 40 (58.8)              | 21 (4.9)            | <0.001  |
| Central                                | 37 (9.3)        | 14 (20.6)              | 20 (4.7)            | 0.002   |
| Environmental                          | 6 (1.5)         | 1 (1.5)                | 4 (0.9)             | 0.999   |
| Central and peripheral composition     | 72 (18.1)       | 30 (44.1)              | 35 (12.5)           | <0.001  |
| Lymphadenopathy                        | 72 (18.1)       | 30 (44.1)              | 22 (6.3)            | <0.001  |
| Nodules                                | 27 (6.8)        | 7 (10.3)               | 18 (6.4)            | 0.294   |
| Crazy paving                           | 11 (2.7)        | 0 (0)                  | 3 (0.7)             | <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                                | 56 (13.9)       | 21 (31.3)              | 29 (10.2)           |         |
| Mild                                   | 56 (13.9)       | 21 (31.3)              | 29 (10.2)           |         |
| Moderate                               | 56 (13.9)       | 21 (31.3)              | 29 (10.2)           |         |
| Severe                                 | 56 (13.9)       | 21 (31.3)              | 29 (10.2)           |         |
| 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  | Non-survivors | Survivors | P-value |
|----------------------------|--------|---------------|-----------|---------|
|                            | (n = 573) | (n = 93)      | (n = 426) |         |
| 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*|
| Hemoglobin (g/dL)          | 1.51 ± 4.46  | 1.80 ± 1.35  | 1.48 ± 5.11  | 0.553   |
|                            | 200.80 ± 329.47  | 338.47 ± 545.62  | 166.94 ± 248.42  | 0.021   |
|                            | < 0.001* | < 0.001* | < 0.001* |         |
| Platelet (10^9/L)          | 530.65 ± 282.76 | 760.05 ± 510.24 | 484.29 ± 191.58 |         |
|                            | 39.27 ± 37.05 | 55.18 ± 48.22 | 34.92 ± 30.91 | 0.284   |
| Lymphocyte (10^2/µL)       | 32.55 ± 26.10 | 54.85 ± 48.70 | 27.54 ± 14.51 | < 0.001* |
| Blood sugar (mg/dL)        | 197.32 ± 178.28 | 249.45 ± 375.91 | 185.56 ± 76.29 | 0.329   |
| BUN (mg/dL)                | 1.31 ± 1.76  | 1.68 ± 2.26  | 0.40 ± 1.10  | 0.021   |
| Serum creatinine (mg/dL)   | 136.82 ± 3.80 | 135.25 ± 4.54 | 4.00 ± 0.44 | < 0.001* |
| CPK (mcg/L)                | 1.21 ± 1.62  | 1.21 ± 1.62  | 1.21 ± 1.62  | 0.180   |
| LDH (U/L)                  | 0.48 ± 1.21  | 0.78 ± 1.67  | 137.31 ± 3.51 | 0.004*  |
| AST (U/L)                  | 1.31 ± 1.76  | 1.68 ± 2.26  | 0.40 ± 1.10  | 0.001*  |
| ALT (U/L)                  | 4.05 ± 0.50  | 4.23 ± 0.68  | 8.33 ± 0.59  | < 0.001* |
| ALKP (IU/L)                | 3.66 ± 0.96  | 4.00 ± 1.53  | 1.88 ± 0.42  | < 0.001* |
| BIL (mg/dL)                | 1.88 ± 0.96  | 1.92 ± 0.38  | 3.98 ± 0.48  | 0.034*  |
| Serum sodium (mEq/L)       | 3.78 ± 0.58  | 3.27 ± 0.51  | 1.28 ± 0.34  | < 0.001* |
| Serum potassium (mEq/L)    | 1.31 ± 0.32  | 1.34 ± 0.29  | 46.44 ± 28.64 | 0.028*  |
| Calcium (mg/dL)            | 50.01 ± 30.19 | 67.92 ± 30.93 | 102 (27.3) | 0.999   |
| Phosphor (mg/dL)           | 126 (25.4) | 14 (18.4) | 35 (9.4) | 0.034*  |
| Magnesium (mg/dL)          | 43 (8.7) | 5 (6.6) | 76 (20.3) | 0.952   |
| Serum albumin (g/dL)       | 113 (22.7) | 25 (32.9) | 123 (32.9) | 0.012*  |
| INR                        | 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       |                |                        |                     |         |
| Negative  |                |                        |                     |         |
| Poor positive                     | 7.40 ± 0.12       | 37.16 ± 10.68         | 24.31 ± 6.98       |
| +1        |                |                        |                     |         |
| +2        |                |                        |                     |         |
| +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 (Kalletra) (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 ± 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 (%)**      |                 |                        |                     |         |
| Sepsis                     | 67 (13.1)       | 60 (69.0)              | 7 (1.7)             | < 0.001*|
| Septic shock               | 35 (6.8)        | 35 (40.2)              | 0 (0)               | < 0.001*|
| Respiratory failure        | 77 (15.1)       | 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)               | < 0.001*|
| 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                                                                 |                |                        |                     |         |
| Hospital readmission (%)                                                 | 27 (5.2)       | 10 (11.1)              | 17 (4.0)            | 0.015*  |
| Admission to the intensive care unit (%)                                 | 103 (20.5)     | 79 (91.9)              | 24 (5.8)            | < 0.001*|
| Duration of hospitalization (days) (mean ± SD)                           | 6.79 ± 4.98    | 8.36 ± 7.91            | 5.97 ± 3.62         | < 0.001*|
| Duration of hospitalization in the intensive care unit (days) (mean ± SD)| 7.84 ± 7.25    | 15.68 ± 8.00           | 12.52 ± 5.76        | 0.003*  |
| Time between onset of clinical symptoms and outcome (days) (mean ± SD)   | 13.02 ± 6.26   |                        |                     |         |
| Duration between the onset of clinical symptoms and admission to the intensive care unit (day) (mean ± SD) | 10.10 ± 5.24 | 9.90 ± 5.12 | 11.00 ± 5.97 | 0.533   |
| Duration between onset of fever and hospital admission (days) (mean ± SD) | 7.11 ± 4.27   | 6.42 ± 3.58            | 7.22 ± 4.36         | 0.310   |
| Duration between cough onset and hospital admission (days) (mean ± SD)   | 6.69 ± 4.04    | 6.26 ± 3.57            | 6.77 ± 4.12         | 0.847   |
| Duration between the onset of dyspnea and hospital admission (days) (mean ± SD) | 6.25 ± 4.58 | 6.38 ± 4.89 | 6.22 ± 4.52 | 0.644   |
| Time between onset of symptoms and onset of corticosteroid treatment (days) (mean ± SD) | 12.34 ± 4.11 | 12.20 ± 4.38 | 13.25 ± 1.71 |         |

* 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   |
| O₂ 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 | 0.303          | < 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                 |
| Plural effusion                  | -2.901| 1.237          | 0.019*  | 0.055| 0.005                 |
| WBC                              | 0.349 | 0.153          | 0.022*  | 1.417| 1.051                 |
| Albumin                          | -4.688| 1.208          | <0.001* | 0.009| 0.001                 |
| Non-invasive mechanical ventilation | 3.536 | 0.799          | <0.001* | 34.315| 7.172                 |
| ARDS                             | 4.190 | 1.274          | 0.001*  | 66.039| 5.437                 |

* 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 ± 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 ± 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 ± SD of PR and RR per minute in this study were significantly higher in non-survivors. On the other hand, the percentage of O\textsubscript{2} 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 ± SD of WBC, blood sugar, urea, LDH, aspartate transaminase (AST), serum potassium, phosphorus, and ESR were higher in non-survivors, but the mean ± 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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