

Original Article



# Factors associated with disease severity and length of stay in hospitalized COVID-19 patients in Tabriz, Iran: A retrospective cohort study

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## Abstract

**Introduction:** The novel coronavirus disease (COVID-19) has spread globally. Early and dynamic detection of prognostic factors is essential to improve the ability to treat COVID-19. The present study aimed to determine clinical characteristics and risk factors associated with the length of hospital stay and disease severity in hospitalized COVID-19 patients in Tabriz, Iran.

**Methods:** This retrospective cohort study included 260 early diagnosed cases with COVID-19 hospitalized at two COVID-19 specialized hospitals in Tabriz, Iran, from April 20 to June 20, 2020. Patients' medical records were used to collect the data. Severe COVID-19 outcomes included need for intubation, admission to the intensive care unit, or death. The data were analyzed using descriptive and analytical statistics, including chi-squared test, Mann-Whitney U test, and logistic regression analysis in SPSS 16.

**Results:** The need for O<sub>2</sub> therapy (adjusted odds ratio [AOR]=4.23; 95% CI: 1.15–15.51; *P*=0.03), the increased creatinine levels (AOR=2.71; 95% CI: 1.25–5.88; *P*=0.01), and the white blood cell counts (AOR=2.44; 95% CI: 1.12–5.33; *P*=0.02) were the main risk factors associated with prolonged hospital stay. Also, having kidney diseases (AOR=7.33; 95% CI=1.94–27.70; *P*=0.01), elevated the white blood cell counts (AOR=4.52; 95% CI=1.67–12.26; *P*=0.003), and lung diseases (AOR=3.97; 95% CI: 1.18–13.29; *P*=0.03) were significant among the predictors of the disease severity.

**Conclusion:** According to the results, hypoxia and underlying diseases might lead to unwanted outcomes. The risk factors identified here confirm previous information and could be helpful to guide early clinical decision-making to reduce the mortality rates and improve the clinical outcomes of COVID-19.

## Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory syndrome that has outspread to most countries in a few months. The burden of COVID-19 has been on the increase globally.<sup>1</sup> Since December 2019, more than 137 million people have been infected, with approximately 3 million deaths.<sup>2</sup>

Patients with COVID-19 mainly have a fever, myalgia or fatigue, and dry cough. Although most patients are believed to have a favorable prognosis, elderly patients and those with chronic diseases are at risk for more severe illness and mortality. Patients who have the severe disease might develop shortness of breath and hypoxemia within one week of the onset of the disease, which can rapidly progress to acute respiratory distress

syndrome (ARDS) or organ failure.<sup>3</sup> Initial analysis of patients hospitalized in China with COVID-19 have shown that diabetes, hypertension, and cardiovascular diseases are very common among them, and patients with these comorbidities are more exposed to have poor clinical outcomes.<sup>4</sup> In a recent study of 201 patients with COVID-19 pneumonia, risk factors associated with ARDS development and progression from ARDS to death included age, neutrophilia, organ dysfunction, and coagulation disorders.<sup>3</sup>

The time of clearance of coronavirus RNA depended on sex, disease severity, and lymphocyte function.<sup>5</sup> The clinical spectrum of COVID-19 infection is wide, including asymptomatic infection, mild upper respiratory tract disease, and severe viral pneumonia associated

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with respiratory failure and even death.<sup>6</sup> Although many studies have been carried out, many aspects of the disease, including the prognosis and related factors, remain unknown.<sup>7</sup> On the other hand, there is still a long way to go before the universal coverage of the vaccine is achieved. Furthermore, there is no definitive cure for it, the gene mutations of the virus continue, and most importantly, there is an increase in the number of daily deaths.<sup>5</sup> For this reason, it is important to identify factors associated with disease severity and prolonged hospital stay. The present study aimed to determine clinical characteristics and risk factors related to the length of hospital stay and disease severity in hospitalized COVID-19 patients in Tabriz, Iran.

## Methods

The present retrospective cohort study recruited 260 early cases of COVID-19 diagnosed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) and hospitalized at the Sina and Imam Reza educational hospitals (the general referral hospitals for COVID-19 patients) in Tabriz, Iran, from April 20 to June 20, 2020.

We reviewed the medical records of patients and extracted demographic data, underlying comorbidities, signs, symptoms, laboratory results, treatment (including antiviral therapy, antibacterial therapy, oxygen therapy, and other supportive treatments), and outcome data (length of hospital stay, severity of disease, and mortality) of the patients. The patients' laboratory results were acquired on the day of admission, and the changes were reviewed.

As the distribution of some quantitative variables was not normal, the descriptive statistics consisted of medians and interquartile ranges (IQR) for continuous data. Mann-Whitney U test was performed for continuous variables, and chi-squared and Fisher's exact tests were employed for categorical variables as appropriate. To explore the risk factors associated with the dependent variables (length of hospital stay and severity of disease), univariate and multivariate binary logistic regression analysis were used. Variables were chosen for multivariable logistic regression model based on univariate analysis ( $P < 0.2$ ), previous findings, and clinical importance, including age, sex, hospitalized ward, having fever, fatigue, anorexia, and coronary heart disease at admission, O<sub>2</sub> therapy, white blood cell counts at admission and increased white blood cell counts and creatinine during hospitalization.

Because the median length of stay (LOS) was 5.0 days, patients who stayed longer than five days were compared with those who stayed for five days or less. Severe COVID-19 outcome was defined based on the need for intubation and mechanical ventilation, admission to the intensive care unit, or mortality. The odds ratio (OR) with the 95% confidence interval (CI) were reported.  $P$  value  $< 0.05$  was regarded as statistically significant. All the statistical analyses were performed by the SPSS 16

(Inc., Chicago, Illinois, USA).

## Results

A total of 260 early patients with laboratory-confirmed COVID-19 were studied. The median age of the patients was 62.5 years old (IQR, 48.0-73.0). The most common symptom was dry cough (69.2%). The records indicated that 93.8% of the patients received oxygen, and 21.2% were mechanically ventilated. A review of laboratory results on admission showed that 92.3% (240/260) of the patients had elevated white blood cell counts. The demographic, clinical characteristics, laboratory findings, and treatments provided to patients with COVID-19 at the initial admission are presented in [Table 1](#).

Based on the median as the cut-off point, the study population was divided into two groups by LOS of  $\leq 5$  days ( $n = 129$ ) and  $> 5$  days ( $n = 131$ ) ([Table 2](#)).

The multivariate logistic regression model, based on stepwise forward variable selection, contained the predictor variables. As presented in [Table 3](#), need for O<sub>2</sub> therapy (adjusted odds ratio [AOR] = 4.23; 95% CI: 1.15-15.51;  $P = 0.03$ ), increased creatinine level (AOR = 2.71; 95% CI: 1.25-5.88;  $P = 0.01$ ), and white blood cell counts (AOR = 2.44; 95% CI: 1.12-5.33;  $P = 0.02$ ) were the main risk factors associated with increased odds of prolonged LOS.

Based on the need or no need for intubation, ICU admission, or death from disease, the study population was divided into two groups by severe COVID-19 outcome ( $n = 79$ ) and non-severe COVID-19 outcome ( $n = 181$ ). Having kidney diseases (AOR = 7.33; 95% CI: 1.94-27.70;  $P = 0.01$ ), elevated white blood cell counts (AOR = 4.52; 95% CI: 1.67-12.26;  $P = 0.003$ ), and lung diseases (AOR = 3.97; 95% CI: 1.18-13.29;  $P = 0.03$ ) were significant among predictors of disease severity ([Tables 3 and 4](#)).

## Discussion

The present study aimed to determine clinical characteristics and risk factors associated with the length of hospital stay and disease severity in hospitalized COVID-19 patients in Tabriz, Iran. According to the results, the main predictors of prolonged LOS (including hypoxia and leukocytosis) and severity (including hypoxia, leukocytosis, and comorbidities) are discussed below.

### Hypoxia

Two factors indicating oxygen deficiency, i.e., intubation and low SpO<sub>2</sub> levels, were associated with LOS and severe outcomes. Prolonged and untreated hypoxia can lead to poor patient outcomes.<sup>8</sup> In a study of 140 patients with COVID-19 pneumonia, higher SpO<sub>2</sub> levels after oxygen supplementation were associated with a reduction in mortality regardless of age and sex (hazard ratio per 1-U SpO<sub>2</sub>, 0.93; 95% CI: 0.91-0.95;  $P < 0.001$ ). The SpO<sub>2</sub> cut-

**Table 1.** Demographic, clinical, treatment, and laboratory characteristics of COVID-19 patients by hospital length of stay (LOS)

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| Age, Median (IQR), years                          | 62.5 (48.0–73.0)     | 63.0 (47.5–72.0)             | 61.0 (48.0–73.0)             | 0.51    |
| Age groups (y)                                    |                      |                              |                              | -       |
| <20   | 4 (1.5)              | 2 (1.6)                      | 2 (1.5)                      |         |
| 20-34   | 18 (6.9)             | 7 (5.4)                      | 11 (8.4)                     |         |
| 35-49   | 50 (19.2)            | 27 (20.9)                    | 23 (17.6)                    | -       |
| 50-65   | 75 (28.8)            | 36 (27.9)                    | 39 (29.8)                    |         |
| ≥66   | 113 (43.5)           | 57 (44.2)                    | 56 (42.7)                    |         |
| Gender  |                      |                              |                              | 0.67    |
| Male  | 166 (63.8)           | 84 (65.1)                    | 82 (62.6)                    |         |
| Female  | 94 (36.2)            | 45 (34.9)                    | 49 (37.4)                    |         |
| Marital status                                    |                      |                              |                              | 0.79    |
| Single or divorced or widowed                     | 23 (8.8)             | 12 (9.3)                     | 11 (8.4)                     |         |
| Married   | 237 (91.2)           | 117 (90.7)                   | 121 (91.6)                   |         |
| Education   |                      |                              |                              | -       |
| Illiterate  | 84 (32.3)            | 33 (25.6)                    | 51 (38.9)                    |         |
| Elementary- Mid school                            | 76 (29.2)            | 47 (36.4)                    | 29 (22.1)                    |         |
| High school                                       | 55 (21.2)            | 32 (24.8)                    | 23 (17.6)                    |         |
| Graduate  | 30 (11.5)            | 9 (7.0)                      | 21 (16.0)                    |         |
| Unknown   | 15 (5.8)             | 8 (6.2)                      | 7 (5.3)                      |         |
| Location  |                      |                              |                              | 0.96    |
| Urban   | 222 (85.4)           | 110 (85.3)                   | 112 (85.5)                   |         |
| Rural   | 38 (14.6)            | 19 (14.7)                    | 19 (14.5)                    |         |
| Occupation  |                      |                              |                              | 0.99    |
| Manual worker                                     | 17 (6.5)             | 8 (6.2)                      | 9 (6.9)                      |         |
| Employee  | 36 (13.8)            | 17 (13.2)                    | 19 (14.5)                    |         |
| Retired   | 17 (6.5)             | 8 (6.2)                      | 9 (6.9)                      |         |
| Housekeeper                                       | 82 (31.5)            | 40 (31.0)                    | 42 (32.1)                    |         |
| Other   | 95 (36.5)            | 48 (37.2)                    | 47 (35.9)                    |         |
| Unknown   | 13 (5.0)             | 8 (6.2)                      | 5 (3.8)                      |         |
| Admit type  |                      |                              |                              | 0.52    |
| Ambulance   | 17 (11.2)            | 16 (12.4)                    | 13 (9.9)                     |         |
| Own   | 231 (88.8)           | 113 (87.6)                   | 118 (90.1)                   |         |
| Hospital ward                                     |                      |                              |                              | 0.04    |
| Ward  | 213 (81.9)           | 112 (86.8)                   | 101 (77.1)                   |         |
| ICU   | 47 (18.1)            | 17 (13.2)                    | 30 (22.9)                    |         |
| Fever at admission                                |                      |                              |                              | 0.10    |
| No  | 142 (54.6)           | 77 (59.7)                    | 65 (49.6)                    |         |
| Yes   | 118 (45.4)           | 52 (40.3)                    | 66 (50.4)                    |         |
| Chills and fever at admission                     |                      |                              |                              | 0.92    |
| No  | 160 (61.5)           | 79 (61.2)                    | 81 (61.2)                    |         |
| Yes   | 100 (38.5)           | 50 (38.8)                    | 50 (38.2)                    |         |
| Dry cough at admission                            |                      |                              |                              | 0.72    |

**Table 1.** Continued

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| No  | 80 (30.8)            | 41 (31.8)                    | 39 (29.8)                    |         |
| Yes   | 180 (69.2)           | 88 (68.2)                    | 92 (70.2)                    |         |
| Sore throat (pharyngitis) at admission            |                      |                              |                              | 0.35    |
| No  | 238 (91.5)           | 116 (89.9)                   | 122 (93.1)                   |         |
| Yes   | 22 (8.5)             | 13 (10.1)                    | 9 (6.9)                      |         |
| Hyposmia (low smell) at admission                 |                      |                              |                              | -       |
| No  | 259 (99.6)           | 129 (100.0)                  | 130 (99.2)                   |         |
| Yes   | 1 (0.4)              | 0 (0.0)                      | 1 (0.8)                      |         |
| Shortness of breath at admission (breath gasp)    |                      |                              |                              | 0.60    |
| No  | 107 (41.2)           | 51 (39.5)                    | 56 (42.7)                    |         |
| Yes   | 153 (58.8)           | 78 (60.4)                    | 75 (57.3)                    |         |
| Nausea at admission                               |                      |                              |                              | 0.33    |
| No  | 220 (84.6)           | 112 (86.8)                   | 108 (82.4)                   |         |
| Yes   | 40 (15.4)            | 17 (13.2)                    | 23 (17.6)                    |         |
| Vomiting at admission                             |                      |                              |                              | 0.84    |
| No  | 241 (92.7)           | 120 (93.0)                   | 121 (92.4)                   |         |
| Yes   | 19 (7.3)             | 9 (7.0)                      | 10 (7.6)                     |         |
| Diarrhea at admission                             |                      |                              |                              | 0.26    |
| No  | 246 (94.6)           | 120 (93.0)                   | 126 (96.2)                   |         |
| Yes   | 14 (5.4)             | 9 (7.0)                      | 5 (3.8)                      |         |
| Myalgia (muscular pain) at admission              |                      |                              |                              | 0.83    |
| No  | 177 (68.1)           | 87 (67.4)                    | 90 (68.7)                    |         |
| Yes   | 83 (31.9)            | 42 (32.6)                    | 41 (31.3)                    |         |
| Headache at admission                             |                      |                              |                              | 0.82    |
| No  | 225 (86.5)           | 111 (86.0)                   | 114 (87.0)                   |         |
| Yes   | 35 (13.5)            | 18 (14.0)                    | 17 (13.0)                    |         |
| Tachypnea at admission                            |                      |                              |                              | 0.75    |
| No  | 247 (95.0)           | 122 (94.6)                   | 125 (95.4)                   |         |
| Yes   | 13 (5.0)             | 7 (5.4)                      | 6 (4.6)                      |         |
| Fatigue at admission                              |                      |                              |                              | 0.12    |
| No  | 212 (81.5)           | 110 (85.3)                   | 102 (77.9)                   |         |
| Yes   | 48 (18.5)            | 19 (14.7)                    | 29 (22.1)                    |         |
| Anorexia at admission                             |                      |                              |                              | 0.07    |
| No  | 240 (92.3)           | 123 (95.3)                   | 117 (89.3)                   |         |
| Yes   | 20 (7.7)             | 6 (4.7)                      | 14 (10.7)                    |         |
| Abnormal ABG at admission                         |                      |                              |                              | 0.67    |
| No  | 240 (92.3)           | 120 (93.0)                   | 120 (91.6)                   |         |
| Yes   | 20 (7.7)             | 9 (7.0)                      | 11 (8.4)                     |         |

Table 1. Continued

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| Admit SaO <sub>2</sub> , Mean (SD)                | 89.9 (6.5)           | 90.0 (5.7)                   | 89.7 (7.3)                   | 0.82    |
| Current Smoker                                    |                      |                              |                              | 0.32    |
| No  | 226 (86.9)           | 109 (84.5)                   | 117 (89.3)                   |         |
| Yes   | 33 (12.7)            | 19 (14.7)                    | 14 (10.7)                    |         |
| Current alcohol user                              |                      |                              |                              | -       |
| No  | 254 (97.7)           | 125 (96.9)                   | 129 (98.5)                   |         |
| Yes   | 5 (1.7)              | 3 (2.3)                      | 2 (1.5)                      |         |
| Current hookah user                               |                      |                              |                              | 0.37    |
| No  | 248 (95.4)           | 124 (96.1)                   | 124 (94.7)                   |         |
| Yes   | 11 (4.2)             | 4 (3.1)                      | 7 (5.3)                      |         |
| Current Opiate user                               |                      |                              |                              | -       |
| No  | 253 (97.3)           | 123 (95.3)                   | 129 (98.5)                   |         |
| Yes   | 6 (2.3)              | 4 (3.1)                      | 2 (1.5)                      |         |
| <b>Comorbidity—history condition</b>              |                      |                              |                              |         |
| Hypertension                                      |                      |                              |                              | 0.49    |
| No  | 166 (63.8)           | 85 (65.9)                    | 81 (61.8)                    |         |
| Yes   | 94 (36.2)            | 44 (34.1)                    | 50 (38.2)                    |         |
| Diabetes  |                      |                              |                              | 0.94    |
| No  | 184 (70.8)           | 91 (70.5)                    | 93 (71.0)                    |         |
| Yes   | 76 (29.2)            | 38 (29.5)                    | 38 (29.0)                    |         |
| Coronary heart disease                            |                      |                              |                              | 0.17    |
| No  | 216 (83.1)           | 103 (79.8)                   | 113 (86.3)                   |         |
| Yes   | 44 (16.9)            | 26 (20.2)                    | 18 (13.7)                    |         |
| Lung (COPD)                                       |                      |                              |                              | 0.97    |
| No  | 242 (93.1)           | 120 (93.0)                   | 122 (93.1)                   |         |
| Yes   | 18 (6.9)             | 9 (7.0)                      | 9 (6.9)                      |         |
| Kidney  |                      |                              |                              | 0.41    |
| No  | 247 (95.0)           | 124 (96.1)                   | 123 (93.9)                   |         |
| Yes   | 13 (5.0)             | 5 (3.9)                      | 8 (6.1)                      |         |
| Liver   |                      |                              |                              | -       |
| No  | 258 (99.2)           | 128 (99.2)                   | 130 (99.2)                   |         |
| Yes   | 2 (0.8)              | 1 (0.8)                      | 1 (0.8)                      |         |
| Cancer  |                      |                              |                              | -       |
| No  | 257 (98.8)           | 128 (99.2)                   | 129 (98.5)                   |         |
| Yes   | 3 (1.2)              | 1 (0.8)                      | 2 (1.5)                      |         |
| Others  |                      |                              |                              | 0.96    |
| No  | 222 (85.4)           | 110 (85.3)                   | 112 (85.5)                   |         |
| Yes   | 38 (14.6)            | 19 (14.7)                    | 19 (14.5)                    |         |
| At least one comorbidity                          |                      |                              |                              | 0.34    |
| No  | 92 (35.4)            | 42 (32.6)                    | 50 (38.2)                    |         |
| Yes   | 168 (64.6)           | 87 (67.4)                    | 81 (61.8)                    |         |
| Exacerbation of symptoms                          |                      |                              |                              | 0.51    |

Table 1. Continued

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| No  | 197 (75.8)           | 100 (77.5)                   | 97 (74.0)                    |         |
| Yes   | 63 (24.2)            | 29 (22.5)                    | 34 (26.0)                    |         |
| New manifestations                                |                      |                              |                              | 0.33    |
| No  | 201 (77.3)           | 103 (79.8)                   | 98 (74.8)                    |         |
| Yes   | 59 (22.7)            | 26 (20.2)                    | 33 (25.2)                    |         |
| New cardiovascular manifestations                 |                      |                              |                              | 0.92    |
| No  | 213 (81.9)           | 106 (82.2)                   | 107 (81.7)                   |         |
| Yes   | 47 (18.1)            | 23 (17.8)                    | 24 (18.3)                    |         |
| Kidney manifestations                             |                      |                              |                              | 0.26    |
| No  | 230 (88.5)           | 117 (90.7)                   | 113 (86.3)                   |         |
| Yes   | 30 (11.5)            | 12 (9.3)                     | 18 (13.7)                    |         |
| Liver manifestations                              |                      |                              |                              | -       |
| No  | 252 (96.9)           | 126 (97.7)                   | 126 (96.2)                   |         |
| Yes   | 8 (3.1)              | 3 (2.3)                      | 5 (3.8)                      |         |
| O <sub>2</sub> therapy                            |                      |                              |                              | 0.009   |
| No  | 16 (6.2)             | 13 (10.1)                    | 3 (2.3)                      |         |
| Yes   | 244 (93.8)           | 116 (89.9)                   | 128 (97.7)                   |         |
| Intubation  |                      |                              |                              | 0.59    |
| No  | 202 (77.7)           | 102 (79.1)                   | 100 (76.3)                   |         |
| Yes   | 58 (22.3)            | 27 (20.9)                    | 31 (23.7)                    |         |
| Death outcome                                     |                      |                              |                              | 0.61    |
| No  | 198 (76.2)           | 100 (77.5)                   | 98 (74.8)                    |         |
| Yes   | 62 (23.8)            | 29 (22.5)                    | 33 (25.2)                    |         |
| Hydroxychloroquine treatment                      |                      |                              |                              | -       |
| No  | 18 (6.9)             | 9 (7.0)                      | 9 (6.9)                      |         |
| Yes   | 242 (93.1)           | 120 (93.0)                   | 122 (93.1)                   |         |
| Oseltamivir treatment                             |                      |                              |                              | -       |
| No  | 107 (41.2)           | 66 (51.2)                    | 41 (31.3)                    |         |
| Yes   | 153 (58.8)           | 63 (48.8)                    | 90 (68.7)                    |         |
| Kaletra treatment                                 |                      |                              |                              | -       |
| No  | 42 (16.2)            | 24 (18.6)                    | 18 (13.7)                    |         |
| Yes   | 218 (83.8)           | 105 (81.4)                   | 113 (86.3)                   |         |
| Ribavirin treatment                               |                      |                              |                              | -       |
| No  | 209 (80.4)           | 115 (89.1)                   | 94 (71.8)                    |         |
| Yes   | 51 (19.6)            | 14 (10.9)                    | 37 (28.2)                    |         |
| Spry treatment                                    |                      |                              |                              | -       |
| No  | 93 (35.8)            | 56 (43.4)                    | 37 (28.2)                    |         |
| Yes   | 167 (64.2)           | 73 (56.6)                    | 94 (71.8)                    |         |
| Antibiotics treatment                             |                      |                              |                              | -       |
| No  | 73 (28.1)            | 47 (36.4)                    | 26 (19.8)                    |         |
| Yes   | 187 (71.9)           | 82 (63.6)                    | 105 (80.2)                   |         |
| Vitamin C   |                      |                              |                              | -       |

**Table 1.** Continued

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| No  | 178 (68.5)           | 93 (72.1)                    | 85 (64.9)                    |         |
| Yes   | 82 (31.5)            | 36 (27.9)                    | 46 (35.1)                    |         |
| Drug complication, No (%)                         |                      |                              |                              | -       |
| Nausea/vomiting                                   | 129 (49.6)           | 57 (44.2)                    | 72 (55.0)                    |         |
| Arrhythmia  | 131 (50.4)           | 72 (55.8)                    | 59 (45.0)                    |         |
| First WBC   |                      |                              |                              | 0.01    |
| Normal  | 188 (72.3)           | 102 (79.1)                   | 86 (65.6)                    |         |
| Low   | 41 (15.8)            | 12 (9.3)                     | 29 (22.1)                    |         |
| High  | 28 (10.8)            | 15 (11.6)                    | 13 (9.9)                     |         |
| First CRP   |                      |                              |                              | 0.58    |
| Normal  | 14 (5.4)             | 8 (6.2)                      | 6 (4.6)                      |         |
| Low   | -                    | -                            | -                            |         |
| High  | 240 (92.3)           | 119 (92.2)                   | 121 (92.4)                   |         |
| First NA (blood sodium)                           |                      |                              |                              | -       |
| Normal  | 205 (78.8)           | 100 (77.5)                   | 105 (80.2)                   |         |
| Low   | 40 (15.4)            | 20 (15.5)                    | 20 (15.3)                    |         |
| High  | 5 (1.9)              | 4 (3.1)                      | 1 (0.8)                      |         |
| First K (blood potassium)                         |                      |                              |                              | -       |
| Normal  | 230 (88.5)           | 118 (91.5)                   | 112 (85.5)                   |         |
| Low   | 13 (5.0)             | 5 (3.9)                      | 8 (6.1)                      |         |
| High  | 8 (3.1)              | 3 (2.3)                      | 5 (3.8)                      |         |
| First urea  |                      |                              |                              | 0.32    |
| Normal  | 33 (12.7)            | 14 (10.9)                    | 19 (14.5)                    |         |
| Low   | 219 (84.2)           | 113 (87.6)                   | 106 (80.9)                   |         |
| High  | -                    | -                            | -                            |         |
| First Cr  |                      |                              |                              | 0.68    |
| Normal  | 211 (81.2)           | 109 (84.5)                   | 102 (77.9)                   |         |
| Low   | 3 (1.2)              | 1 (0.8)                      | 2 (1.5)                      |         |
| High  | 37 (14.2)            | 17 (13.2)                    | 20 (15.3)                    |         |
| First Calcium                                     |                      |                              |                              | 0.83    |
| Normal  | 49 (18.8)            | 24 (18.6)                    | 25 (19.1)                    |         |
| Low   | 175 (78.3)           | 88 (68.2)                    | 87 (66.4)                    |         |
| High  | 3 (1.2)              | 1 (0.8)                      | 2 (1.5)                      |         |
| WBC increase                                      |                      |                              |                              | 0.005   |
| No  | 205 (78.8)           | 112 (86.8)                   | 93 (71.0)                    |         |
| Yes   | 52 (20.0)            | 17 (13.2)                    | 35 (26.7)                    |         |
| CRP increase                                      |                      |                              |                              | 0.96    |
| No  | 149 (57.3)           | 74 (57.4)                    | 75 (57.3)                    |         |
| Yes   | 108 (41.5)           | 54 (41.9)                    | 54 (41.2)                    |         |
| Urea increase                                     |                      |                              |                              | 0.22    |
| No  | 209 (80.4)           | 108 (83.7)                   | 101 (77.1)                   |         |
| Yes   | 50 (19.2)            | 21 (16.3)                    | 29 (22.1)                    |         |
| Cr increase                                       |                      |                              |                              | 0.06    |

**Table 1.** Continued

| Demographic and clinical characteristics, No. (%) | All patients (n=260) | Hospital LOS <5 days (n=129) | Hospital LOS ≥5 days (n=131) | P value |
|---|----------------------|------------------------------|------------------------------|---------|
| No  | 209 (80.4)           | 110 (85.3)                   | 99 (75.6)                    |         |
| Yes   | 48 (18.5)            | 18 (14.0)                    | 30 (22.9)                    |         |
| SGOT increase (AST)                               |                      |                              |                              | 0.47    |
| No  | 237 (91.2)           | 116 (89.9)                   | 121 (92.4)                   |         |
| Yes   | 21 (8.1)             | 12 (9.3)                     | 9 (6.9)                      |         |
| SGPT increase (ALT)                               |                      |                              |                              | 0.97    |
| No  | 240 (92.3)           | 119 (92.2)                   | 121 (92.4)                   |         |
| Yes   | 18 (6.9)             | 9 (7.0)                      | 9 (6.9)                      |         |
| LDH increase                                      |                      |                              |                              | 0.71    |
| No  | 198 (76.2)           | 97 (75.2)                    | 101 (77.1)                   |         |
| Yes   | 58 (22.3)            | 30 (23.3)                    | 28 (21.4)                    |         |

IQR: Interquartile range, ICU: intensive care unit, AdmiteSaO<sub>2</sub>: oxyhemoglobin saturation in admission time, WBC: white blood cell count, CRP: C-reactive protein, Cr: Creatinine, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase.

off value of 90.5% yielded a sensitivity of 84.6% and a specificity of 97.2% for predicting survival. Dyspnea was also independently associated with multivariate analysis of death (hazard ratio = 2.60; 95% CI: 1.24-5.43; P = 0.01).<sup>9</sup>

However, Liu et al reported no significant differences in blood oxygen saturation between the progression and recovery/stabilization groups.<sup>10</sup> An easily obtainable and clinically relevant measure, SpO<sub>2</sub> of ≤90%, despite oxygen supplementation, provides a major risk factor for fatal outcomes; in fact, this measure is the most powerful predictor of multiple measures,<sup>11</sup> including the standard demographic and inflammatory measures reported in previous studies.<sup>3,12</sup> Further studies are necessary to assess the prognostic importance of such models in COVID-19 pneumonia.

### Coronary artery disease

Ischemic heart disease is another predictor of severe outcomes. Coronary artery disease has also been shown to be associated with acute cardiac events and adverse outcomes of COVID-19, influenza, and other respiratory viral infections.<sup>11,13</sup> A descriptive study of 8,910 COVID-19 patients discharged at the time of analysis showed that coronary artery disease was a factor independently associated with an increased risk of death in hospital (10.2% versus 5.2% among patients without disease; OR = 2.70; 95% CI: 2.08-3.51), heart failure (15.3% versus 5.6% among those who did not have heart failure; OR = 2.48; 95% CI: 1.62-3.79), cardiac arrhythmia (11.5% versus 5.6% among people without arrhythmia; OR = 1.95; 95% CI: 1.33-2.86).<sup>14</sup> The present study confirmed previous observations indicating that underlying cardiovascular disease is associated with an increased risk of hospital death among patients admitted

**Table 2.** Risk factors associated with prolonged hospital LOS ( $\geq 5$  days)

| Demographic and clinical characteristics   | Crude OR (95%)    | P value | Adjusted OR (95%) | P value |
|--|-------------------|---------|-------------------|---------|
| Age (per additional year)                  | 1.0 (.99–1.01)    | 0.98    | -                 | -       |
| Male sex (vs female)                       | 0.90 (.54–1.49)   | 0.67    | -                 | -       |
| Hospital ward (disease severity status)    |                   |         |                   |         |
| ICU (vs. ward)                             | 1.96 (1.02–3.76)  | 0.04    | -                 | -       |
| Having fever at admission                  |                   |         |                   |         |
| Yes (vs. no)                               | 1.50 (0.92–2.46)  | 0.10    | -                 | -       |
| Having anorexia at admission               |                   |         |                   |         |
| Yes (vs. no)                               | 2.45 (0.91–6.60)  | 0.07    | -                 | -       |
| Having fatigue at admission                |                   |         |                   |         |
| Yes (vs. no)                               | 1.64 (.87–3.12)   | 0.13    | -                 | -       |
| O <sub>2</sub> therapy                     |                   |         |                   |         |
| Yes (vs. no)                               | 4.78 (1.33–17.20) | 0.02    | 4.23 (1.15–15.51) | 0.03    |
| Having coronary heart disease at admission |                   |         |                   |         |
| Yes (vs. no)                               | 0.63 (.63–1.22)   | 0.17    | -                 | -       |
| First WBC                                  |                   |         |                   |         |
| Normal                                     | reference         | -       | -                 | -       |
| Low  | 2.87 (1.38–5.96)  | 0.005   | 2.44 (1.12–5.33)  | 0.02    |
| High                                       | 1.03 (0.46–2.28)  | 0.95    | 0.52 (0.20–1.34)  | 0.17    |
| WBC increase                               |                   |         |                   |         |
| Yes (vs. no)                               | 2.48 (1.31–4.71)  | 0.006   | 2.71 (1.24–5.88)  | 0.01    |
| Cr increase                                |                   |         |                   |         |
| Yes (vs. no)                               | 1.85 (0.97–3.53)  | 0.06    | -                 | -       |

OR, odds ratio; CI, 95% confidence interval; WBC, white blood cell.

Nagelkerke R square=0.115; Hosmer and Lemeshow test=1.26; df=3, P=0.74.

with COVID-19.

### **Chronic obstructive pulmonary disease (COPD)**

In the present study, COPD was significantly associated with severe COVID-19. A meta-analysis showed that COPD was significantly associated with severe COVID-19 (OR = 5.69, 95% CI: 2.49–13.00,  $I^2=0.0\%$ , Cochran's Q,  $P=0.95$ ). Changes in the local/systemic inflammatory response, host immunodeficiency, microbiome imbalance, persistent mucus production, structural damage, and the use of inhaled corticosteroids might have been associated with such risks.<sup>15</sup> Also, due to COVID-19, in patients with COPD, levels of the angiotensin-converting enzyme (ACE2), the receptor reported for the virus responsible for COVID-19, is increased,<sup>16,17</sup> which might explain the severity of the patients with COPD.

In a series of 11 meta-analyses, the incidence of COPD and the development of severe COVID-19 was 4.38 (fixed effects model; 95% CI: 2.34–8.20), while the ongoing OR smoking was 1.98 (fixed effects model; 95% CI: 1.29–3.05).<sup>11</sup> Another meta-analysis with 123 cases showed that the pooled prevalence rates of COPD patients and smokers in COVID-19 cases were 2% (95% CI: 1–3%) and 9% (95% CI: 4–14%), respectively. Patients with COPD were at a higher risk of more severe disease (severity risk=63%, [22/35] compared with patients without COPD [33.4%

[409/1224], calculated RR=1.88 (95% CI: 1.4–2.4). This rate was associated with higher mortality (60%), and their results showed that 22% (319/139) of current smokers and 46% (28/13) of former smokers had severe complications. The calculated RR of smokers was 1.45 times higher (95% CI: 1.03–2.04) than former smokers and had never had severe side effects, and current smokers had a higher mortality rate of 38.5%.<sup>18</sup> However, in a study by Liu et al, there was no significant difference in COPD between the progression and improvement/stabilization groups.<sup>10</sup> Hence, the rate of smoking and COPD is high worldwide, suggesting COPD as an important risk factor for severe outcomes of COVID-19.

### **Kidney**

The results showed that kidney disease is a predictor of serious outcomes. However, Wang et al concluded that AKI (acute kidney injury) is not common in COVID-19. SARS-CoV-2 infection does not lead to AKI and does not worsen chronic kidney disease in COVID-19 patients,<sup>19</sup> and most studies are consistent with our findings. For example, in the cohort of Cheng et al, patients with high basal serum creatinine levels are more likely to be admitted to the intensive care unit and mechanically ventilated, indicating that kidney disease at the time of admission poses a higher risk of worsening. It has

**Table 3.** Demographic, clinical, treatment, and laboratory characteristics of COVID-19 patients by non-severe or severe outcome (requiring intubation during hospitalization or ICU admission, or death outcome)

| Demographic and clinical characteristics, No. (%) | All patients (N=260) | Non-severe outcome (n=181) | Severe outcome (n=79) | P value |
|---|----------------------|----------------------------|-----------------------|---------|
| Age—Median (IQR), years                           | 62.5 (48.0–73.0)     | 59.0 (44.0–69.0)           | 68.0 (52.0–77.0)      | 0.004   |
| Age groups (g)                                    |                      |                            |                       | -       |
| <20   | 4 (1.5)              | 3 (1.7)                    | 1 (1.3)               |         |
| 20-34   | 18 (6.9)             | 13 (7.2)                   | 5 (6.3)               |         |
| 35-49   | 50 (19.2)            | 41 (22.7)                  | 9 (11.4)              | -       |
| 50-65   | 75 (28.8)            | 55 (30.4)                  | 20 (25.3)             |         |
| ≥66   | 113 (43.5)           | 69 (38.1)                  | 44 (55.7)             |         |
| Gender  |                      |                            |                       | 0.47    |
| Male  | 166 (63.8)           | 113 (62.4)                 | 53 (67.1)             |         |
| Female  | 94 (36.2)            | 68 (37.6)                  | 26 (32.99)            |         |
| Marital status                                    |                      |                            |                       | 0.64    |
| Single or divorced or widowed                     | 23 (8.8)             | 17 (9.4)                   | 6 (7.6)               |         |
| Married   | 237 (91.2)           | 164 (90.6)                 | 73 (92.4)             |         |
| Education   |                      |                            |                       | 0.43    |
| illiterate  | 84 (32.3)            | 55 (30.4)                  | 29 (36.7)             |         |
| Elementary- Mid school                            | 76 (29.2)            | 55 (30.4)                  | 21 (26.6)             |         |
| High school                                       | 55 (21.2)            | 43 (23.8)                  | 12 (15.2)             |         |
| Graduate  | 30 (11.5)            | 22 (12.2)                  | 8 (10.1)              |         |
| Unknown   | 15 (5.8)             | 6 (3.3)                    | 9 (11.4)              |         |
| Location  |                      |                            |                       | 0.60    |
| Urban   | 222 (85.4)           | 157 (86.7)                 | 65 (82.3)             |         |
| Rural   | 38 (14.6)            | 24 (13.3)                  | 14 (17.7)             |         |
| Occupation  |                      |                            |                       | 0.88    |
| Manual worker                                     | 17 (6.5)             | 13 (7.2)                   | 4 (5.1)               |         |
| Employee  | 36 (13.8)            | 23 (12.7)                  | 13 (16.5)             |         |
| Retired   | 17 (6.5)             | 12 (6.6)                   | 5 (6.3)               |         |
| Housekeeper                                       | 82 (31.5)            | 59 (32.6)                  | 23 (29.1)             |         |
| Other   | 95 (36.5)            | 68 (37.6)                  | 27 (34.2)             |         |
| Unknown   | 13 (5.0)             | 6 (3.3)                    | 7 (8.9)               |         |
| Admit type  |                      |                            |                       | -       |
| Ambulance   | 17 (11.2)            | 4 (2.2)                    | 25 (31.6)             |         |
| Own   | 231 (88.8)           | 177 (97.8)                 | 54 (68.4)             |         |
| Hospital ward                                     |                      |                            |                       | -       |
| Ward  | 213 (81.9)           | 181 (100.0)                | 32 (40.5)             |         |
| Critical  | 47 (18.1)            | 0 (0.0)                    | 47 (59.5)             |         |
| Fever   |                      |                            |                       | 0.97    |
| No  | 142 (54.6)           | 99 (54.7)                  | 43 (54.4)             |         |
| Yes   | 118 (45.4)           | 82 (45.3)                  | 36 (45.6)             |         |
| Chills and fever                                  |                      |                            |                       | 0.70    |
| No  | 160 (61.5)           | 110 (60.8)                 | 50 (63.3)             |         |
| Yes   | 100 (38.5)           | 71 (39.2)                  | 29 (36.7)             |         |
| Dry cough   |                      |                            |                       | 0.001   |

**Table 3.** Continued

| Demographic and clinical characteristics, No. (%) | All patients (N=260) | Non-severe outcome (n=181) | Severe outcome (n=79) | P value |
|---|----------------------|----------------------------|-----------------------|---------|
| No  | 80 (30.8)            | 44 (24.3)                  | 36 (45.6)             |         |
| Yes   | 180 (69.2)           | 137 (75.7)                 | 43 (54.4)             |         |
| Sore throat (pharyngitis)                         |                      |                            |                       | 0.19    |
| No  | 238 (91.5)           | 163 (90.1)                 | 75 (94.9)             |         |
| Yes   | 22 (8.5)             | 18 (9.9)                   | 4 (5.1)               |         |
| Hyposmia (low smell)                              |                      |                            |                       | -       |
| No  | 259 (99.6)           | 180 (99.4)                 | 79 (100.0)            |         |
| Yes   | 1 (0.4)              | 1 (0.6)                    | 0 (0.0)               |         |
| Shortness of breath (breath gasp)                 |                      |                            |                       | 0.22    |
| No  | 107 (41.2)           | 79 (43.6)                  | 28 (35.4)             |         |
| Yes   | 153 (58.8)           | 102 (56.4)                 | 51 (64.6)             |         |
| Nausea  |                      |                            |                       | 0.24    |
| No  | 220 (84.6)           | 150 (82.9)                 | 70 (88.6)             |         |
| Yes   | 40 (15.4)            | 31 (17.1)                  | 9 (11.4)              |         |
| Vomiting  |                      |                            |                       | 0.69    |
| No  | 241 (92.7)           | 167 (92.3)                 | 74 (93.7)             |         |
| Yes   | 19 (7.3)             | 14 (7.7)                   | 5 (6.3)               |         |
| Diarrhea  |                      |                            |                       | 0.10    |
| No  | 246 (94.6)           | 174 (96.1)                 | 72 (91.1)             |         |
| Yes   | 14 (5.4)             | 7 (3.9)                    | 7 (8.9)               |         |
| Myalgia (muscular pain)                           |                      |                            |                       | 0.82    |
| No  | 177 (68.1)           | 124 (68.5)                 | 53 (67.1)             |         |
| Yes   | 83 (31.9)            | 57 (31.5)                  | 26 (32.9)             |         |
| Headache  |                      |                            |                       | 0.07    |
| No  | 225 (86.5)           | 152 (84.0)                 | 73 (92.4)             |         |
| Yes   | 35 (13.5)            | 29 (16.0)                  | 6 (7.6)               |         |
| Tachypnea   |                      |                            |                       | 0.01    |
| No  | 247 (95.0)           | 176 (97.2)                 | 71 (89.9)             |         |
| Yes   | 13 (5.0)             | 5 (2.8)                    | 8 (10.1)              |         |
| Fatigue   |                      |                            |                       | 0.84    |
| No  | 212 (81.5)           | 147 (81.2)                 | 65 (82.3)             |         |
| Yes   | 48 (18.5)            | 34 (18.8)                  | 14 (17.7)             |         |
| Anorexia  |                      |                            |                       | 0.97    |
| No  | 240 (92.3)           | 167 (92.3)                 | 73 (92.4)             |         |
| Yes   | 20 (7.7)             | 14 (7.7)                   | 6 (7.6)               |         |
| Abnormal ABG                                      |                      |                            |                       | <0.001  |
| No  | 240 (92.3)           | 179 (98.9)                 | 61 (77.2)             |         |
| Yes   | 20 (7.7)             | 2 (1.1)                    | 18 (22.9)             |         |
| Admit SaO <sub>2</sub> , Mean (SD)                | 89.9 (6.5)           | 91.5 (3.9)                 | 86.0 (9.3)            | <0.001  |
| SaO <sub>2</sub> low                              |                      |                            |                       | <0.001  |
| No  | 153 (58.8)           | 123 (68.0)                 | 30 (38.0)             |         |
| Yes   | 107 (41.2)           | 58 (32.0)                  | 49 (62.0)             |         |
| Current Smoker                                    |                      |                            |                       | 0.70    |

Table 3. Continued

| Demographic and clinical characteristics, No. (%) | All patients (N=260) | Non-severe outcome (n=181) | Severe outcome (n=79) | P value |
|---|----------------------|----------------------------|-----------------------|---------|
| No  | 226 (86.9)           | 157 (86.7)                 | 69 (87.3)             |         |
| Yes   | 33 (12.7)            | 24 (13.3)                  | 9 (11.4)              |         |
| Current alcohol user                              |                      |                            |                       | -       |
| No  | 254 (97.7)           | 179 (98.9)                 | 75 (96.2)             |         |
| Yes   | 5 (1.7)              | 2 (1.1)                    | 3 (3.8)               |         |
| Current hookah user                               |                      |                            |                       | 0.64    |
| No  | 248 (95.4)           | 173 (96.1)                 | 74 (93.7)             |         |
| Yes   | 11 (4.2)             | 7 (3.9)                    | 4 (5.1)               |         |
| Current Opiate user                               |                      |                            |                       | 0.049   |
| No  | 253 (97.3)           | 178 (98.3)                 | 74 (93.7)             |         |
| Yes   | 6 (2.3)              | 2 (1.1)                    | 4 (5.1)               |         |
| <b>Comorbidity— history condition</b>             |                      |                            |                       |         |
| Hypertension                                      |                      |                            |                       | 0.33    |
| No  | 166 (63.8)           | 119 (65.9)                 | 47 (59.5)             |         |
| Yes   | 94 (36.2)            | 62 (34.3)                  | 32 (40.5)             |         |
| Diabetes  |                      |                            |                       | 0.57    |
| No  | 184 (70.8)           | 130 (71.8)                 | 54 (68.4)             |         |
| Yes   | 76 (29.2)            | 51 (28.2)                  | 25 (31.6)             |         |
| Coronary heart disease                            |                      |                            |                       | 0.001   |
| No  | 216 (83.1)           | 160 (88.4)                 | 56 (70.9)             |         |
| Yes   | 44 (16.9)            | 21 (11.6)                  | 23 (29.1)             |         |
| Lung (COPD)                                       |                      |                            |                       | 0.02    |
| No  | 242 (93.1)           | 173 (95.6)                 | 69 (87.3)             |         |
| Yes   | 18 (6.9)             | 8 (4.4)                    | 10 (12.7)             |         |
| Kidney  |                      |                            |                       | 0.01    |
| No  | 247 (95.0)           | 176 (97.2)                 | 71 (89.9)             |         |
| Yes   | 13 (5.0)             | 5 (2.8)                    | 8 (10.1)              |         |
| Liver   |                      |                            |                       | -       |
| No  | 258 (99.2)           | 180 (99.4)                 | 78 (98.7)             |         |
| Yes   | 2 (0.8)              | 1 (0.6)                    | 1 (1.3)               |         |
| Cancer  |                      |                            |                       | -       |
| No  | 257 (98.8)           | 179 (98.9)                 | 78 (98.7)             |         |
| Yes   | 3 (1.2)              | 2 (1.1)                    | 1 (1.3)               |         |
| Others  |                      |                            |                       | 0.004   |
| No  | 222 (85.4)           | 162 (89.5)                 | 60 (75.9)             |         |
| Yes   | 38 (14.6)            | 19 (10.5)                  | 19 (24.1)             |         |
| At least one comorbidity                          |                      |                            |                       | 0.002   |
| No  | 92 (35.4)            | 75 (41.4)                  | 17 (21.5)             |         |
| Yes   | 168 (64.6)           | 106 (58.6)                 | 62 (78.5)             |         |
| Exacerbation of symptoms                          |                      |                            |                       | -       |
| No  | 197 (75.8)           | 179 (98.9)                 | 18 (22.8)             |         |
| Yes   | 63 (24.2)            | 2 (1.1)                    | 61 (77.2)             |         |
| New manifestations                                |                      |                            |                       | -       |

Table 3. Continued

| Demographic and clinical characteristics, No. (%) | All patients (N=260) | Non-severe outcome (n=181) | Severe outcome (n=79) | P value |
|---|----------------------|----------------------------|-----------------------|---------|
| No  | 201 (77.3)           | 178 (98.3)                 | 23 (29.1)             |         |
| Yes   | 59 (22.7)            | 3 (1.7)                    | 56 (70.9)             |         |
| New cardiovascular manifestations                 |                      |                            |                       | -       |
| No  | 213 (81.9)           | 181 (100.0)                | 32 (40.5)             |         |
| Yes   | 47 (18.1)            | 0 (0.0)                    | 47 (59.5)             |         |
| New kidney manifestations                         |                      |                            |                       | -       |
| No  | 230 (88.5)           | 181 (100.0)                | 49 (62.0)             |         |
| Yes   | 30 (11.5)            | 0 (0.0)                    | 30 (38.0)             |         |
| New liver manifestations                          |                      |                            |                       | -       |
| No  | 252 (96.9)           | 181 (100.0)                | 71 (89.9)             |         |
| Yes   | 8 (3.1)              | 0 (0.0)                    | 8 (10.1)              |         |
| O <sub>2</sub> therapy                            |                      |                            |                       | -       |
| No  | 16 (6.2)             | 15 (8.3)                   | 1 (1.3)               |         |
| Yes   | 244 (93.8)           | 166 (91.7)                 | 78 (98.8)             |         |
| Intubation durance - Median (IQR), days           | -                    | -                          | 1.0 (1-4)             | -       |
| Admit durance - Median (IQR), days                | 5.0 (3-7)            | 4.0 (3-6)                  | 5.0 (3-9)             | -       |
| Hydroxychloroquine treatment                      |                      |                            |                       | -       |
| No  | 18 (6.9)             | 10 (5.5)                   | 8 (10.1)              |         |
| Yes   | 242 (93.1)           | 171 (94.5)                 | 71 (89.9)             |         |
| Oseltamivir treatment                             |                      |                            |                       | -       |
| No  | 107 (41.2)           | 78 (43.1)                  | 29 (36.7)             |         |
| Yes   | 153 (58.8)           | 103 (56.9)                 | 50 (63.3)             |         |
| Kaletra (lopinavir/ritonavir) treatment           |                      |                            |                       | -       |
| No  | 42 (16.2)            | 29 (16.0)                  | 13 (16.5)             |         |
| Yes   | 218 (83.8)           | 152 (84.0)                 | 66 (83.5)             |         |
| Ribavirin treatment                               |                      |                            |                       | -       |
| No  | 209 (80.4)           | 158 (87.3)                 | 51 (64.6)             |         |
| Yes   | 51 (19.6)            | 23 (12.7)                  | 28 (35.4)             |         |
| Spray treatment                                   |                      |                            |                       | -       |
| No  | 93 (35.8)            | 76 (42.0)                  | 17 (21.5)             |         |
| Yes   | 167 (64.2)           | 105 (58.0)                 | 62 (78.5)             |         |
| Antibiotics treatment                             |                      |                            |                       | -       |
| No  | 73 (28.1)            | 58 (32.0)                  | 15 (19.0)             |         |
| Yes   | 187 (71.9)           | 123 (68.0)                 | 64 (81.0)             |         |
| Vitamin C   |                      |                            |                       | -       |
| No  | 178 (68.5)           | 128 (70.7)                 | 50 (63.3)             |         |
| Yes   | 82 (31.5)            | 53 (29.3)                  | 29 (36.7)             |         |
| Drug complication, No (%)                         |                      |                            |                       | -       |
| Nausea/vomiting                                   | 129 (49.6)           | 94 (51.9)                  | 35 (44.3)             |         |
| Arrhythmia  | 131 (50.4)           | 87 (48.1)                  | 44 (55.7)             |         |
| First WBC   |                      |                            |                       | <0.001  |



Table 3. Continued

| Demographic and clinical characteristics, No. (%) | All patients (N=260) | Non-severe outcome (n=181) | Severe outcome (n=79) | P value |
|---|----------------------|----------------------------|-----------------------|---------|
| Normal  | 188 (72.3)           | 145 (80.1)                 | 43 (54.4)             |         |
| Low   | 41 (15.8)            | 26 (14.4)                  | 15 (19.0)             |         |
| High  | 28 (10.8)            | 8 (4.4)                    | 20 (25.3)             |         |
| First CRP   |                      |                            |                       | -       |
| Normal  | 14 (5.4)             | 12 (6.6)                   | 2 (2.5)               |         |
| Low   | 0 (0.0)              | 0 (0.0)                    | 0 (0.0)               |         |
| High  | 240 (92.3)           | 168 (92.8)                 | 72 (91.1)             |         |
| First NA  |                      |                            |                       | -       |
| Normal  | 205 (78.8)           | 150 (82.9)                 | 55 (69.6)             |         |
| Low   | 40 (15.4)            | 25 (13.8)                  | 15 (19.0)             |         |
| High  | 5 (1.9)              | 1 (0.6)                    | 4 (2.8)               |         |
| First K   |                      |                            |                       | -       |
| Normal  | 230 (88.5)           | 169 (93.4)                 | 61 (77.2)             |         |
| Low   | 13 (5.0)             | 8 (4.4)                    | 5 (6.3)               |         |
| High  | 8 (3.1)              | 2 (1.1)                    | 6 (7.6)               |         |
| First Urea  |                      |                            |                       | -       |
| Normal  | 33 (12.7)            | 5 (2.8)                    | 28 (35.4)             |         |
| Low   | 219 (84.2)           | 172 (95.0)                 | 47 (59.5)             |         |
| High  | 0 (0.0)              | 0 (0.0)                    | 0 (0.0)               |         |
| First Creatinine                                  |                      |                            |                       | -       |
| Normal  | 211 (81.2)           | 162 (89.5)                 | 49 (62.0)             |         |
| Low   | 3 (1.2)              | 2 (1.1)                    | 1 (1.3)               |         |
| High  | 37 (14.2)            | 13 (7.2)                   | 24 (30.4)             |         |
| First Calcium                                     |                      |                            |                       | -       |
| Normal  | 49 (18.8)            | 39 (21.5)                  | 10 (12.7)             |         |
| Low   | 175 (78.3)           | 123 (68.0)                 | 52 (65.8)             |         |
| High  | 3 (1.2)              | 2 (1.1)                    | 1 (1.3)               |         |

previously been reported that kidney damage is associated with an increased risk of death in patients with influenza H1N1 and SARS.<sup>20,21</sup>

In a cohort study by Cheng et al, approximately 13% of patients had underlying kidney disease; >40% had signs of impaired renal function, and 5.1% had AKI during their hospital stay. A dose-dependent relationship was observed between AKI stages and death, with the risk of death among people with stage 3 AKI exceeding at least four times. Thus, kidney disease is a severe complication of COVID-19 and a significant risk factor for death.<sup>22</sup> One possible explanation for the high prevalence of kidney damage in inpatients with COVID-19 is that some patients with COVID-19 have a history of chronic kidney disease. In such patients, an anti-inflammatory state with functional defects in the populations of innate and adaptive immune cells is observed<sup>23</sup>; these patients have a higher risk of upper respiratory tract infections<sup>24,25</sup> and pneumonia.<sup>26</sup> Thus, our studies provided direct evidence for the association of SARS-CoV-2 with kidney tissue.

### Comorbidity

Of 38 patients with concomitant pathology, except for these diseases, 19 had a severe outcome. Previous studies have consistently reported that comorbidities are strong risk factors for adverse clinical outcomes.<sup>10,26</sup> Mortality in patients with viral pneumonia appears to have increased during the underlying illness and mixed bacterial infection, consistent with the present study.

The mortality rate of patients with viral pneumonia during the underlying illness and mixed bacterial infection appears to have increased,<sup>27</sup> consistent with the present study. However, in some studies such as Jung et al, no correlation was found between comorbidity and clinical outcome.<sup>21</sup> In addition, in the study by Liu et al, there were no significant differences concerning any comorbidities, including hypertension, diabetes, COPD, cancer, and others, between the progression and recovery/stabilization groups.<sup>28</sup> These conflicting results highlight the importance of additional research in this area.

### Leukocytosis

In the present study, only 20.0% of patients with leukocytosis showed the most severe results. Similar to the present study, survival analysis showed that leukocytosis was associated with death in patients with severe COVID-19.<sup>27,29</sup> Importantly, in the meta-analysis, most patients had normal leukocyte counts (69.7%; 95% CI: 62.8–76.2%), and only a few patients had leukocytosis (12.6%), confirming that the disease is transmitted by a virus. Hence, the physician must be careful to detect bacterial infections, and conventional antibiotics should be avoided.<sup>30</sup> This training has several limitations. First, only discharged or deceased patients were examined due to limited medical resources, and medical histories were not reviewed. Second, not all laboratory studies were performed in all patients due to the retrospective nature of this study. Third, this study used relatively small sample sizes, which can lead to biased results. Thus, the interpretation of our results might be limited by the sample size. Despite these limitations, we could identify several risk factors using appropriate statistical tools to predict disease severity and length of hospital stay for COVID-19 patients. However, a large-scale multicenter study with additional investigators is required. In addition, the interpretation of our results might be limited by the sample size. Despite these limitations, with the help of appropriate statistical tools, we could identify several risk factors to predict disease severity and length of hospital stay in COVID-19 patients.

### Conclusion

According to the results, hypoxia and the underlying disease can lead to undesirable consequences. The risk factors identified here confirm previous information and could be helpful for early clinical surveillance of disease progression in patients with COVID-19. Currently, the

**Table 4.** Risk factors associated with severe COVID-19 outcomes (requiring intubation during hospitalization or ICU admission, or death outcome)

| Demographic and clinical characteristics | Crude OR (95%)    | P value | Adjusted OR (95%) | P value |
|--|-------------------|---------|-------------------|---------|
| Age (per additional year)                | 1.02 (1.01–1.04)  | 0.005   | -                 | -       |
| Male sex (vs. female)                    | 1.23 (.70–2.14)   | 0.47    | -                 | -       |
| <b>Dry Cough</b>                         |                   |         |                   |         |
| Yes (vs. no)                             | 2.61 (2.61–4.55)  | 0.001   | 0.49 (0.25–0.96)  | 0.04    |
| <b>Headache</b>                          |                   |         |                   |         |
| Yes (vs. no)                             | 0.43 (.17–1.08)   | 0.07    | -                 | -       |
| <b>Tachypnea</b>                         |                   |         |                   |         |
| Yes (vs. no)                             | 3.97 (1.25–12.54) | 0.02    | -                 | -       |
| <b>SaO<sub>2</sub> low</b>               |                   |         |                   |         |
| Yes (vs. no)                             | 3.46 (1.20–6.01)  | <0.001  | 3.26 (1.72–6.18)  | <0.001  |
| <b>Current opiate user</b>               |                   |         |                   |         |
| Yes (vs. no)                             | 4.81 (.86–26.84)  | 0.07    | -                 | -       |
| <b>Coronary heart disease</b>            |                   |         |                   |         |
| Yes (vs. no)                             | 3.13 (1.61–6.09)  | 0.001   | 3.39 (1.51–7.64)  | 0.003   |
| <b>Lung (COPD)</b>                       |                   |         |                   |         |
| Yes (vs. no)                             | 3.13 (1.19–8.27)  | 0.02    | 3.97 (1.18–13.29) | 0.03    |
| <b>Kidney</b>                            |                   |         |                   |         |
| Yes (vs. no)                             | 3.97 (1.25–12.54) | 0.003   | 7.33 (1.94–27.70) | 0.01    |
| <b>Others comorbidity disease</b>        |                   |         |                   |         |
| Yes (vs. no)                             | 2.70 (1.34–5.44)  | 0.01    | 2.89 (1.27–6.69)  | 0.01    |
| <b>First WBC</b>                         |                   |         |                   |         |
| Normal                                   | reference         | -       | -                 | -       |
| Low                                      | 1.94 (.95–4.00)   | 0.07    | 1.95 (.86–4.41)   | 0.11    |
| High                                     | 8.43 (3.47–20.48) | <0.001  | 4.52 (1.67–12.26) | 0.003   |

OR, odds ratio; CI, 95% confidence interval; COPD, Chronic obstructive pulmonary disease; WBC, white blood cell. Nagelkerke R square=0.34; Hosmer and Lemeshow test=10.36; df=6, P=0.11.

best prognostic, diagnostic, and therapeutic protocols for COVID-19 are under revision; the results of this study could be included until special attention and consideration are paid to the patients with identified risk factors.

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#### Ethical Approval

The study was approved by the Ethics Committee of Tabriz University of Medical Sciences (ethical code: IR.TBZMED.REC.1398.1317). Due to the educational nature of the hospital, at the time of admission, consent was obtained to access patients' medical records.

#### Conflict of Interest

None to declare.

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#### Study Highlights

##### What is current knowledge?

- Elderly patients and those with chronic diseases are at risk for more severe illness and mortality.
- Diabetes, hypertension, and cardiovascular diseases are very common among hospitalized patients with COVID-19

##### What is new here?

- The main predictors of prolonged length of stay includes hypoxia and leukocytosis.
- The main predictors of severity includes hypoxia, leukocytosis, and co-morbidities.

- in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med.* 2020;180(7):934-43. doi: [10.1001/jamainternmed.2020.0994](https://doi.org/10.1001/jamainternmed.2020.0994).
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