Clinical features and disease severity in an Iranian population of COVID-19 patients

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Abstract

Objectives: Coronavirus disease 2019 (COVID-19) can present with a variety of symptoms. Severity of the disease may be associated with several factors. Here, we review clinical features of COVID-19 patients with different severities.

Methods: This cross-sectional study was performed in Imam Reza hospital, Mashhad, Iran, during February-April 2020. COVID-19 patients with typical computed tomography (CT) patterns and/or positive reverse-transcriptase polymerase chain reaction (RT-PCR) were included. The patients were classified into three groups of moderate, severe, and critical based on disease severity. Demographic, clinical, laboratory, and radiologic findings were collected and compared. P<0.05 was considered statistically significant.

Results: Overall, 200 patients with mean age of 69.75±6.39 years, of whom 82 (41%) were female were studied. Disease was severe/critical in the majority of patients (167, 83.5%). Disease severity was significantly associated with age, malignant comorbidities, dyspnea, nausea/vomiting, confusion, respiratory rate, pulse rate, O₂ saturation, extent of CT involvement, serum C-reactive protein (CRP), pH, pO₂, and aspartate transaminase (P<0.05). Moreover, complications including shock, coagulopathy, acidosis, sepsis, acute respiratory distress syndrome (ARDS), intensive care unit (ICU) admission, and intubation were significantly higher in patients with higher severities. O₂ saturation, nausea/vomiting, and extent of lung CT involvement were independent predictors of severe/critical COVID-19 (OR=0.342, 45.93, and 25.48, respectively; P<0.05).

Conclusions: Our results indicate O₂ saturation, nausea/vomiting, and extent of lung CT involvement as independent predictors of severe COVID-19 conditions. Serum CRP levels and pO₂ were also considerably higher patients with higher severity and can be used along with other factors as possible predictors of severe disease in COVID-19 patients.

Introduction

In December 2019, a novel coronavirus emerged in Wuhan city of Hubei Province in China (1). The virus mainly involved the lungs, leading to a severe acute respiratory syndrome; thus it was initially named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The world health organization (WHO) named the condition as coronavirus disease of 2019 (COVID-19) and announced it as a global health emergency, which soon was recognized a pandemic (2).

Compared to the two previously known diseases caused by coronaviruses, namely Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), COVID-19 is more contagious and can easily spread between individuals (3, 4). However, the disease is less lethal than was the case in SARS and MERS (5). It seems that most of COVID-19 cases develop a mild or even asymptomatic disease. Other patients mostly show signs and symptoms of mild upper respiratory tract illness. However, some cases develop severe pneumonia that is accompanied by respiratory failure and even death (6, 7).
Previous studies on Chinese population have reported different underlying diseases and demographic factors to be associated with further deterioration of the condition of COVID-19 patients and worse outcomes (7-9). Old age, smoking, male sex, and underlying diseases such as chronic kidney disease, chronic obstructive pulmonary disease (COPD), and cerebrovascular disease are reportedly associated with higher disease severity. Higher levels of serum biomarkers including lactate dehydrogenase (LDH), C-reactive protein (CRP), and D-dimer, as well as decreased blood platelet and lymphocyte count have also been associated with more lethal conditions (10). However, most of our knowledge regarding COVID-19 comes from Chinese studies and there is little known about the clinical and paraclinical findings of the patients in other regions. Our study aims to investigate further demographic, clinical, laboratory, and radiologic findings to design a protocol in order to assess the condition, prognosis, and response to treatment of COVID-19 infected patients.

Methods

Study design and approval

This cross-sectional study was conducted in Imam Reza tertiary hospital, an officially recognized center for COVID-19 patients in Mashhad, the second largest city of Iran, during February-April 2020.

All enrolled patients provided informed written consent before entrance in the study. Patients’ data were kept coded without names and confidentiality was observed. The study was in accordance with the ethical codes of Helsinki declaration and was approved by the Ethics Committee of Mashhad University of Medical Sciences (approval code: IR.MUMS.REC.1398.308).

Patients with confirmed diagnoses of COVID-19 according to a positive RT-PCR and/or typical chest computed tomography (CT) findings were included. The patients were classified based on the severity of disease according to the criteria proposed by WHO (11), into the following groups:

- Mild/Moderate: no or mild pneumonia;
- Severe: with dyspnea (respiratory rate >30) or hypoxia ($O_2$ saturation <93);
- Critical: with respiratory failure, shock, or multi-organ dysfunction.

Data collection

In order to gather patients’ data, we designed a checklist according to the standards of reporting COVID-19 cases, proposed by WHO (12). The checklist was discussed in a group of internal medicine specialists and subspecialists using a focus group technique to optimize the list by removing/adding some items.

Demographic data including age and gender, as well as medical and social history were recorded. In addition, clinical symptoms and vital signs were evaluated and recorded. Complications and outcomes including shock, sepsis, acute respiratory distress syndrome (ARDS), diastolic heart failure (DHF), acute tubular necrosis (ATN), intensive care unit (ICU) admission, intubation, coagulopathy, and acidosis were evaluated.
All patients were evaluated for pulmonary involvement using chest CT. Blood samples were taken and analyzed for several biomarkers. Laboratory findings including lymphocyte count and serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), LDH, and CRP levels, as well as blood gas analysis were assessed and recorded.

**Statistical analysis**

All the analyses were performed using SPSS software (version 23 for Windows; IBM Statistics, Chicago, IL). Kolmogorov-Smirnov test was used to assess the normality of data. We made comparisons between all the three groups as well as between mild/moderate and severe/critical groups (merging the severe and critical cases). Chi-square test, independent samples t-test, Mann-Whitney test, one-way ANOVA test, and Kruskal-Wallis test were used to compare data between different subgroups of patients.

Binary logistic regression analyses was used to assess the factors associated with morbidity and severity of disease. Odds ratio (OR) along with 95% confidence interval (95%CI) were used to report the data. P<0.05 was considered statistically significant in all tests.

**Results**

Overall, 200 patients were enrolled in the study, of whom 118 (59%) were male and 82 (41%) were female. Mean age of the patients was 69.75±6.39 years. Overall, 33 cases (16.5%) were in mild/moderate group, 139 (69.5%) were severe, and 28 (14%) were critical. There was no significant difference regarding gender between the three groups of patients. Critical cases were significantly older compared with the mild/moderate and severe groups (P=0.009). However, there was no significant difference in the mean age when comparing the two groups of mild/moderate and severe/critical (P=0.149). Table 1 compares the demographic data and comorbid conditions in patients with different degrees of disease severity. Among all comorbid conditions, only malignancy had a significantly different frequency between the three groups (P<0.001).

Regarding vital signs, pulse rate, respiratory rate, and oxygen saturation were significantly associated with the severity of disease, both in two-group and three-group comparisons (P<0.05; Table 2). The frequency of dyspnea was significantly higher in severe/critical group, while nausea/vomiting was significantly more common among the mild/moderate cases (P=0.023 and 0.016, respectively). Confusion was significantly more common among critical cases, compared to the mild/moderate and severe groups (P=0.043). Furthermore, most of COVID-19-associated morbidities including shock, sepsis, coagulopathy, acidosis, ARDS, ICU admission, and intubation were significantly more common among the critical cases, compared with mild/moderate and severe groups (P<0.001).

Table 3 details the paraclinical findings of patients. As shown in the table, CRP, AST, pH, and pO$_2$ were significantly associated with disease severity in three-group comparisons (P<0.05). However, two-group comparison showed that only CRP and pO$_2$ were significantly associated with disease severity (P<0.05; Table 3). Chest CT showed that the extent of both ground-glass consolidative pulmonary involvement was
significantly higher in the critical and severe cases, compared with mild/moderate ones, in both two- and three-group comparisons (P<0.01). Severity of COVID-19 was not significantly associated with pleural effusion and bronchiectasis in chest CT.

Multivariate logistic regression showed that O₂ saturation, nausea/vomiting, and extent of lung involvement in CT were independent predictors of severe/critical COVID-19, while for critical disease alone, only O₂ saturation showed a significant association in multivariate analyses (Table 4). However, none of the assessed variables were significantly associated with ICU admission in a multivariate regression model.

**Discussion And Conclusion**

COVID-19 infection often causes a mild or even asymptomatic disease; however, some patients may proceed to severe and critical condition. Various clinical and paraclinical factors have been associated with higher disease severity (13). However, most of the studies are from a restricted geographical region and there is a paucity of evidence regarding the determinant factors of poor prognosis in different ethnicities, as the features of COVID-19 might differ in patients with different characteristics. Thus, we reviewed the clinical, laboratory, and imaging characteristics of COVID-19 patients in a center in Iran and assessed the factors that might possibly associate with disease severity.

We found that critical cases of COVID-19 were significantly older compared to patients with lower severity. Malignant comorbidities were found to be considerably higher in critical and severe cases. Among vital signs, pulse rate, respiratory rate, and oxygen saturation were significantly associated with the severity of disease. Among symptoms, dyspnea, confusion, and nausea/vomiting were associated with higher disease severities. COVID-19-associated complications including shock, sepsis, coagulopathy, acidosis, ARDS, ICU admission, and intubation were significantly more common among the critical cases. Paraclinical factors that were associated with higher disease severity were increased CRP and AST, as well as decreased pH and pO₂. Multivariate analyses showed that O₂ saturation, nausea/vomiting, and extent of lung involvement in CT were independent predictors of severe COVID-19 in absence of other factors. O₂ saturation was the sole independent predictor of critical condition in COVID-19 patients.

In line with the findings of our study, several studies proposed that malignancy is associated with more severe disease and poorer outcomes (14-16). Therefore, it has been proposed that continuing antitumor treatment may further help the outcome of these patients (14). Although we found no significant association between disease severity and diabetes, hypertension, or cardiovascular diseases, a recently published meta-analysis proposed that diabetes, hypertension, and cardiovascular diseases are linked with more severe infection. This inconsistency might be because their study only included Chinese population and proposed a high heterogeneity between studies (14). Moreover, our sample is relatively small, compared with a meta-analysis, and larger samples can yield results that are statistically significant.

As expected, we observed considerably lower O₂ saturation and higher values of respiratory and pulse rate in patients with higher severities of the disease. It seems that the pulmonary involvement of COVID-19 and the subsequent respiratory distress, impairs cardiopulmonary functions causing a ventilation-perfusion
mismatch (17), which in turn leads to development of tachypnea and tachycardia. On the other hand, tachycardia can be related to fever in these patients (18). However, we found no notable difference in the frequency of fever between patients with different disease severities.

AST was also found to be notably higher in severe COVID-19 infection in our patients. It might be hypothesized that the higher rate of hypoxia in more severe stages of the disease may be the cause of liver injury and subsequent enzyme release as it is evident with AST release. However, the direct invasion of the virus to hepatocytes can also be proposed as an etiologic factor, which was reported by some studies (19). Han et al. reported that AST could be an independent risk factor for COVID-19 infection severity (20), which was not the case in our multivariate assessments.

Another important finding of our study was the markedly higher level of CRP in patients with severe and critical COVID-19 disease. This factor is reported to be independently related to disease severity; CRP levels >37.3 mg/L have been reportedly associated with poorer outcomes (20). In our study, the serum level of CRP showed an incremental increase with the rise in disease severity from mild/moderate to critical. Consistently, Wang et al. reported that higher CRP levels were associated with more lung involvement and more severe diseases (21).

Our results indicate that higher severities of COVID-19 are associated with higher rates of serious complications such as shock, sepsis, ARDS, intubation, coagulopathy, and acidosis, which require ICU admission. It is generally believed that most of the COVID-19 cases develop mild to moderate symptoms and do not need hospitalization or ICU admission. However, some of them may need hospitalization and even intensive care. These patients are more prone to develop sepsis, shock, ARDS, and eventually death (22). Furthermore, despite the usual presence of thrombocytopenia, coagulopathy is predictable in COVID-19 infected patients. Studies have reported elevated levels of D-dimer and thrombotic events in these patients, which might be related to inflammatory processes (23). Acidosis can be present in some of the COVID-19 patients, which heralds a more severe stage of the disease (6). In the present study, we found markedly lower pH levels in the VBG of patients with critical condition, compared to other groups. This implies that acidosis is significantly associated with higher severities of the disease.

We found that low O₂ saturation was the only independent predictor of critical condition and poor prognosis in COVID-19 patients. Lower O₂ saturation was linked to a one-third lower risk for developing critical disease. In line with our findings, a recent study on 167 patients in Anhui, China, reported that fingertip oxygen saturation and decreased CD4 cell count were the only independent risk factors for severe COVID-19 (24).

We also found that the extent and severity of lung involvement in CT scan, as the number of involved lobes with consolidation or ground-glass opacification, was a significant and independent predictor of severe/critical COVID-19 infection. Similarly, Chaganti et al. developed a score for lung involvement that was composed of the number of lobes with consolidation or ground-glass opacification and found that this score is positively correlated with severe stages of COVID-19 (25).
Among all symptoms, nausea/vomiting proved to be an independent predictive factor for severe disease and poorer prognosis. Several studies have indicated that gastrointestinal manifestations, namely nausea and vomiting, are common among COVID-19 patients. However, nausea and vomiting have not been alluded to as risk factors for severe conditions in these patients (26, 27).

A recent systematic review and meta-analysis on 1813 COVID-19 patients showed that dyspnea, COPD, cardiovascular diseases, and hypertension were predictive factors for severe disease and ICU admission (28). A recent study on 548 patients from Wuhan indicated older age, comorbid hypertension, high LDH, and D-dimer were significantly associated with higher severity in cases with COVID-19 (29). LDH was also identified as a risk factor for severe disease in another retrospective study of 47 patients from Wuhan, which also indicated lymphocyte count, especially CD3, CD4, and CD8 cells, as a predictive factor for higher severity (30). Although age was significantly related to disease severity, inconsistent with the mentioned studies, our multivariate analyses did not find significant associations between disease severity and age, comorbid conditions, LDH, and lymphocyte count.

Our study can provide insights into the factors associated with higher risk for developing severe COVID-19 in the Iranian population. The present study had some limitations. First of all, we had limited access to RT-PCR testing and could not perform it for all patients. Second, further survival and prognosis analyses was not performed, which may be applicable for further studies. However, besides these shortcomings, we enrolled an acceptable sample of patients.

In conclusion, O₂ saturation, nausea/vomiting, and extent of lung involvement in chest CT can be potential factors that contribute to early prediction of severe and critical conditions in COVID-19 patients. It is therefore recommended to further evaluate the role of these factors in diagnosis and prognosis of patients with COVID-19 in future studies.

**Declarations**

All enrolled patients provided informed written consent before entrance in the study. Patients’ data were kept coded without names and confidentiality was observed. The study was in accordance with the ethical codes of Helsinki declaration and was approved by the Ethics Committee of Mashhad University of Medical Sciences (approval code: IR.MUMS.REC.1398.308).

**Conflict of interest statement**

None to disclose

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**Competing Interests**
The authors declare no competing interests

References

1. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. 2020;395(10223):514-23.

2. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. New England Journal of Medicine. 2020.

3. Arabi YM, Balkhy HH, Hayden FG, Bouchama A, Luke T, Baillie JK, et al. Middle East respiratory syndrome. New England Journal of Medicine. 2017;376(6):584-94.

4. Peiris JS, Yuen KY, Osterhaus AD, Stöhr K. The severe acute respiratory syndrome. New England Journal of Medicine. 2003;349(25):2431-41.

5. Mahase E. Covid-19: WHO declares pandemic because of “alarming levels” of spread, severity, and inaction. British Medical Journal Publishing Group; 2020.

6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506.

7. Bai T, Tu S, Wei Y, Xiao L, Jin Y, Zhang L, et al. Clinical and Laboratory Factors Predicting the Prognosis of Patients with COVID-19: An Analysis of 127 Patients in Wuhan, China. China (2/26/2020). 2020.

8. Liu J, Tu C, Zhu M, Wang J, Yang C, Liu W, et al. Exploring the Law of Development and Prognostic Factors of Common and Severe COVID-19: A Retrospective Case-Control Study in 122 Patients with Complete Course of Disease. Available at SSRN 3555209. 2020.

9. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020.

10. Zhao X, Zhang B, Li P, Ma C, Gu J, Hou P, et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis. medRxiv. 2020.

11. Organization WH. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: Interim guidance2020. p. 21.

12. Organization WH. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. World Health Organization; 2020.

13. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of COVID-19 disease. MedRxiv. 2020.

14. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. Annals of Oncology. 2020.

15. Oh WK. COVID-19 Infection in Cancer Patients: Early Observations and Unanswered Questions. Annals of Oncology. 2020.
16. Ma J, Yin J, Qian Y, Wu Y. Clinical Characteristics and Prognosis in Cancer Patients with COVID-19: a Single Center's Retrospective Study. Journal of Infection. 2020.
17. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? BioMed Central; 2020.
18. Hui H, Zhang Y, Yang X, Wang X, He B, Li L, et al. Clinical and radiographic features of cardiac injury in patients with 2019 novel coronavirus pneumonia. medRxiv. 2020.
19. Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: management and challenges. The Lancet Gastroenterology & Hepatology. 2020.
20. Han Y, Zhang H, Mu S, Wei W, Jin C, Xue Y, et al. Lactate dehydrogenase, a Risk Factor of Severe COVID-19 Patients. medRxiv. 2020.
21. Ling W. C-reactive protein levels in the early stage of COVID-19. Medecine et Maladies Infectieuses. 2020.
22. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). Statpearls [internet]: StatPearls Publishing; 2020.
23. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. American Journal of Hematology. 2020.
24. Wei YY, Wang RR, Zhang DW, Tu YH, Chen CS, Ji S, et al. Risk factors for severe COVID-19: Evidence from 167 hospitalized patients in Anhui, China. The Journal of infection. 2020.
25. Chaganti S, Balachandran A, Chabin G, Cohen S, Flohr T, Georgescu B, et al. Quantification of Tomographic Patterns associated with COVID-19 from Chest CT. arXiv preprint arXiv:200401279. 2020.
26. Wong SH, Lui RN, Sung JJ. Covid-19 and the digestive system. Journal of gastroenterology and hepatology. 2020;35(5):744-8.
27. Tian Y, Rong L, Nian W, He Y. gastrointestinal features in COVID-19 and the possibility of faecal transmission. Alimentary pharmacology & therapeutics. 2020;51(9):843-51.
28. Jain V, Yuan J-M. Systematic review and meta-analysis of predictive symptoms and comorbidities for severe COVID-19 infection. medRxiv; 2020.
29. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. Journal of Allergy and Clinical Immunology. 2020.
30. Han Y, Zhang H, Mu S, Wei W, Jin C, Xue Y, et al. Lactate dehydrogenase, a Risk Factor of Severe COVID-19 Patients. medRxiv; 2020.

Tables

Table 1. Demographic data and comorbid conditions in patients with different disease severities
### Feature

| Disease severity | Mild/moderate (N=33) | Severe (N=139) | Critical (N=28) | \(P_1\) | \(P_2***\) |
|------------------|-----------------------|---------------|----------------|---------|-----------|
| **Demographic Data** |                       |               |                |         |           |
| Sex (Female)     | 15 (45.5)             | 55 (39.6)     | 12 (42.9)      | 0.569*  | 0.807     |
| Age             | 54.87±18.35           | 57.80±14.80   | 66.71±16.61    | 0.149** | **0.009** |
| **Comorbid Conditions** |                       |               |                |         |           |
| DM              | 6 (18.2)              | 43 (30.9)     | 12 (42.9)      | 0.093*  | 0.111     |
| IHD             | 5 (15.2)              | 22 (15.8)     | 7 (25.0)       | 0.757*  | 0.476     |
| Hypertension    | 7 (21.2)              | 40 (28.8)     | 10 (35.7)      | 0.310*  | 0.454     |
| Asthma          | 0 (0.0)               | 5 (3.6)       | 0 (0.0)        | 0.314*  | 0.325     |
| Autoimmune disease | 1 (3.0)               | 3 (2.2)       | 1 (3.6)        | >0.999* | 0.888     |
| CKD             | 0 (0.0)               | 2 (1.4)       | 1 (3.6)        | 0.438*  | 0.517     |
| Transplantation | 1 (3.0)               | 0 (0.0)       | 0 (0.0)        | 0.024*  | 0.079     |
| COPD            | 2 (6.1)               | 13 (9.4)      | 1 (3.6)        | 0.653*  | 0.721     |
| Cerebrovascular disease | 0 (0.0)               | 3 (2.2)       | 0 (0.0)        | 0.438*  | 0.513     |
| CNS disease     | 0 (0.0)               | 2 (1.4)       | 0 (0.0)        | 0.528*  | 0.642     |
| Hepatitis       | 1 (3.0)               | 0 (0.0)       | 0 (0.0)        | 0.024*  | 0.079     |
| Hypothyroidism  | 0 (0.0)               | 2 (1.4)       | 1 (3.6)        | 0.438*  | 0.517     |
| Malignancy      | 0 (0.0)               | 3 (2.2)       | 5 (17.9)       | 0.199*  | <0.001    |
| Smoking         | 5 (15.2)              | 14 (10.1)     | 4 (14.3)       | 0.822*  | 0.544     |
| Addiction       | 0 (0.0)               | 5 (3.6)       | 0 (0.0)        | 0.593*  | 0.325     |
| Alcohol use     | 0 (0.0)               | 1 (0.7)       | 0 (0.0)        | >0.999* | 0.802     |
| **Clinical Characteristics of COVID-19** |                       |               |                |         |           |
| Symptomatic period (days) | 6.00±6.50             | 7.09±4.31     | 6.81±3.54      | 0.294** | 0.555     |
| Hospital stay (days) | 6.48±3.94             | 7.27±3.39     | 7.56±4.74      | 0.249** | 0.484     |

DM: diabetes mellitus; IHD: ischemic heart disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CNS: central nervous system

\(P_1\): Comparison between mild/moderate and severe/critical groups
\(P_2\): Comparison between mild/moderate, severe, and critical groups

*Chi-square or Fisher's exact test
**Mann-Whitney test
***Kruskal-Wallis test

Table 2. Vital signs, clinical symptoms, and morbidity in patients with different disease severities
## Feature

| Feature                  | Mild/moderate (N=33) | Severe (N=139) | Critical (N=28) | P₁   | P₂ *** |
|--------------------------|----------------------|----------------|-----------------|------|-------|
| **Vital signs**          |                      |                |                 |      |       |
| Pulse rate               | 87.12±20.12          | 94.71±26.64    | 106.48±26.36    | **0.003** | <0.001 |
| Respiratory rate         | 20.12±1.97           | 26.64±6.87     | 26.36±6.76      | **<0.001** | **<0.001** |
| BP (mmHg)                | 126.71±21.98         | 126.74±15.42   | 129.68±23.68    | 0.478 | 0.467 |
| Temperature (°C)         | 37.63±0.65           | 37.65±0.66     | 37.98±0.83      | 0.742 | 0.084 |
| O₂ saturation (%)        | 95.48±1.25           | 87.80±6.37     | 82.15±10.00     | **<0.001** | **<0.001** |
| **Symptoms**             |                      |                |                 |      |       |
| Fever                    | 23 (69.7)            | 101 (72.7)     | 19 (67.9)       | 0.802 | 0.849 |
| Dyspnea                  | 24 (72.7)            | 123 (88.5)     | 24 (85.7)       | **0.023** | 0.069 |
| Nausea/vomiting          | 11 (33.3)            | 22 (15.8)      | 4 (14.3)        | **0.016** | 0.055 |
| Cough                    | 29 (87.9)            | 129 (92.8)     | 25 (89.3)       | 0.414 | 0.595 |
| Diarrhea                 | 8 (24.2)             | 19 (13.7)      | 2 (7.1)         | 0.082 | 0.148 |
| Conjunctivitis           | 0 (0.0)              | 2 (1.4)        | 0 (0.0)         | 0.528 | 0.642 |
| Myalgia                  | 16 (48.5)            | 69 (49.6)      | 15 (53.6)       | 0.849 | 0.914 |
| Arthralgia               | 7 (21.2)             | 18 (12.9)      | 2 (7.1)         | 0.156 | 0.261 |
| Weakness                 | 16 (48.5)            | 65 (46.8)      | 14 (50.0)       | 0.901 | 0.945 |
| Abdominal pain           | 1 (3.0)              | 6 (4.3)        | 0 (0.0)         | 0.872 | 0.519 |
| Seizure                  | 0 (0.0)              | 1 (0.7)        | 0 (0.0)         | 0.656 | 0.802 |
| Headache                 | 3 (9.1)              | 26 (18.7)      | 2 (7.1)         | 0.266 | 0.164 |
| Sore throat              | 1 (3.0)              | 19 (13.7)      | 2 (7.1)         | 0.109 | 0.167 |
| Chill                    | 10 (30.3)            | 28 (20.1)      | 7 (25.0)        | 0.240 | 0.428 |
| Hyposmia                 | 4 (12.1)             | 11 (7.9)       | 2 (7.1)         | 0.414 | 0.710 |
| Fatigue                  | 9 (27.3)             | 40 (28.8)      | 7 (25.0)        | 0.919 | 0.916 |
| Confusion                | 0 (0.0)              | 2 (1.4)        | 3 (10.7)        | 0.517 | **0.043** |
| Rhinorrhea               | 1 (3.0)              | 3 (2.2)        | 0 (0.0)         | 0.802 | 0.681 |
| **Morbidity**            |                      |                |                 |      |       |
| Shock                    | 0 (0.0)              | 1 (0.7)        | 6 (21.4)        | 0.231 | **<0.001** |
| Sepsis                   | 0 (0.0)              | 1 (0.7)        | 8 (28.6)        | 0.172 | **<0.001** |
| ARDS                     | 0 (0.0)              | 1 (0.7)        | 27 (96.4)       | **0.011** | **<0.001** |
| DHF                      | 0 (0.0)              | 1 (0.7)        | 0 (0.0)         | >0.999 | 0.802 |
| ATN                      | 0 (0.0)              | 1 (0.7)        | 1 (3.6)         | >0.999 | 0.288 |
| Coagulopathy             | 0 (0.0)              | 0 (0.0)        | 1 (3.6)         | >0.999 | **0.046** |
| Acidosis                 | 0 (0.0)              | 0 (0.0)        | 1 (3.6)         | >0.999 | **0.046** |
| ICU admission            | 0 (0.0)              | 0 (0.0)        | 14 (50.0)       | 0.085 | **<0.001** |
| Intubation               | 0 (0.0)              | 0 (0.0)        | 23 (82.1)       | **0.023** | **<0.001** |

BP: blood pressure; ARDS: acute respiratory distress syndrome; DHF: diastolic heart failure; ATN: acute tubular necrosis; ICU: intensive care unit

P₁: Comparison between mild/moderate and severe/critical groups

P₂: Comparison between mild/moderate, severe, and critical groups

*Chi-square or Fisher’s exact test

**Mann-Whitney test

***Kruskal-Wallis test

Table 3. Paraclinical data in patients with different disease severities
| Feature                      | Mild/moderate (N=33) | Severe (N=139) | Critical (N=28) | P₁     | P₂*** |
|------------------------------|----------------------|----------------|----------------|--------|-------|
| **Laboratory Findings**      |                      |                |                |        |       |
| Lymphopenia                  | 24 (75.0)            | 99 (76.2)      | 19 (70.4)      | 0.985* | 0.818 |
| VBG pH                       | 7.42±0.05            | 7.41±0.05      | 7.10±1.29      | 0.572**| 0.030 |
| VBG pO₂ (mmHg)               | 36.27±9.11           | 32.21±9.48     | 31.85±8.51     | 0.037**| 0.021 |
| VBG pCO₂ (mmHg)              | 39.01±6.81           | 40.33±7.84     | 35.12±7.92     | 0.824**| 0.112 |
| VBG pHCO₃ (mmHg)             | 25.86±4.05           | 25.94±5.05     | 23.14±4.32     | 0.705**| 0.054 |
| AST (IU/L)                   | 57.92±76.53          | 48.55±74.94    | 54.42±31.50    | 0.470**| 0.031 |
| ALT (IU/L)                   | 59.64±87.35          | 50.94±77.99    | 49.78±60.37    | 0.210**| 0.384 |
| LDH (U/L)                    | 560.20±200.34        | 660.74±434.76  | 897.70±287.47  | 0.310**| 0.137 |
| CRP (mg/L)                   | 51.64±52.07          | 86.22±62.33    | 167.59±146.86  | 0.003**| 0.001 |
| **Chest CT Findings**        |                      |                |                |        |       |
| Consolidation                |                      |                |                |        |       |
| None                         | 8 (24.2)             | 36 (25.9)      | 5 (17.9)       |        |       |
| 1 lobe                       | 1 (3.0)              | 3 (2.2)        | 0 (0.0)        |        |       |
| 2 lobes                      | 21 (63.6)            | 55 (39.6)      | 6 (21.4)       |        |       |
| 3 lobes                      | 0 (0.0)              | 1 (0.7)        | 2 (7.1)        |        |       |
| 4 lobes                      | 3 (9.1)              | 44 (31.7)      | 15 (53.6)      |        |       |
| GGO                          |                      |                |                |        |       |
| None                         | 7 (21.2)             | 32 (23.0)      | 9 (32.1)       |        | <0.001*<0.001 |
| 1 lobe                       | 3 (9.1)              | 0 (0.0)        | 0 (0.0)        |        |       |
| 2 lobes                      | 13 (39.4)            | 25 (18.0)      | 6 (3.6)        |        |       |
| 3 lobes                      | 0 (0.0)              | 4 (2.9)        | 0 (0.0)        |        |       |
| 4 lobes                      | 10 (30.3)            | 78 (56.1)      | 18 (64.3)      |        |       |
| PE                           | 1 (3.0)              | 8 (5.8)        | 4 (14.3)       | 0.376* | 0.168 |
| Bronchiectasis               | 0 (0.0)              | 1 (0.7)        | 0 (0.0)        | 0.656* | 0.802 |

VBG: venous blood gas; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; CT: computed tomography; GGO: ground-glass opacity; PE: pleural effusion

P₁: Comparison between mild/moderate and severe/critical groups
P₂: Comparison between mild/moderate, severe, and critical groups

*Chi-square or Fisher’s exact test
**Mann-Whitney test
***Kruskal-Wallis test

Table 4. Multivariate regression for prediction of severe COVID-19
| Predictor                        | Odds Ratio | 95% Confidence Interval | P    |
|---------------------------------|------------|-------------------------|------|
|                                 |            | Lower bound             | Upper bound |
| **Severe or critical disease**  |            |                         |      |
| $O_2$ saturation                | 0.342      | 0.146                   | 0.800 | **0.013** |
| Nausea/vomiting                 | 45.937     | 1.513                   | 1395.069 | **0.028** |
| Extent of CT involvement        | 25.483     | 1.148                   | 565.455 | **0.041** |
| **Critical disease**            |            |                         |      |
| $O_2$ saturation                | 0.906      | 0.824                   | 0.997 | **0.043** |