RESEARCH ARTICLE

Risk factors prediction, clinical outcomes, and mortality in COVID-19 patients

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Abstract
Preventing communicable diseases requires understanding the spread, epidemiology, clinical features, progression, and prognosis of the disease. Early identification of risk factors and clinical outcomes might help in identifying critically ill patients, providing appropriate treatment, and preventing mortality. We conducted a prospective study in patients with flu-like symptoms referred to the imaging department of a tertiary hospital in Iran between March 3, 2020, and April 8, 2020. Patients with COVID-19 were followed up after two months to check their health condition. The categorical data between groups were analyzed by Fisher's exact test and continuous data by Wilcoxon rank-sum test. Three hundred and nineteen patients (mean age 45.48 ± 18.50 years, 177 women) were enrolled. Fever, dyspnea, weakness, shivering, C-reactive protein, fatigue, dry cough, anorexia, anosmia, ageusia, dizziness, sweating, and age were the most important symptoms of
COVID-19 infection. Traveling in the past 3 months, asthma, taking corticosteroids, liver disease, rheumatological disease, cough with sputum, eczema, conjunctivitis, tobacco use, and chest pain did not show any relationship with COVID-19. To the best of our knowledge, a number of factors associated with mortality due to COVID-19 have been investigated for the first time in this study. Our results might be helpful in early prediction and risk reduction of mortality in patients infected with COVID-19.

**KEYWORDS**
COVID-19, effective features on prediction, effective features on the mortality, risk factors

1 | INTRODUCTION

In December 2019, a cohort of patients suffered from acute respiratory disease with unknown etiology in Wuhan, China. The Chinese Center for Disease Control and Prevention detected a new coronavirus, that was previously known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, formerly dubbed as 2019-nCoV) by the International Committee on Taxonomy of Viruses. The virus is highly infectious and causes fatigue, cough, fever, and severe or mild respiratory impediments. SARS-CoV-2 is termed as coronavirus disease 2019 (COVID-19), of which most patients exhibited mild symptoms. But a fraction of the critical patients developed acute respiratory failure, septic shock, and other severe complications including acute respiratory distress syndrome (ARDS), and multiple organ dysfunction syndromes that may lead to fatal outcomes. COVID-19 has been recognized as a Class B respiratory contagious ailment by the China Health Committee.

The WHO, on March 12, 2020, declared the COVID-19 as a global pandemic. Several measures were implemented to restrain the outbreak of the disease by different governments across the globe. These measures include restrictive face-to-face communications via obligatory “social distancing” and closure of public education and recreation sites such as parks, schools, colleges, and universities. The majority of the world’s population have gone through an unprecedented experience by following stern observance to the new measures. Elderly persons with co-morbid diseases such as acute kidney injury, diabetes mellitus, cardiovascular diseases, cancer, and hypertension are at higher risk of mortality or may have a more critical COVID-19. 13.8%-19.1% reported COVID-19 patients in Wuhan, China became patients critically. An astonishing fatality rate of 61.5% was recorded in the latest reports that increased significantly with age and for patients with comorbidities. This has led to the scarcity of intensive care facilities in hospitals due to the exponential increase in the number of cases and also put enormous pressure on medical staff and services. It is unfortunate not to have any prognostic biomarker to identify patients that may need urgent medical care and the associated fatality rate. Besides this, although there is a rapid increase in COVID-19 cases, information concerning the clinical symptoms (features) is inadequate. Liu et al. compared the clinical characteristics of elderly patients of COVID-19 with middle-aged and young patients. The common symptoms were fever, sputum, and cough.

The proportion of multiple lobe involvement and pneumonia severity index score was significantly higher in old patient’s group compared to those in middle and young aged cohort.

Early detection of disease helps clinicians to provide necessary, timely treatment. Zheng et al. explored the clinical and epidemiological characteristics of coronavirus. They used the treatment, radiological, laboratory, clinical, demographic, and epidemiological data of 99 confirmed COVID-19 patients in China. They identified fever, fatigue, and dry cough as common symptoms. The median age of the patients were 49 years, 41% had underlying disease, 49% came in close contact with COVID-19 affected patients, and 42% lived in or traveled to Wuhan. Lower CD8 and CD4 counts, smaller white blood cells, lymphocytes, and neutrophils; higher brain natriuretic peptide levels; higher levels of myocardial damage and higher C-reactive protein levels may be used for the early recognition of severely ill patients of the disease.

Previous studies have shown that COVID-19 patients present with different signs and symptoms. Abnormal liver function is observed in some of the COVID-19 patients. Fan et al. studied the features related to COVID-19 associated liver damage for providing treatment. The study included 75 male and 73 female patients from China with a mean age of 50 years. Enhanced levels of total bilirubin, alkaline phosphatase, gamma-glutamyltransferase, and aspartate and alanine aminotransferase are considered markers of abnormal liver function. The patients with abnormal liver function were treated with lopinavir/ritonavir drug after hospital admission and reported more extended hospital stays than patients with normal liver function. Case-fatality rates and confirmed cases of COVID-19 are different among countries. One probable reason may be that the universal bacilli Calmette-Guérin (BCG) vaccine coverage varies from country to country. Hamiel et al. reviewed 72,060 test results among COVID-19 affected patients from Israel and did not find a statistical difference between the positive test results in the unvaccinated group and BCG vaccinated cohort.

Heart transplant (HT) patients may have higher risk levels from COVID-19 due to clinically significant immunosuppression and several other comorbidities. Latif et al. studied the treatment, outcomes, and characteristics of patients having COVID-19 with HT. Their study recorded a fatality rate of 25% in patients with HT related to COVID-19. Wu et al. explored the outcomes and the clinical characteristics in COVID-19 infected patients who died or
had ARDS. They extracted the risk factors related to ARDS development and death as coagulation dysfunction, neutrophilia, and older age by using bivariate Cox regression and concluded that due to less immune response, aged patients had a higher risk of ARDS development and death. Rothe et al.\(^\text{12}\) examined the transmission of COVID-19 disease from asymptomatic contacts in Germany to conclude that asymptomatic patients were potential carriers of COVID-19 infection, and there was an urgent need for the examination of the transmission dynamics of the pandemic.

Oxley et al.\(^\text{13}\) investigated five patients with large-vessel stroke who were diagnosed with COVID-19 in a New York City hospital with a 5% prevalence of stroke among COVID-19 patients. Reluctance to present to the hospital, isolation, and social distancing were the causes of the poor outcome. They asserted the need for further study of the association between COVID-19 in young patients and large-vessel stroke. The first COVID-19 case in Iceland was recorded in late February 2020. Gudbjartsson et al.\(^\text{14}\) carried out screening with random samples from 2283 subjects, invited samples from 10,797 persons, out of which 643 tested positive. Most of the positive persons had an international travel history at the early stage of the study. The haplotypes of the COVID-19 changed over time and were found to be diverse.

Type 2 diabetes (T2D) has been identified as prime comorbidity of COVID-19. We are uncertain about the effect of blood glucose control on medical attention or mortality in patients with T2D as well as COVID-19. Zhu et al.\(^\text{15}\) conducted a multi-center, retrospective study of 7337 patients in China, of which 952 had T2D disease. They observed that T2D were more prone to multiple organ injury, mortality, and needed more medical attention than nondiabetic persons. Early, fast, and accurate clinical assessment of the COVID-19 severity level is crucial to support healthcare planning and decision making. Yan et al.\(^\text{16}\) collected blood samples from 485 COVID-19 patients in Wuhan, China, to detect critical biomarkers of the disease. Their machine learning method picked high-sensitivity C-reactive protein, lymphocyte, and lactic dehydrogenase as potential biomarkers that achieved 90% accuracy in mortality prediction. However, some of the features that have important effects on COVID-19 mortality rate were not investigated in these previous studies. Therefore, in this study, we analysed additional risk factors of COVID-19 in Iran.

2 | MATERIALS AND METHODS

This study was performed prospectively from March 3, 2020 to April 8, 2020 at the imaging department of OMID hospital, Tehran, Iran. We included 319 patients with flu-like symptoms during the COVID-19 pandemic. All clinical data, including general information, epidemiological and medical history, symptoms, signs, epidemiological and clinical characteristics of patients were included. Finally, we selected 32 features (symptoms) based on consultation with four infection disease specialists. This study was approved by the local ethical committee of the university. Our patients were informed about the study aims, and written consent was obtained before enrollment and data collection.

For patients with symptoms, lung computed tomography (CT) was performed as a noninvasive test for lung situation assessment. Unlike reverse-transcription polymerase chain reaction, which requires specific laboratory environments, CT-scan was used to provide a faster diagnosis of lung diseases. All the suspected patients underwent a thin-slice high-resolution multi-slice spiral CT scan in a supine position, and high-resolution computed tomography (HRCT) images of all patients were reviewed by a radiologist with more than 14 years of experience in chest imaging. In this manner, COVID-19 was diagnosed in suspicious cases. We followed-up with patients for two months after participation to determine their health status.

2.1 | Statistical analysis

Data are presented as means (± standard deviations). We analyzed the features using Matlab 2016a software. Fisher’s exact test\(^\text{17}\) and Wilcoxon Rank-Sum Test\(^\text{18}\) are used for categorical and continuous data respectively, to specify differences between the two groups. Statistical significance was set at \( p \leq .05 \).

3 | RESULTS

A total of 319 patients (mean age 45.48 ± 18.50 years, 177 women) were recruited. Of the patients with COVID-19, one had leukemia, one advanced thyroid, and one bone marrow cancer and unfortunately, the patients with leukemia and bone marrow cancer died. Meanwhile, two cases had a stroke, and one of them was cured. One patient with a history of tuberculosis died. Two cases had kidney disease and both of them died.

Our data showed a significant difference between healthy and COVID-19 cases with regard to the symptoms like fever \(( p = 1.99E−12)\), dyspnea \(( p = 2.99E−11)\), weakness \(( p = 3.16E−11)\), shivering \(( p = 1.01E−09)\), fatigue \(( p = 6.60E−09)\), and dry cough \(( p = 9.53E−09)\). Indeed, symptoms such as anorexia \(( p = 1.68E−08)\), anosmia \(( p = 5.46E−08)\), ageusia \(( p = 1.19E−07)\), dizziness \(( p = 2.10E−05)\), and sweating \(( p = 2.15E−05)\) showed a significant difference between healthy versus COVID-19 cases as well. All of these symptoms are more prevalent in COVID-19 affected cases than healthy subjects. When considering symptoms such as chest pain, sore throat, and cough with sputum, there is no significant difference between healthy versus COVID-19 cases \(( p = .411, .666, \text{and } 1, \text{respectively})\). A significantly higher mean age is seen in COVID-19 cases \((52.02 ± 17.63\text{-year-old})\) versus healthy subjects \((44.13 ± 16.17\text{ years old})\) \(( p = 1.54E−04)\). Abnormal CRP is significantly more in COVID-19 affected cases compared with healthy subjects \(( p = 1.59E−09)\). The O− blood group (BG) \(( p = .0066)\) is found to be lower for COVID-19 cases compared to normal subjects. There is no significant difference between healthy and COVID-19 cases regarding AB−, A−, A+, B+, AB+, B−, and O+ BG carriers with
$p$ of .641, .6251, .6561, .7291, .8044, 1, and 1, respectively. Past history of BCG vaccination did not show any significant difference between COVID-19 and healthy subjects ($p = .1057$). There is no significant difference between healthy and COVID-19 cases regarding DM ($p = .269$), immune deficiency ($p = .302$), HEM ($p = .377$), hematologic diseases ($p = .377$), corticosteroid therapy ($p = .385$), tobacco use ($p = .38$), and gender ($p = .411$). History of travel within the past 3 months showed no significant difference between the two classes ($p = .546$). We observed no significant difference between healthy and COVID-19 cases with regard to asthma ($p = .715$), liver disease ($p = .746$), cancer ($p = .754$), heart disease ($p = 1$), kidney disease ($p = 1$), and organ transplant ($p = 1$). The summary of this data is shown in Table 1. Features with a significant relationship with COVID-19 are illustrated in Figure 1. Meanwhile, the age distribution and a number of different blood type groups of COVID-19 patients are shown in Figure 2. Figure 2A shows that the groups with the highest infection risk are people in the age group between 25 and 55. They form an active labor force of society and have a higher rate of interaction with others. It is clear from Figure 2B that the negative blood groups are infected extremely less than positive groups. In positive blood groups, O+ BG, A+ BG, B+ BG, and AB+ BG are more infected, respectively.

We observed a significant association between older age ($p = 2.82\times10^{-5}$), history of heart disease ($p = 5.0654$), and history of cancer ($p = 1.01286$) with COVID-19 mortality compared with healthy subjects. Carriers of O+ BG showed protective features against COVID-19 with regard to mortality ($p = 0.0057$). Regarding symptoms, anosmia ($p = 0.010612$), dry cough ($p = 0.011324$), ageusia ($p = 0.011741$), fever ($p = 0.024933$), and anorexia ($p = 0.038981$) are significantly related to COVID-19 with regard to mortality compared with healthy subjects. Other features did not show a significant relationship with COVID-19 with regard to mortality. The summary of this data is shown in Table 2. Features with a significant relationship with regard to mortality in COVID-19 are shown in Figure 3. The age distribution of dead patients because of COVID-19 is illustrated in Figure 4. According to this figure, although most of the infected people are in the range of 25 and 55, the mortality rate is very low. There is no mortality in the ages between 40 and 60. But, this does not mean that the youth are completely immune from death. There are two cases that died in the range of 30 and 40. These two young cases have some common features. The 30-year-old case was a female with diabetes and dyspnea. The 40-year-old case was a male with Respiratory disease and dyspnea. There were no other diseases recorded for them. Although the infection rate is not high among older people, their mortality rate is high.

| TABLE 1 Clinical characteristics of COVID-19 patients |
|--------------------------------------|------|---------|-----|
| Feature                             | Covid-19 | Healthy | $p$ value |
| Fever                               | 50    | 15      | 1.99E-12 |
| Dyspnea                             | 61    | 29      | 2.99E-11 |
| Weakness                            | 34    | 5       | 3.16E-11 |
| Shivering                           | 32    | 6       | 1.01E-09 |
| CRP                                 | 84    | 66      | 1.59E-09 |
| Fatigue                             | 38    | 12      | 6.60E-09 |
| Dry cough                           | 55    | 29      | 9.53E-09 |
| Anorexia                            | 26    | 4       | 1.68E-08 |
| Ageusia                             | 33    | 10      | 5.46E-08 |
| Dizziness                           | 11    | 0       | 2.10E-05 |
| Sweating                            | 15    | 2       | 2.15E-05 |
| Age                                 | 52.02 ± 17.63 | 44.13 ± 16.17 | 1.54E-04 |
| Blood type                          |       |         |        |
| O-                                  | 1     | 15      | .0066  |
| AB-                                 | 2     | 2       | .641   |
| A-                                  | 1     | 4       | .6524  |
| A+                                  | 24    | 34      | .6561  |
| B+                                  | 16    | 23      | .7291  |
| AB+                                 | 6     | 12      | .8044  |
| B-                                  | 1     | 2       | 1      |
| O+                                  | 35    | 55      | 1      |
| BCG vaccine                         | 88    | 158     | .1057  |
| Diabetes                            | 10    | 24      | .269539|
| Immunodeficiency                    | 0     | 4       | .302357|
| HEM                                 | 3     | 2       | .37745 |
| Rheumatological disease             | 3     | 2       | .37745 |
| Corticosteroids                     | 1     | 0       | .38558 |
| Tobacco                             | 1     | 0       | .38558 |
| Gender                              |       |         |        |
| Male                                | 62    | 80      | .4116  |
| Female                              | 61    | 116     |       |
| Chest Pain                          | 1     | 5       | .411622|
| Traveling in past 3 months ago      | 6     | 6       | .546959|
| Sore throat                         | 8     | 16      | .666779|
| Asthma                              | 2     | 6       | .715367|
| Liver disease                       | 3     | 7       | .746248|
| Cancer                              | 5     | 6       | .754812|
| Heart disease                       | 12    | 20      | 1      |
| Kidney disease                      | 5     | 8       | 1      |
| Transplant                          | 0     | 1       | 1      |
| Cough with sputum                   | 2     | 4       | 1      |

Note: The bold values significant at $p < .05$. 

4 | DISCUSSION

The main findings of our study are the significant association between symptoms such as fever, dyspnea, weakness, shivering, fatigue, dry cough, anorexia, anosmia, ageusia, dizziness, and sweating with COVID-19. We also observed an association between higher mean
FIGURE 1 Features with a significant relationship with COVID-19

FIGURE 2 (A) The age distribution of COVID-19 patients. (B) Blood types of COVID-19 patients

| Feature                        | Dead | Alive | p Value |
|--------------------------------|------|-------|---------|
| Age                            | 71.13 ± 16.89 | 49.21 ± 15.97 | 2.82E−05 |
| Blood type                     |      |       |         |
| O+                             | 0    | 35    | .0057   |
| A+                             | 4    | 20    | .4897   |
| AB+                            | 0    | 6     | 1       |
| AB−                            | 0    | 2     | 1       |
| A−                             | 0    | 1     | 1       |
| B+                             | 2    | 14    | 1       |
| B−                             | 0    | 1     | 1       |
| O−                             | 0    | 1     | 1       |
| Heart disease                  | 5    | 7     | .00654  |
| Anosmia                        | 0    | 33    | .010612 |
| Dry cough                      | 2    | 53    | .011324 |
| Ageusia                        | 0    | 31    | .011741 |
| Cancer                         | 3    | 2     | .012863 |
| Fever                          | 2    | 48    | Anorexia|
| Anorexia                       | 0    | 26    | .038981 |
| Respiratory disease            | 4    | 10    | .068973 |
| CRP                            | 7    | 77    | .0751066|
| Diabetes                       | 3    | 7     | .010612 |
| Kidney disease                 | 2    | 3     | .112073 |
| Sweating                       | 0    | 15    | .211765 |
| Chest pain                     | 0    | 16    | .214526 |
| Gender                         |      |       |         |
| Male                           | 10   | 52    | .270425 |
| Female                         | 5    | 56    |         |
| Dyspnea                        | 5    | 56    | .270425 |
| BCG vaccine                    | 4    | 84    | .3238626|
| HEM                            | 1    | 2     | .325374 |
| Shivering                      | 2    | 30    | .349559 |
| Dizziness                      | 0    | 11    | .356602 |
| Nausea_Diarrhea                | 0    | 11    | .356602 |
| Fatigue                        | 3    | 35    | .389313 |
| Sore throat                    | 0    | 8     | .593884 |
| Blood pressure                 | 0    | 9     | .5987395|
| Weakness                       | 3    | 31    | .758468 |
| Traveling in past 3 months ago | 0    | 6     | 1       |
| Asthma                         | 0    | 2     | 1       |
| Corticosteroids                | 0    | 1     | 1       |
| Liver disease                  | 0    | 3     | 1       |
age and abnormal CRP in COVID-19 patients. Interestingly, O− BG showed a protective effect against COVID-19. Among Iranian people with Rh-negative blood group, O− BG has the highest percentage (about 4%). The percentage of other Rh-negative blood groups A− BG, B− BG, and AB− BG are about 3%, 2.5%, and 0.8%, respectively.19,20 However, another possibility is that O− BG people are more likely to get flu-like symptoms in the healthy group. Therefore, more research is needed to understand this relationship which is beyond the scope of this study. Also, we showed a relationship between older age, history of heart disease, and cancer, and COVID-19 related mortality. Development of symptoms such as anosmia, dry cough, ageusia, fever, and anorexia are also predictors of mortality of COVID-19 cases. O+ BG is a protective factor against COVID-19 related mortality.

In our study, fever is the most significantly associated symptom with COVID-19, which is in line with findings by Zhang et al.21 and Chen et al.22 In contrast, Liang et al.,23 DeBiasi et al.,24 Tian et al.,25 Zho et al.,26 and Qin et al.27 found a nonsignificant association between fever and COVID-19. Indeed, dyspnea is a relevant symptom with COVID-19 that is in agreement with Tian et al.,25 DeBiasi et al.,24 and Qin et al.27 but is in contrast with the findings of Liang et al.23 and Yan et al.28 Dizziness is associated with COVID-19 in our study, which is similar to the findings of Zhou et al.29 and Zhang et al.30 But Shi et al.,17 Chen et al.,22 and Liang et al.23 found no association with this. We did not find a study regarding sweating, and to the best of our knowledge, this is the first work to report this. Nikpouraghdam et al.31 suggested an association between weakness and COVID-19 that is the same as our data but is in contrast with the findings of Shi et al.17 Shivering is observed in the cohort of COVID-19, which is reported by Zhu et al.32 too. Fatigue is significantly related with COVID-19 in our cohort which confirms the findings of Qin et al.27 but is in contrast to the findings of Liang et al.23 Tian et al.,25 Lei et al.,33 and Yan et al.34 A dry cough is reported by Du et al.35 to be related with COVID-19, which is similar with our findings, while such an association is not found by Qin et al.,27 Lei et al.,33 and Shi et al.17 Anorexia is found to be a significant symptom for COVID-19 in our study. The association between anorexia and COVID-19 in our study is similar to Zhang et al.21 and Chen et al.22 but is not in line with the findings of Shi et al.,17 Lei et al.,33 and Qin et al.27 Anosmia is associated with COVID-19 in our cohort, which confirms the findings of Yan et al.28 Bagheri et al.,36 and Lee et al.37 Yan et al.28 and Lee et al.37 also introduced ageusia as an associated symptom with COVID-19 that is in line with our findings.

Regarding the association between age and COVID-19, we observed old age, as an indicator, which is in line with Fan et al.,38 but is in contrast with the findings of Fu et al.,39 Fang et al.,40 and Omrani-Nava et al.41 who did not find a significant association between age and COVID-19. This discrepancy could be explained by different demographic features (symptoms). We observed elevated CRP as a related feature to COVID-19 in our investigation that is in agreement with Fu et al.39 and is in contrast with the findings of Omrani-Nava et al.41 BCG vaccination showed no significant relationship between COVID-19 versus healthy subjects in our cohort that is in agreement with the findings of Li et al.42 and Hamiel et al.10 and in contrast to Dayal et al.13

Currently, there are additional data regarding predictor features of mortality related to COVID-19. Interestingly, some features with no obvious relationship with COVID-19 infection are associated with

### TABLE 2 (Continued)

| Feature          | Dead | Alive | p Value |
|------------------|------|-------|---------|
| Rheumatological disease | 0    | 3     | 1       |
| Cough with sputum | 0    | 2     | 1       |
| Eczema           | 0    | 3     | 1       |
| Conjunctivitis   | 0    | 2     | 1       |
| Tobacco          | 0    | 1     | 1       |
| Chest pain       | 0    | 1     | 1       |
COVID-19 related mortality, O+ BG, history of heart disease, and cancer are with COVID-19 infection showed a significant relationship with COVID-19 related mortality. However, the development of symptoms such as anosmia, dry cough, ageusia, fever, and anorexia are the predictors of both COVID-19 infection and mortality. Old age is a predictor of mortality in the Zhou et al.26 report, which is also observed in our findings. Zhou et al.26 reported other predictors of mortality such as fever, fatigue, myalgia, nausea, vomiting, diarrhea, cough, and sputum that are not mortality predictors in our cohort. Fever and dyspnea are also considered as predictors of mortality by Iftime et al.44 and Chen et al.45 respectively, while we did not find an association between these symptoms with COVID-19 related mortality.

Interestingly, we observed more features associated with mortality in our cohort, but age seems to be the most important risk factor for COVID-19, which is in line with other published studies.26,44-47 The predictive role of age is also confirmed by Sun et al., De Smet et al.,47 and Chen et al.45 studies. In the old age group, immune impairment can occur, and also there is a possibility of increased respiratory disease. As mentioned above, comorbidities such as cancer and underlying heart diseases are associated with COVID-19 mortality. Iftime et al.44 observed such an association with T2D and cancer, but they negated the relationship between the history of heart disease and COVID-19 related mortality. Regarding comorbidities, Ruan et al.48 and Chen et al.45 demonstrated a link between a history of heart disease and COVID-19 related mortality. Furthermore, a history of cerebrovascular disease is also a determinant in predicting the disease while age, O+ BG, heart disease, anosmia, and dry cough are the most crucial factors in the mortality of patients. This study may be helpful in early prediction and risk reduction of mortality in patients infected with COVID-19. Further studies with longitudinal follow-ups are needed to confirm our findings.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
Continued to prepare the first draft: Roohallah Alizadehsani, Mohamad Roshanzamir, Zahra Roshanzamir, Zahra Alizadeh Sani, Mohaddeseh Behjati, Sadiq Hussain, Afshin Shoeibi, Fahime Khozeimeh. Contributed to editing the final draft: Saeid Nahavandi, Abbas Khorosvari, Sheikh M. S. Islam, and U. Rajendra Acharya. Contributed to all analysis of the data and produced the results accordingly: Niloofar Abединي, Fereshteh Hasanzadeh, Roohallah Alizadehsani, Assef Zare, Maryam Panahiazar, Abbas Khorosvari, and Maryam Panahiazar. Searching for papers and then extracted data: Roohallah Alizadehsani, Pardis Moradnejad, Sadiq Hussain, and Mohaddeseh Behjati. Provided overall guidance and managed the project: Sheikh M. S. Islam and U. Rajendra Acharya.

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### APPENDIX A

#### TABLE A1  Summary of common findings reported by other state-of-the-art studies

| Ref No. | Population of samples | Country | Feature name | p value |
|---------|------------------------|---------|--------------|---------|
| Fan et al.38 | 69 | Singapore | Age | .02 |
|  |  |  | Hb (g/dl) | .07 |
|  |  |  | WBC (<10^9/L) | .87 |
|  |  |  | ALC (<10^9/L) | .0002 |
|  |  |  | ANC (<10^9/L) | .17 |
|  |  |  | Platelets (<10^9/L) | .81 |
|  |  |  | LDH (U/L) | .003 |
| Fu et al.39 | 75 | China | Age | .095 |
|  |  |  | CRP (mg/L) | .001 |
|  |  |  | WBC count (10^9/L) | .026 |
|  |  |  | Neutrophil count (10^9/L) | .008 |
|  |  |  | Lymphocyte level (10^9/L) | .009 |
|  |  |  | NLR | .001 |
|  |  |  | D-dimer level (μg/L) | .001 |
|  |  |  | Hemoglobin (%) | .548 |
| Omrani-Nava et al.41 | 279 | Iran | CRP (positive) | .248 |
|  |  |  | Age | .125 |
|  |  |  | Lymphopenia | .676 |
|  |  |  | WBC, per mm^3 | .473 |
|  |  |  | Lymphocyte, per mm^3 | <.001 |
|  |  |  | Hemoglobin, g/dL | .421 |
|  |  |  | Platelet, per mm^3 | <.001 |
| Zhao et al.53 | 1775 | China | Blood Group A | <.001 |
|  |  |  | Blood Group B | .240 |
|  |  |  | Blood Group AB | .291 |
|  |  |  | Blood Group O | <.001 |
| Zietz et al.50 | 1,559 | The U.S. and China | Blood Group A | .009 |
|  |  |  | Blood Group B | .446 |
|  |  |  | Blood Group AB | .033 |
|  |  |  | Blood Group O | .036 |
| Guo et al.51 | 174 | China | Red blood cells (×10^{12}/L) | <.01 |
|  |  |  | Hemoglobin (g/dl) | <.01 |
|  |  |  | C-reactive protein (mg/L) | <.01 |
|  |  |  | Lymphocytes (×10^9/L) | <.01 |
|  |  |  | Neutrophils (×10^9/L) | .02 |
|  |  |  | Immunodeficiency | .294 |
|  |  |  | Chronic liver disease | .288 |
|  |  |  | Chronic kidney disease | .373 |
| Li et al.42 | NA | 91 countries | BCG | .3948 |
| Dayal et al.43 | NA | High Burden Countries: 12 | BCG | <.0001 |
|  |  | Countries that follow BCG vaccination:12 |  |
| Hamiel et al.50 | 297340 (1979-1981: BCG vaccinated) 301600 (1983-1985: BCG unvaccinated) | Israel | BCG | .09 |
| Zheng et al.54 | 3027 | Different countries | Respiratory disease | <.00001 |
| Liang et al.23 | 88 | China | Fever | .816 |
|  |  |  | Cough | .001 |
| Ref No. | Population of samples | Country      | Feature name                          | p value |
|---------|-----------------------|--------------|--------------------------------------|---------|
|         |                       |              | Dyspnea or shortness of breath       |         |
|         |                       |              | Expectoration                        | .354    |
|         |                       |              | Fatigue                              | .175    |
|         |                       |              | Sore throat                          | .193    |
|         |                       |              | Nasal symptoms                       | .219    |
|         |                       |              | Headache or dizziness                | .153    |
|         |                       |              | Diarrhea                             | .343    |
| DeBiasi et al. 24 | 177                | The U.S.     | Fever                                | .06     |
|         |                       |              | Sore throat or congestion             | .004    |
|         |                       |              | Cough                                | .003    |
|         |                       |              | Shortness of breath                  | .04     |
|         |                       |              | Diarrhea or vomiting                 | .89     |
|         |                       |              | Chest pain                           | .22     |
|         |                       |              | Loss of sense of taste and/or smell  | .28     |
|         |                       |              | Headache                             | .01     |
| Tian et al. 25 | 262                | China        | Fever                                | .752    |
|         |                       |              | Cough                                | .201    |
|         |                       |              | Fatigue                              | .288    |
|         |                       |              | Dyspnea                              | <.001   |
|         |                       |              | Headache                             | .992    |
|         |                       |              | Respiratory rate                     | .333    |
| Qin et al. 27 | 452               | China        | Fever                                | .232    |
|         |                       |              | Dry cough                            | 1.000   |
|         |                       |              | Expectoration                        | .843    |
|         |                       |              | Shortness of breath                  | <.001   |
|         |                       |              | Myalgia                              | .407    |
|         |                       |              | Confusion                            | .301    |
|         |                       |              | Headache                             | .068    |
|         |                       |              | Dizziness                            | .112    |
|         |                       |              | Fatigue                              | .014    |
|         |                       |              | Nausea and vomiting                  | .092    |
|         |                       |              | Diarrhea                             | .913    |
|         |                       |              | Abdominal pain                       | .073    |
|         |                       |              | Anorexia                             | .234    |
| Lei et al. 33 | 34                 | China        | Dry cough                            | .51     |
|         |                       |              | Anorexia                             | .63     |
|         |                       |              | Nausea                               | >.99    |
|         |                       |              | Diarrhea                             | >.99    |
|         |                       |              | C-reactive protein, mg/L             | .55     |
|         |                       |              | Fatigue                              | .70     |
|         |                       |              | Dizziness or headache                | .41     |
|         |                       |              | Chronic kidney disease               | .44     |
|         |                       |              | Cancer                               | .62     |
|         |                       |              | Diabetes                             | .78     |
| Yan et al. 28 | 262                  | The U.S.     | Ageusia                              | <.001   |
|         |                       |              | Anosmia                              | <.001   |
|         |                       |              | Headache                             | .019    |
|         |                       |              | Dyspnea                              | .14     |
|         |                       |              |                                      | (Continues) |
| Ref No. | Population of samples | Country     | Feature name                     | p value |
|--------|----------------------|-------------|----------------------------------|---------|
| Yan et al. 34 | 128 | The U.S. | Anosmia                          | <.001   |
|         |         |             | Fatigue                          | .19     |
|         |         |             | Dysgeusia                        | <.001   |
|         |         |             | Headache                         | .86     |
|         |         |             | Cough                            | .14     |
|         |         |             | Cardiac disease                  | .71     |
|         |         |             | Cancer                           | .62     |
|         |         |             | Diabetes                         | .78     |
| Bagheri et al. 36 | 10069 | Iran | Anosmia                          | <.001   |
| Lee et al. 37 | 3,191 | Korea | Anosmia                          | <.001   |
| Shi et al. 17 | 81 | China | Anorexia                         | .6296   |
|         |         |             | Headache                         | .8645   |
|         |         |             | Diarrhea                         | .913    |
|         |         |             | Nausea and vomiting              | .092    |
|         |         |             | Dry cough                        | 1.00    |
|         |         |             | Headache                         | .068    |
|         |         |             | Dizziness                        | .8056   |
|         |         |             | Weakness                         | .4065   |
| Guertler et al. 55 | 114 | Germany | Hand eczema                      | .99     |
| Zhang et al. 21 | 221 | China | Sex                              | .011    |
|         |         |             | Fever                            | .006    |
|         |         |             | Anorexia                         | <.001   |
| Chen et al. 22 | 145 | China | Fever                            | .01     |
|         |         |             | Anorexia                         | .01     |
|         |         |             | Dizziness                        | .24     |
| Du et al. 35 | 67 | China | Dry cough                        | .03     |
| Zhu et al. 32 | 4394 | China | Shivering                        | <.001   |
| Nikpouraghdam et al. 31 | 120 | Iran | Weakness                         | .031    |
| Wang et al. 56 | 1480 | China | Liver disease                    | .326    |
| Feng et al. 57 | 476 | China | Chest pain                       | .13     |
| Siegler et al. 58 | 328 | United States | Prior stroke                  | .90     |
| Chen et al. 59 | 236 | China | Sore throat                      | .1726   |
| Gold et al. 60 | 305 | Georgia | Asthma                           | .12     |
|         |         |             | Rheumatologic or autoimmune condition | .22 |
|         |         |             | Immunocompromising conditions or therapies | .91 |
| Pereira et al. 61 | 90 | United States | Organ transplant Kidney         | .90     |
| Webb et al. 62 | 39 | Different Countries | Liver transplant               | .580    |
| Fang et al. 40 | 78 | China | Kidney                           | .959    |
### TABLE A1 (Continued)

| Ref No. | Population of samples | Country | Feature name | p value |
|---------|------------------------|---------|--------------|---------|
| Fadel et al.\(^63\) | 213 | United States | Corticosteroid use and age general group (n = 55) | .33 |
| | | | Severe group (n = 23) | |
| Liu et al.\(^7\) | 56 | China | Smoking history | .0615 |
| Zhou et al.\(^29\) | 254 | China | Cough with sputum | .284 |
| Zhang et al.\(^30\) | 663 | China | Dizziness | .032 |
| Liu et al.\(^64\) | 245 | China | Dizziness | .009 |

Abbreviations: ALC, absolute lymphocyte count; AMC, absolute monocyte count; ANC, absolute neutrophil count; Hb, hemoglobin; LDH, lactate dehydrogenase; WBC, white blood cell.

### TABLE A2 Some of the common clinical characteristics of COVID-19 patients with fatality

| Ref no. | Population of samples | Country | Feature name | p Value |
|---------|------------------------|---------|--------------|---------|
| Zhou et al.\(^26\) | 171 | China | Age | .0043 |
| | | | Coronary heart disease | .48 |
| | | | Fever (temperature ≥ 37.3°C) | .94 |
| | | | Cough | .15 |
| | | | Sputum | .55 |
| | | | Myalgia | .93 |
| | | | Fatigue | .33 |
| | | | Diarrhea | .67 |
| | | | Nausea or vomiting | .40 |
| | | | White blood cell count, ×10⁹/L | <.0001 |
| | | | Lymphocyte count, ×10⁹/L | <.0001 |
| | | | Hemoglobin, g/L | .30 |
| | | | Anemia | .0094 |
| | | | Platelet count, ×10⁹/L | <.0001 |
| Sun et al.\(^46\) | 244 | China | Age | .037 |
| | | | Sex | .270 |
| | | | SpO₂, % | .565 |
| | | | Heart rate, beats/min | .977 |
| | | | Respiratory rate, breaths/min | .181 |
| | | | Consciousness disorders (disorders vs. clear) | .827 |
| | | | Hypertension (yes vs. no) | .744 |
| | | | Previous respiratory diseases (yes vs. no) | .245 |
| | | | WBC count, ×10⁹/L | .052 |
| | | | LYM count, ×10⁹/L | .001 |
| | | | NT-proBNP, ×10⁵ pg/ml | .514 |
| | | | PCT, ng/ml | .791 |
| | | | hs-TnI, pg/ml | .065 |
| | | | D-dimer, μg/ml FEU | .278 |
| | | | ALT, U/L | .231 |
| | | | AST, U/L | .137 |
| | | | Creatinine, μmol/L | .340 |
| | | | eGFR, ml/min/1.73 m² | .543 |
| | | | hs-CRP, mg/L | .122 |

(Continues)
| Ref no.       | Population of samples | Country    | Feature name                        | p Value |
|--------------|------------------------|------------|-------------------------------------|---------|
| De Smet et al.⁴⁷ | 81                     | Belgium    | Age                                 | .03     |
| Lftime et al.⁴⁴ | 188                    | Spain      | Age                                 | <.001   |
|               |                        |            | Fever                               | .046    |
|               |                        |            | Cough                               | .901    |
|               |                        |            | Diarrhea                            | .232    |
|               |                        |            | Gender                              | .084    |
|               |                        |            | Smoking status                      | .471    |
|               |                        |            | Cardiovascular diseases             | .714    |
|               |                        |            | Chronic liver diseases              | .457    |
|               |                        |            | Chronic lung diseases               | .658    |
|               |                        |            | Cancer                              | .009    |
| Chen et al.⁴⁵  | 1,590                  | China      | Chronic kidney diseases             | .576    |
|               |                        |            | Age (≥75 vs. <65)                   | <.001   |
|               |                        |            | Age (65–74 vs. <65)                 | .018    |
|               |                        |            | Coronary heart disease              | .032    |
|               |                        |            | Cerebrovascular disease             | .037    |
|               |                        |            | Dyspnea                             | .008    |
| Ruan et al.⁴⁸  | 150                    | China      | Creatinine, μmol/L                  | .093    |
|               |                        |            | Cardiovascular disease              | <.001   |
|               |                        |            | C-reactive protein                  | <.001   |
|               |                        |            | Sex                                 | .43     |
|               |                        |            | Age                                 | <.001   |
| Li et al.⁴⁹   | 269                    | China      | Sex, male vs. female                | .032    |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; eGFR, estimated glomerular filtration rate; FEU, fibrinogen equivalent units; hs-CRP, high-sensitivity C-reactive protein; hs-TnI, high-sensitivity cardiac troponin I; LYM, lymphocyte; NT-proBNP, amino-terminal pro-brain natriuretic peptide; OR, odds ratio; PCT, procalcitonin; SpO₂, oxygen saturation; WBC, white blood cell.