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RESEARCH ARTICLE

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

Roohallah Alizadehsani[1] | Zahra Alizadeh Sani[2,3] | Mohaddeseh Behjati[2] | Zahra Roshanzamir[4] | Sadiq Hussain[5] | Niloofar Abedini[6] | Fereshteh Hasanzadeh[3] | Abbas Khosravi[1] | Afshin Shoeibi[7,8] | Mohamad Roshanzamir[9] | Pardis Moradnejad[2] | Saeid Nahavandi[1] | Fahime Khozeimeh[1] | Assef Zare[10] | Maryam Panahiazar[11] | U. Rajendra Acharya[12,13,14] | Sheikh Mohammed Shariful Islam[15]

[1]Institute for Intelligent Systems Research and Innovation (IISRI), Deakin University, Victoria, Australia

[2]Rajaei Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

[3]Department of Cardiac MRI, Omid Hospital, Tehran, Iran

[4]Pediatric Respiratory and Sleep Medicine Research Center, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

[5]System Administrator at Dibrugarh University, Dibrugarh, Assam, India

[6]Tehran University of Medical Science, Imam Khomeini Hospital Complex, Tehran, Iran

[7]Faculty of Electrical and Computer Engineering, Biomedical Data Acquisition Lab, K. N. Toosi University of Technology, Tehran, Iran

[8]Department of Computer Engineering, Ferdowsi University of Mashhad, Mashhad, Iran

[9]Department of Engineering, Islamic Azad University, Fasa, Fars, Iran

[10]Faculty of Electrical Engineering, Gonabad Branch, Islamic Azad University, Gonabad, Iran

[11]Institute for Computational Health Sciences, University of California San Francisco, San Francisco, CA, USA

[12]Department of Electronics and Computer Engineering, Ngee Ann Polytechnic, Singapore, Singapore

[13]Department of Biomedical Informatics and Medical Engineering, Asia University, Taichung, Taiwan

[14]Department of Biomedical Engineering, School of Science and Technology, Singapore University of Social Sciences, Singapore

[15]Institute for Physical Activity and Nutrition, Faculty of Health, Deakin University, Melbourne, Victoria, Australia

Correspondence
Dr. Sheikh Mohammed Shariful Islam, MBBS, MPH, PhD, FESC, National Heart Foundation Senior Research Fellow and NHMRC Emerging Leader, Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Faculty of Health, Deakin University, 221 Burwood Highway, Burwood, Melbourne, Victoria 3125, Australia.
Email: shariful.islam@deakin.edu.au

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.[1] 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.[2] 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.[3] 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.[4] 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.[5] 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.[4] 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.[6] 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.[7] 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.[8] 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.[9] 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.[10] 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.[11] 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.[12] 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.[13] 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.[14] 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.[15] 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.[16] 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.[4] 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[17] and Wilcoxon Rank-Sum Test[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 ($p = \mathbf{1.99E{-}12}$), dyspnea ($p = \mathbf{2.99E{-}11}$), weakness ($p = \mathbf{3.16E{-}11}$), shivering ($p = \mathbf{1.01E{-}09}$), fatigue ($p = \mathbf{6.60E{-}09}$), and dry cough ($p = \mathbf{9.53E{-}09}$). Indeed, symptoms such as anorexia ($p = \mathbf{1.68E{-}08}$), anosmia ($p = \mathbf{5.46E{-}08}$), ageusia ($p = \mathbf{1.19E{-}07}$), dizziness ($p = \mathbf{2.10E{-}05}$), and sweating ($p = \mathbf{2.15E{-}05}$) 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 of .411, .666, and 1, respectively). A significantly higher *mean* age is seen in COVID-19 cases (52.02 ± 17.63-year-old) versus healthy subjects (44.13 ± 16.17 years old) ($p = \mathbf{1.54E{-}04}$). Abnormal CRP is significantly more in COVID-19 affected cases compared with healthy subjects ($p = \mathbf{1.59E{-}09}$). 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 ($p = .377$), rheumatologic 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 ($p = \mathbf{2.82E{-}05}$), history of heart disease ($p = \mathbf{.00654}$), and history of cancer ($p = \mathbf{.012863}$) with COVID-19 mortality compared with healthy subjects. Carriers of O+ BG showed protective features against COVID-19 with regard to mortality ($p = \mathbf{.0057}$). Regarding symptoms, anosmia ($p = \mathbf{.010612}$), dry cough ($p = \mathbf{.011324}$), ageusia ($p = \mathbf{.011741}$), fever ($p = \mathbf{.024933}$), and anorexia ($p = \mathbf{.038981}$) 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.

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

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**
Anosmia	33	10	**5.46E−08**
Ageusia	31	9	**1.19E−07**
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			.4116
Male	62	80	
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 $p < .05$.

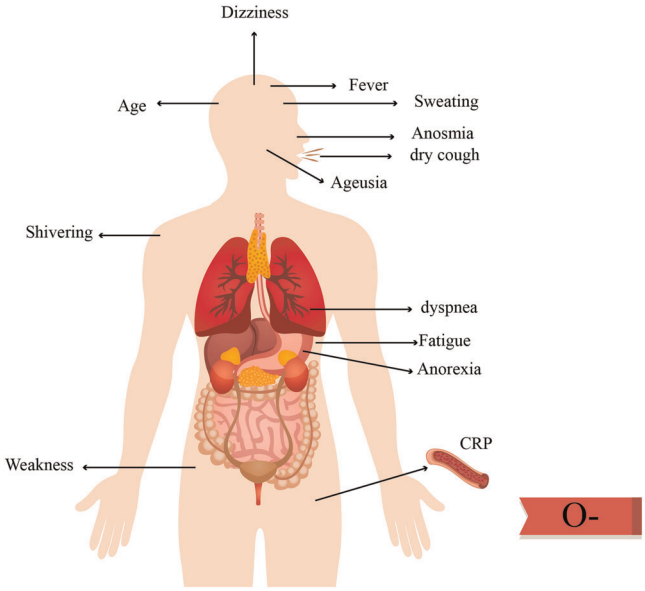

FIGURE 1 Features with a significant relationship with COVID-19

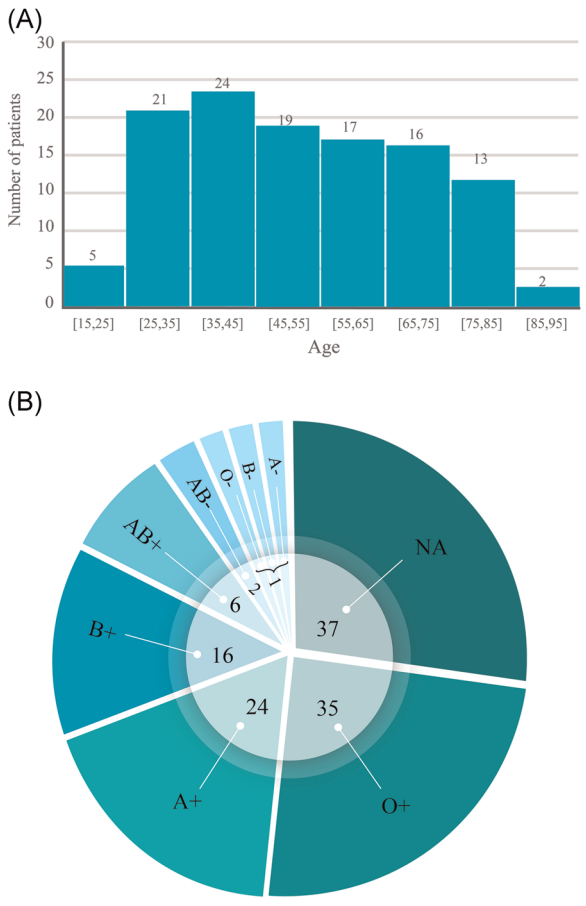

FIGURE 2 (A) The age distribution of COVID-19 patients. (B) Blood types of COVID-19 patients

TABLE 2 Clinical characteristics of COVID-19 patients with mortality

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	.1043992
Kidney disease	2	3	.112073
Sweating	0	15	.211765
Chest pain	0	16	.214526
Gender			.270425
Male	10	52	
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

(Continues)

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

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]

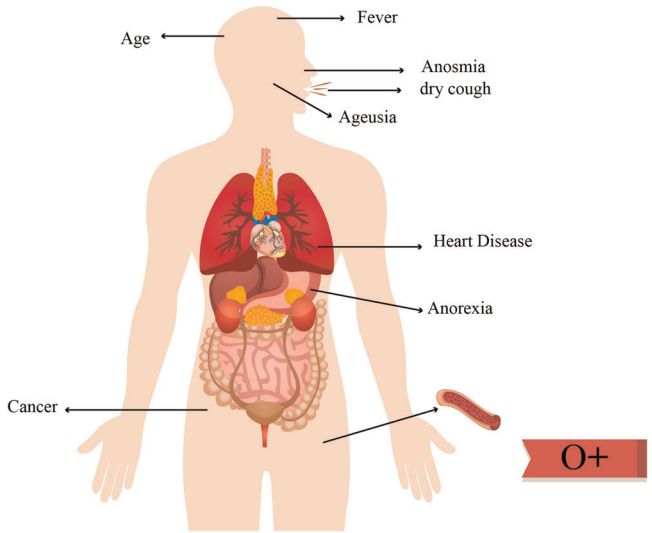

FIGURE 3 Features with a significant relationship with mortality in COVID-19

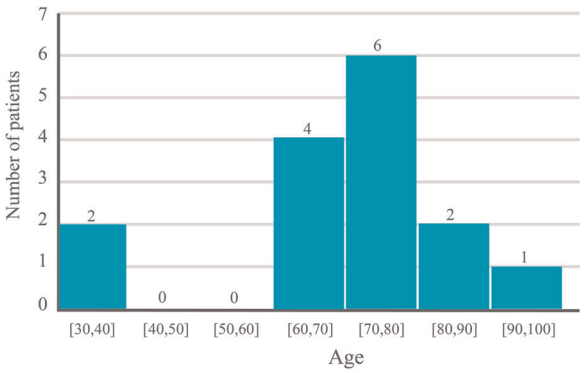

FIGURE 4 Age distribution of patients died because of COVID-19

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.[43]

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

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. Iftimie 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 the Chen et al.[45] cohort. Male gender was associated with COVID-19 related mortality in a study by Li et al.[49] study, but we did not observe such an association in our cohort. Positive CRP is a predictor in Ruan et al.[48] study, while it did not have any association with mortality in our investigation.

The association between a certain type of blood group and COVID-19 related mortality is the novel finding of our investigation. We observed a protective role for O− BG against COVID-19 in our cohort that is similar to the findings of Zietz et al.[50] and Guo et al.[51] Currently, there is no clear reason for such an association between certain BG and risk of COVID-19, but it has been suggested that O− BG or in other words, lack of A or B antigens might not permit viral entrance to cells with a subsequent lower chance for carriers to get infected by this virus. Guillon et al.[52] specifically inhibited adhesion of SARS-CoV S protein-expressing cells into ACE2-expressing cell lines with anti-A antibodies. Interestingly, we demonstrated a lower chance of mortality for O+ BG carriers, and further study is needed to support this. The summary of common findings reported by other state-of-the-art studies is listed in Tables A1 and A2. In Table A1, the effective features of COVID-19 infection are listed while in Table A2, the effective features on the mortality rate of COVID-19 patients are listed.

The novelty of our study is that we have investigated the predictive role of many reported features (symptoms) for both COVID-19 and its related mortality using 319 Iranian cases. This may provide a clear trend of the whole population as the enrolled cases are selected from different regions of Iran. Indeed, data of mortality predictors are not yet widely available, especially in Middle Eastern countries. Another point is that a combination of these features can help to manage the patient better and the need for upgrading the features associated with COVID-19 related mortality is essential in this pandemic era.

In conclusion, this is one of the first studies that investigated the effect of certain risk factors in prediction, clinical outcomes, and mortality of COVID-19. Our results indicate that risk factors like fever, dyspnea, weakness, shivering and CRP are the most important factors 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 Khosravi, Sheikh M. S. Islam, and U. Rajendra Acharya. *Contributed to all analysis of the data and produced the results accordingly*: Niloofar Abedini, Fereshteh Hasanzadeh, Roohallah Alizadehsani, Assef Zare, Maryam Panahiazar, Abbas Khosravi, and Maryam Panahiazar. *Searched 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.

ORCID

Roohallah Alizadehsani http://orcid.org/0000-0002-3069-7932
Sadiq Hussain http://orcid.org/0000-0002-9840-4796
Sheikh Mohammed Shariful Islam https://orcid.org/0000-0001-7926-9368

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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)1	.07
			WBC ($\times 10^9$/L)	.87
			ALC ($\times 10^9$/L)	.0002
			ANC ($\times 10^9$/L)	.17
			Platelets ($\times 10^9$/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
			Hemoglobulin (%)	.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 ($\times 10^{12}$/L)	<.01
			Hemoglobin (g/dl)	<.01
			C-reactive protein (mg/L)	<.01
			Lymphocytes ($\times 10^9$/L)	<.01
			Neutrophils ($\times 10^9$/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 Countries that follow BCG vaccination:12	BCG	<.0001
Hamiel et al.[10]	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

TABLE A1 (Continued)

Ref No.	Population of samples	Country	Feature name	*p* value
			Dyspnea or shortness of breath	.174
			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)

TABLE A1 (Continued)

Ref No.	Population of samples	Country	Feature name	*p* value
			Diarrhea	.001
			Nausea	.004
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
			Ageusia	<.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	.90
			Kidney	
Webb et al.[62]	39	Different Countries	Liver transplant	.580
Fang et al.[40]	78	China		.959

TABLE A1 (Continued)

Ref No.	Population of samples	Country	Feature name	*p* value
			Corticosteroid use and age general group ($n = 55$)	
			Severe group ($n = 23$)	.33
Fadel et al.[63]	213	United States	Smoking history	.0615
Liu et al.[7]	56	China	Cough with sputum	.284
Zhou et al.[29]	254	China	Dizziness	.032
Zhang et al.[30]	663	China	Dizziness	.009
Liu et al.[64]	245	China	Dizziness	.490

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, $\times 10^9$/L	<.0001
			Lymphocyte count, $\times 10^9$/L	<.0001
			Hemoglobin, g/L	.30
			Anemia	.0094
			Platelet count, $\times 10^9$/L	<.0001
Sun et al.[46]	244	China	Age	.037
			Sex	.270
			SpO_2, %	.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, $\times 10^9$/L	.052
			LYM count, $\times 10^9$/L	.001
			NT-proBNP, $\times 10^2$ 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 m^2	.543
			hs-CRP, mg/L	.122

(Continues)

TABLE A2 (Continued)

Ref no.	Population of samples	Country	Feature name	*p* Value
De Smet et al.[47]	81	Belgium	Age	.03
Iftime 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
			Chronic kidney diseases	.576
Chen et al.[45]	1,590	China	Age (≥75 vs. <65)	<.001
			Age (65–74 vs. <65)	.018
			Coronary heart disease	.032
			Cerebrovascular disease	.037
			Dyspnea	.008
			Creatinine, μmol/L	.093
Ruan et al.[48]	150	China	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; SpO_2, oxygen saturation; WBC, white blood cell.