Identification of Risk Factors Associated With Mortality Among Patients With COVID-19 Using Random Forest Model: A Historical Cohort Study

Fatemeh Moghaddam-Tabrizi[1], Tahereh Omidi[2], Masoomeh Mahdi-Akhgar[3], Robabeh Bahadori[4], Rohollah Valizadeh[5,6,7], Hamidreza Farrokh-Eslamlou[8,9]

[1] *Reproductive Health Research Center, Clinical Research Institute, Urmia University of Medical Sciences, Urmia, Iran*
[2] *Department of Biostatistics, Hamadan University of Medical Sciences, Hamadan, Iran*
[3] *Department of Biostatistics, Tarbiat Modares University, Tehran, Iran*
[4] *Department of Pediatric, Urmia University of Medical Sciences, Urmia, Iran*
[5] *Department of Epidemiology, School of Public Health, Iran University of Medical Sciences, Tehran, Iran*
[6] *Minimally Invasive Surgery Research Center, Hazrat-e Rasool General Hospital, Iran University of Medical Sciences, Tehran, Iran*
[7] *Student Research Committee, Iran University of Medical Sciences, Tehran, Iran*
[8] *Department of Public Health, School of Health, Urmia University of Medical Sciences, Urmia, Iran*
[9] *Reproductive Health Research Center, Urmia University of Medical Sciences, Urmia, Iran*

Received: 11 Jan. 2021; Accepted: 23 Jul. 2021

Abstract- There is conflicting evidence about factors associated with Clinical course and risk factors for mortality of adult inpatients. We aimed to identify the demographic, clinical, treatment, and laboratory data factors associated with mortality in the Khoy district. We performed a retrospective cohort study including COVID-19 infected patients who were admitted to Qamar-Bani Hashim hospital from 2 November 2020 to 4 December 2020. We used random forest methods to explore the risk factors associated with death. The applied method was evaluated using sensitivity, specificity, accuracy, and the area under the curve. Age, pulmonary symptoms, patients need a ventilator, brain symptoms, nasal airway, job were the most important risk factors for mortality of COVID-19 in the random forest (RF) method. The RF method showed the highest accuracy, 82.9 and 79.3, for training and testing samples, respectively. However, this method resulted in the highest specificity (89.5% for training and 95.7% for testing sample) and the highest sensitivity (91.9% for training and 94.5% for testing sample). The potential risk factors consisting of older age, pulmonary symptoms, the use of a ventilator, brain symptoms, nasal airway, and the job could help clinicians to identify patients with poor prognosis at an early stage.

Acta Med Iran 2021;59(8):457-465.

Keywords: Decision tree; Random forests; Variable importance; Coronavirus disease 2019 (COVID-19); Mortality

Introduction

Based on the Epidemiologic transition theory, infectious disease pandemics are replaced as major causes of death by chronic diseases in modern human history (1,2). Therefore, the focus on reducing the risks associated with chronic diseases, especially in high-income countries, has been overshadowed the continuing threat from infectious diseases. In recent decades, some emerging infectious diseases have been threatened public health several times, such as Avian influenza A H7N9 in 2013 and Middle East Respiratory Syndrome (MERS) in 2012. Coronavirus Disease 2019 caused by the novel Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is an ongoing emerging pandemic (3-5). It was first identified in Wuhan, China, in December 2019, has spread rapidly through the globe and became a public health emergency of international

Corresponding Author: R. Valizadeh
Department of Epidemiology, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
Tel: +98 9142664745, Fax: +98 443469932, E-mail address: rohvali4@gmail.com

concern (3). On February 19, 2020, the first confirmed case died by COVID-10 in Iran was reported from Qom, a region of central Iran (6). On November 21, 2020, more than 57.5 million cases of coronavirus had been confirmed. More than 1.37 million deaths have also been reported due to COVID.19 (3). Since the increasing number of cases reported throughout all 31 provinces of the country led Iran to be the second most distributer country in the world, after the China. Considerable differences in disease severity have been documented. Most patients infected with COVID-19 were asymptomatic, but a few patients have developed life-threatening complications including sever pneumonia, pulmonary edema, Acute Respiratory Distress Syndrome (ARDS), multiple organ failure and death (7,8). In response to the emergence of COVID-19, one hospital in every city of Iran was assigned to admit COVID-19 patients. Our study was started on 17 January 2020, in time to enroll the first case of COVID-19 patient was admitted to the hospital in Khoy district located in north-western Iran. Based on the admission criteria in different countries, hospital admission rate for patients with covid-19 were different. However, patients have been admitted with severe acute respiratory infection according to Iran's national guideline for COVID-19 infection (9). Accordingly, studies from many countries have found the percentage of patients who required intensive has varied from 5% to 32% (7,10). Information on the incidence and clinical characteristics of critically ill patients diagnosed with COVID-19 in Iran is still limited. In this study, we did a comprehensive exploration of the demographics, baseline comorbidities, presenting clinical features and outcomes of 401 hospitalized patients with confirmed COVID-19 during the growth phase of the first wave of this outbreak in north-western Iran, up to 4 December 2020.

Materials and Methods

Participants and study design

In a retrospective cohort study, we identified all patients admitted to Ghamar-Banihashem Hospital in Khoy district, Iran, which was assigned to admit COVID-19 adult patients. Patients recruited from November 2, 2020 to December 4, 2020. The clinical status of the patients as of December 4, 2020, was categorized as discharged alive or dead. The Urmia Medical Sciences University (UMSU) ethics committee approved this study (IR. UMSU. REC. 1399.044) and the requirement for informed consent was waived by the ethics committee. All consecutive patients who require hospital admission based on Iran's national guideline for the diagnosis and treatment of COVID-19 were included (11). Admitted patients were considered to have confirmed infection if the result on Real-Time reverse transcriptase-Polymerase Chain Reaction (RT-PCR) testing of a nasopharyngeal sample was positive or CT scan of chest was typical for the COVID-19 infection. Patients with acute respiratory failure (partial pressure of oxygen less than 70%) received mechanical ventilation or high-level supplemental oxygen during hospitalization. All critically ill patients requiring invasive mechanical ventilation were admitted to ICU.

The demographic data were obtained by face-to-face interviews. The data source for clinical symptoms, laboratory, and radiological findings on admission, as well as the complications, treatment, and outcomes during hospitalization, was a modified standard form from the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) (12). Any missing records were clarified through direct communication with involved hospital providers and patients` families.

The variables registered included demographic data, epidemiological information, comorbidities (chronic cardiac disease, chronic pulmonary disease, cerebrovascular disease, chronic neurological disorder, diabetes, and malignancy), baseline laboratory tests results (hemoglobin concentration, lymphocyte count, platelet count, arterial blood gas analysis, FiO_2, partial pressure of oxygen (PaO_2), and lactate concentration), signs and symptoms at admission (fever, cough, dyspnea, myalgia, arthralgia, chest pain, headache, and vomiting), chest radiographic findings, electrocardiogram results, development of ARDS and other complications during hospitalization, inpatient medications, oxygen therapy, treatments (vasoconstrictive agents, antiviral agents, antibacterial agents, corticosteroids, immunoglobulin, and mechanical ventilation), and outcomes (including length of stay, ICU admission, palliative discharge, and mortality in hospital). For variables such as initial laboratory testing and clinical studies for which not all patients had values, percentages of total patients with completed tests are shown.

Patients were divided into two groups based on the outcomes. The following two conditions were defined as outcome improvement: 1- Patients with mild or severe illness who were discharged or were going to be discharged at the end of the follow-up. 2- Patients who received continuous treatment in the ward or ICU were considered to have non-improved (death) outcomes. Therefore, the response associated with this study was the patient's final status (death or recovery), which is recorded as a binary variable.

Statistical model

Random forest (RF)

RF is an ensemble learning technique for classification and regression (13). RF method consisting of the aggregation of the set of Decision Tree (DT) by selecting the subset of the main dataset and selecting a random subset of prediction variable, finally aggregating the result of a large number of DT models to obtain a random forest (14). Multiple classifications tree of the RF is obtained from a bootstrap sample drawn randomly from the main dataset using the CART method and the decrease in the Gini impurity criterion (13). The tree training parameters used in the present study are (i) ntree=500, the number of trees generated (ii) ntry=8, the number of predictor variables used in each tree, and (iii) node size=5, the minimum number of observations in a leaf node. One of the most important features of a random forest is the output of the variable importance. RF can be used to rank the variables based on their importance for the response variable (15). Gini index is commonly used for variable importance (13). The importance of variable in a tree is determined based on comparing means decrease in accuracy and Gini index.

The Gini index at a node D is given by:

$$\text{Gini (D)} = 1 - \sum_{i=1}^{m} p_i^2$$

When pi is probability of an observation on a node D belongs to category Ci and estimated by $|Ci.\ C\ |/|D|$ (16).

This study aimed to identify Risk Factors Associated with Mortality among patients With Coronavirus disease using random forest model.

Evaluation model performance

In the present study, the results derived from the training and validation samples were evaluated by utilizing sensitivity (SE), specificity (SP) and the area under curve (AUC). Summary Indices of Test Performance:

Accuracy=(TP+TN)/(TP+FP+TN+FN)
Sensitivity=TP/(TP+FN)
Specificity= TN/(FP+TN)

Here TP, TN, FP, and FN are truly positive, true negative, false positive, and false negative, respectively (17). The receiver operating characteristic (ROC) curve is a graphical plot that illustrates the full picture of the trade-off between the true positive rate (TPR) and false-positive rate (FPR) across a series of cutoff points (18). The area under the curve (AUC) is considered as an effective measure of the accuracy of a diagnostic test (17). Statistical analyses were performed using R4.0.3 packages randomForest ' and ' pROC.’

Results

Of 401 patients with COVID-19, 36.2% were male, 95.6% were married, and 67.7% were living in the urban area. The mean (standard deviation) age of females was 57 (18.01) years, and the mean (standard deviation) age of males was 58 (18.61) years. The demographic and clinical characteristics of the study population are summarized in Tables 1 to 5. To identify the risk factors affecting the death of patients with COVID-19, LR was performed to the data. The results of the independent *chi*-square test showed that the age, job status, place of birth, shortness of breath, cough, history of hypertension, brain disease, chronic kidney disease, diabetes, heart disease, and drug use, heart symptoms, kidney symptoms, pulmonary symptoms, brain symptoms, prescription of IV Immunoglobulins, liver function tests, ECG, dyspnea, and weakness in dead patients was significantly higher than non-dead patients (P<0.001).

The socio-demographic characteristics, comorbidities, admission signs and symptoms, vital signs, and laboratory parameters were considered as the explanatory variables for the performed methods. Based on the result of the random forest model age, pulmonary symptoms, patients need a ventilator, brain symptoms, nasal airway, job, gastrointestinal symptoms, history of brain disease and heart disease, heart symptoms, history of chronic kidney disease, psychological symptoms, dyspnea symptom, history of drug use and hypertension were the most important risk factors related to the death of patients with COVID-19 (Figure 1).

A comparison of sensitivity, specificity, and accuracy for training and testing sample of classification method RF is shown in Table 6 and Figure 2.

Sensitivity (95% CI) and specificity (95% CI) of random forest in training sample were 91.9% (87.6, 95.1) and 89.5% (77.3, 96.5), respectively. Sensitivity (95% CI) and specificity (95% CI) of random forest in validation sample were 89.5% (77.3, 96.5) and 95.7% (73.9, 99.8), respectively. The accuracy (95% CI) in training and validation sample were 89.8% (85.6, 93.1) and 94.7% (89.4, 97.9), respectively. We used the area under the curve (AUC) in the validation and training to evaluate the random forest model. The related value in the case of the validation sample amounted to 79.3% and 82.9% for the training sample. The RF model has a better performance in the training sample (Figure 2).

Table 1. Comparison of demographic characteristics between the alive and dead group, N (%)

Characteristic demographics		Total (No.=401)	Alive (No.=316)	Death (No.=85)	*P*
Age (year)	<20	8 (2.0)	8 (2.5)	0 (0.0)	<0.001
	21-30	22 (5.5)	21 (6.6)	1 (1.2)	
	31-40	56 (14.0)	53 (16.8)	3 (3.5)	
	41-50	55 (13.7)	48 (15.2)	7 (8.2)	
	51-60	83 (20.7)	69 (21.8)	14 (16.5)	
	61-70	65 (16.2)	53 (16.8)	12 (14.1)	
	>70	112(27.9)	64(20.3)	48(56.5)	
Gender	Male	213 (53.1)	161 (50.9)	52 (61.2)	0.093
	Female	188 (46.9)	155 (49.1)	33 (38.8)	
Marriage status	Single	21(5.2)	20(6.3)	1(1.2)	0.058
	Married	380(94.8)	296(93.7)	84(98.8)	
Job Status	Housewife	175(46.2)	142(47.5)	33(41.2)	<0.001
	Azad	119(31.4)	97(32.4)	22(27.5)	
	Employee	51(13.5)	44(14.7)	7(8.8)	
	Unemployed	34(19)	16(5.4)	18(22.5)	
Resident place	Urban	273(68.2)	212(67.3)	61(71.8)	0.433
	Rural	127(31.8)	103(32.7)	24(28.2)	
Place of Birth	Khoy	327(82.6)	266(85.5)	61(71.8)	0.003
	Western Azerbaijan	61(15.4)	38(12.2)	28.2(27.1)	
	Others	8(19)	7(2.3)	1(1.2)	

Table 2. Comparison of symptoms between the alive and dead group, N (%)

Symptoms		Total (No.=401)	Alive (No.=316)	Death (No.=85)	*P*
Shortness of breath	No	114(28.4)	102(32.3)	12(14.1)	0.001
	Yes	287(71.6)	214(67.7)	73(85.9)	
Fever	No	234(58.5)	185(58.7)	49(57.6)	0.857
	Yes	166(41.4)	130(41.3)	36(42.4)	
Cough	No	134(33.4)	95(30.1)	39(45.9)	0.006
	Yes	267(66.6)	221(69.9)	46(54.1)	
Myalgia	No	211(52.6)	160(50.6)	51(60)	0.125
	Yes	190(47.4)	156(49.4)	34(40)	
Diarrhea	No	376(93.8)	298(94.3)	78(91.8)	0.390
	Yes	25(6.2)	18(5.7)	7(8.2)	
Nausea and vomiting	No	337(84)	263(83.2)	74(87.1)	0.392
	Yes	64(16)	53(16.8)	11(12.9)	

Table 3. Comparison of comorbidities between the alive and dead group, N (%)

Comorbidities		Total (No.=401)	Alive (No.=316)	Death (No.=85)	*P*
History of Surgery	No	306(82.7)	247(84)	59(77.6)	0.340
	Yes	64(17.3)	47(16)	17(22.4)	
Hypertension	No	274(68.3)	224(70.9)	50(58.8)	0.034
	Yes	127(31.7)	92(29.1)	35(41.2)	
Brain disease	No	374(93.3)	305(96.5)	69(81.2)	<0.001
	Yes	27(6.7)	11(3.5)	16(18.8)	
Chronic Kidney Disease	No	397(99)	315(99.7)	82(96.5)	0.008
	Yes	4(19)	1(.3)	3(3.5)	
Chronic obstructive pulmonary diseases	No	347(86.5)	277(87.7)	70(82.4)	0.203
	Yes	54(13.5)	39(12.3)	15(17.6)	
Diabetes	No	321(80)	261(82.6)	60(70.6)	0.014
	Yes	80(19)	55(17.4)	25(29.4)	
Heart disease	No	292(72.8)	245(77.5)	47(55.3)	<0.001
	Yes	109(27.2)	71(22.5)	38(44.7)	
History of drug use	No	194(48.4)	170(54.1)	24(28.2)	<0.001
	Yes	205(51.1)	144(45.9)	61(71.8)	
Addiction history	No	354(88.3)	279(88.3)	75(88.2)	0.873
	Yes	45(11.2)	35(11.1)	10(11.8)	
Family History covid 19	No	375(97.4)	298(97.4)	77(97.5)	0.837
	Yes	10(2.6)	8(2.6)	2(2.5)	

Table 4. Comparison of vital signs between the alive and dead group, N (%)

Vital signs		Total (No.=401)	Alive (No.=316)	Death (No.=85)	*P*
Heart symptoms	No	303(75.6)	263(83.2)	40(47.1)	<0.001
	Arrhythmia	7(1.7)	3(.9)	4(4.7)	
	Chest pain	91(22.7)	50(15.8)	41(48.2)	
Kidney symptoms	No	384(95.8)	314(99.4)	70(82.4)	<0.001
	Yes	17(4.2)	2(.6)	15(17.6)	
Pulmonary symptoms	No	51(12.7)	50(15.8)	1(1.2)	<0.001
	Mild shortness of breath	287(71.6)	259(82)	28(32.9)	
	Severe shortness of breath	63(15.7)	7(2.2)	56(65.9)	
Brain symptoms	No	353(88.2)	313(99.1)	40(47.6)	<0.001
	Yes	47(11.8)	3(.9)	44(52.4)	
Psychological symptoms	No	31(7.7)	24(7.6)	7(8.2)	0.71
	Anxiety	322(80.3)	252(79.7)	70(82.4)	
	Depression	48(12)	40(12.7)	8(9.4)	

Table 5. Comparison of laboratory parameters between the alive and dead group, N (%)

Laboratory parameters		Total (No.=401)	Alive (No.=316)	Death (No.=85)	*P*
Prescription of Actemra	No	78(19.7)	59(19)	19(22.4)	0.487
	Yes	318(80.3)	252(81)	66(77.6)	
Prescription of Hydroxychloroquine	No	101(25.5)	78(25.1)	23(27.1)	0.711
	Yes	295(74.5)	233(74.9)	62(72.9)	
Prescription of IV Immunoglobulins	No	386(97.5)	311(100)	75(88.2)	<0.001
	Yes	10(2.5)	0(19)	10(11.8)	
D-Dimer	Negative	24(32)	20(40)	4(16)	0.056
	Positive	51(68)	30(60)	21(84)	
Liver Function tests	Abnormal	109(44.1)	68(36.2)	41(69.5)	<0.001
	Normal	138(55.9)	120(63.8)	18(30.5)	
CT Scan	Negative	12(3.2)	11(3.8)	1(1.2)	0.247
	Positive	362(96.8)	281(96.2)	81(98.8)	
ECG	Abnormal	70(18.2)	37(12.3)	33(40.2)	<0.001
	Normal	314(81.8)	265(83.9)	49(59.8)	
Dyspnea	No	165(41.4)	151(48.1)	14(16.5)	<0.001
	Yes	234(58.6)	163(51.9)	71(83.5)	
Weakness	No	45(11.3)	44(14)	1(1.2)	0.001
	Yes	354(88.7)	270(86)	84(98.8)	

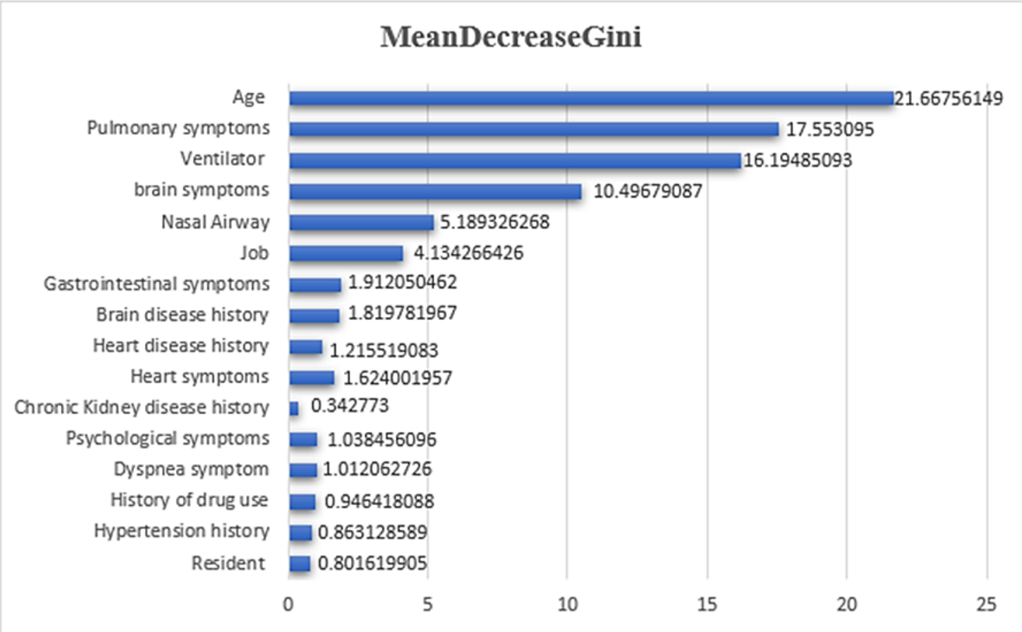

Figure 1. The importance of input variables based on the Gini importance index in random forest model

Table 6. Comparison of performed method in the training sample and validation sample

Variable (95% CI)	Training sample	Validation sample
Sensitivity (95% CI)	91.9 (87.6, 95.1)	94.5(88.5, 97.9)
Specificity (95% CI)	89.5 (77.3, 96.5)	95.7 (73.9, 99.8)
Accuracy (95% CI)	89.8 (85.6, 93.1)	94.7 (89.4, 97.9)

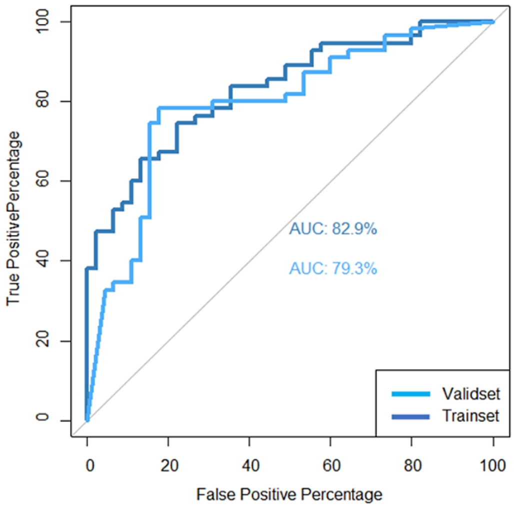

Figure 2. The area under the curve for the performed method in the training sample and validation sample

Discussion

Considering the undeniable importance of medical decisions based on clinical evidence of patients with COVID-19 disease, the present study aimed at Identifying Risk Factors Associated with Mortality among patients with COVID-19 in West Azerbaijan province and the city of Khoy was designed. In the present study, we identified all patients admitted to Ghamar-Banihashem Hospital in Khoy, Iran, which was assigned to admit COVID-19 adult patients. Patients were recruited from November 2, 2020, to December 4, 2020. The clinical status of the patients as of December 4, 2020, was categorized as discharged alive or dead. Based on the result of the random forest model old age (>70), pulmonary symptoms, patients need a ventilator, brain symptoms, nasal airway, job, gastrointestinal symptoms, brain disease history, heart disease history, heart symptoms, chronic kidney disease history, psychological symptoms, dyspnea symptom, history of drug use and hypertension history were the most important risk factors related to the death of patients with COVID-19. Recent studies have found that there are several risk factors associated with Covid-19 disease that increase patient mortality showing the need for new agents (19,20). Therefore, it is necessary to consider these factors when controlling and managing this epidemic (21). Among the most important of these risk factors are pre-existing non-communicable diseases such as cancer, diabetes, hypertension, cardiovascular disease, chronic kidney disease, chronic lung disease, and other chronic diseases (22). Therefore, knowing the mentioned risk factors in the patient with Covid-19 can help decision-makers, physicians, and scientists in reducing the burden of COVID-19. Also, many researchers have shown that knowing the incidence of mortality during outbreaks of infectious diseases, such as COVID-19, can help epidemiologists and health care professionals to address abnormalities in a population. Identify and help researchers estimate early mortality from the disease. Many recent studies have highlighted the epidemiological features of COVID-19 and the assessment of underlying diseases in affected patients and have recognized that these features can help public health officials, decision-makers, and physicians to take the initiative in Reduce the burden of infectious disease and thus control the epidemic (23). Although several studies have recently reported some epidemiological features of Covid-19 disease in the United States, Europe, Iran, and China (3,24-28), no comprehensive study has been conducted to assess these important factors in the population of Iran, particularly in the city of Khoy in West Azerbaijan Province. Zali *et al.,* (2020) showed a high case fatality rate among suspected and confirmed COVID-19 cases and highlighted the main associated risk factors including age, sex, underlying non-communicable diseases, and ICU/CCU admission affecting survival of COVID-19 patients in hospitals affiliated to Shahid Beheshti University of Medical Sciences of Iran (29). In many studies, age >60 years has been identified as a major risk factor and risk of dying from COVID-19 in men is higher than women (30,31). But in our study age>70 years has been identified as a major risk factor and risk of dying from COVID-19 in men and women was equal. Richardson *et al*., (2020) revealed that 50% of deaths had occurred in the ICUs (32). Zhou *et al*., (2020) revealed that older age, high SOFA score, and d-dimer greater than 1µg/mL are the potential risk factors of COVID-19. These could help clinicians to identify patients with poor prognosis at an early stage (33). Hou *et al.,* (2020) designed a study with title" Risk factors for disease progression in hospitalized patients with COVID-19: a retrospective cohort study" in China. Results of their study showed that older age increased CRP and decreased lymphocyte count resulted in potential risk factors for COVID-19 progression. Therefore, this may be helpful in identifying patients whose condition worsens at an early stage (34). Some risk factors for Mortality in Patients with COVID-19 that extracted from Mikami *et al.*, (2020) were older age, male sex, hypotension, tachypnea, hypoxia, impaired renal function, elevated D-dimer. Also, elevated troponin was associated with increased in-hospital mortality and hydroxychloroquine use was associated with decreased in-hospital mortality (35). Given that COVID-19 can affect the function of kidney, however medications used for the treatment of the COVID-19 can induce nephropathy as well (36,37). Padilla-Raygoza *et al*., (2020) showed that age and gender a confounding effect on dying due COVID-19 disease (38).

Some limitations in our study are worth noting. First, due to the retrospective study design, not all clinical and laboratory tests were done in all patients. Second, some confounding factors such as social economic status was not recorded for all patients and could have a plausible impact on the COVID-19 severity and mortality. Therefore, their role might be underestimated in predicting in-hospital death. These findings should be confirmed in larger, prospective, adequately powered studies.

Based on the result of our study, age, pulmonary symptoms, patients need a ventilator, brain symptoms, nasal airway, job, gastrointestinal symptoms, brain disease history, heart disease history, heart symptoms; chronic kidney disease history, psychological symptoms, dyspnea symptom, history of drug use and hypertension history can be used for identification of severe patients with COVID-19 on hospital admission. Also, these characteristics can be considered as important risk factors for patients with Covid-19 in khoy city that increase their mortality. Physicians and administrators can use them to reduce the mortality rate of this disease.

Acknowledgments

This study was financially supported by Urmia Medical Sciences University (UMSU) ethics committee approved this study (IR.TUMS.VCR.REC.1398.1036). In addition, all participants and personnel in health care centers who helped in the research process are appreciated.

References

1. McKeown RE. The epidemiologic transition: changing patterns of mortality and population dynamics. Am J Lifestyle Med 2009;3:19S-26.
2. Daneshfar M, Dadashzadeh N, Ahmadpour M, Ragati Haghi H, Rahmani V, Forouzesh M, et al. Lessons of mortality following COVID-19 epidemic in the United States especially in the geriatrics. J Nephropharmacol 2021;10:e06.
3. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.
4. Tabatabaii SA, Soltani P, Khanbabaee G, Sharma D, Valizadeh R, Farahbakhsh N, et al. SARS Coronavirus 2, Severe Acute Respiratory Syndrome, and Middle East Respiratory Syndrome in Children: A Review on Epidemiology, Clinical Presentation, and Diagnosis. Arch Pediatr Infect Dis 2020;8:e104860.
5. Valizadeh R, Dadashzadeh N, Zakeri R, James Kellner S, Rahimi MM. Drug therapy in hospitalized patients with very severe symptoms following COVID-19. J Nephropharmacol 2020;9:e21.
6. Raoofi A, Takian A, Sari AA, Olyaeemanesh A, Haghighi H, Aarabi M. COVID-19 pandemic and comparative health policy learning in Iran. Arch Iran Med 2020;23:220-34.
7. 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. Lancet 2020;395:497-506.
8. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 2020;20:669-77.
9. Ahmadinejad Z, Assari R, Yazdi NA, Mazloomi SH, Javanshayani P, Afousi HK, et al. COVID-19 pandemic and biological therapy in rheumatologic disorders: how to deal with? Reumatismo 2020;72:173-7.
10. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al.. Clinical characteristics of coronavirus disease. N Engl J Med 2020;382:1708-720.
11. Lim LW, Yip LW, Tay HW, Ang XL, Lee LK, Chin CF, et al. Sustainable practice of ophthalmology during COVID-19: challenges and solutions. Graefes Arch Clin Exp Ophthalmol 2020;258:1427-36.
12. Mohamed-Ahmed O, McDonald B, Pardinaz-Solis R, Sigfrid L, McMullen C, Moore S, et al. The International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) response to the Zika virus outbreak. F1000Res 2016;5.
13. Breiman L. Random forests. Mach Learn 2001;45:5-32.
14. Khalifa M, Zabani I. Improving Utilization of Clinical Decision Support Systems by Reducing Alert Fatigue: Strategies and Recommendations. Stud Health Technol Inform 2016;226:51-4.
15. Buntine W, Niblett T. A further comparison of splitting rules for decision-tree induction. Mach Learn 1992;8:75-85.
16. Tayefi M, Esmaeili H, Karimian MS, Zadeh AA, Ebrahimi M, Safarian M, et al. The application of a decision tree to establish the parameters associated with hypertension. Comput Methods Programs Biomed 2017;139:83-91.
17. Alberti KG, Zimmet P, Shaw J. International Diabetes Federation: a consensus on Type 2 diabetes prevention. Diabet Med 2007;24:451-63.
18. Kumar R, Indrayan A. Receiver operating characteristic (ROC) curve for medical researchers. Indian pediatr 2011;48:277-87.
19. Barzegar A, Ghadipasha M, Rezaei N, Forouzesh M, Valizadeh R. New hope for treatment of respiratory involvement following COVID-19 by bromhexine. J Nephropharmacol 2021;10:e11.
20. Mirsoleymani S, Taherifard E, Taherifard E, Taghrir MH, Ahmadi Marzaleh M, Nekooghadam SM, et al. Predictors of Mortality Among COVID-19 Patients With or Without Comorbid Diabetes Mellitus. Acta Med Iran 2021;59:393-9.
21. Shankar A, Saini D, Roy S, Mosavi Jarrahi A, Chakraborty A, Bharti SJ, et al. Cancer care delivery challenges amidst coronavirus disease–19 (COVID-19) outbreak: specific precautions for cancer patients and cancer care providers to prevent spread. Asian Pac J Cancer Prev 2020;21:569-73.
22. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. PloS one 2020;15:e0238215.
23. Modi C, Boehm V, Ferraro S, Stein G, Seljak U. How

deadly is COVID-19? A rigorous analysis of excess mortality and age-dependent fatality rates in Italy. medRxiv, 2020.
24. CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children—United States, February 12–April 2, 2020. MMWR Morb Mortal Wkly Rep 2020;69:422-6.
25. Lippi G, Mattiuzzi C, Sanchis-Gomar F, Henry BM. Clinical and demographic characteristics of patients dying from COVID-19 in Italy versus China. J Med Virol 2020;92:1759-60.
26. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
27. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43.
28. Valizadeh R. Clinical and Demographic Characteristics of Patients with COVID-19 Who Died in Modarres Hospital. Maced J Med Sci 2020;8:144-9.
29. Zali A, Gholamzadeh S, Mohammadi G, Looha MA, Akrami F, Zarean E, et al. Baseline Characteristics and Associated Factors of Mortality in COVID-19 Patients; an Analysis of 16000 Cases in Tehran, Iran. Arch Acad Emerg Med 2020;8:e70.
30. 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. J Allergy Clin Immunol 2020;146:110-8.
31. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020;81:e16-25.
32. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323:2052-9.
33. 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. Lancet 2020;395:1054-62.
34. Hou W, Zhang W, Jin R, Liang L, Xu B, Hu Z. Risk factors for disease progression in hospitalized patients with COVID-19: a retrospective cohort study. Infect Dis (Lond) 2020:1-8.
35. Mikami T, Miyashita H, Yamada T, Harrington M, Steinberg D, Dunn A, et al. Risk factors for mortality in patients with COVID-19 in New York City. J Gen Intern Med 2021;36:17-26.
36. Lotfi B, Farshid S, Dadashzadeh N, Valizadeh R, Rahimi MM. Is Coronavirus Disease 2019 (COVID-19) Associated with Renal Involvement? A Review of Century Infection. Jundishapur J Microbiol 2020;13:e102899.
37. Rahimi MM, Jahantabi E, Lotfi B, Forouzesh M, Valizadeh R, Farshid S. Renal and liver injury following the treatment of COVID-19 by remdesivir. J Nephropathol 2021;10:e10.
38. Padilla-Raygoza N, Sandoval-Salazar C, León-Verdín MG, de Jesús Gallardo-Luna M, Navarro-Olivos E, Magos-Vazquez FJ, et al. Risk Factors for Mortality by Novel Corona Virus Disease, in Mexico: A Cross-Sectional Study. ARC J Public Health Community Med 2020;5:14-9.