Original Article

Risk Factors for In-Hospital Mortality among Patients with Coronavirus-19 in Isfahan City, Iran

Roya Riahi[1], Marziye Ghasemi[2], Zahra Montazeri Shatouri[3], Mojgan Gharipour[4], Mahboobeh Maghami[1], Hamid Melali[5], Ramin Sami[6], Aminreza Tabatabaei[7], Sayed Mohsen Hosseini[1]

[1]Department of Biostatistics and Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Department of Medical Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, [3]Department of Biostatistics and Epidemiology, Shahrekord University of Medical Sciences, Shahrekord, Iran, [4]Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran, [5]Department of Surgery, Isfahan Minimally Invasive Surgery and Obesity Research Center, Amin University Hospital, Isfahan University of Medical Sciences, Isfahan, Iran, [6]Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, [7]Department of Education and Research, Hajj and Pilgrimage Medical Center, Tehran, Iran

Abstract

Background: The aim of the study is to explore the risk factors of mortality for hospitalized patients in three designated hospitals in Isfahan province.

Materials and Methods: This retrospective cohort study was conducted on all positive coronavirus disease (COVID)-19 patients admitted to Khorshid, Isabn Maryam, and Amin hospitals in Isfahan province. The demographic, clinical, laboratory, and outcome data of patients who were died or discharged from February 24, 2020, to April 18, 2020, were extracted from patient's medical records.

Results: Overall 1044 COVID-19 patients were included in this analysis. Based on the findings of this study, older age (≥65 years) (adjusted hazard ratio [aHR]: 2.06; 95% confidence interval [CI]: 1.13–3.76), chronic obstructive pulmonary disease (COPD) history (aHR: 2.52; 95% CI: 1.09–5.83), white blood cell (WBC) counts more than 10 × 10^3/L (aHR: 3.05; 95% CI: 1.42–6.55), Hb level <13 gr/L (aHR: 2.82; 95% CI: 1.34–5.93), bilateral pulmonary infiltrates (aHR: 2.02; 95% CI: 1.12–3.64) at admission, development of acute respiratory distress syndrome (ARDS) (aHR: 1.87; 95% CI: 1.01–3.47), and intensive care unit (ICU) admission (aHR: 2.09; 95% CI: 1.04–4.18) during hospitalization were risk factors for in-hospital mortality in patients with COVID-19.

Conclusions: Multiple factors were found related to the severity and death among COVID-19 patients. We were found that older age (≥65 years) with COPD history, high level of WBC, low level of Hb (<13 g/L), bilateral pulmonary infiltrates at admission, development of ARDS, and ICU admission during hospitalization were identified as risk factors of death among COVID-19 patients. More related studies are needed in the future.

Keywords: Coronavirus disease 2019, hospitalization, risk factors

Address for correspondence: Dr. Sayed Mohsen Hosseini, Department of Biostatistics and Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: hosseini@hlth.mui.ac.ir
Submitted: 18-Apr-2021; **Revised:** 27-Jun-2021; **Accepted:** 04-Aug-2021; **Published:** 26-Dec-2022

Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by the COVID. It can be transmitted from an infected person to an average of 3 other people in a population.[1] This emerging disease is similar to the severe acute respiratory syndrome (SARS) and the middle east respiratory syndrome.[2] Although most people have mild

Access this article online

Quick Response Code:

Website: www.advbiores.net

DOI: 10.4103/abr.abr_86_21

How to cite this article: Riahi R, Ghasemi M, Montazeri Shatouri Z, Gharipour M, Maghami M, Melali H, *et al*. Risk factors for in-hospital mortality among patients with coronavirus-19 in Isfahan city, Iran. Adv Biomed Res 2022;11:121.

symptoms, some may experience respiratory failure, arrhythmia, shock, kidney failure, cardiovascular damage, or sometimes liver failure.[3] There is currently no effective antiviral treatment. Only supportive care such as mechanical ventilation and extracorporeal membrane oxygenation to resistant patients with refractory hypoxemia may be useful.[4] A study reported that more than 90% of COVID-19-related deaths in the UK were in people over 60 and 60% in men.[5,6] Given that no drug has been proved to be clinically effective directly targeting SARSCoV-2, identifying the risk factors associated with disease progression and mortality is of particular importance.[7,8] Various preexisting medical conditions have been associated with an increased risk of death. For example, in a study of 44,672 individuals (1,023 deaths), the Chinese Center for Disease Control and Prevention reported an increased risk of death for patients with cardiovascular disease, high blood pressure, diabetes, respiratory diseases, and cancer,[6] but the relationships with age was not clear in this study. A UK cross-sectional survey of 16,749 patients with COVID-19 showed that the risk of death was higher in patients with heart, lung, and kidney disease, as well as cancer, dementia, and obesity.[9] Obesity was associated with intensified treatment in French intensive care (n = 124)[10] and a New York hospital presentation cohort (n = 3,615).[11] The risks associated with smoking are unclear. In a study of 17,278,392 adults and 10,926 COVID19-related deaths, COVID-19 mortality was associated with the following: male gender, greater age, diabetes, severe asthma, and various other medical conditions.[12] Since the mentioned studies have been done in other countries and studies in Iran to identify the risk factors for death of COVID-19 among hospitalized patients are restricted[13,14] and also due to the widespread prevalence of this disease and limited medical resources to control this epidemic, therefore identify the risk factors of COVID-19 mortality is important and can help to manage the crisis in this regard. Here, we study all COVID-19 patients in detail admitted from February 24 to April 15, 2020, in three designated hospitals of Isfahan University of Medical Sciences with the approval of COVID-19 laboratory and a specific clinical outcome (death or discharge). This study is aimed to investigate the risk factors of in-hospital death.

Materials and Methods

Study design and participants

This retrospective cohort study included two groups (survivors and nonsurvivors) of patients from three hospitals in Isfahan province. The study population included all patients who were diagnosed with COVID-19 disease and hospitalized in Khorshid hospital, Isabn Maryam hospital, and Amin hospital between February 24, 2020, and April 19, 2020. To identify definitive cases of COVID-19, the real-time reverse transcriptase–polymerase chain reaction test on nasopharyngeal swab specimens was used according to the criteria of the World Health Organization.[15] Inclusion criteria included hospitalization in hospitals under the auspices of Isfahan University of Medical Sciences. Individuals who have a positive test but have not been hospitalized during the study time were excluded from this study. Patients whose most of their information were not available were excluded from the study. The consent was received from all participants, emphasizing the observance of patient confidentiality. All information of COVID-19 patients was recorded and tracked from medical records based on the specified checklist, test results, computed tomography (CT) scan, and chest radiograph using a patient record.

Data collection

Demographic, clinical, laboratory, and outcome data were extracted from the medical records based on the specified checklist for this study. Routine blood tests and serum biochemical tests were performed to complete count blood cells, liver, kidney, heart enzymes measurement to identify possible damage. Hemodynamic and respiratory parameters were measured by respiratory devices. Furthermore, the measurement of body temperature was done using a thermometer. Record and image of chest radiograph or CT scan were for all inpatients.

Definitions

The following demographic/clinical characteristics, symptoms, and laboratory findings were extracted from the patient's medical records: age, gender, smoking status, comorbidities including diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease (COPD), carcinoma, and anemia; symptoms including fever, diarrhea, nausea or vomiting, cough, shortness of breath (difficult or short breathing, in which the patient feels uncomfortable and difficult to breathe); and laboratory findings and vital signs including white blood cell count (WBC), hemoglobin, and lymphocytes count, peripheral oxygen saturation (SpO2), heart rate, respiratory rate, and systolic blood pressure. Fever was defined as an axillary temperature of at least 37.3°C.[16] Sepsis patients with COVID-19 have a significantly higher mortality rate than nonsepsis patients.[17] Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition.[18] Thus, the early identification and diagnosis of sepsis in patients with COVID-19 are particularly necessary.

The presence of bilateral pulmonary infiltration, consolidation, and ground-glass opacity lesions were identified based on the radiographic findings. Acute respiratory distress syndrome (ARDS) will be diagnosed according to the Berlin definition.[19] Cardiac damage is assessed by monitoring serum levels of cardiac biomarkers. Diagnosis of kidney and liver damage will be made according to clinical guidelines.[20]

Statistical analysis

Categorical variables were reported as frequency (percentage) and continuous variables were described as median (interquartile range) for total cases and all in survivors and nonsurvivors. To compare the differences between the survivor and nonsurvivor cases, Chi-square or Fisher's exact test was used for categorical

variables, and independent *t*-test or Mann–Whitney U-test was performed for continuous variables. The unadjusted and adjusted Cox proportional-hazard models were conducted to detect the risk factors associated with in-hospital mortality in patients with COVID-19. Survival time was defined as the time length between hospital admission and discharge or death: days from hospital admission to death (event). At the censoring time, patients might be alive in the hospital or improved and discharged. The results were reported as hazard ratio (HR) with a 95% confidence interval (CI). Variables with nonsignificant differences between survivors and nonsurvivors and if the number of events was too small to calculate the desired effect size were excluded from univariate analysis. Nominate factors for the multivariate analysis were selected based on the findings of the univariate analysis and the previous findings.[13] To assess the proportional hazard assumption, the Schoenfeld residuals test was performed. A $P < 0.05$ was considered as statistically significant. All statistical analyses were performed using Stata package (stata statistical software: Release 14, STATA Corporation 2015 College Station, TX, USA).

Results

During the study period, 1076 patients with COVID-19 were confirmed, of whom 1044 patients were included in the analysis (excluding patients that were still hospitalized at the study endpoint, and those without available key information in the patient's medical records). Of all patients, 118 died (11.3%) in hospital and 926 were discharged (88.7%). The mean standard deviation (SD) of age was 59.35 (17.29) years (survivors: 57.88 (17.1) years vs. nonsurvivors: 70.97 (14.29) years, $P < 0.001$), and 59.2% were younger than 65 years. About 56.1% of patients were male, and 6.5% were smoker.

The demographics characteristics, comorbidities, and related symptoms on admission according to vital status are shown in Table 1. Compared with survivor cases, nonsurvivors were older (71.8% aged 65 years or older vs. 36%; $P < 0.001$) and had a higher prevalence of comorbidities included diabetes (48.7% vs. 30.2%; $P < 0.001$), hypertension (57.3% vs. 34.7%; $P < 0.001$), cardiovascular disease (38.5% vs. 27.8%; $P = 0.012$), COPD (19.5% vs. 8.5%; $P < 0.001$), carcinoma (7.7% vs. 2.8%; $P = 0.006$), and anemia (19.3% vs. 9.9%; $P = 0.003$) [Table 1].

Top three most common-related symptoms on admission included cough (81.4%), shortness of breath (73.3%), and fever (48%). Clinical symptoms including shortness of breath (88.1% vs. 71.4%; $P < 0.001$) and fever (64.5% vs. 46%; $P < 0.001$) were more frequent in nonsurvived cases than survived cases. While at admission, the proportion of patients with diarrhea was higher in survivors than nonsurvivors (6.5% vs. 1.7%; $P = 0.037$) [Table 1].

The comparison of clinical, laboratory, imaging findings on admission and complications during hospitalization are presented in Table 2. On admission, most patients had normal Hb level (51.1%), WBC (69.7%), and lymphocyte (59.6%) counts. In comparison with survivors, nonsurvivors had higher WBC counts (median: 7.4 vs. 5.6; $P < 0.001$) and had lower counts of lymphocyte (median: 0.84 vs. 1.19; $P < 0.001$) and Hb (median: 11.3 vs. 13.1; $P < 0.001$) [Table 2]. According to the imaging manifestations, ground-glass opacities were the common findings in patients with COVID-19 (76.5%). Ground-glass opacities (88.5% vs. 74.7%; $P < 0.001$) and bilateral pulmonary infiltrates (59.8% vs. 34.6%; $P < 0.001$) were more common in nonsurvivors than survivors [Table 2]. About 55% of patients had low level of SpO2 (<92%). Nonsurvivors were more likely to have abnormal SpO2 (median: 88% vs. 91%; $P < 0.001$) and also had higher prevalence of elevated heart rate (≥120 beats/min) (7.3% vs. 2.1%; $P = 0.006$).

ARDS (7.7%) and acute cardiac injury (6.8%) were most common complications during hospitalization. Admission to the intensive care unit (ICU) was required for 171 (16.5%) patients, with a median interquartile range (IQR) duration of ICU stay 7 (3–12) days. Survivors were less likely to require to ICU admission compared to nonsurvivors (8.6% vs. 78%; $P < 0.001$). Compared with survivor cases, nonsurvivors were more likely to developed sepsis (16.7% vs. 1.1%; $P < 0.001$), ARDS (39.8% vs. 3.7%; $P < 0.001$), acute cardiac injury (28.4% vs. 4%; $P < 0.001$), acute kidney injury (23.7% vs. 2.3%; $P < 0.001$), acute liver injury (8% vs. 0.9%; $P < 0.001$) during hospitalization [Table 2].

The median (IQR) duration of hospital stay was 7 (4–10) days: 6 (4–10) days for survivor cases and 8 (4–13) days for nonsurvivor cases ($P = 0.02$). As shown in Table 3, based on the univariate cox analysis, independent factors associated with mortality in hospitalized patients included older age (≥65 years), history of diabetes, hypertension, COPD, carcinoma, fever, shortness of breath, bilateral pulmonary infiltrates, WBC, and lymphocyte counts, Hb level, SpO2 (%), development of ARDS, acute cardiac injury, acute kidney injury, and ICU admission ($P < 0.05$). Multivariable Cox proportional hazards regression model illustrated that older age (≥65 years) (aHR: 2.06; 95% CI: 1.13–3.76), COPD history (aHR: 2.52; 95% CI: 1.09–5.83), WBC counts more than 10 × 10^3/L (aHR: 3.05; 95% CI: 1.42–6.55), Hb level <13 gr/L (aHR: 2.82; 95% CI: 1.34–5.93), bilateral pulmonary infiltrates (aHR: 2.02; 95% CI: 1.12–3.64) at admission, development of ARDS (adjusted HR [aHR]: 1.87; 95% CI: 1.01–3.47), and ICU admission (aHR: 2.09; 95% CI: 1.04–4.18) during hospitalization were factors associated with higher risk of in-hospital mortality in patients with COVID-19. The Harrell's C statistic (a measure of the model's ability to distinguish between the survivor and nonsurvivor patients with COVID-19) was 0.86. Based on the Schoenfeld residue analysis, there was no evidence of nonproportional hazards ($P = 0.92$).

The Kaplan–Meier survival curves according to the risk factors of COVID-19 mortality are depicted in Figure 1.

Table 1: Demographics characteristics, comorbidities, and symptoms of patients with coronavirus disease 2019

Variables	Total (n=1044), n (%)	Vital status		P
		Survived (n=926), n (%)	Nonsurvived (n=118), n (%)	
Demographic characteristics				
Age (≥65 years)	422 (40.8)	338 (36.9)	84 (71.8)	<0.001*
Gender (male)	579 (56.1)	511 (55.8)	68 (58.1)	0.63
Smoking status (smoker)	62 (6.5)	54 (6.4)	8 (7.4)	0.69
Comorbidities				
Diabetes	328 (32.3)	272 (30.2)	56 (48.7)	<0.001*
Hypertension	385 (37.2)	318 (34.7)	67 (57.3)	<0.001*
Cardiovascular disease	294 (28.5)	249 (27.8)	45 (38.5)	0.012*
COPD	101 (9.8)	78 (8.5)	23 (19.5)	<0.001*
Carcinoma	35 (3.4)	26 (2.8)	9 (7.7)	0.006*
Anemia	112 (11)	90 (9.9)	22 (19.3)	0.003*
Signs and symptoms				
Body temperature	37.2 (37-37.9)	37.1 (37-37.8)	37.5 (37-38.2)	<0.001*
Fever (temperature ≥37.3°C)	488 (48)	417 (46)	71 (64.5)	<0.001*
Cough	839 (81.4)	747 (81.6)	92 (80)	0.69
Nausea or vomiting	230 (22.6)	213 (23.5)	17 (15.2)	0.05
Diarrhea	61 (5.9)	59 (6.5)	2 (1.7)	0.037*
Shortness of breath	761 (73.3)	657 (71.4)	104 (88.1)	<0.001*

*P<0.05 is considered statistically significant between survivors and nonsurvivors. Data are shown as, n (%) or median (IQR). P values were calculated using Chi-squared test, Fisher's exact test, or Mann-Whitney U-test. COPD: Chronic obstructive pulmonary disease, IQR: Interquartile range

Discussion

Our results demonstrated the higher mortality rate among older patients, the mean age of nonsurvivors was higher than survivor patients which is line with other studies. Previous studies in Isfahan demonstrated signs and symptoms, vital symptoms, and laboratory findings of 490 patients admitted to a COVID-19 referral hospital in Isfahan. Eight percent of the admitted patients were transferred to the ICU (48% male). Thirty-four patients (7%) died. The top three leading causes of admission were fever (77%), dry cough (73%), and fatigue (69%). Sneeze (10%), runny nose (14%), and abdominal pain (17%) were the least frequent symptoms among COVID-19 patients. The top three prevalent comorbidities with COVID-19 were hypertension (35%), diabetes (28%), and ischemic heart disease (14%). Angioni *et al*. demonstrated a key factor in COVID-19 morbidity and mortality. They investigated the immune profile of COVID-19 hospitalized patients identifying a distinctive age-dependent immune signature associated with disease severity. Indeed, longer hospitalization and severity of signs in COVID-19 patients are related to circulating factors-CXCL8, interleukin-10 (IL-10), IL-15, IL-27, and tumor necrosis factor-α in older age patients.[21] Similarly, Qian showed that age ≥75 years was important risk factor for mortality.[17] Similar to findings, other investigations in the world try to found impact of different risk factors that affecting morbidity and mortality by COVID-19. Our results showed that nonsurvivors had a higher prevalence of comorbidities included diabetes, hypertension, cardiovascular disease COPD, carcinoma, and anemia. Medetalibeyoglu *et al*. have shown that mortality and ICU admission rates were statistically significantly higher in patients with cardiac injury than in those without. There was a positive correlation between levels of high-sensitivity TNT and fibrinogen, D-dimer, ferritin, procalcitonin, and C-reactive protein. They concluded and particular treatment algorithms specific to our center

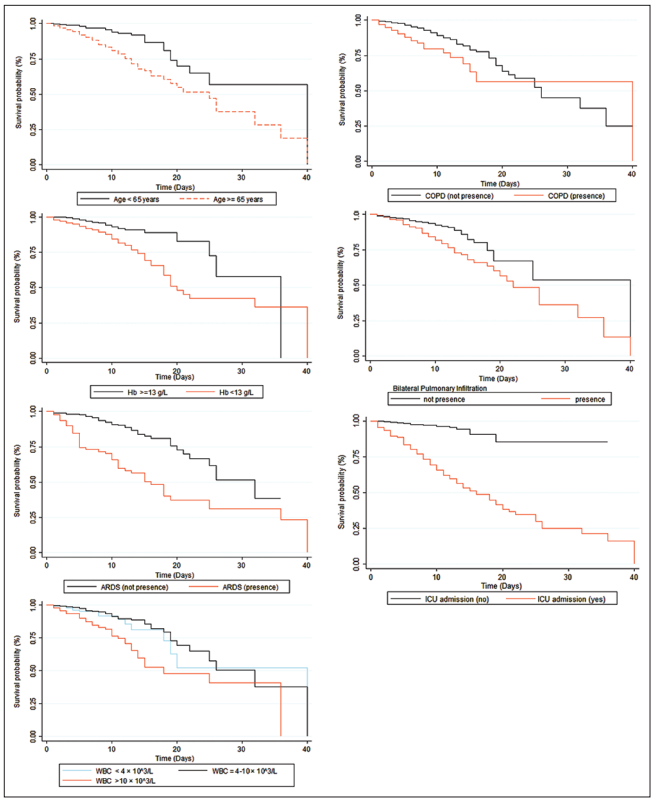

Figure 1: Survival curves of COVID-19 patients with significant risk factors based on multivariate analysis

Table 2: Clinical, laboratory, imaging findings on admission, and complications hospitalization of patients with coronavirus disease 2019

Variables	Total (n=1044)	Vital status		P
		Survived (n=926)	Nonsurvived (n=118)	
Laboratory findings on admission				
WBC (×10³/L), median (IQR)	5.7 (4.3-7.9)	5.6 (4.3-7.5)	7.4 (5-11.3)	<0.001*
<4, *n* (%)	149 (18.2)	133 (18.3)	16 (17.4)	<0.001*
4-10	570 (69.7)	524 (72.2)	46 (50)	
>10	99 (12.1)	69 (9.5)	30 (32.6)	
Lymphocytes (×10³/L), median (IQR)	1.1 (0.77-1.66)	1.19 (0.82-1.70)	0.84 (0.48-1.24)	<0.001*
<1 (×10³/L), *n* (%)	313 (40.4)	260 (37.3)	53 (62.4)	<0.001*
Hemoglobin (gr/dl) median (IQR)	13 (11.7-14.2)	13.1 (12-14.3)	11.3 (10.1-12.8)	<0.001*
<13 (×10³/L), *n* (%)	398 (48.9)	327 (45.4)	71 (75.5)	<0.001*
Imaging findings on admission				
Bilateral pulmonary infiltrates	360 (37.5)	293 (34.6)	67 (59.8)	<0.001*
Consolidation	89 (9.5)	75 (9)	14 (13.9)	0.12
Ground-glass opacities	745 (76.3)	645 (74.7)	100 (88.5)	0.001*
Vital signs on admission				
SpO_2 (%), median (IQR)	91 (88-94)	91 (88-94)	88 (83-92)	<0.001*
<92, *n* (%)	558 (54.9)	474 (52.5)	84 (74.3)	<0.001*
SBP (mm Hg), median (IQR)	120 (110-138)	120 (110-137)	125.5 (110-140)	0.61*
>120 mmHg, *n* (%)	512 (49.7)	451 (49.3)	61 (52.6)	0.50
Heart rate (pulse/min), median (IQR)	85.5 (80-95.8)	85 (80-96)	88 (80-96)	0.28
≥120 beats/min, n (%)	27 (2.7)	19 (2.1)	8 (7.3)	0.01*
Respiratory rate (breaths/min), median (IQR)	20 (18-23)	20 (18-23)	20 (18-25)	0.95
≥21 breath/min, *n* (%)	412 (40.5)	367 (40.6)	45 (39.1)	0.76
Complications, *n* (%)				
Species	27 (2.8)	17 (1.1)	10 (16.7)	<0.001*
ARDS	79 (7.7)	34 (3.7)	45 (39.8)	<0.001*
Acute cardiac injury	70 (6.8)	37 (4)	33 (28.4)	<0.001*
Acute kidney injury	48 (4.7)	21 (2.3)	27 (23.7)	<0.001*
Acute liver injury	17 (1.7)	8 (0.9)	9 (8)	<0.001*
ICU admission	171 (16.5)	79 (8.6)	92 (78)	<0.001*

*P<0.05 is considered statistically significant between survivors and nonsurvivors. P values were calculated using Chi-squared test, Fisher's exact test, or Mann-Whitney U-test. WBC: White blood cell count, SpO_2: Oxygen saturation, SBP: Systolic blood pressure, ARDS: Acute respiratory distress syndrome, ICU: Intensive care unit, IQR: Interquartile range

should be helpful in determining better treatment strategies in the future.[22] Our study emphasizes the importance and frequency of cardiovascular outcomes and the significance of some cardiac biomarkers in predicting COVID-19 prognosis. Similar to our results, Qian *et al*. indicated that patients with myocardial injury had higher prevalence of underlying CVD, and in-ICU CVD complications. Myocardial injury on admission increased the risk of 28-day mortality.[17]

This study concluded that critically ill patients with COVID-19 had a high risk of CVD complications. Myocardial injury on admission may be a common comorbidity and is associated with severity and a high risk of mortality in this population.[17] The results from Zheng *et al*. indicated that fever was negatively associated with the progression of COVID-19 such as severe illness and death and shortness of breath/dyspnea was positively associated with the progression of COVID-19 such as severe illness and death, which suggests that COVID-19 patients with fever may have a lower risk to develop to severe and critical disease outcomes and COVID-19 patients with dyspnea may have a higher risk to develop to severe and critical disease outcomes.[16] However, Fu *et al*. observed that there was no statistically significant association between fever or shortness of breath and the severity of patients with COVID-19.[23] To definitely recognize the risk factors for predicting mortality in patients with COVID-19, Shi *et al*. carry out a meta-analysis to assess whether fever and dyspnea (not included shortness of breath) were related with the risk of mortality in COVID-19 patients. Likewise, our results indicated that clinical symptoms including shortness of breath and fever were more frequent in nonsurvived cases than survived cases. While, diarrhea was not considered as a risk factor for mortality in these patients.[8]

Shi *et al*. found that dyspnea was significantly associated with higher mortality in COVID-19 patients on the basis of 11 studies with 2091 cases (odds ratio [OR] = 4.34). However, they did not observe a significant association between fever and the risk of mortality in patients with COVID-19 on the basis of 15 studies with 2818 cases.[8] In our study,

Table 3: Risk factors associated with in-hospital death using cox proportional hazard model

Variables	Crude HR (95% CI)	*P*	Adjusted HR (95% CI)[a]	*P*
Patient characteristics				
Age (<65 years)	3.09 (2.05-4.65)	<0.001*	2.06 (1.13-3.76)	0.02*
Comorbidities				
Diabetes (not presence)	1.64 (1.13-2.37)	0.01*	1.32 (0.74-2.40)	0.35
Hypertension (not presence)	1.88 (1.30-2.74)	−0.001*	1.25 (0.64-2.43)	0.52
Cardiovascular disease (not presence)	1.30 (0.89-1.90)	−0.17		
COPD (not presence)	1.84 (1.15-2.96)	0.01*	2.52 (1.09-5.83)	0.03*
Carcinoma (not presence)	3.36 (1.69-6.70)	−0.001*	1.57 (0.33-7.45)	0.69
Anemia (not presence)	1.19 (0.73-1.93)	−0.49		
Signs and symptoms				
Fever (temperature <37.3°C)	1.63 (1.10-2.43)	0.02*	1.73 (0.94-3.19)	0.08
Shortness of breath (not presence)	2.14 (1.22-3.75)	0.01*	1.83 (0.70-4.80)	0.22
Laboratory variable				
WBC (4-10×10^3/L)				
<4	1.31 (0.73-2.36)	0.36	1.66 (0.77-3.58)	0.20
>10	2.69 (1.68-4.30)	<0.001*	3.05 (1.42-6.55)	0.004*
Lymphocytes (≥1×10^3/L)	1.84 (1.17-2.87)	0.01*	1.51 (0.78-2.93)	0.22
Hemoglobin (≥13 gr/L)	2.75 (1.70-4.45)	<0.001*	2.82 (1.34-5.93)	0.006*
Imaging findings				
Bilateral pulmonary infiltrates (not presence)	2.00-(1.37-2.92)	<0.001*	2.02 (1.12-3.64)	0.02*
Ground-glass opacities (not presence)	1.55 (0.86-2.77)	0.14		
Vital signs on admission				
SpO_2 (≥92%)	1.57 (1.02-2.41)	0.02*	1.12 (0.59-2.10)	0.74
Heart rate (>120 pulse per min)	1.21 (0.57-2.59)	0.62		
Complications				
ARDS (not presence)	3.69 (2.46-5.53)	<0.001*	1.87 (1.01-3.47)	0.048*
Acute cardiac injury (not presence)	3.77 (2.49-5.71)	<0.001*	1.96 (0.71-5.37)	0.19
Acute kidney injury (not presence)	3.86 (2.48-6.02)	<0.001*	1.16 (0.53-2.57)	0.70
ICU admission (not presence)	9.42 (5.96 14.91)	<0.001*	2.09 (1.04-4.18)	0.04*

**P*<0.05 is considered statistically significant. [a]The model is adjusted for all significant factors from the univariate analysis plus history of cardiovascular disease. The reference group is shown in the parenthesis. *P* values are calculated from cox proportional hazards regression model. HR: Hazard ratio, CI: Confidence interval, WBC: White blood cell count, SpO_2: Oxygen saturation, ARDS: Acute respiratory distress syndrome, ICU: Intensive care unit, COPD: Chronic obstructive pulmonary disease

nonsurvivors had higher WBC counts and had lower counts of lymphocyte and Hb. About 55% of patients had low level of SpO2 (<92%). Nonsurvivors were more likely to have abnormal SpO2 and also had higher prevalence of elevated heart rate (≥120 beats/min). Lezzeri *et al*. demonstrated that in COVID-19 patients, ARDS is related to the level of troponin T. The increase in systolic pulmonary arterial pressures observed in all patients may be related to hypoxic vasoconstriction.[24-26] Likewise, in our study population, ARDS and acute cardiac injury were most common complications during hospitalization. Nonsurvivors were more likely to developed sepsis, ARDS acute cardiac injury, acute kidney injury, acute liver injury during hospitalization.

Limitation

This study has some limitations as follows: information collection was based on electronic medical records and some important measures were not evaluated in all patients. Therefore, the presence of missing data might cause bias in findings. Moreover, we exclude patients who remained hospitalized at the end of study time of our comparisons between survivors and nonsurvivors. Furthermore, due to the lack of information and observational design of the study, we are not able to enter body mass index and received treatments in our analyses.

Conclusions

This study was different from previous similar studies because of it is the first study that done in the area to identify risk factors related to death and hospitalization of patients with COVID-19 disease in Isfahan province, which offered another perspective on risk factors novel coronavirus. Similar to the previous study in other area, we found that the higher mortality rate among older patients. Furthermore, our results showed that nonsurvivors had a higher prevalence of comorbidities included diabetes, hypertension, cardiovascular disease, COPD, carcinoma, and anemia.

In summary, multiple factors were found related to the severity and death among COVID-19 patients. We were found that older age (≥65 years) with COPD history, high level of WBC,

low level of Hb (<13 g/L), bilateral pulmonary infiltrates at admission, development of ARDS, and ICU admission during hospitalization were identified as risk factors of death among COVID-19 patients. More related studies are needed in the future.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Alimohamadi Y, Taghdir M, Sepandi M. Estimate of the basic reproduction number for COVID-19: A systematic review and meta-analysis. J Prev Med Public Health 2020;53:151-7.
2. Bonilla-Aldana DK, Dhama K, Rodriguez-Morales AJ. Revisiting the one health approach in the context of COVID-19: A look into the ecology of this emerging disease. Adv Anim Vet Sci 2020;8:234-7.
3. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? Lancet 2020;395:931-4.
4. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, *et al.* The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – An update on the status. Mil Med Res 2020;7:11.
5. Statistics COVID-19 Daily Deaths. Available from: https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-daily-deaths/. [Last acessed on 2021 Feb 12].
6. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. Crit Care 2020;24:179.
7. Li H, Wang YM, Xu JY, Cao B. Potential antiviral therapeutics for 2019 novel coronavirus. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:E002.
8. Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: Findings of 487 cases outside Wuhan. Crit Care 2020;24:108.
9. Docherty A, Harrison E, Green C, Hardwick H, Pius R, Norman L, *et al.* Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. medRxive 2020.
10. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, *et al.* High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity 2020;28:1195-9.
11. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, *et al.* Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission. Clin Infect Dis 2020;71:896-7.
12. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, *et al.* Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430-6.
13. Adham D, Habibzadeh S, Ghobadi H, Jajin SA, Abbasi-Ghahramanloo A, Moradi-Asl E. Epidemiological characteristics and mortality risk factors among COVID-19 patients in Ardabil, Northwest of Iran. BMC Emerg Med 2021;21:67.
14. Arman A, Tajik M, Nazemipour M, Ahmadinejad Z, Shahrestanaki SK, Hazrati E, *et al.* Risk factors of developing critical conditions in Iranian patients with COVID-19. Glob Epidemiol 2021;3:100046.
15. COVID Live Update: 187,368,359 Cases and 4,045,085 Deaths from the Coronavirus-Worldometer. Available from: https://www.worldometers.info/coronavirus/. [Last accessed on 2021 Jul 11].
16. 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.
17. Qian H, Gao P, Tian R, Yang X, Guo F, Li T, *et al.* Myocardial injury on admission as a risk in critically ill COVID-19 patients: A retrospective in-ICU study. J Cardiothorac Vasc Anesth 2021;35:846-53.
18. 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.
19. Force AD, Ranieri VM, Rubenfeld GD, Thompson B, Ferguson N, Caldwell E. Acute respiratory distress syndrome. JAMA 2012;307:2526-33.
20. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120:c179-84.
21. Angioni R, Sánchez-Rodríguez R, Munari F, Bertoldi N, Arcidiacono D, Cavinato S, *et al.* Age-severity matched cytokine profiling reveals specific signatures in Covid-19 patients. Cell Death Dis 2020;11:957.
22. Medetalibeyoglu A, Emet S, Senkal N, Aydogan M, Kose M, Tukek T. Cardiovascular view of intermediate and high-risk COVID-19 patients: Single-centre experience with low mortality and intensive care hospitalisation rates. Cardiovasc J Afr 2021;32:79-86.
23. Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T, *et al.* Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. J Infect 2020;80:656-65.
24. Sami R, Soltaninejad F, Amra B, Naderi Z, Haghjooy Javanmard S, Iraj B, *et al.* A one-year hospital-based prospective COVID-19 open-cohort in the Eastern Mediterranean region: The Khorshid COVID Cohort (KCC) study. PLoS One 2020;15:e0241537.
25. Javanmard SH, Nasirian M, Ataei B, Vaseghi G, Vaezi A, Changiz T. Isfahan COvid-19 REgistry (I-CORE): Design and methodology. J Res Med Sci 2020;25:32.
26. Janani M, Beheshti-Nia F, Ahmadi H, Khazeni A, Yadegarafar G. Epidemiological features and hotspot of COVID-19 in Isfahan province of Iran: Results of a cohort study. 2020.