ISSN: 2538-5887; Pathobiology Research. 2021;24(1):55-61

Prediction of the Risk Factors for COVID-19 Infection in Progression to Severe Disease in Bu-Ali Sina Hospital, Qazvin, Iran

Running title:

Factors for COVID-19 in progression to Severe Disease

ARTICLE INFO

Article Type
Original Research

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Article History
Received: Augest 3, 2020
Accepted: April 10, 2021
ePublished: March 6, 2021

ABSTRACT

Background and Aim: Given the widespread epidemic of COVID-19 around the world and the irreparable damage to all aspects of human life, surveying methods to cope with this epidemic is one of the research priorities of societies. The aim of this study was to find the factors that predict the severity of the disease and the resulting death.

Methods: This descriptive-analytical study was performed on COVID-19 patients admitted to Bu-Ali Sina hospital in Qazvin during March 2020. Epidemiological, clinical, laboratory, and radiological characteristics of patients were collected. Data were analyzed by independent t-test and Mann-Whitney U test (for normally and non-normally distributed quantitative variables, respectively) and Chi-square test (for qualitative variables) using SPSS software Version 22. A *p* value of <.05 was considered as significant.

Results: The study population included 119 admitted COVID-19 patients. Among whom 94 patients recovered, and 25 patients died. The deceased patients were significantly older than the recovered patients (*p*=.0007). The frequency of smoking among patients in this study was 5.4%. Lymphopenia (*p*=.015), neutrophil number (*p*=.009), blood urea nitrogen (*p*=.012), and creatinine (*p*=.032) were significantly higher, and blood oxygen saturation (*p*=.001) was significantly lower in the deceased patients than in the recovered patients.

Conclusion: The percentage of smokers in hospitalized patients with COVID-19 disease was significantly lower than in the general population. If COVID-19 patients are in the high-risk group, including older people with sever hypoxia, lymphopenia, neutrophilia, impaired renal function, and sever lung involvement in CT scan, they should be examined with extra care due to the increased risk of death in these patients.

Keywords: COVID-19, Hospital, Qazvin

Introduction

In late December 2019, a type of pneumonia due to a novel variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China (1). The novel coronavirus was officially named Coronavirus 2019 (COVID-19) by the WHO on February 11, 2020. The prevalence of Chinese COVID-19 infected cases escalated rapidly. Then the virus spread from one country to another. Eventually, the WHO declared COVID-19 a pandemic on March 11, 2020. COVID-19 appears to be the greatest threat to humanity in the 21st century (2).

COVID-19 symptoms include fever, exhaustion, cough, upper respiratory infection, and difficulty in breathing or shortness of breath. The majority of COVID-19 patients develop mild to moderate illness and recover without hospitalization. However, prominent laboratory abnormalities associated with severe disease progression are observed in approximately 15-20% of cases, indicating that a mild infection could lead to a severe one requiring intensive care and hospitalization (3, 4). Organ dysfunction, including acute respiratory distress syndrome (ARDS), shock, acute cardiac injury, and acute kidney injury, may appear in 5% of severe COVID-19 cases (3, 5). As of January 17, 2021, the latest update indicates that 95,007,057 laboratory-confirmed COVID-19 cases have been identified around the globe. Data on the epidemiological and clinical characteristics of COVID-19 patients are obtained primarily from Chinese (6), Italian (7), and American (8) research studies. However, knowledge about this disease and its characteristics has been recently developed in Iran. Since the disease is highly contagious and potentially fatal (9), understanding all the clinical impacts of the virus helps improve disease management and thus control the pandemic.

The present study outlined the demographic characteristics and results of each COVID-19 patient admitted to Bu-Ali Sina hospital in Qazvin during March 2019. This comprehensive assessment aimed to identify demographic, clinical, and laboratory characteristics of all cases that recovered or passed away. In this retrospective study, 119 laboratory-confirmed COVID-19 cases admitted to the hospital during March 2019 were examined to identify the factors affecting the outcomes with the hope of improving treatment and reducing mortality.

Methods

The present descriptive-analytical study was conducted during one month (March 2019) on COVID-19 patients admitted to ICU (intensive care unit) and non-ICU wards of Bu-Ali Sina hospital in Qazvin, Iran. The Ethics Committee of Qazvin University of Medical Sciences approved the present study protocol with the following ethics code: IR.QUMS.REC.1399.379. Clinical symptoms suggestive of COVID-19 pneumonia, including cough (with or without sputum), fever, pleuritic chest pain, or dyspnea as well as chest computed tomography (CT) scan findings compatible with COVID-19 and positive reverse polymerase chain reaction (RT-PCR) test of nasopharyngeal swab specimens determined COVID-19 confirmed cases as the inclusion criteria (10).

In general, epidemiological (rural/urban), clinical, laboratory, and radiological characteristics of patients were extracted from their medical records using data collection forms.

The following information was collected through data collection forms: age; sex; personal health record (PHR) of hypertension (HTN), diabetes melitus (DM), cardiovascular disease (CVD), chronic kidney disease (CKD), smoking cigarettes, and drug addiction; length of hospital stay (LOS); admission to ICU and non-ICU wards; intubation and non-intubation; complete blood count (CBC) including white blood cells (WBCs), lymphocyte, neutrophil, neutrophil to lymphocyte ratio, platelet, hemoglobin, and erythrocyte sedimentation rate (ESR); urea (BUN) and creatinine (Cr); peripheral capillary oxygen saturation (SpO_2); and computed tomography (CT) of the chest. Furthermore, the patients' outcomes (death and recovery) were extracted from their medical records.

Data were analyzed using SPSS Statistics Ver. 22.0. Independent t-test and Mann-Whitney U test

were used to compare normally and non-normally distributed quantitative variables, respectively. Chi-square (χ^2) and Fisher's exact tests were used to compare qualitative variables. The significance level was considered at $p < .05$.

Results

Demographic and Clinical Characteristics

The study population consisted of 119 COVID-19 patients admitted to Bu-Ali Sina hospital. The mean age of patients was 54.38 ± 16.95. Among whom 65 (54.6%) cases were male (Table 1). Out of 119 patients, 77 cases had at least one underlying disease, including HTN (35, 20.41%), DM (25, 21%), coronary heart disease (CHD) (12, 10.08%), and CKD (5, 4.2%). Also, six patients (5.04%) were smokers, and five patients (4.2%) were addicted to drugs. The frequency of smoking among patients in this study was 5.4%. In addition, 84 patients (70.58%) lived in urban areas, while 35 patients (29.42%) lived in rural areas.

The mean LOS was 7.71±6.78 days. The patients included in this study were hospitalized in March 2019. Out of 119 cases, 94 COVID-19 patients (79%) recovered and were discharged from the hospital. The other 25 COVID-19 patients (21%) passed away. Oddly enough, the first person to pass away due to COVID-19 in the province was a 26-year-old female medical staff member.

The deceased cases were significantly older than the recovered cases (mean age of 64 vs. 51) (p=.0007). Male gender was the prevalent gender among the deceased patients (14, 56%) as opposed to the recovered patients (51, 54%). The deceased patients were more likely to have underlying diseases, such as HTN (14, 56% vs. 21, 4.6%).

The deceased patients were more likely to have DM, CHD, and CKD; however, there was no significant difference between the two groups. All COVID-19 infected smokers recovered and were discharged. Only one drug addict, a 77-year-old smoker with a record of cerebrovascular accident (CVA), passed away. Urban patients were the prevalent population among the deceased patients (20, 80%) as opposed to the recovered patients (64, 68%); however, there was no significant difference between the urban and rural populations. Moreover, there was no significant difference between the two groups in terms of LOS. Only 19 patients were admitted to ICU, of whom nine cases (four intubated cases & five non-intubated cases) recovered. Of the other 100 patients admitted to non-ICU wards, 85 patients recovered. All of them were non-intubated.

Table 1: Demographic and clinical characteristics of patients who died and recovered following COVID-19

Demographic and Clinical Information	Total Patients with COVID-19 (119)	Recovered Patients	Died Patients	*P*-Value
Age (year) / Mean± SD	54.38±16.95	51.34±15.4	64.26±19.28	.0007
Sex/Number (%)				.9525
Male	65 (54.36)	51 (54)	14 (56)	
Female	54 (45.4)	43 (46)	11 (44)	
Residence/Number (%)				.2451
City resident	84 (70.58)	64 (68.08)	20 (80)	
Village resident	35 (29.42)	30 (31.92)	5 (20)	
History of diabetes Number (%)	25 (21)	19 (20.21)	6 (24)	.6973
History of coronary heart disease Number (%)	12 (10.08)	6 (6.38)	6 (24)	.0624
History of chronic kidney disease Number (%)	5 (4.2)	1 (1.06)	4 (16)	.0592
Smoking Number (%)	6 (5.04)	6 (6.38)	0 (0)	.3962
Having an addiction Number (%)	5 (4.2)	4 (4.25)	1 (4)	.7993
Duration of hospitalization	7.71±6.78	7.61±6.32	8.42±8.08	.7993

Mean± SD					
ICU Number (%)	Intubated	9 (7.56)	4 (4.25)	5 (20)	.8087
	Un-intubated	10 (8.4)	5 (5.31)	5 (20)	
Non ICU Number (%)	Intubated	3 (2.52)	0 (0)	3 (12)	<.001
	Un-intubated	97 (81.51)	85 (90.42)	12 (48)	

Table 2: Laboratory findings and the chest CT scans of patients who died and recovered following COVID-19

Laboratory Findings	Total Patients with COVID-19 (119)	Recovered Patients	Died Patients	*P*-Value
WBC($\times10^3/\mu$/L) Mean± SD	6.95±3.96	6.63±3.86	4.18±8.22	.0426
Neutrophil %	73.36	72.11	78.39	.0086
Lymphocyte %	21.16	22.3	16.56	.0148
Plt ($\times10^3/\mu$/L) Mean± SD	179.09±80.92	176.71±81.34	188.73±80.26	.5254
Hb (mg/dL) Mean± SD	13.6±2.05	13.73±2.0	13.08±2.21	.2125
ESR (mm/h) Mean± SD	39.64±20.17	38.05±19.90	47.0±20.29	.398
BUN (mg/dL) Mean± SD	18.66±16.95	15.41±10.35	30.88±28.30	.0124
Cr (mg/dL) Mean± SD	1.11±0.81	0.98±0.57	1.58±1.28	.0325
Spo_2*	83.14±14.7	85.39±14.10	74.04±13.78	.0012
CT Number (%)				
Normal	3 (2.88)	3 (3.7)	0 (0)	.0012
Mild	14 (13.46)	14 (17.3)	0 (0)	
Moderate	32 (30.76)	29 (35.8)	3 (13.04)	
Severe	55 (52.9)	35(43.2)	20 (86.96)	

* Oxygen saturation

Laboratory and Radiological Findings

Several abnormal results were found in the laboratory findings (Table 2). Abnormalities included leukopenia, lymphopenia, and a higher ESR. Significant differences were detected in laboratory findings between the deceased patients and the recovered ones in this hospital (Table 2). Lymphopenia (p =.015) and the mean neutrophil number (p =.009) were significantly higher in the deceased patients. Besides, BUN (p =.012) and Cr (p=.032) concentrations were significantly higher in the deceased patients than in the recovered patients. The blood oxygen saturation (14.7±83.15) in COVID-19 patients decreased significantly more in the deceased patients than in the recovered ones (p=.001). Out of 104 patients, only three patients (recovered) had normal chest CT results (Table 2). Meanwhile, out of 55 severely infected patients, 20 cases passed away.

Discussion

In the present study, mortality predictors in COVID-19 patients were evaluated. The mean age of the deceased COVID-19 patients was 64.26 years as opposed to 51.34 years in the recovered patients. Thus, age was an influential factor in determining COVID-19 recovery. This finding is compatible with those of international studies. Previous studies have reported that the deceased patients had a mean age of 68 years, and that 80% of COVID-19 related deaths occurred among adults aged ≥ 60 years (6, 11). Therefore, old age was recognized as a fatality risk factor for

COVID-19 patients. Regarding age, the same fatality pattern has been reported for SARS and MERS patients (12, 13). Elderly patients are more prone to acute respiratory distress syndrome and thus undergo a higher mortality rate (2). Elderly patients develop age-related immune deficiencies that reduce cellular and humoral immune function, impairing viral replication control, and inducing long-term pro-inflammatory responses (6, 14).

Most COVID-19 patients lived in urban areas (70.58%), and less than one-third of the patients (29.42%) lived in rural areas. This finding might be due to the incidence of this determinant in the study population. The percentages of urban and rural population in Qazvin are 74.7% and 25.3% of the total population, respectively (15). Accordingly, many researchers are investigating the dynamics of the pandemic in urban areas to figure out the impacts of COVID-19 on cities. Overall, existing knowledge indicates that the COVID-19 crisis provides an exceptional opportunity for planners and policymakers to take innovative measures and initiatives towards building more resilient cities (16).

Many papers have proposed that HTN is a risk factor for COVID-19. Also, HTN has been reported to be a highly influential factor in determining the infection severity and mortality rate in patients (3, 4, 7, 17, 18). In this study, HTN was the most common (29.41%) underlying disease among patients, of whom 56% passed away. Research has shown that treating DM and HTN with angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) increases ACE2 expression in patients, resulting in an increased risk of severe COVID-19 infection. However, so far, there is no evidence to show that ACE or ARB inhibitors in COVID-19 patients affect the risk of mortality (ROM) (19, 20).

In the present study, no statistically significant association was found between DM, CHD, and CKD and the risk of mortality in COVID-19 patients. However, in a meta-analysis study investigating 14 mortality predictors in COVID-19 patients in 2020, high blood pressure, DM, CVD, CVA, and CKD were identified as mortality risk factors in hospitalized patients. This inconsistency could be due to an error in the data collection procedure or the small sample size in this research. Nevertheless, the meta-analysis recorded HTN as the most prevalent underlying disease among the deceased patients, consistent with this study result.

The frequency of smoking in the present study was low (5.4% of patients vs. 13% of general population in Qazvin). In all studies, the percentages of smokers in hospitalized patients with COVID-19 disease have been reported to be significantly lower than in the reference general population (21, 22). Hence, it has been hypothesized that smoking has a protective role against COVID-19 disease (23). Although the use of a patient self-report method could lead to miscalculation about smoking behaviors. Previous studies have raised concerns about the validity of the patient self-report method for evaluating smoking status, as some smokers may be introduced as non-smokers (24, 25) Hence, another hypothesis is that smoking behavior is underestimated among COVID patients. Moreover, no significant correlation was reported between smoking and mortality risk in COVID-19 patients neither in this study nor in the meta-analysis study (26).

Out of 119 patients in this study, 19 patients were admitted to ICU, of whom 10 cases passed away. Out of 25 deceased cases, 15 were not admitted to ICU. The reasons are as follows. First, due to the sudden and unforeseen outbreak of this health crisis, there were not enough empty beds available. Therefore, patients who needed healthcare services, including admission to ICU, did not receive their required services well. Secondly, since physicians and healthcare personnel had inadequate knowledge of COVID-19 mortality predictors, they could not accurately identify patients who needed extra care.

In line with previous studies (27), LOS was not associated with COVID-19 mortality.

In the present study, leukopenia, lymphopenia, neutrophilia, and BUN/Cr were identified as significant laboratory characteristics. They were significantly associated with the disease severity and mortality in patients. Also, several of these laboratory features have been identified in other retrospective studies investigating COVID-19

mortality outcomes (28, 29). Moreover, increased BUN and Cr levels are clinical signs of impaired renal function with a poor prognosis (30).

According to this study findings, oxygen saturation percentage in patients, whether ill or not, is a primary factor in determining the risk of mortality. Likewise, lung involvement percentage is a determining factor in mortality. Based on these findings, performing CT scans for COVID-19 patients is recommended to determine the treatment protocol, including ICU admission or initiation of antiviral therapy. Because the severity of symptoms, including fever and shortness of breath, has been reported to be not as helpful in measuring the severity of the disease as para-clinical findings. Therefore, it is recommended that healthcare providers working in respiratory disease screening centers use para-clinical assessments, including lung CT scans as well as hematology, serology, and biochemistry tests.

One limitation of the present study was the insufficient number of COVID-19 positive samples diagnosed by PCR test at the start point of the pandemic due to the lack of test kits. This lack of facilities prompted physicians to request PCR testing from patients who were more likely to be infected with the virus, resulting in a smaller study sample size. The research is still ongoing to investigate other aspects and with a larger sample size of COVID-19 patients, the findings of which will be discussed in future papers.

Conclusion

The percentage of smokers in hospitalized patients with COVID-19 disease was significantly lower than in the general population. If COVID-19 patients are in the high-risk group, including older people with sever hypoxia, lymphopenia, neutrophilia, impaired renal function, and sever lung involvement in CT scan, they should be examined with extra care due to the increased risk of death in these patients.

Conflicts of interest:

The authors declared no conflict of interest.

Acknowledgments:

The authors thank the staff of Bu-Ali Sina hospital for their support during the study.

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