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Original Article

Clinical Characteristics and Outcomes of 905 COVID-19 Patients Admitted to Imam Khomeini Hospital Complex in the Capital City of Tehran, Iran

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Abstract
Background: We studied the clinical characteristics and outcomes of 905 hospitalized coronavirus disease 2019 (COVID-19) patients admitted to Imam Khomeini Hospital Complex (IKHC), Tehran, Iran.
Methods: COVID-19 patients were recruited based on clinical symptoms and patterns of computed tomography (CT) imaging between February 20 and March 19. All patients were tested for the presence of COVID-19 RNA. The Poisson regression model estimated the incidence rate ratio (IRR) for different parameters.
Results: The average age (± standard deviation) was 56.9 (±15.7) years and 61.77% were male. The most common symptoms were fever (93.59%), dry cough (79.78%), and dyspnea (75.69%). Only 43.76% of patients were positive for the RT-PCR COVID-19 test. Prevalence of lymphopenia was 42.9% and more than 90% had elevated lactate dehydrogenase (LDH) or C-reactive protein (CRP). About 11% were severe cases, and 13.7% died in the hospital. The median length of stay (LOS) was 3 days. We found higher risks of mortality in patients who were older than 70 years (IRR = 11.77, 95% CI 3.63–38.18), underwent mechanical ventilation (IRR = 7.36, 95% CI 5.06–10.7), were admitted to the intensive care unit (ICU) (IRR = 5.47, 95% CI 4.00–8.38), tested positive on the COVID-19 test (IRR = 2.80, 95% CI 1.64–3.55), and reported a history of comorbidity (IRR = 1.76, 95% CI 1.07–2.89) compared to their corresponding reference groups. Hydroxychloroquine therapy was not associated with mortality in our study.
Conclusion: Older age, experiencing a severe form of the disease, and having a comorbidity were the most important prognostic factors for COVID-19 infection. Larger studies are needed to perform further subgroup analyses and verify high-risk groups.
Keywords: Clinical characteristics, Iran, Mortality, Outcome, SARS-CoV-2
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Introduction

The coronavirus disease 2019 (COVID-19) is the latest epidemic to threaten human communities. This disease, a type of viral pneumonia, is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) which was first found and reported in late December in Wuhan, China. After rapid spread of the infection worldwide, the WHO declared the disease a pandemic on March 11, 2020.[1] The rate of contagiousness of COVID-19 via human-to-human transmission is frightening[2] with a total of 10 905 501 persons infected worldwide as of July 1, 2020.[3] Thus, the real concern is that health-care systems may not be ready to battle this epidemic, especially regarding the provision of care to severe cases that need intensive care units (ICUs), which comprise roughly 16% of hospitalized patients.[4]

Iran is facing a grave epidemic caused by SARS-CoV-2. When the pandemic first began to spread outside of China, our country was on the frontline of the battle against COVID-19 alongside Italy and Spain.[3] The recognition of COVID-19 in the Iranian health-care system dates back to February 19 when two primary cases were detected in Qom city, 150 km to the south of Tehran.[5] On July 2, 2020, the Iranian Ministry of Health and Medical Education (MOHME) announced 232,863 confirmed cases and a total of 11 106 deaths in the daily press conference on the COVID-19 situation. The MOHME counts only those with positive real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) tests in the official statistics.[6] The health-care system of Iran, although one of the best in the region, is already negatively influenced by the sanctions imposed by the United States.[7] However, all health-care personnel have done their best to overcome logistic deficits and save the lives of COVID-19 patients.

After the alleviation of new cases of infection in China, considering the rapid emergence and expansion of the epidemic, many countries, especially middle-income and developing countries may be faced with a situation similar to that currently present in Iran.[8] Thus, the study of clinical data and outcomes of patients who were admitted to hospitals and those transferred to the ICU may lead to better preparedness for management of critically ill patients in future epidemics in Iran and other countries. Imam Khomeini Hospital Complex (IKHC), the largest Iranian university hospital, was the first center assigned to provide care for patients suspected to have COVID-19 from the beginning of the epidemic in Tehran. IKHC is a comprehensive medical center affiliated to Tehran University of Medical Sciences. This hospital complex was established in 1941 and provides diagnostic and treatment services for most diseases. In this study, we report the clinical characteristics and outcomes of patients who were admitted to IKHC in the first month following the onset of the COVID-19 epidemic in Iran. To the best of our knowledge, this is the largest series of hospitalized COVID-19 patients from Iran that comprehensively reports the prognostic factors and outcomes of hospitalized patients.

Materials and Methods

Study Design and Participants

We conducted a retrospective case-series and obtained data from COVID-19 patients who were admitted to IKHC. In IKHC, physicians triaged suspicious patients using history and physical examination (including pulse oximetry) and ordered chest CT scans for suspicious cases. The admission criteria were as follows; 1) an oxygen saturation (SO_2) level of less than 93% without supplementary oxygen and 2) observing characteristics of novel COVID-19 disease on the patient's CT scan, i.e. involvement of more than half of the lungs. However, patients with comorbidities were admitted if they had severe symptoms, or had suggestive signs of COVID-19 on their CT scan but did not have a low SO_2 level. The final diagnosis of COVID-19 was made by an infectious disease specialist or pulmonologist using a compilation of clinical signs, symptoms and CT scan features, irrespective of RT-PCR test results.

At the time of admission, patients provided written informed consent for the use of their medical records in different research projects.

Data Collection

We recruited all patients who were admitted to IKHC between February 20 and March 17, 2020 and were discharged or died during this period. We utilized the health information system (HIS) to access the medical records of the patients. The HIS contained demographic data, the drugs prescribed for the patients and date of admission, discharge or death and ICU admission. Data on signs, symptoms and comorbidities and results of RT-PCR assay were obtained from the national COVID-19 portal system and were merged with the patient data using their national identification number. The RT-PCR assay was performed for all patients using pharyngeal swab specimens. Data on comorbidities or co-existing conditions and smoking was gathered based on patients' self-report. The complications of COVID-19 were not counted as comorbidities. We used mortality data from the hospital records and did not follow-up on the patients after discharge.

Statistical Analysis

We used descriptive analysis to study the distribution of patients' characteristics and clinical data and mortality across different strata of the studied variables, including age, sex, symptoms, major comorbidities and RT-PCR test status, ICU admission, length of hospital stay and severity. Patient status was assumed to be severe if they had PSO_2 lower than 60% or received noninvasive or invasive (mechanical) ventilation. Since the length of stay (LOS) had a skewed distribution, we reported the median and interquartile range (Q1 and Q3) for these patients. Since the follow-up time was short and patients died after the third day, the proportion hazard assumption was not met in this data. Therefore, we used the Poisson regression model and estimated incidence rate ratio (IRR) to study associations between the different variables and patient outcomes. For model generation, we entered each variable into a simple model and then selected the most influential variables (P value < 0.2) for the multiple regression model. We also checked co-linearity and then used a stepwise approach to build a model with the best fit. As there was an association between comorbidity, ICU admission and severity, we ran a different model to assess the association between the aforementioned variables and adjusted for mortality for all other confounders. We were unable to study the survival of patients by different treatment regimens in detail due to limited power. Therefore, we categorized medical treatments into hydroxychloroquine-based and non-hydroxychloroquine groups.

During the study period, 12 461 individual patients visited the respiratory triage of IKHC with symptoms and were suspected to be infected with COVID-19. We recruited 905 patients who were admitted to IKHC between February 20 and March 17, 2020. We observed 124 deaths due to COVID-19 in these patients. We studied associations between risk of death due to COVID-19 and different parameters, including age-group, gender, comorbidities, etc. We used the Stata software and estimated that this sample size would provide more than 90% power to estimate an IRR of more than two, indicating that this study had sufficient power to evaluate our hypotheses.

Although the interaction between the results of the RT-PCR test and other variables was not statistically significant, we have reported the results of analyses exclusively among the RT-PCR positive group. We used the Stata statistical analyses software (ver. 14.1, College Station, Texas, USA).

Results

Out of the 905 patients who were recruited in this study, 396 (43.75%) had a positive RT-PCR result, 146 (16.13%) were admitted to the ICU, and 124 (13.7%) died of the disease during their hospital stay. The average age [±standard deviation (SD)] of the patients was 56.9 (±15.7) years and 61.77% were male (Table 1). The most common symptoms were fever (93.59%), dry cough (79.78%) and dyspnea (75.69%). Our data showed that 63.31% of study participants had at least one comorbid condition, such as hypertension (30.72%), diabetes (26.96%), and cardiovascular diseases (CVD) (16.80%).

Only 43.76% of patients were positive for the SARS-CoV-2 RT-PCR test. The demographic and clinical characteristics of patients with a positive RT-PCR result were similar to the overall data except that the former group had a higher prevalence of fever (94.19%) and

Table 1. Personal and Clinical Characteristics of COVID-19 Patients Admitted to Imam Khomeini Hospital Complex (IKHC) in Tehran in March 2019

Variables	Overall, No. (%)	Test Positive, No. (%)
Total	**905 (100)**	**396 (100)**
Sex		
Men	559 (61.77)	262 (66.16)
Women	346 (38.23)	134 (33.84)
Age group		
Under 20	5 (0.55)	-
21–30	42 (4.64)	17 (4.29)
31–40	103 (11.38)	40 (10.10)
41–50	156 (17.24)	63 (15.91)
51–60	202 (22.32)	90 (22.73)
61–70	217 (23.98)	104 (26.26)
Over 70	180 (19.89)	82 (20.71)
Symptoms		
Any symptoms	903 (99.78)	396 (100)
Fever	847 (93.59)	373 (94.19)
Dry cough	722 (79.78)	321 (81.06)
Dyspnea	685 (75.69)	304 (76.77)
Sorethroat	487 (53.81)	226 (57.07)
Myalgia	430 (47.51)	189 (47.73)
Shivering	351 (38.78)	156 (39.39)
Lethargy	218 (24.09)	106 (26.77)
Body pain	209 (23.09)	106 (26.77)
Nausea	179 (19.78)	81 (20.45)
Wet cough	147 (16.24)	74 (18.69)
Vomiting	139 (15.36)	67 (16.92)
Headache	118 (13.04)	54 (13.64)
Anorexia	115 (12.71)	52 (13.13)
Diarrhea	84 (9.28)	45 (11.36)
Chest pain	60 (6.63)	25 (6.31)
Epigastric pain	37 (4.09)	15 (3.79)
Fatigue	37 (4.09)	14 (3.54)
Dizziness	26 (2.87)	13 (3.28)
Sweetening	26 (2.87)	11 (2.78)
Rhinorrhea	25 (2.76)	9 (2.27)
Loss of consciousness	24 (2.65)	11 (2.78)
Hemoptysis	12 (1.33)	5 (1.26)
Arthralgia	5 (0.55)	2 (0.51)
Cardiac arrhythmia	4 (0.44)	1 (0.25)
Bleeding	2 (0.22)	1 (0.25)
Anosmia	1 (0.11)	1 (0.25)
Rush	1 (0.11)	1 (0.25)
Other	237 (26.19)	124 (31.31)
Temperature		
Under 37.5	523 (57.79)	232 (58.59)
Over 37.5	352 (38.90)	153 (38.64)
Missing	30 (3.31)	11 (2.78)
PSO_2%		
Under 93	303 (33.48)	120 (30.30)
Over 93	557 (61.55)	256 (64.65)
Missing	45 (4.97)	20 (5.05)
Pulse rate		
Under 100	635 (70.17)	271 (68.43)
Over 100	245 (27.07)	115 (29.04)
Missing	25 (2.76)	10 (2.53)

Table 1. Continued

Variables	Overall, No. (%)	Test Positive, No. (%)
Respiratory rate		
Under 24	630 (69.61)	287 (72.47)
Over 24	153 (16.91)	67 (16.92)
Missing	122 (13.48)	42 (10.61)
Comorbidity		
No comorbidity	332 (36.69)	114 (28.79)
Any comorbidity	573 (63.31)	282 (71.21)
Hypertension	278 (30.72)	146 (36.87)
Diabetes	244 (26.96)	122 (30.81)
CVD	152 (16.80)	88 (22.22)
Hyperlipidemia	63 (6.96)	45 (11.36)
Hypothyroidism	44 (4.86)	23 (5.81)
Chronic kidney diseases	42 (4.64)	26 (6.57)
Cancers	39 (4.31)	18 (4.55)
Asthma	33 (3.65)	16 (4.04)
COPD	19 (2.10)	9 (2.27)
CVA	12 (1.33)	4 (1.01)
Chronic liver diseases	12 (1.33)	5 (1.26)
Transplantation	11 (1.22)	7 (1.77)
Rheumatologic diseases	11 (1.22)	8 (2.02)
Fatty Liver	8 (0.88)	3 (0.76)
Neurological diseases	3 (0.33)	2 (0.51)
Schizophrenia	3 (0.33)	1 (0.25)
HIV/AIDS	1 (0.11)	0 (0.0)
Immunodeficiency syndrome	1 (0.11)	1 (0.25)
Other	98 (10.83)	53 (13.38)
No. of comorbidities		
One comorbidity	275 (30.39)	117 (29.55)
Two comorbidities	149 (16.46)	76 (19.19)
>2 comorbidities	149 (16.46)	89 (22.47)
BMI		
Underweight	4 (0.44)	3 (0.75)
Normal	108 (11.93)	58 (14.64)
Overweight	159 (17.56)	73 (18.43)
Obesity Class I	72 (7.95)	38 (9.59)
Obesity Class II	26 (2.87)	11 (2.77)
Missing	536 (59.22)	213 (53.78)
Cigarette smoking	41 (4.53)	22 (5.56)
Hookah smoking	20 (2.21)	10 (2.53)
Alcohol consumption	6 (0.66)	4 (1.01)
Drug abuse	16 (1.77)	6 (1.52)
Drug regimes		
Hydroxychloroquine-based	729 (80.55)	337 (85.10)
Non-hydroxychloroquine-based	154 (17.02)	51 (12.88)
Unknown	22 (2.43)	8 (2.02)
ICU admission		
No	759 (83.87)	315 (79.55)
Yes	146 (16.13)	81 (20.45)
Severity		
Non-Severe	805 (88.95)	340 (85.86)
Severe	100 (11.05)	56 (14.14)
Mechanical (invasive) ventilation	69 (7.62)	45 (11.36)
Re-admission	19 (2.10)	14 (3.5)
Vital Status		
Alive	781 (86.30)	311 (78.54)
Dead	124 (13.70)	85 (21.46)

comorbidities (71.21%). We also showed that 43.09% were overweight, and the proportion of obesity was estimated to be around 26.56%. Forty-one patients were considered ever-smokers and prevalence of ever-use of hookah was 2.21%. Moreover, according to severity criteria 11.0% of our study participants were classified as severe cases (Table 1). Regarding laboratory values on admission (Table 2), the most frequent abnormalities were elevated lactate dehydrogenase (LDH) and C-reactive protein (CRP) in over 90% of patients. The rate of lymphopenia was 42.91%. The drugs prescribed for COVID-19 patients included hydroxychloroquine and oseltamivir, lopinavir/ritonavir, naproxen and ribavirin and were administered as single or combination regimens.

The median LOS was 3 days overall and 8.0 days among ICU patients (Table 3). The difference across age groups was statistically significant (*P* value = 0.001). In addition, LOS was significantly higher among deceased patients (6.0 days) compared to survivors (3.0 days) (P-value < 0.001). We also observed that patients with a positive RT-PCR test stayed longer in the hospital (LOS = 4) compared to those who were negative (LOS = 3) (*P* value = 0.009). The difference of LOS between severe (LOS- 7) and non-severe patients (LOS = 3) was also highly statistically significant (*P* value < 0.00) (Table 3).

The mortality rate ranged from 2% in patients who were younger than 40 to 31.1% among those aged 70 years or above (Table 4). Case fatality rate was estimated at 15.56% in men and 10.69% in women. After adjustment for all confounding factors, the highest relative risks were observed in patients who were older than 70 (IRR = 11.77, 95% CI 3.63, 38.18) compared to patients who were younger than 40 and among patients who underwent invasive ventilation (IRR = 7.36, 95% CI 5.06–10.7) compared to other patients.

We found that 146 patients (16.13%) were transferred to the ICU and 124 patients (13.70%) died of COVID-19 during hospitalization. Case fatality rate was higher in ICU admitted patients (50%) compared to non-ICU patients (6.72%) (IRR = 5.79, 95% CI = 4.00, 8.38). Mortality was also much higher in severe cases (58.00%) in comparison with non-severe cases (8.20%); after adjustment for all confounders, the IRR was 5.47 times higher in severe patients (95% CI = 3.79, 7.89) compared to mild/moderate patients. Mortality was higher among patients who had a positive RT-PCR test (21.46%) than those who tested negative (7.66%) (IRR = 2.80, 95% CI = 1.91, 4.09) (Table 4). Difference in the survival of patients who were treated with the hydroxychloroquine-based regimen was not statistically significant from patients who received non-hydroxychloroquine combinations (OR = 1.07, 95% CI = 0.62, 1.81). We also observed a higher IRR in patients who suffered from co-existing disorders (IRR = 1.76, 95% CI = 1.07, 2.89) compared to patients without any comorbidity. However, the association between each

Table 2. Results of Laboratory Tests in COVID-19 Patients Admitted to Imam Khomeini Hospital Complex (IKHC) in Tehran in March 2019

Laboratory Test	Distribution			Patients with Abnormal Results	
	No. of Patients	Mean (SD)	Median (Q1-Q3)	Abnormal Range	No. (%)
WBC (count)	860	7307.4 (9063)	6000 (4400–8550)	<4100	182 (21.16)
Lymphocyte (count)	846	1544.1 (6139.2)	1085.4 (748–1544)	<1000	363 (42.91)
Neutrophil (count)	840	5340.0 (4118.9)	4408.8 (2766–6735)	<1500	69 (8.21)
Hb (g/dL)	864	13.2 (2.0)	13.3 (12–14.5)	<12	214 (24.77)
Platelet (count)	865	219342.2 (95395.3)	200 000 (156 000–268 000)	<145 000	170 (19.65)
Urea (mg/dL)	864	40.12 (31.2)	31.0 (23.0–46.0)	>43	242 (28.01)
Creatinine (mg/dL)	864	1.2 (0.9)	1.1 (0.9–1.3)	>1.5	104 (12.04)
Na (mmol/L)	858	139.0 (4.0)	139 (137–142)	<135 or >150	103 (12.00)
K (mmol/L)	852	4.2 (0.6)	4.2 (3.8–4.6)	<2.5 or >5	61 (7.16)
FBS (mg/dL)	255	154.7 (83.8)	122 (99–186)	>100	186 (72.94)
BS (mg/dl)	519	146.7 (72.4)	122 (101–165)	>200 or <60	83 (15.99)
ESR (mm/h)	748	64.0 (33.2)	63 (36–90)	>30 (Men)/>42 (women)	572 (76.47)
CRP (mg/L)	805	93.84 (73.6)	76.0 (29–150)	>10	738 (91.68)
pH value	369	7.4 (0.08)	7.4 (7.3–7.4)	<7.35 or >7.45	137 (37.13)
AST (units/L)	460	58.3 (202.0)	38 (27–54)	(Female) >31 or (male) >37	250 (54.35)
ALT (units/L)	458	46.9 (87.5)	35 (22–52)	>31 (women)/>41(men)	194 (42.36)
ALP (units/L)	457	194.5 (166.6)	156 (126–207)	>360	29 (6.35)
Total bil (mg/dL)	416	1.0 (1.6)	0.7 (0.5–1.0)	>1.3	60 (14.42)
Direct bil (mg/dL)	415	0.4 (0.9)	0.3 (0.2–0.5)	>0.3	156 (37.59)
Calcium (mg/dL)	370	8.2 (0.6)	8.3 (7.9–8.7)	>11 or <8.6	257 (69.46)
Phosphorus (mmol/L)	323	3.2 (1.1)	3.1 (2.5–3.8)	>4.5	34 (10.53)
LDH (Units/L)	319	708.7 (683.5)	591 (461– 773)	>280	**312 (97.81)**
NT-ProBNP (pg/mL)	244	2234.6 (5486.2)	252 (68–881)	>125 (age 0–74)/>450 (age +75)	**116 (82.27)**

*Number of observations is less than the total number of patients due to missing information in the patient documents. Some tests were not performed for all patients due to clinical decisions.

Table 3. Distribution of the Length of Stay (LOS) of COVID-19 Patients Admitted to Imam Khomeini Hospital Complex (IKHC) in Tehran in March 2019

	Overall		RT-PCR Positive Patients	
Variables	Median of LOS (Q1-Q3)	*P* Value	Median of LOS (Q1-Q3)	*P* Value
Overall	3.0 (2.0–5.0)	—	4.0 (2.0–7.0)	—
Sex				
Women	3.0 (2.0–5.0)		4.0 (2.0–8.0)	
Men	3.0 (2.0–5.0)	0.483	3.0 (2.0–6.0)	0.428
Age group				
Lower than 40	2.0 (1.0–4.0)		2.0 (1.0–6.0)	
41–50	3.0 (1.0–4.0)		3.0 (2.0–6.0)	
51–60	3.5 (2.0–6.0)		4.0 (2.0–8.0)	
61–70	3.0 (2.0–6.0)		3.0 (2.0–6.0)	
Higher than 70	4.0 (2.0–6.0)	0.001	4.0 (3.0–6.0)	0.003
ICU admission				
No	3.0 (2.0–4.0)		3.0 (2.0–5.0)	
Yes	8.0 (5.0–14.0)	<0.001	9.0 (6.0–15.0)	<0.001
Comorbidity				
No	2.0 (1.0–4.0)		3.0 (1.0–5.0)	
Yes	4.0 (2.0–7.0)	<0.001	4.0 (2.0–7.0)	0.001
RT-PCR test				
Negative	3.0 (2.0–5.0)		—	
Positive	4.0 (2.0–7.0)	0.009	—	—
Vital status				
Alive	3.0 (2.0–5.0)		3.0 (2.0–6.0)	
Dead	5.0 (3.0–9.0)	<0.001	5.0 (3.0–9.0)	0.002
Severity index				
Severe	7.0 (4.0–13.0)		8.0 (5.5–15.0)	
Mild/Moderate	3.0 (2.0–5.0)	<0.001	3.0 (2.0–5.0)	<0.001

specific comorbidity and risk of death was not statistically significant (Table 4).

Discussion

We studied the clinical characteristics and outcomes of 905 patients who were admitted to the IKHC hospital in Tehran. We found that older patients and those with comorbidities, patients with a positive RT-PCR test and those who were admitted to the ICU stayed longer in the hospital. In addition, we observed that deceased patients had a higher probability of suffering from severe disease, having a comorbid condition, being in the ICU, being older and testing positive for SARS-CoV-2 RNA.

We used clinical diagnosis and CT scan findings compatible with COVID-19 for patient admission. CT scan findings have been shown to have higher sensitivity than the RT-PCR test.[9] Indeed, our RT-PCR test results were only 43% positive in clinically suspicious COVID-19 patients who were admitted to this center. This low rate of test positivity in clinical practice was due to multiple reasons. Firstly, the difficult sampling procedure and type of sample taken (i.e. oropharyngeal, nasopharyngeal, or bronchoalveolar lavage), limited experience of medical staff, and the overwhelming situation during the first month of this epidemic might have affected the quality of samples that were sent to the lab for PCR assay.[10] Secondly, the sensitivity of the RT-PCR test depends on the number of samples taken and tested from each patient. Considering limitations in the availability of kits in Iran, almost all patients were tested only once. In spite of the clear clinical presentation of patients as COVID-19, tests were not repeated for patients who were negative in the first round. In addition, the quality of the test kit itself and the laboratory procedure may also affect the sensitivity of the RT-PCR test. To sum up, false-negative test results with sampling in these conditions were estimated to be

Table 4. Crude and Adjusted Relative Risk of Death and 95% Confidence Intervals for Different Variables in All Patients Admitted as COVID-19 and Patients Who Were Tested Positive Based on RT-PCR Assays in IKHC, Tehran, Iran in March 2019

Variable	All Patients (N = 905)			Patients Positive for RT-PCR Test (n = 396)		
	No. of Death (%)*	Crude RR (95% CI)	Adjusted RR (95% CI)	No . of death (%)*	Crude RR (95% CI)	Adjusted RR (95% CI)
Sex						
Women	37 (10.69)	Reference	Reference	24 (17.91)	Reference	Reference
Men	87 (15.56)	1.45 (0.99, 2.13)	1.16 (0.78, 1.73)	61 (23.28)	1.29 (0.81, 2.08)	**1.06 (0.65, 1.73)**
Age group						
Less than 40	3 (2.00)	Reference	Reference	2 (3.51)	Reference	Reference
41–50	5 (3.21)	1.60 (0.38, 6.70)	1.51 (0.36, 6.33)	2 (3.17)	0.90 (0.12, 6.42)	0.83 (0.11, 5.94)
51–60	22 (10.89)	5.44 (1.62, 18.19)	4.56 (1.35, 15.32)	16 (17.78)	**5.06 (1.16, 22.03)**	**4.55 (1.03, 19.97)**
61–70	38 (17.51)	8.75 (2.70, 28.36)	6.76 (2.06, 22.13)	27 (25.96)	**7.39 (1.75, 31.11)**	**6.59 (1.54, 28.11)**
Higher than70	56 (31.11)	15.55 (4.86, 49.69)	11.77 (3.63, 38.18)	38 (46.34)	**13.20 (3.18, 54.74)**	**11.76 (2.78, 49.70)**
Comorbidity						
No	20 (6.02)	Reference	Reference	16 (14.04)	Reference	Reference
Yes	104 (18.15)	3.00 (1.86, 4.86)	1.76 (1.07, 2.89)	69 (24.47)	**1.74 (1.01, 3.00)**	1.04 (0.59, 1.83)
Diabetes	42 (17.21)	2.85 (1.67, 4.86)	1.50 (0.86, 2.63)	25 (20.49)	1.46 (0.77, 2.73)	0.82 (0.43, 1.59)
Hypertesnsion	54 (19.42)	3.22 (1.93, 5.38)	1.55 (0.89, 2.69)	35 (23.97)	1.70 (0.94, 3.08)	0.88 (0.46, 1.65)
CVD	37 (24.34)	4.04 (2.34, 6.96)	1.58 (0.88, 2.83)	24 (27.27)	**1.94 (1.03, 3.65)**	0.92 (0.47, 1.80)
No. of comorbidity						
No	20 (6.02)	Reference	Reference	16 (14.04)	**Reference**	**Reference**
1 co-existing disease	45 (16.36)	2.70 (1.60, 4.59)	1.88 (1.10, 3.23)	31 (26.50)	1.88 (1.03, 3.45)	1.24 (0.67, 2.31)
Two or more	59 (19.80)	3.28 (1.97, 5.45)	1.67 (0.99, 2.82)	38 (23.03)	1.64 (0.91, 2.94)	0.92 (0.50, 1.68)
RT-PCR test						
No	39 (7.66)	Reference	Reference	—	—	—
Yes	85 (21.46)	2.80 (1.91, 4.09)	2.41 (1.64, 3.55)	—	—	—
Drug regime						
Hydroxychloroquine-based	108 (14.38)	Reference	Reference	80 (23.19)	Reference	Reference
Non-hydroxychloroqiune-based	16 (10.39)	1.38 (0.81, 2.33)	1.07 (0.62, 1.81)	5 (9.80)	0.42 (0.17, 1.04)	0.53 (0.21, 1.32)
ICU admission						
No	51 (6.72)	Reference	Reference	38 (12.06)	Reference	Reference
Yes	73 (50.00)	7.44 (5.20, 10.64)	5.79 (4.00, 8.38)	47 (58.02)	**4.80 (3.13, 7.37)**	**4.07 (2.61, 6.33)**
Severity						
Mild/Moderate	66 (8.20)	Reference	Reference	45 (13.24)	**Reference**	**Reference**
Severe	58 (58.00)	7.07 (4.97, 10.06)	5.47 (3.79, 7.89)	40 (71.43)	**5.39 (3.52, 8.26)**	**4.30 (2.76, 6.70)**
Invasive (mechanical) ventilation						
No	66 (7.9)	Reference	Reference	50 (14.24)	**Reference**	**Reference**
Yes	58 (84.1)	10.64 (7.48–15.15)	7.36 (5.06–10.7)	35 (77.77)	**6.01 (3.9–9.2)**	**5.09 (3.23–8.01)**

*Percentages are raw percentages of death from the admitted patients in each category reported in Table 1.

between 30%–50%.[9] In this situation, the hospital should not rely on the results of RT-PCR test for evaluation and management of COVID-19 patients. A clinical evaluation including signs and symptoms, low oxygen saturation, and pattern of lung involvement on CT scan was felt to be sufficient to admit and treat patients, especially during the epidemic.[11]

Interestingly, although those with positive PCR tests for SARS-CoV-2 mirrored the results of all patients admitted to our hospital, the mortality rate was higher among the RT-PCR positive group. These findings may be explained by the fact that in people with more severe disease due to heavier viremia, the possibility of a positive test is increased.[12] Another possibility is that some of the negative RT-PCR cases suffered from other viral pneumonias such as seasonal influenza with much lower fatality (as low as one twentieth) compared to COVID-19.[13]

The most common symptoms on admission were fever, followed by cough and dyspnea. These findings are consistent with other reports from both inside and outside Wuhan.[14] The rate of dyspnea is reported to be lower outside of Wuhan in China as a reflection of milder disease compared to reports from Wuhan.[15]

About 63% of our patients suffered from at least one comorbidity. The most common comorbidities were hypertension, diabetes mellitus (DM) and CVD. Patients who died were more likely to have a comorbidity. However, there was no significant association between a specific condition and death. Some reports showed that comorbidity was associated with higher mortality[16] but others suggested that the association faded in multivariate analyses.[17,18] However, we did not find a significant relationship between more important comorbidities such as DM, CVD and HTN and death. Some studies reported DM as a potent risk factor for death from COVID-19.[19] The hypothesis beyond the role of comorbidities, especially hypertension and diabetes, is that these patients usually consume angiotensin-converting enzyme (ACE) inhibitors. The target of SARS-CoV-2 is the ACE enzyme that is more highly expressed in the presence of ACE inhibitors. Also, this hypothesis is supported by the polymorphisms of ACE, a fact that may explain the role of genetic predisposition.[20] Larger data with detailed information on severity and duration of each comorbidity is needed to study the association between different comorbidities and the incidence and prognosis of the COVID-19 disease.

Forty-three percent and 26.5% of our patients were overweight and obese, respectively. These rates in the Iranian population are 32.3% and 22.3%, respectively, based on national representative reports.[21] The association between obesity and hospitalization due to COVID-19 has been investigated before. Overall, there is no relationship; however, obesity in younger patients with COVID-19 could make them prone to more severe disease which requires hospitalization and ICU admission.[22]

The percentage of cigarette smoking was much lower in this study compared to the general Iranian population (4.5% vs. 15.9%).[23] Contrary to the theoretical effects of nicotine on overexpression of ACE2 in respiratory airways, this low prevalence of smoking in the hospitalized COVID-19 patients has been previously reported by other investigators from China, US and Spain.[19,24,25] There are multiple explanations for such findings. Due to the immunomodulatory effects of nicotine, it may protect against coronavirus infection. In addition, the majority of our patients are old and have comorbidities that may encourage them to quit smoking. In addition, since we used administrative data in this study, under-reporting could be one of the main explanations for this finding. Epidemiological studies with active data collection are needed to study the association of tobacco use with the incidence and mortality of COVID-19.

Regarding laboratory findings, due to the presence of various definitions for normal ranges, it is hard to compare studies. For example, the rate of lymphopenia in our study was lower than other studies that used higher thresholds for low lymphocyte count (below 1500).[26] One other reason is that the severity of the disease is different among various studies. Protocols for admission of COVID-19 patients in different hospitals vary and may depend on several factors including patient load, availability of beds, ICU care, etc. This issue could affect the distribution of laboratory abnormalities in the patient population.

In our study, 16% of the patients were admitted to the ICU during their hospital stay. This figure is in accordance with previous estimates of the need for ICU service at some point in the COVID-19 process. In the overwhelming conditions of an emergent epidemic and the low preparedness of medical centers in the early days, we had limitations in ICU beds. Thus, some patients might have needed ICU care but were kept in non-ICU wards. Looking at the mortality rate of our patients (13.7%) and the mortality rates in the ICU (50%), bearing in mind that death should occur among the critically ill, we may speculate that about 28% of our patients needed ICU care but only half of them were able to get transferred to this unit. Hospitals that are preparing for the management of COVID-19 disease should expand their critical care units and further support severely ill patients who need intensive care during their hospitalization.

The reported mortality rates for COVID-19 in previous studies are somewhere between 2%–3% without follow-up of diagnosed patients.[27] This number is the rate among all tested subjects with a spectrum of disease from mild to severe, which also includes asymptomatic patients.[28] We should keep in mind that in hospitalized patients who usually suffer from moderate to severe disease, the rate is expected to be much higher and reported between 10–21%.[29-32] Another report from Iran showed that the mortality ranged between 1.85% and 8% in outpatient and inpatient settings, respectively.[33] In the aforementioned report, patients were younger and had better underlying conditions than ours. Overall mortality rates in different studies vary due to various admission criteria and follow-up policies.[17,34,35] For example, among ICU patients, a report from Italy suggested a considerably low mortality rate of 26%. It is worth noting that 58% of their patients were still in the ICU with unknown outcome that could dramatically change this figure to expectedly higher rates.[36] In cohorts similar to ours, mortality rates are close to what we have reported.

We assumed that male gender and older age are risk factors for being hospitalized with COVID-19 disease.[37,38] In our study, the majority of the patients were more than 50 years of age while the death rate was significantly higher among those aged 50 years or higher compared to those below 40. Likewise, over 60% of the patients in our study were male with a significantly higher fatality rate, about one and a half-fold, compared to females. Similar to previous reports, being male was not an independent risk factor of death from COVID-19 in our study.[38]

The LOS at the hospital was significantly greater among those admitted to the ICU. Without any specific treatments available, supportive measures in the ICU take longer to heal cases of severe disease, or they may simply delay death. Here, increasing age was again accompanied by a corresponding increase in LOS. This finding is in line with the fact that the disease is more severe in the elderly with higher proportions of ICU admission and death in this population. Survivors also had lower LOS, indicating the prolonged course of disease in the severe cases.

Odds of death in hydroxychloroquine-based treatment and non-hydroxychloroquine-based regimen were not statistically significant in this study. Although the Food and Drug Administration (FDA) did not approve hydroxychloroquine for treatment of COVID-19 patients,[39] it has been used based on encouraging results from preliminary Chinese investigations. The rationale behind the use of hydroxychloroquine in COVID-19 rests on the efficacy of this drug for the SARS outbreak caused by SARS-CoV-1.[40] In addition, multiple antiviral mechanisms of hydroxychloroquine against SARS-CoV-2 have been shown in *in-vitro* studies. In addition, French investigators suggested that it may reduce viral load in patients with COVID-19.[41] Thus, many clinical trials are being conducted on the effectiveness of HCQ on COVID-19. [42] We did not have the power to perform analyses in the different subgroups of treatment regimens. Larger data with detailed analyses of treatment regimens may provide some clue on the effectiveness of some treatment regimens in COVID-19 disease.

In spite of several strengths voiced above, this study has some limitations. We did not have information about the risk factors of COVID-19 infection in this study, including travel to China or other endemic areas inside Iran, the patients' race and ethnicity, or exposure to an infected family member or co-worker. In addition, we did not have information about the severity of the co-existing disorders. Severity of the comorbidities is an important predictor of the patient's outcome and should be taken into consideration in future research. In addition, we did not follow the patients after discharge from hospital to evaluate their final outcome. Our study was based on the data from one hospital and the number of deaths was too small to perform subgroup analyses. Recruiting more patients from this hospital and combining data from different registries may shed light on the management of COVID-19 patients in Iran and other countries that face this epidemic, especially low- and middle-income countries with limitations in diagnostic and treatment services.

In conclusion, age above 50 years, having a positive RT-PCR test, presence of any comorbidity, ICU admission, severity of disease, and receiving invasive ventilation were the main risk factors for death from COVID-19. Treatment with hydroxychloroquine did not improve patient survival in this study. Fewer than 50% of the patients had positive RT-PCR results, either due to challenges in acquiring proper samples or sensitivity of the laboratory techniques to detect COVID-19. Rigorous attempts are required to monitor and improve the quality of COVID-19 testing and clinical decision-making for the diagnosis and treatment of these patients in hospitals.

Authors' Contribution

SFA, and KZ prepared study, designed and supervised the project. SN performed statistical analysis. RG prepared the first draft of the paper. All authors actively collaborated in the design and conduct of the study and contributed in the design, data collection, interpretation of the results, critical review and approval of the final version of this paper.

Conflict of Interest Disclosures

The authors declare no conflicts of interest.

Ethical Statement

This study was approved by the ethics committee of Tehran University of Medical Sciences, Tehran, Iran (No.: IR.TUMS.VCR.REC.1399.027).

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