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Epidemiological Characteristics, Clinical Features, and Outcome of COVID-19 Patients in Northern Tehran, Iran; a Cross-Sectional Study

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Abstract

Introduction: Following the widespread pandemic of the novel coronavirus diseases (COVID-19), this study has reported demographic and laboratory findings and clinical outcomes of patients with COVID-19 admitted to a tertiary educational hospital in 99 days in Iran.

Objective: We aimed to investigate in-hospital death risk factors including underlying diseases and describe the signs, symptoms, and demographic features of COVID-19 patients.

Methods: All confirmed COVID-19 cases admitted from 22 February to 30 May 2020 were extracted from hospital records. A follow-up telephone survey was conducted 30 days after discharge to acquire additional data such as survival status. Distribution of demographic and clinical characteristics was presented based on survival status during hospitalization. All analyses were performed using STATA version 14 with a level of significance below 5%.

Results: Among 1083 recorded patients, the rate of survival and death was 89.2% (n=966) and 10.8% (n=117), respectively. 62% of the cases (n=671) were male. The mean recovery time was 1.90 (3.4) days in survived cases, which was significantly lower than that in deceased cases 4.5 (5.2) days, p<0.001). A significantly higher rate of death was observed among patients above the age of 60 years (24.8%, p<0.001), cases with hypertension (25.4%, P<0.001) and cases without cough (17 %, p=0.002) but with shortness of breath (16.5%, p=0.001).

Conclusions: Our study emphasized the significant effect of different underlying conditions as mortality factors among COVID-19 patients, namely older age spectrum, hypertension, and ischemic heart disease. By acknowledging the epidemiologic pattern and mortality factors, we have more tools to prioritize and make better judgments, and more lives can be saved.

Key words: : COVID-19; Coronavirus; Epidemiology; Iran; Patient Outcome Assessment

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INTRODUCTION

Wuhan city, the capital of China's Hubei province, became the site of an epidemic of unexplained cause of pneumonia in December 2019 (1, 2). The World Health Organization (WHO) chose the official name of COVID-19 (standing for coronavirus disease 2019), for the disease, as well as the term SARS-COV- 2 (severe acute respiratory syndrome coronavirus 2) for the virus. The clinical continuum of SARS-CoV-2 infection appears to be broad, including asymptomatic infection, moderate upper respiratory tract disease, and extreme respiratory failure and even death (3). The disease is highly contagious and each infected person could infect three people, on average (4, 5). As of Aug 5, 2020, a total of 317483 COVID-19 cases have been identified in Iran and 17802 deaths (5.6% of total cases) have occurred due to infection with the virus (6). Although a number of epidemiological studies have been done in each of the highly infected regions (7-10), most of them investigated the

patients during their hospitalization without post-discharge follow-up. Therefore, a full clinical and laboratory characterization of this disease is required. Besides, due to genetic differences around the world, previous studies may not precisely represent the clinical features among the Iranian population. In the present study, we presented the epidemiological and laboratory information of all COVID-19 patients admitted to one of the major COVID-19 academic tertiary hospitals in Tehran, Iran, and reported laboratory findings and definite clinical outcomes as of February 1, 2020. We aimed to investigate in-hospital death risk factors, including underlying diseases, and describe the signs, symptoms, and demographic features of COVID-19 patients.

Methods

Study design and data collection

The study was designed as a cross-sectional study conducted in Shohadaye Tajrish Hospital, Tehran, Iran: a referral COVID-19 medical center since the early days of the disease when it was still considered endemic. All cases admitted to the hospital between the period of 16 February 2020 and 8 April 2020 were included in the sampling and all medical records were extracted. This also included patients who expired during the course of the diseases while admitted. Confirmed cases that were eligible for inclusion in this investigation had a positive result of the SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction (RT-PCR). Waiver of informed consent for the acquisition of clinical data from infected cases was granted by Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.119), under the supervision of the Ministry of Health and Medical Education, as part of the COVID-19 outbreak research. Written informed consent was obtained from study participants for the collection of biological samples after review and approval of the study protocol by the institutional ethics committee. Samples (nasopharyngeal swabs; blood, urine, and stool samples) were collected in the first week after study enrollment at multiple time points and tested via RT-PCR for SARS-CoV-2. The RT-PCR cycle threshold values were recorded.

Clinical Management

Complete blood cell (CBC) count, liver and kidney function tests, and evaluation of C-reactive protein and lactate dehydrogenase levels were performed as part of the routine care. A multiplex PCR assay was used to screen the respiratory samples for influenza and other respiratory viruses. Every patient underwent supportive treatment, including supplementary oxygen, once pulse oximeter saturation fell below 92%. Oral Oseltamivir 75mg and Hydroxychloroquine 200 mg twice a day or Lopinavir / Ritonavir 200/50 mg once a day was given to COVID-19 patients (Based on national guideline on the time of study). If the patient was clinically suspected of developing community-acquired pneumonia, proper antibiotic therapy would be considered. Corticosteroids were shunned, following extended mortality with their use in severe influenza.

Statistical analysis

Data were described using mean and standard deviation (SD) or frequency (%). Binary comparisons were done using the Chi-squared test or Fisher's exact test for categorical variables or Independent Samples t-test for continuous variables. The odds of death due to COVID-19 according to various predictors was calculated using generalized linear regression models (GLM) with logarithm link function. The Change-In-Estimate strategy was used to select the confounder for the final model. In this strategy, a confounder is defined as a variable in which the adjusted effect size falls outside a predefined range of 10% for unadjusted effect size (11). Accordingly, current smoking, diabetes, hypertension, ischemic heart disease, renal chronic disease, neurologic disorders, and clinical symptoms of fever, cough, and shortness of breath were included in the final model. Furthermore, setting up time to death as the outcome, the Proportional-Hazards Cox Regression model was employed. All the analyses were performed using STATA software version 14. A p-value less than 5% was considered statistically significant.

Results

Overall, information on 1083 cases of COVID-19 with the mean age of 50.75 $\pm$19.33 (age range 1-102) years was collected. Figure 1 presents the epidemic curve of the reported cases depicting alive and expired patients based on the date of admission. The percentage of survival and death was estimated as 89.2% (n=966) and 10.8% (n=117), respectively. More than half of the cases (n=671, 61.9%) were male, while only 5% of the cases (n=42) were working in a healthcare setting. Only one case (0.1%) reported travel to China during the COVID-19 pandemic and twenty-eight cases (2.6%) reported travel to epicenter of the COVID-19 in Iran (including Qom and Gilan provinces). Although people of all age groups were susceptible to get infected with COVID-19, the proportion of occurrence was highest in patients

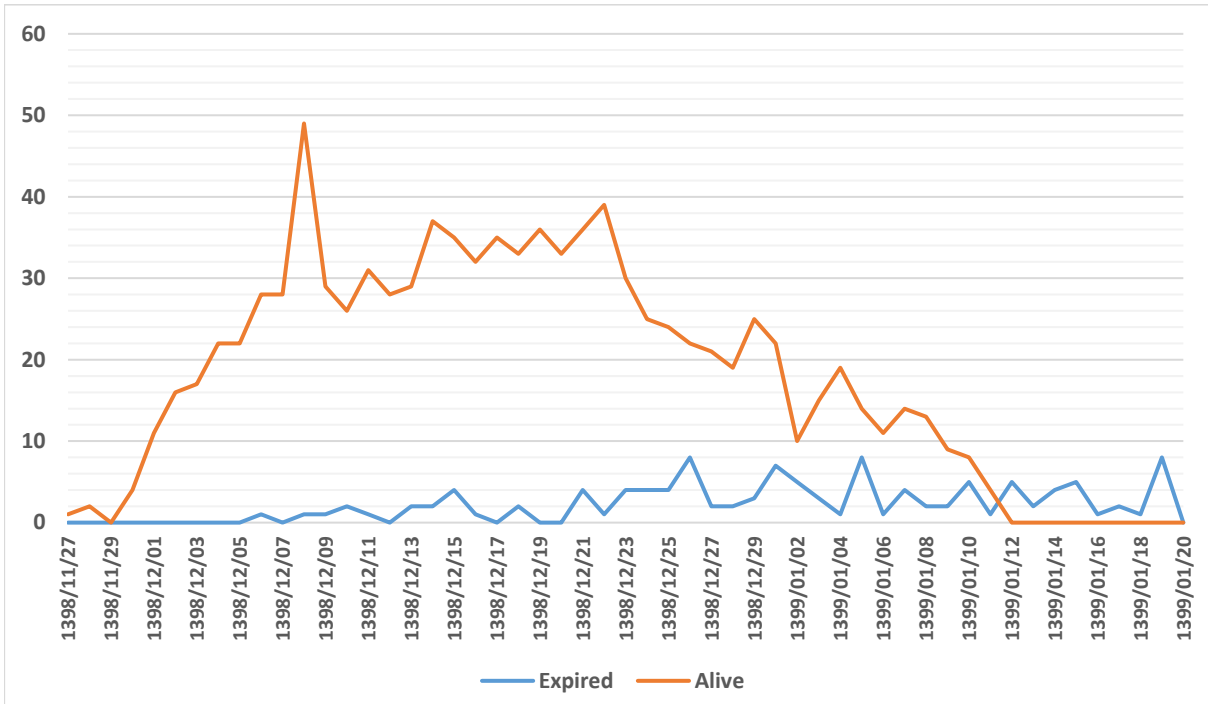

Figure 1: Epidemic curve of COVID-19 cases based on the date of hospital admission

above the age of 60 (34.6%, P<0.001). Fever (67% of cases), shortness of breath (56%) and cough (54%) were the most prevalent presentations of patients. Runny nose and skin rash was found in few cases (7% and 2.5%, respectively). While 31.5% of patients only needed nasal cannula as the oxygenation method during their hospitalization, 9.5% of patients needed mechanical ventilation. Moreover, 22.7% of patients were complicated with acute respiratory distress syndrome (ARDS) (Table 1).

Table 2 presents the distribution of laboratory findings of the COVID-19 patients. Accordingly, D-dimer was the least required test (3% of the patients) and complete blood count test was the most required test (73% of all cases).

The comparison of survival status based on demographic characteristics showed that compared to other age groups, patients aged 60 years or higher had the highest rate of death (24.8%), while patients in age groups of 19-29 years and 30-39 years had the lowest rate of mortality (0.7% and 0.5%, respectively; p<0.001).

The rate of death due to COVID-19 based on gender showed that men had higher a rate of mortality, but the difference was not statistically significant (11% vs. 10.4%; p=0.761). The rate of death due to COVID-19 was significantly higher among cases with diabetes (20.9% vs. 11.3% in cases free of diabetes, p=0.003), hypertensive cases (25.4% vs. 10% in normotensive cases, p<0.001), cases with ischemic heart diseases (24.6% vs. 10.3%, p<0.001), and cases with chronic renal disorders (31.3% vs. 11.7%, p<0.001). Significantly higher mortality was also observed among cases who were recipients of organ transplants (66.6% vs. 12.7% in non-recipients, p=0.005), those with neurologic disorders (34.1% vs. 11.8%; p<0.001), and those with a history of cancer (57.1% vs. 12.1% in patients with no history of cancer, p<0.001).

When comparing the patients based on their survival status, laboratory findings did not differ significantly, except for neutrophil count and Platelet count. The mean (SD) of the neutrophil count was 71.6 (13.3) in alive cases, which was significantly lower than that in deceased cases (82.6 (12.2); p<0.001). Similarly, the mean (SD) of platelet count was 185 (81.4) in alive cases, which was significantly lower than deceased cases (201.8 (74.4); p=0.032).

With regards to BMI, we could not calculate the distribution of BMI based on the patients' survival status, since there were only 8 records for BMI, all of which belonged to expired cases. To compensate for that, we used the distribution of weight, which was recorded for 423 cases (39% of all registered cases). Accordingly, the mean (SD) of weight was 76.3 (15.4) kg in alive cases, which was statistically significantly higher than deceased cases (57.4 (32.4), p<0.001). Study of recovery time also

revealed that the mean recovery time was 1.90 (3.4) days in survived cases, which was significantly lower than that of deceased cases (4.5 (5.2) days, p<0.001).

A significantly lower rate of death was observed among patients with cough (9.8% vs. 17% in

Table 1: Epidemiological and baseline features and clinical outcomes of patients with COVID-19 in Shohadaye-Tajrish Medical Center in Tehran, Iran (n=1083)

Variable	Frequency (%)
Age (in years)	
≤18	22 (2.0)
19-29	133 (12.3)
30-39	215 (19.9)
40-49	183 (16.9)
50-59	154 (14.2)
>60	374 (34.6)
Gender	
Male	671 (61.9)
Female	412 (38.1)
Smoking	
Current smoker	76 (8.9)
History of smoking	61 (7.1)
Working in a healthcare setting	42 (4.9)
History of travel to China	1 (0.1)
History of travel to epicenter in Iran*	28 (2.6)
Reason for referral to the hospital* **	
Suspected symptoms	745 (89.1)
Contact with suspected/probable case	70 (10.4)
Other	70 (10.3)
Clinical characteristics	
Fever	609 (67.0)
Cough	469 (54.3)
Shortness of breath	484 (56.0)
Myalgia	286 (33.1)
Sore throat	125 (14.6)
Runny nose	60 (7.0)
Diarrhea	125 (14.6)
Nausea and vomiting	177 (16.6)
Headache/Dizziness	254 (23.4)
Skin rash	27 (2.5)
Admission to intensive care unit	87 (8.0)
Facial mask	218 (20.1)
Nasal cannula	341 (31.5)
Facial Mask with Reserve Bag	132 (12.1)
Non-invasive Positive-Pressure Ventilation (NIPPV)	25 (2.3)
Intensive ventilation	103 (9.5)
Acute respiratory distress syndrome (ARDS)	63 (22.7)
Chronic underlying disease	
Cardiovascular diseases	264 (30.5)
Endocrine system diseases	134 (15.7)
Respiratory system diseases	172 (15.9)
Chronic renal disorders	51(6.0)
Chronic liver disorders	12 (1.4)
Neurological disorders	41 (4.8)
Malignant tumors	14 (1.6)
Organ transplantation	3 (0.3)
Immunocompromised disorders	9 (1.0)
Receiving Flu vaccine within the last 12 months	29 (3.4)
Receiving Pneumococci vaccine within the last 5 years	1 (0.1)
Clinical outcome during hospitalization	
Discharged	966 (89.2)
Died	117 (10.8)
Clinical outcome during follow-up**	
Survived	952 (87.9)
Died	14 (1.3)

*Including Qom and Gilan provinces; **Among survived subjects (n=966); *** More than one answer was allowed

Table 2: Laboratory parameters of patients with COVID-19 upon admission

Variable	Number	Mean ± SD	Median (IQR)	Range
Neutrophil count, %	796	73.07 ±13.69	75 (20)	2 - 95
Lymphocyte count, %	789	23.23±12.28	20 (17)	1- 85
Monocyte count, %	509	3.41± 4.01	3 (1)	1-51
Hemoglobin, g/dL	797	13.34 ±3.78	13.2 (2.3)	4.5-21.8
Platelet count, 10*3/uL	799	186.90± 80.80	175 (87)	12 -1050
Prothrombin time, s	398	14.23± 2.93	13 (1.2)	13- 46
D-dimer, mg/L	40	3494.05± 4560.23	1486.5(2741)	153-15000
Alkaline phosphatase, U/L	353	213.45±140.67	182(89)	12-1585
Aspartate aminotransferase, U/L	372	57.62 ±101.15	30.5(597.8)	11-854
Alanine aminotransferase, U/L	370	48.28 ±108.82	25 (22)	9-1282
Serum total bilirubin, mg/dL	179	0.9748±1.03	0.71 (0.52)	0.18 - 10.25
Blood urea nitrogen, mg/dL	734	20.93±18.38	15 (11)	5- 174
Serum creatinine, mg/dL	725	1.48±1.34	1.19 (0.4)	0.52-10.2
Creatine kinase, U/L	476	513.86±3589.31	115 (164.5)	6.1-75000
Creatine Kinase MB, U/L	442	33.12±65.29	22(14)	6 -1200
Lactate dehydrogenase, U/L	355	608.04±342.13	530 (304)	3.4 - 3010
C-reactive protein, mg/L	699	34.54±33.32	23.5 (39)	0.1-188
Amylase, U/L	44	80.42±88.19	57.2 (48.9)	8.9 -462
Erythrocyte sedimentation rate, mm/hr	597	32.22±26.24	25 (33)	1-130
Sodium, meq/L	718	136.43± 7.74	137(21.2)	123-166.5
Potasium, meq/L	716	4.19 ± 2.48	4(3)	3.1-6.7

Table 3: Laboratory parameters of patients with COVID-19 upon admission

Variable	Outcome		P value*
	Survived	Expired	
	Number (%)		
Age			
<19	20 (90.9)	2 (9%)	
19-29	132 (99.2%)	1 (0.7%)	
30-39	214 (99.5%)	1 (0.5%)	< 0.001
40-49	174 (95%)	9 (5%)	
50-59	144 (93.5%)	10 (6.4%)	
>60	281 (75.1%)	93 (24.8%)	
Gender			
Male	597 (88.9%)	74 (11%)	0.761
Female	369 (89.5%)	43 (10.4%)	
Current smoking	74 (97.3%)	2 (2.6%)	0.022Ω
Underlying diseases			
Diabetes	106 (79.1%)	28 (20.9%)	0.003
Hypertension	117 (74.5%)	40 (25.4%)	< 0.001
Stroke	21 (91.3%)	2 (8.7%)	0.837Ω
Chronic respiratory diseases	52 (88%)	7 (11%)	0.835Ω
Asthma	23(79.3%)	6 (20.6%)	0.097Ω
Ischemic Heart Diseases	113 (75.3%)	37 (24.6%)	< 0.001
Renal chronic disorders	35 (68.6%)	16 (31.3%)	< 0.001
Liver chronic disorders	12 (100%)	0 (0%)	0.179Ω
Organ transplantation	1 (33.3%)	2 (66.6%)	0.005Ω
Immunocompromised diseases	7 (77.7%)	2 (22.2%)	0.402Ω
Neurological disorders	27(65.8%)	14 (34.1%)	< 0.001
History of cancer	6 (42.8%)	8 (57.1%)	< 0.001Ω
Clinical symptoms			
Fever	544(89.3%)	65 (10.6%)	0.192
Chills	301(89.5%)	35(10.4%)	0.272
Cough	423 (90.1%)	46 (9.8%)	0.002
Shortness of breath	404 (83.4%)	80 (16.5%)	0.001
Loss of sleep	57 (82.6%)	12 (17.4%)	0.114Ω
Skin rash	24(88.8%)	3 (11.1%)	0.986Ω
Loss of appetite	157(91.2%)	15 (8.8%)	0.258Ω
Smell impairment	93 (87.7%)	13 (12.2%)	0.501
Taste impairment	93 (88.5%)	12 (11.5%)	0.712
Dizziness	106 (93.8%)	7 (6.1%)	0.088Ω
Sore throat	115 (92%)	10 (8%)	0.368Ω
Pleuritic chest pain	116 (96.6%)	4 (3.4%)	0.003Ω

*Chi-Squared test; ε Independent samples T-Test; ΩFisher's exact test

Table 3 (in continue): Laboratory parameters of patients with COVID-19 upon admission

Variable	Survival status		P value*
	Survived	Expired	
	Number (%)		
Nausea/vomiting	156 (88.1%)	21 (11.8%)	0.590
Neck pain	12 (85.7%)	2 (14.2%)	0.715Ω
Headache	193(90.6%)	20(9.4%)	0.436
Abdominal pain	86 (92.4%)	7 (7.5%)	0.234Ω
Diarrhea	114 (91.2%)	11 (8.8%)	0.447
Myalgia	256(89.5%)	30(10.4%)	0.546
Rhinorrhea	57 (95%)	3 (5%)	0.120Ω
	Mean ±SD		
Laboratory findings			
Neutrophil count, %	71.63±13.32	82.64±12.26	< 0.001£
Lymphocyte count, %	23.23±12.44	23.25±11.03	0.492£
Monocyte count, %	3.45± 4.23	3.11±1.39	0.265£
Haemoglobin, g/dL	14.72±16.20	15.61±21.65	0.318£
Platelet count, 10*3/uL	185.04±81.40	201.89±74.47	0.032£
Alanine aminotransferase, U/L	49.05±112.80	40.47± 53.66	0.333£
Serum total bilirubin, mg/dL	1.00±1.07	0.67± 0.28	0.126£
Blood urea nitrogen, mg/dL	21.28±19.08	17.93±10.19	0.065£
Serum creatinine, mg/dL	1.86±5.82	1.20±0.47	0.161£
C-reactive protein, mg/L	34.64± 33.59	33.68±31.12	0.406£
Lactate dehydrogenase, U/L	598.57±333.44	680.58±399.77	0.074£
Vital signs			
Heart rate, bpm	88.59±15.21	88.06 ±15.47	0.362£
Respiratory rate, bpm	18.62±5.32	19.31±7.96	0.112£
O2 saturation on admission, %	91.51±7.51	91.47±6.53	0.482£
Weight, Kg	76.31±15.4	57.47±32.5	< 0.001£
Hospitalization duration (days)	1.90±3.4	4.54 ± 5.2	< 0.001£
Time from onset to admission (days)	5.00±6.08	4.30±4.25	0.1707£

*Chi-Squared test; £ Independent samples T-Test; ΩFisher's exact test

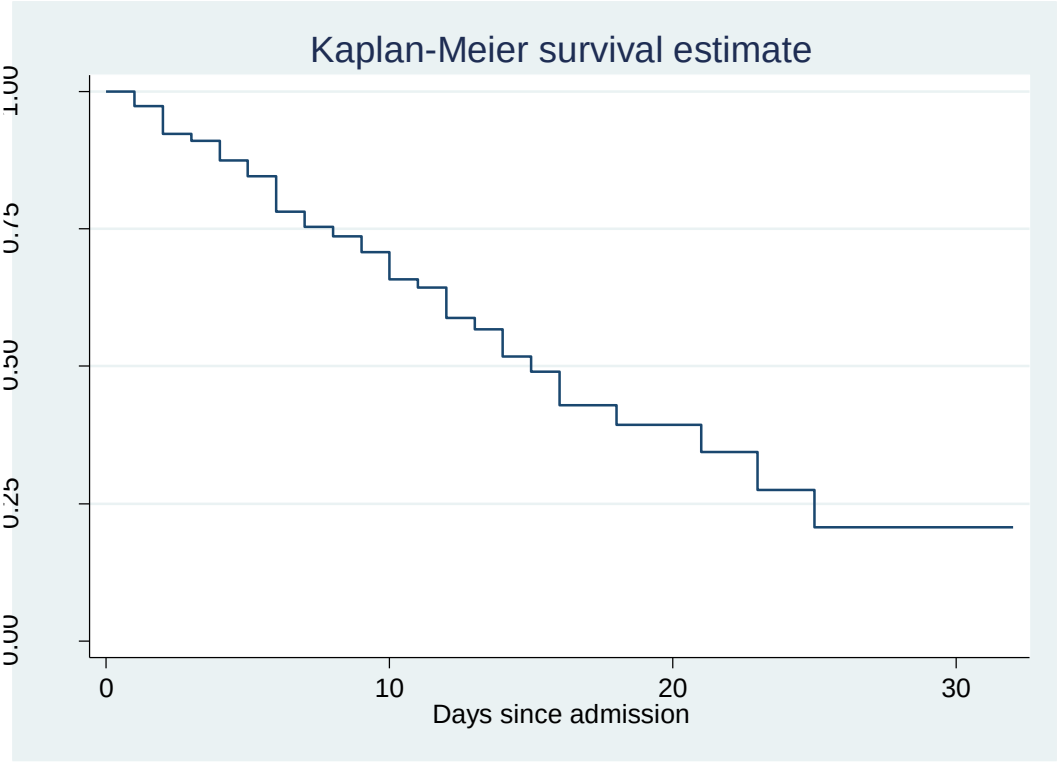

Figure 2: Kaplan-Meier curve of survival following hospital admission due to COVID-19

Table 4: Multiple Logistic Regression on death due to COVID-19

Predictor	Unadjusted model			Adjusted model		
	OR	95%CI	P	OR	95%CI	P Value
Current smoking	0.21	0.05, 0.91	0.037	0.40	0.08,1.89	0.248
Diabetes	2.05	1.27, 3.30	0.003	1.13	0.52, 2.43	0.745
Hypertension	3.06	1.98, 4.73	<0.001	0.85	0.40,1.79	0.681
Ischemic Heart Disease	2.83	1.82, 4.42	<0.001	0.86	0.41, 1.80	0.694
Renal chronic disorders	3.43	1.83, 6.45	<0.001	2.07	0.59,7.21	0.251
Neurological disorders	3.86	1.95, 7.62	<0.001	0.61	0.16, 2.26	0.466
Fever	0.47	0.32, 0.71	<0.001	0.91	0.48, 1.75	0.795
Cough	0.53	0.35, 0.79	0.002	0.48	0.25, 0.92	0.028
Shortness of breath	2.07	1.35, 3.19	0.001	3.39	1.64, 7.00	0.001
Age	**1.07**	1.05, 1.08	<0.001	1.07	1.05, 1.09	<0.001
Weight	0.93	0.90, 0.97	0.001	Removed		
Cancer history	9.62	3.27, 28.28	<0.001	Removed		
Organ transplant	13.74	1.23, 152.82	0.033	Removed		
Neutrophil count	1.09	1.06, 1.11	<0.001	Removed		
Platelet count	1.00	0.99, 1.00	0.070	Removed		
Hospitalization duration	1.13	1.08, 1.17	<0.001	Removed		
Loss of sleep	1.69	0.87, 3.28	0.117	Removed		
Pleuritic pain	1.52	0.86, 2.69	0.144	Removed		

Table 5: Hazard of death associated with COVID-19

Predictor	Category	Univariate model			Multivariate model		
		Hazard Ratio (HR)	HR 95%CI	P	Hazard Ratio (HR)	HR 95%CI	P
Age (in years)		1.03	1.02,1.05	<0.001	1.03	1.01,1.05	<0.001
Gender	Female	1.00			1.00		
	Male	0.95	0.62, 1.45	0.819	1.12	0.68, 1.84	0.505
Diabetes	No	1.00			1.00		
	Yes	0.88	0.55, 1.42	0.616	0.70	0.41, 1.18	0.189
Hypertension	No	1.00			1.00		
	Yes	1.74	1.13, 2.69	0.012	1.48	1.12, 2.92	0.015
Ischemic heart disease	No	1.00			1.00		
	Yes	1.06	0.67, 1.68	0.777	1.53	0.92, 2.54	0.100
Chronic renal disease	No	1.00			1.00		
	Yes	1.33	0.73,2.41	0.346	1.26	0.63, 2.53	0.504
Neurological disorder	No	1.00			1.00		
	Yes	2.13	1.18, 3.85	0.012	2.22	1.19, 4.12	0.012
Fever	No	1.00			1.00		
	Yes	1.15	0.72, 1.85	0.541	1.14	0.69, 1.88	0.605
Cough	No	1.00			1.00		
	Yes	0.58	0.38, 0.88	0.012	0.51	0.31, 0.83	0.007
Shortness of breath	No	1.00			1.00		
	Yes	1.41	0.89,2.24	0.133	1.65	0.97, 2.79	0.062

patients without cough, p=0.002) and those with pleuritic chest pain (3.4% vs. 12.4% in patients free of that symptom, p=0.003). On the other hand, patients with shortness of breath experienced a higher rate of death (16.5% vs. 8.7%, p=0.001) (Table 3).

The results of the multiple logistic regression model showed that the odds of death due to COVID-19 significantly decreased by 52% in patients with cough (AOR=0.48, 95%CI: 0.25, 0.92). Moreover, the odds of death significantly increased by 3.4 times in patients with shortness of breath (AOR=3.39, 95%CI: 1.64, 7.00) and by 7% per each year increase in age (AOR=1.07, 95%CI: 1.05, 1.09) (Table 4). Median (SD) of survival time (in days) was 15 (1.31) (Figure 2). Specifically, it was 15 (1.47) days for males and 21 (5.43) days in females. The difference in survival time between males and females was not statistically significant (p-value = 0.815). The results of the final Cox regression model showed that the hazard of death due to COVID-19 significantly increased by 3% per each year of increase in age (HR=1.03, 95%CI: 1.01, 1.05), by 48% in patients with hypertension (HR=1.48, 95%CI: 1.12, 2.92), and by more than two-fold in patients with neurological disorders (HR=2.22, 95%CI: 1.19, 4.12). The hazard of death, on the other hand, significantly decreased by half among patients with cough at admission (HR=0.51, 95%CI: 0.31, 0.83) (Table 5).

Discussion

This descriptive cross-sectional investigation reports the clinical characteristics, risk factors, and demographic features of COVID-19 in Iran. Data of 1083 COVID-19 cases admitted to a tertiary educational hospital in Tehran, Iran, from 22 February to 30 May 2020, were extracted from patients' hospital records and were analyzed.

Even though at the beginning of the outbreak investigations demonstrated the overall fatality rate of 2.3% (12), the overall fatality rate in our investigation was 10.8%. This controversy might be due to the undetermined destiny of cases in the previous study, an issue which this research rectified by further following patients after their discharge from hospital to determine their final status. Moreover, in this study, only hospitalized cases were included. A recent study by Nikpourghadam et al. in Tehran revealed the case fatality rate to be 1.85% based on the total number of patients (both outpatients and inpatients) and 8.06% among hospitalized patients (9). Consistently, a recent systematic review and meta-analysis reported a case fatality rate of over 13% in 632 hospitalized patients (13).

Although some previous studies have reported male predilection for death from COVID-19 (9), gender was not significantly associated with the risk of death in our study. We also observed a greater number of males than females in the 1083 cases of COVID-19 infection, which is consistent with other studies in Iran and other countries (7, 9, 14). Out of the 117 death cases, the majority were about 60 years of age and/or had pre-existing comorbidities such as hypertension (P value<0.001), ischemic heart disease (P value<0.001), diabetes (P value=0.003), renal chronic disorders (P value<0.001), and organ transplantation (P value=0.005). A higher prevalence of diabetes and high blood pressure among non-survivor has been seen in previous Iranian investigations (9). Multivariate analyses revealed that patients with neurological disorders were at the highest risk of death from COVID-19 infection. A pooled analysis of published literature until April 2020 revealed a ~2.5-fold increase in odds of severe COVID-19 illness with a history of cerebrovascular disease (15). Garcia-Azorin et al. also reported that the presence of chronic neuroimmune disease (CND) is an independent predictor of mortality in hospitalized COVID-19 patients. That could not be explained neither by a worse immune response to COVID-19 nor by differences in the level of care received by patients with CND (16). Our results show that the association of neurological disorders with mortality of COVID-19 is independent of age, cough, fever, and shortness of breath or other co-existing comorbidities. Hence, higher mortality in patients with neurological disorders cannot be explained only by the higher severity of COVID-19 pneumonia at presentation in these patients. A plausible explanation could be the higher fragility and lower reserve of CND population. Delirium, malnutrition, impaired respiratory function, and poor self-management are frequently seen in patients with neurological disorders; many of them can be worsened by COVID-19 disease and the use of personal protective equipment makes its management arduous (16). Further studies are needed to better elucidate the pattern of association between neurological disorders and COVID-19.

The most frequent clinical manifestations were fever (67.0%), shortness of breath (56.0%), cough (54.3%), and myalgia (33.1%), respectively. Ashraf et al. studied one hundred hospitalized patients with COVID-19 in Tehran and revealed that fever was present in less than half (45.2%) of the patients on admission, while the most common clinical symptoms were shortness of breath (74%) and cough (68%) (10). Our findings are similar to Guan et al. and Ashraf et al. who reported 43.8% and 45.2% fever on admission and differs from Chen et al. and Wang et al. who reported 83% and 98.6%, respectively (7, 14, 17). This might show that fever cannot be accounted as a specific finding in COVID-19. However, cough and shortness of breath have been two consistent prominent clinical symptoms in hospitalized COVID-19 patients. Our results also showed that fever, cough, and pleuritic pain were significantly higher in survivors. Consistently, the Cox regression model revealed that the hazard of death significantly decreases by half among patients with cough on admission. This finding indicates that the presence of signs of body reaction to infection, such as fever and cough, is associated with a better prognosis in COVID-19. However, high-grade fever may deteriorate prognosis and further studies are needed to elucidate that. Although shortness of breath increased the odds of death by 8%, respiratory rate and O2 saturation were not significantly different between survivors and non-survivors. This finding indicates that the subjective status of patient's breath can be considered as a prognostic factor.

In terms of laboratory findings, Neutrophil and Platelet count was significantly higher in the non-survivor group. Increase in white blood cells (WBCs) with the predominance of neutrophils can

be a sign of secondary bacterial infection.

Although smoking and higher weight were more prevalent in survived compared to non-survived patients, considering potential confounders is needed before any conclusive statement. Smoking is more prevalent in young people in Iran and many patients with pre-existing comorbidities may have a lower weight due to their disease compared to healthy ones. Further studies are needed to better elucidate the association of body weight and smoking with COVID-19 prognosis.

14 (1.3%) patients died after discharge. Previously, Ashraf et al. had reported symptom relapse, readmission, and death in about 40%, 8.6% and 4.3% of patients after discharge (10). Lan et al. reported that certain patients could recover and test negative, only to test positive again (18, 19). These findings emphasize the need for close follow-up after symptom improvement and discharge.

Limitations

Our findings should be interpreted in light of certain limitations. First, the limited number of laboratory studies was due to the high patient load and limited resources. Second, some patients' medical records were not complete due to the emergency situation. Further studies in outpatient, primary care, or community settings would help to get a full picture of the clinical presentation, natural history, risk factors, and the spectrum of clinical severity of the disease.

Conclusions

COVID-19 can present with a set of non-specific signs and symptoms, but affects older individuals more adversely. To the best of our knowledge, the present study is one of the first descriptive studies of COVID-19 with a large sample size in Iran. Patients with pre-existing comorbidities such as hypertension, ischemic heart disease, diabetes, renal chronic disorders, organ transplantation, neurologic disorders and a history of cancer are more vulnerable to the adverse effects of COVID-19. Special attention should be paid to patients with neurological disorders, as they were found to be at the highest risk of death in multivariate analyses. Besides, shortness of breath, and higher neutrophil and platelet counts can be considered as adverse prognostic factors in our population.

By acknowledging mortality factors, especially when facing patients on admission, and making a more accurate estimation of disease progression in the future, we can make better judgments and save more lives through more precise prioritization and more appropriate healthcare provision considering the ongoing pandemic and resources shrinking and being limited.

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Authors' contribution

Conceptualization: RJK, DO, AZ, FA, SN. Methodology: RJK, DO, AZ, FA. Data collection and first analysis: MV, AA, DS, GS, LJK, MHM, TH, YK. Supervision: AF. Writing-original draft: RJK, DO, FA, SN. Draft editing: MAA, RT, MK. Data analysis and interpretation: RJK, DO, FA, SN. Writing, review, and editing: RJK, DO, AZ, FA, MV, AA, DS, GS, LJK, SN, SN, MAA, MHM, TH, RT, MK, YK, AF. All authors read the manuscript and approved the final version.

Conflict of interest

The authors declare that they have no conflict of interest.

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. The N Engl J Med. 2020;382(8):727-33.
2. Vahidi E, Jalili M. Why COVID-19? Adv J Emerg Med. 2020;4(2s):e36.
3. 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(10223):497-506.
4. 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(3):151-7.
5. Naderpour Z, Saeedi M. A Primer on COVID-19 for Clinicians: Clinical Manifestation and Natural Course. Adv J Emerg Med. 2020;4(2s):e62.

6. Worldometers. COVID-19 CORONAVIRUS PANDEMIC 2020 [Available from: https://www.worldometers.info/coronavirus/].
7. 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(10223):507-13.
8. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, 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(7):1-11.
9. Nikpouraghdam M, Jalali Farahani A, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. J Clin Virol. 2020;127:104378.
10. Ashraf MA, Shokouhi N, Shirali E, Davari-tanha F, Memar O, Kamalipour A, et al. COVID-19 in Iran, a comprehensive investigation from exposure to treatment outcomes. medRxiv. 2020; Preprint.
11. Greenland S, Pearce N. (2015). Statistical Foundations for Model-Based Adjustments. Annu Rev Public Health. 2015;36:89-108.
12. Surveillances V. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. China CDC Weekly. 2020;2(8):113-22.
13. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623.
14. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
15. Aggarwal G, Lippi G, Michael Henry B. Cerebrovascular disease is associated with an increased disease severity in patients with Coronavirus Disease 2019 (COVID-19): A pooled analysis of published literature. Int J Stroke. 2020;15(4):385-9.
16. García-Azorín D, Martínez-Pías E, Trigo J, Hernández-Pérez I, Valle-Peñacoba G, Talavera B, et al. Neurological Comorbidity Is a Predictor of Death in Covid-19 Disease: A Cohort Study on 576 Patients. Front Neurol. 2020;11:781.
17. 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(11):1061-9.
18. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA. 2020;323(15):1502-3.
19. Zhang JF, Yan K, Ye HH, Lin J, Zheng JJ, Cai T. SARS-CoV-2 turned positive in a discharged patient with COVID-19 arouses concern regarding the present standard for discharge. Int J Infect Dis. 2020;97:212-4.