Original Article

TANAFFOS

Clinical and Epidemiological Characteristics of Coronavirus Disease 2019 in Iran: a Hospital-Based Observational Study

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Background: Coronavirus disease 2019 (COVID-19) has been pandemic and has caused a great burden on almost all countries across the world. Different perspectives of this novel disease are poorly understood. This study sought to investigate the clinical and epidemiological characteristics of COVID-19 to efficiently assist the health system of Iran to conquer the outbreak.

Materials and Methods: This retrospective observational study was performed on 394 patients with a diagnosis of COVID-19. The patients should have a history of hospitalization at Loghman-Hakim hospital, Tehran, Iran, for 10 weeks, beginning from the first official report of the disease in Iran. In the subsequent step, the baseline demographic and clinical and paraclinical information of the patients was documented. Finally, the patients were assessed if they had exhibited any morbidity or mortality.

Results: The epidemiological examination of the COVID-19 population suggested a bell diagram pattern for the hospitalization rate, in which the 4th week of the study was the peak. The highest rate of secondary adverse events due to the virus was observed at the 6th and 7th weeks of the study course. On another note, clinical evaluations resulted in identifying specific abnormalities, such as bilateral opacity in chest computed tomography scans or low oxygen saturation in laboratory data.

Conclusion: This study provides evidence concerning the clinical and epidemiological characteristics of COVID-19 in the first phase of the virus outbreak in Iran. Further studies comparing the disease features in the subsequent phases with findings of this study can pave the way for additional information in this regard.

Key words: COVID-19; Iran; Loghman-Hakim Hospital; Morbidity; Mortality; Observational Study

INTRODUCTION

In December 2019, Wuhan, China, has been recognized as the primary source of a new coronavirus. Since then, the virus, called "severe acute respiratory syndrome coronavirus 2", has rapidly spread to almost all countries across the world and has led to mortality and various types of morbidities in a significant proportion of the worldwide population (1, 2). Almost all healthcare systems introduced specific protocols to conquer the rapid expansion of the disease and minimize its complications,

such as acute respiratory distress syndrome (ARDS), septic shock, acute kidney injury (AKI), cardiac arrhythmia, or even death (3-5). The construction of these protocols requires exact information regarding the virus's behavior.

The first official report of the coronavirus disease 2019 (COVID-19) outbreak in Iran goes back to February 19, when two deaths occurred due to the virus attack in Qom, 150 km south of Tehran, the capital city of Iran (6). Since then, the virus has infected thousands of Iranians; accordingly, the government had to execute several restrictive rules, such as systematic quarantine in some parts of the country. The burden related to COVID-19 does not follow the pattern of other countries. Although the Iranians benefit from one of the most well-organized and flexible health settings in the Eastern Mediterranean region (7), the COVID-19 outbreak has brought about problems, such as limited access to health resources and therefore higher rates of victims.

Each hospital should make specific decisions to manage chronic crises, such as the COVID-19 outbreak. Making appropriate prompt decisions seems essential in this condition for the achievement of which the staff members should be aware of ongoing issues in their hospital. Several things, including but not limited to, the number of patients' entry to the hospital, demographic characteristics of the patients, mortality and morbidity rates, and paraclinical features, should be analyzed to efficiently combat COVID-19. The evaluation of the aforementioned matters can assist the healthcare team in predicting required resources for each patient and provide appropriate strategies to reduce the burden of the disease. In this regard, the current retrospective descriptive study aimed to assess the aforementioned parameters during 10 weeks, which completely cover the first surge of the COVID-19 outbreak in Iran. This hospital-based study reflects the trend of the COVID-19 outbreak and its complications in Tehran. During the outbreak, the patients were referred to Loghman-Hakim hospital from other therapeutic centers across the city; therefore, it is believed that the results obtained from this observation could be extended to the status of the whole city.

MATERIALS AND METHODS
Study Design and Setting

This retrospective cross-sectional study was conducted on patients with COVID-19 at Loghman-Hakim hospital, Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran, within February 2020 to May 2020. After a complete explanation of the study and its objectives, written informed consent was obtained from the patients or their representatives. The Institutional Review Board of SBMU approved the trial protocol (IR.SBMU.RETECH.REC.1399.033; available at: https://ethics.research.ac.ir/ProposalCertificateEn.php?id =128067&Print=true&NoPrintHeader=true&NoPrintFooter =true&NoPrintPageBorder=true&LetterPrint=true).

Participants

This study included patients above 18 years of age with COVID-19 based on clinical and paraclinical features. The clinical criteria were forehead radiation contactless body temperature of ≥ 37.7 ℃, at least one of several symptoms of cough, sputum production, nasal discharge, myalgia, diarrhea, headache, or fatigue on admission, and acute time of onset of symptoms (days≤14). Paraclinical features included specific chest computed tomography (CT) patterns or positive polymerase chain reaction (PCR) of nasopharyngeal samples. The PCR was conducted in a subset of patients before enrollment using LightMix, SarbecoVIRUS E-gene RT-PCR kits (Roche, Berlin, Germany) or Liferiver (W-RR-0479-02, China) for ribonucleic acid (RNA)-dependent RNA polymerase, envelope protein, and nucleocapsid protein genes.

The patients were excluded if their documented data were incomplete. Other exclusion criteria were death occurrence before data documentation, discharge in less

than 1 h, and the exclusion of COVID-19 diagnosis during the clinical management.

Baseline Characteristics of Patients

The demographic characteristics of the subjects, including age, gender, marital status, substance abuse, and comorbidities, were evaluated in this study. Moreover, the drug profiles of the patients, both before and during the hospitalization, were documented. Some additional information, such as the CT scan report, laboratory data, and presenting symptoms, were also obtained.

Longitudinal Status of COVID-19 Wards

This study evaluated the referrals to the hospital each week for a total duration of 10 weeks. The study duration was defined to completely cover the first outbreak in Iran. The rate of referrals, mortality, and morbidities, including ARDS, AKI, septic shock, acute coronary syndrome, arrhythmia, and disseminated intravascular coagulation, were assessed each week.

Statistical Analysis

Statistical Package for the Social Sciences software (SPSS version 25; IBM Company, United States) was used to perform statistical analyses. Graphs were drawn using GraphPad Prism software (version 8; San Diego, CA, USA). Quantitative variables were presented as mean±standard deviation; however, qualitative variables were reported as percentage (%).

RESULTS

Baseline Characteristics of Patients

The total number of COVID-19 referrals during the 10 weeks was 2008 individuals (female: 823 and male: 1185). Out of 2008 subjects, 558 patients were hospitalized. Finally, according to the defined inclusion and exclusion criteria, 394 subjects were selected for this study. The demographic characteristics of the participants are presented in Table 1. As shown in Table 1, most patients were male and from the elderly population. Regarding substance abuse, this study showed that most of the cases

referred to Hakim-Loghman hospital did not report any previous or current history. Finally, blood hypertension, diabetes mellitus, and cardiovascular diseases were the most frequent comorbidities among the COVID-19 positive population, respectively.

Table 1. Demographic characteristics of participants

Age, years (Mean ± SD)	61.44 ± 18.24
Gender	
Male	63.96%
Female	36.04%
Marital status	
Single	23.55%
Married	66.45%
Widowed	8.06%
Divorced	1.93%
Substance addiction	
Unknown	90.65%
Opioid	3.43%
Amphetamine	0.93%
Weed	0.31%
Others	4.67%
Smoking status	
Unknown	92.35%
Current smoker	7.32%
Former smoker	0.31%
Comorbidities	
Diabetes	28.92%
Hypertension	35.22%
Cardiovascular disease	19.94%
Rheumatologic condition	1.88%
Asthma	3.78%
COPD	4.01%
Chronic liver disease	0.27%
Transplantation history	0.53%
Malignancy	1.88%
HIV	1.62%
Hypothyroidism	1.88%

Trend of Patients' Admission and Mortality during the Observation

The number of patients' referrals to Hakim-Loghman hospital followed the pattern of bell diagram throughout the study (Figure 1). There was an increasing trend in the number of hospitalized patients with COVID-19 until the 4th week of the study. Afterward, a significant reduction was observed in the number of new cases, which could be due to the effects of interventional procedures in society.

On another note, the overall mortality rate was observed to be 34.77% of the admitted patients. According to Figure 1, the peak of mortality was at the 6th and 7th weeks of the study.
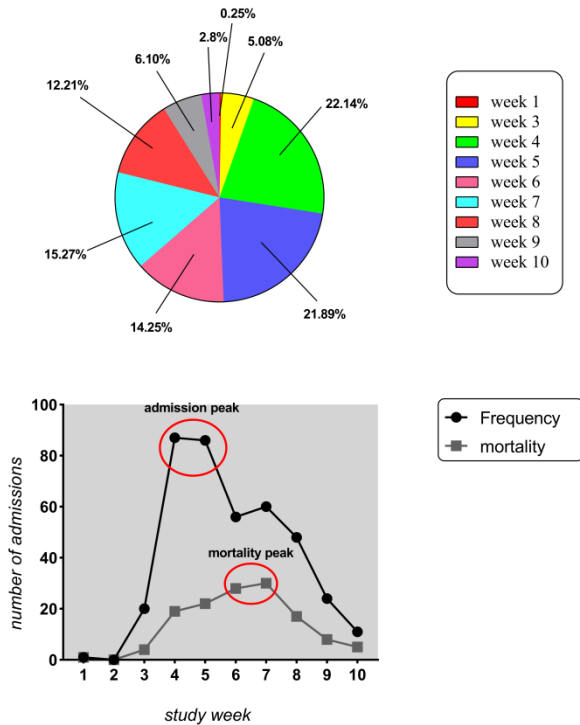

Figure 1. Rates of admission and mortality for patients with COVID-19 diagnosis during 10 weeks

Initial Clinical Symptoms

A long list of initial symptoms was detected in hospitalized patients with COVID-19. However, dyspnea, dry cough, and fever were the most documented initial symptoms, respectively (Table 2). The alterations in the number of referrals with these three symptoms are shown in Figure 2.

Drug Profile of Subjects before and After Hospitalization

The patients reported several medications prescribed before the COVID-19 incidence, mainly due to their chronic disorders, which could be observed in Table 3. During the hospitalization, in addition to their previous medications, the patients were administered a variety of antibiotics plus a specific treatment strategy based on their clinical condition. As shown in Table 3, ceftriaxone and azithromycin were the most applied medications. However, a three-drug regimen, consisting of a combination of hydroxychloroquine, ribavirin, and Kaletra, was reported with the highest usage in the management of the patients during the study. The prescription trend of antiviral drugs during the study is depicted in Figure 3.

Table 2. Proportion of clinical symptoms in hospitalized patients with COVID-19

|	
Fever at presentation	42.89%
Chills	21.12%
Fatigue	31.82%
Pharyngitis	2.40%
Dry cough	60.05%
Productive cough	12.30%
Nasal congestion	3.05%
Rhinorrhea	4.02%
Sneezing	2.41%
Hemoptysis	1.88%
Dyspnea	80.70%
Chest pain	10.72%
Nausea	12.30%
Vomiting	8.55%
Diarrhea	4.01%
Conjunctival congestion	0.53%
Throat burning	1.87%
Tonsil swelling	1.60%
Lymph node enlargement	0.26%
Rash	1.07%
Anorexia	13.90%
Dizziness	5.90%
Headache	6.68%
Abdominal pain	4.54%
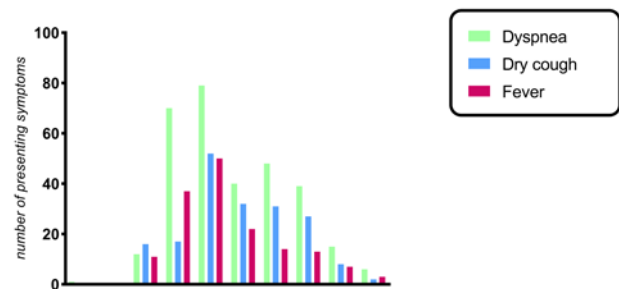
Figure 2. The most common clinical presentations of hospitalized patients with COVID-19

Table 3. Drug profile of the subjects

Previous history	
ARB	16.33%
Metformin	11.14%
β-blocker	11.08%
NSAID	7.29%
ACE inhibitors	3.19%
Acetaminophen	3.19%
Prednisolone	2.90%
Salmeterol	2.62%
Glybenclamide	2.61%
Furosemide	2.04%
Fluticasone	2.03%
Hydrochlorothiazide	1.74%
Salbutamol	1.74%
Levothyroxine	1.44%
Cellcept	0.58%
Azathioprine	0.58%
Chemotherapy	0.28%
During hospitalization	
Antiviral treatment regimen	
0 drug	8.91%
2 drugs	25.14%
3 drugs	42.09%
4 drugs	25.14%
Antibiotics	
Total cases	58.37%
Ceftriaxone	32.42%
Vancomycin	17.16%
Meropenem	16.12%
Azithromycin	28.53%
Levofloxacin	16.25%
Clindamycin	6.90%

Figure 3. Prescription trend of antiviral drugs during the first outbreak of COVID-19 in Iran

Table 4. Frequency of morbidity and mortality due to COVID-19

Death (positive/negative)	34.77%
Septic shock (positive/negative)	9.38%
Acute coronary syndrome (positive/negative)	2.09%
Arrythmia (positive/negative)	8.18%
ARDS (positive/negative)	20.43%
AKI (positive/negative)	1.67%
DIC (positive/negative)	0.66%

Figure 4. The trend of COVID-19 related morbidities and mortality during the study period

Complications Due to COVID-19

A summary of the identified secondary morbidities is shown in Table 4. Most of these deaths were due to adverse events, such as ARDS or septic shock. The trend of change in the occurrence of complications indicated that the highest incidence rate was at the 6th and 7th weeks of the study (Figure 4).
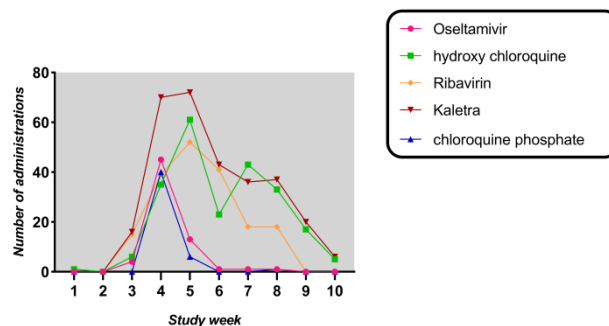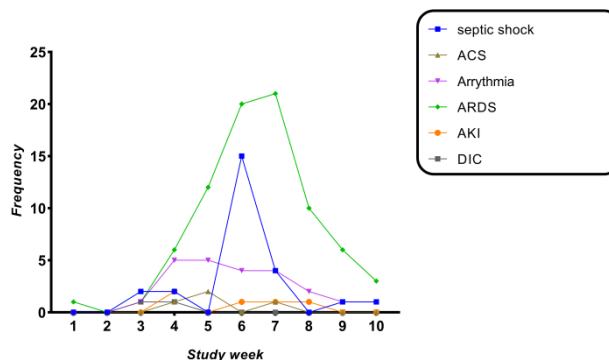
Radiologic Features of COVID-19

The information obtained from CT scan imaging suggested that the disease involved the respiratory system in a significant proportion of the population (Table 5). In detail, bilateral patches and ground-glass opacities were the most frequent (81.82%) findings of lung CT imaging.

Table 5. Computed tomography data of patients with COVID-19

Abnormality	Frequency (positive/total)
Unilateral consolidation	1.56%
Bilateral consolidation	14.02%
Unilateral patch/ground glass opacity	1.03%
Bilateral patch/ground glass opacity	81.82%

Laboratory Features of COVID-19

The laboratory findings are thoroughly listed in Table 6. The presence of inflammatory reactions was confirmed by a high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). However, the mean oxygen saturation was 85.03±11.42, which is suggestive of hypoxia in the majority of the participants. Moreover, a slight lymphopenia (17.19±10.82) was observed among the patients (normal range: 20-40%).

Table 6. Lab data of participants

Variables	Mean	Standard deviation
Heart rate	91.88	16.96
O2 saturation	85.03	11.42
WBC	8837.40	5771.12
Neutrophil percentage	76.73	11.42
Lymphocyte percentage	17.19	10.82
Platelet count	201850.40	81133.67
Hemoglobulin	12.91	2.26
ESR	46.11	26.61
CRP	53.92	36.43
LDH	559.16	343.06
Creatinine	1.46	0.91
Na	136.42	4.38
K	4.19	0.60
ALT	71.47	68.80
AST	74.21	70.55
ALP	237.85	144.23
VBG		
pH	7.38	0.12
PaCO2	43.24	15.66
HCO3	25.14	4.89

DISCUSSION

This study provided evidence regarding the status of a tertiary referral hospital affiliated with SBMU. During the first phase of the COVID-19 outbreak, this hospital was specialized as one of the main centers that admitted COVID-19 patients. The current study showed that this hospital admitted 394 patients with a definite diagnosis of COVID-19 during 10 weeks, with the highest rate at the 4th week of the study course. A variety of complications were also detected throughout the study. Given the referral peak at the 4th week, it is not surprising that the highest rates of virus-related organ failures were at the 6th and 7th weeks.

Growing evidence highlights the role of demographic factors in COVID-19 pathogenesis. In line with most previous relevant studies, COVID-19 was more frequently observed in male subjects than in female subjects in the present study (8). This finding might be justified by the epidemiological differences between the genders. Additionally, the protective effect of the X chromosome and sex hormones could contribute to modulating innate and adaptive immunity (9).

The COVID-19 exhibits diverse clinical manifestations that complicate its diagnosis. Dry cough and fever were the most common presentations, and gastrointestinal symptoms were observed less frequently, in line with a significant number of previous reports (10), which gives additional support to the fact that this virus has different viral tropism in comparison to similar ones (i.e., seasonal influenza, severe acute respiratory syndrome coronavirus, and Middle East respiratory syndrome coronavirus) (11, 12). However, another reason for the higher frequency of fever and dry cough could be the fact that the inclusion criteria were mainly based on these symptoms and no systematic questionnaire was used in this regard. Beyond the presenting clinical symptoms, a subset of patients is involved with different morbidities, such as ARDS, septic shock, and AKI. The precise pathophysiology of the systemic involvement remains vague.

Due to the present similarity between symptoms and signs of COVID-19 with other viral respiratory diseases,

such as common cold or seasonal influenza, paraclinical examinations (e.g., radiologic and laboratory tests) might help distinguish these etiologies; however, all paraclinical features are very similar. The specific patterns of lung involvement in the chest CT of COVID-19 and the suitable accessibility of this modality have turned it into one of the best methods to distinguish COVID-19 from other similar diseases (13, 14). According to the analyses of the present study, 98.96% of the patients represented abnormality in their chest CT scans, indicating the high sensitivity of this modality to detect COVID-19.

Bilateral patch/ground-glass opacity was the most common (81.8%) pattern observed in the subjects' chest CT scans. Bilateral consolidation was also evident in 14.02% of the participants. The aforementioned two patterns that mainly occur in an acute setting could be helpful in COVID-19 diagnosis. This theory has the support of several previous reports (15, 16). However, the above-mentioned radiologic features are not specific for COVID-9, and other viral pneumonitis cases, including influenza, are not distinguishable. Moreover, radiologic involvement could be persistent for several weeks. Additionally, without considering pretest probability and frequency rate in the population, relying on CT scan findings could be misleading.

Other than imaging modalities, there are paraclinical modalities that could help detect COVID-19 (e.g., laboratory data). Two recent random-effects meta-analyses demonstrated that the most common laboratory findings include increased CRP, ESR, lactate dehydrogenase (LDH), and decreased lymphocytes, which are in line with the results of the present study (17, 18). Nevertheless, studies have shown higher LDH and CRP levels in severe patients. However, the exact mechanisms are not completely clear, and further investigations are warranted in this regard (19). Without specific molecular-based tests, including a nucleic acid amplification test and PCR, other laboratory tests are entirely non-specific for differentiating other viral and inflammatory processes.

There are some limitations requiring consideration in this study. Firstly, some cases had incomplete documentation of the clinical and paraclinical measures, mainly due to the clinically driven process of data generation and the critical characteristics of the disease that increase the need for urgent decisions. Secondly, the retrospective design of the study might have led to selection bias. Thirdly, this study only assessed those who had to be hospitalized due to severe symptoms since this was a hospital-based observational study. Fourthly, further assessments, such as exposure history, incubation period, and admission to discharge period, could provide additional insight into the nature of the disease.

In conclusion, this study showed the trend for the first phase of the COVID-19 outbreak. The trend mimicked the bell diagram pattern, probably due to interventional procedures adopted by the government and society to suppress the outburst. However, individuals are not entirely secure from the upcoming epidemics, and sanitary protocols should be released according to the community- and hospital-based experiences from the first outbreak.

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