**The Clinical Characteristics of Early Cases with 2019 Novel Coronavirus Disease in Tabriz, Iran**

Elnaz Asghari1 Farnaz Rahmani2 Mina Hosseinzadeh3* Nader Mahdavi4 Anna Praskova5 Shaqayeq Targhaq6 Mohammad Khajehgoodari7

1. PhD, Department of Medical-Surgical Nursing, Faculty of Nursing & Midwifery, Tabriz University of Medical Sciences, Tabriz, Iran
2. PhD, Research Center of Psychiatry and Behavioral Science, Tabriz University of Medical Sciences, Tabriz, Iran
3. PhD, Department of Community Health Nursing, Nursing and Midwifery Faculty, Tabriz University of Medical Sciences, Tabriz, Iran
4. PhD Candidate in Epidemiology, Department of Epidemiology, Student Research Committee, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
5. PhD, Faculty of Health, Southern Cross University, Gold Coast, QLD, Australia
6. MSc, Nursing Student, Department of Community Health Nursing, Nursing and Midwifery Faculty, Tabriz University of Medical Sciences, Tabriz, Iran
7. PhD, International Valiasr Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

*Correspondence to: Mina Hosseinzadeh
m.hosseinzadeh63@gmail.com

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**Abstract**

**Background and Purpose:** COVID-19 is a new infectious disease first identified in December 2019 in China, and since it spread globally, it resulted in a Pandemic. Much research is needed to understand the disease, and especially its clinical characteristics. The aim of present study was to explore the clinical features, diagnosis, and treatment of COVID-19 in Tabriz, Iran.

**Materials and Methods:** This was a case series single center study that focused retrospectively on the clinical characteristics of 140 early consecutive cases with confirmed COVID-19, who were hospitalized at one of the referral hospitals for COVID-19 patients of Tabriz, from March 20 to May 3, 2020. We used patients’ records to obtain the data, which were analyzed by SPSS Version 16 using descriptive and analytic statistics (Student’s t-test, Mann-Whitney’s, and Chi-square test).

**Results:** Findings showed that 34 out of 140 patients deceased. The highest percentage of patients were in the age range of 65 years and over. The most common symptom on admission was dry-cough (67.9%), followed by shortness of breath (55.7%), and fever (51.5%). During hospitalization, 27.1% showed increase in white-blood-cell count. Only 20% were ventilated and others received oxygen by cannula, and/or mask. Recovered patients reported significant lower rates of pre-existing comorbid conditions than patients who died ($p= .02$).

**Conclusion** This single center study with a relatively small sample size showed that the most common symptom on admission among patients with COVID-19 was dry-cough, shortness of breath, and fever. The finding is mostly in accordance with the current evidence seen around the World.

**Keywords:** COVID-19; Respiratory infection; Epidemiology; Clinical characteristics

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1. Introduction

Coronavirus is a pathogen that primarily targets human respiratory system and can result in severe acute respiratory syndrome (1). In late December 2019, a cluster of patients in China were admitted to hospital with an early diagnosis of pneumonia for an unknown (2). They were later diagnosed with a new infectious disease called the Coronavirus disease 2019 (COVID-19). epidemiologically, these patients were associated with the Huanan Seafood Wholesale Market in Wuhan, Hubei Province, China (3). In previous epidemics that involved animal to human transition, such as SARS, the initial hotspots of diseases were reported in Middle East, Saudi Arabia, and China. Later human to human transmissions of pathogens were reported in other countries (4,5).

According to the early reports from the Chinese Health Officials, this latest outbreak of COVID-19 started at the Seafood market that sells live animals on the 12 December, 2019 (6), although the first case may be traced back to 17 November 2019 (1). Number of COVID-19 cases has risen substantially and fast in China and, before widespread closures of cities, provinces, and state borders, quickly spread globally, resulting in now ongoing pandemic (World Health Organization; 5). The spread has been much more effective compared to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), which adds to the complexity of overcoming it. Based on the modelling of the transmission data and the observed long incubation time, it is likely to take significantly longer to halve the infected cases, and, so, all current control measures will need to stay in place for much longer than in previous epidemics. At the time of writing this article (June 2020), more than 6.19 million of COVID-19 cases have been reported across 188 countries, resulting in more than 376 thousands of deaths. Specific to Iran, there have been 175,927 confirmed cases of COVID-19 since the first confirmed case until 3 April 2020 (1).

The route of transmission of COVID-19 remains undetermined. It is believed that the virus is mainly transmitted through droplets transitioned through air when the infected person coughs or exhales. People then are infected by breathing in the virus or touching surfaces where the droplets fell. While the initial symptoms are known to be respiratory and flu-like, such as coughing and fevers, the disease epidemiology remains largely unknown. To be able to treat new infections and prevent further transmission, it is necessary to review, analyze, and share epidemiological data on the cases reported to date (7).

Governments around the world are at work to establish counter-measures to minimize possible devastating effects. Health organizations coordinate information flows and issue directives and guidelines to best mitigate the impact of the threat (8). At the same time, scientists around the world work tirelessly to provide new information about the transmission mechanisms, the clinical spectrum of the disease, new diagnostics, and develop prevention and therapeutic strategies. Many uncertainties remain with regards to both the virus-host interaction and the evolution of the epidemic, with specific reference to the times when the epidemic will reach its peak (9). This study was carried out to explore the epidemiological characteristics, clinical features, diagnosis, and treatment of COVID-19 in Iran.
2. Materials and Methods
This was a case series study that retrospectively analyzed the epidemiological and clinical characteristics of the first 140 identified consecutive cases with confirmed COVID-19 in the hospital. They were hospitalized at Sina educational hospital (one of the two referral hospitals for COVID-19 patients) of Tabriz city, Iran, between 20 March and 3 May 2020. The inclusion criteria were confirmed cases of COVID-19 based on the Laboratory confirmation of a positive throat swab, tested by real-time polymerase chain reaction for SARS-Cov-2 RNA and being discharged or deceased between 20 March and 3 May 2020. Cases with incomplete data of medical records were excluded from the study. With regard to the inclusion and exclusion criteria, the medical records of 140 identified consecutive cases were selected as the sample of the study.

Data collection involved reviewing existing medical records of the patients diagnosed with COVID-19, and extracting information using a checklist, including demographic data, underlying health comorbidities, vital signs, observed symptoms, laboratory results, received treatment (including antiviral therapy, antibacterial therapy, oxygen therapy, and other supportive treatments), and outcome data (discharged or deceased). Specific to Laboratory results, the initial results on admission were compared to the consecutive tests and reviewed for any changes.

We conducted descriptive statistics on the collected data, using the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA), version 16.0. We reported means and standard deviation if the continuous data were normally distributed or median and interquartile ranges if the data showed signs of a skew. We reported frequency data for categorical variables. Student’s t-test, Mann-Whitney’s chi-square test, or Fisher's exact test were used to compare the epidemiological and clinical characteristics of COVID-19 across the discharge vs. deceased patients. The results of the current study were evaluated using alpha level for statistical significance, where $p<.05$ indicated statistically significant result.

The study was approved by the Ethics Committee of Tabriz University of Medical Sciences (ethics no: IR.TBZMED.REC.1398.1317). Consent was obtained to access patients’ medical records for research purposes at the time of admission.

3. Results
Among the 140 COVID-19 patients, 88 (62.9%) were males and 52 (37.1%) were females. The highest percentage of patients was in the age group of 65 years and over, while the lowest percentage of patients were in an age group of 20 years or less. Only three patients (2.1%) were medical staff. The demographic sample characteristics are reported in Table 1.
Clinical characteristics and treatments provided to patients with COVID-19 are shown in Table 2. On admission, the most common symptom observed among patients was dry cough 95 (67.9%), followed by signs of shortness of breath 78 (55.7%) and fever 72 (51.5%). Most of the patients (84.3%) were administered Hydroxychloroquine and antibiotics. To help with breathing difficulties, records indicated that 87.9% of the patients received oxygen via nasal cannula, 30% by a mask, and 20% with mechanical ventilation. A combination of oxygen methods were used for 37.9% of the patients.

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Clinical Characteristics of Admitted Patients with COVID-19

Review of laboratory results are reported in Table 3, indicating that during hospitalization, 27.1% of the patients showed an increase and 17.1% showed a decrease in white blood cell count.

Specifically, reviewing the patients who deceased due to COVID-19 showed that 55.6% of them experienced an increase in white blood cell count, while 26.5% of them had a decrease in the same value.

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Table 3. Laboratory Results of Patients with COVID-19

| Variables | All patients (n=106) | Deceased (n=3) | Recovered (n=103) | Statistics | p |
|-----------|----------------------|----------------|-------------------|------------|---|
| WBC Increase | Yes | 19(18.1) | 19(19.1) | 3.329 | <0.001 |
| No | 84(80.0) | 84(84.0) | 1(1.9) | - | - |
| CRP Increase | Yes | 3(54.6) | 4(45.6) | 6.22 | - | - |
| No | 60(57.5) | 60(66.0) | 2(1.9) | - | - |
| Urea Increase | Yes | 7(6.7) | 7(6.7) | 33.97 | <.001 |
| No | 119(92.3) | 119(93.0) | 1(1.0) | - | - |
| SGOT increase | Yes | 3(3.1) | 3(3.1) | 33.97 | <.001 |
| No | 103(92.3) | 103(93.0) | 1(1.0) | - | - |
| LDH increase | Yes | 2(1.9) | 2(1.9) | 33.97 | <.001 |
| No | 104(92.3) | 104(93.0) | 1(1.0) | - | - |
| Positive CTNI | Yes | 3(3.1) | 3(3.1) | 33.97 | <.001 |
| No | 103(92.3) | 103(93.0) | 1(1.0) | - | - |
| DDIMER | Yes | 3(3.1) | 3(3.1) | 33.97 | <.001 |
| No | 103(92.3) | 103(93.0) | 1(1.0) | - | - |
| PLT abnormal | Yes | 2(1.9) | 2(1.9) | 33.97 | <.001 |
| No | 104(92.3) | 104(93.0) | 1(1.0) | - | - |

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Reviewing the recovered and deceased cases showed that the median age with median interquartile range (IQR) was significantly lower for recovered patients (58.0(43.0-69.0) years) than for deceased patients (70.0(60.0-74.0) years, p <.001; see Table 1). In line with this finding, the recovered patients reported significantly lower rates of pre-existing comorbid conditions than patients who died (p =.02), including heart disease (10.5% vs 32.4%; p <.002), diabetes (p=.04), and kidney disease (p=.02), but no lung disease (p=.45), hypertension (p=.35), or high cholesterol (p=.82). Patients who eventually died developed significantly more new systemic symptoms after admission than those who recovered (p<.001), including the cases with cardiovascular and kidney symptoms. Notably, no new liver problems were detected in any of the patients after admission. Finally, the patients who died had significantly lower oxygen saturation on admission than patients who recovered (p<.001), and all required mechanical ventilation before they died. On the other hand, none of the recovered patients needed ventilation, instead they received oxygen via nasal cannula significantly more than deceased patients who were more likely to receive oxygen via mask or, later on, via ventilator. More detailed comparative results for recovered and deceased patients are reported in Table 2.

### 4. Discussion

The findings showed that the most common symptom on admission among patients were dry cough, shortness of breath and fever. This is consistent with reported studies to date that revealed the common clinical features include fever, cough, sore throat, and shortness of breath or dyspnea, also called silent hypoxemia (10, 11). In Shiraz, Iran, the most common symptoms were fatigue, cough and fever, respectively (12). The five most common clinical symptoms among patients referred to Northern Tehran, Iran were fever, cough, shortness of breath, myalgia, and sore throat (13). In Mashhad, Iran, the most prevalent symptoms among Covid-19 patients were fever and cold symptoms (14). In a narrative review, it was revealed that a large number of patients were presented to health centers with mild common cold symptoms, such as dry cough, sore throat, low-grade fever or body aches (15). An important concern in the recent pandemic is the capability of the pathogen to establish and induce infection in people with different clinical manifestations. According to a report published by WHO, about 82 percent of COVID-19 patients only experienced mild symptoms and recovered quickly (15). These mild symptoms can be a major factor in transmission and play an important role in effectively spreading this virus (16), as people may not take these seriously or misinterpret them for a common cold (17). Since the advanced symptoms of the disease may manifest during the days of hospitalization, people with mild symptoms, such as fever, cough, or shortness of breath, may not come in time to receive medical intervention (15).

The findings of the present study showed that most of the patients had one or more coexisting chronic disease. For example, diabetes was reported significantly more in deceased patients than in recovered patients. This finding was consistent with the results of a study that showed that people with diabetes (i.e., blood sugar levels higher than recommended target) were more likely to have diabetes-related
health problems, making it much harder to overcome COVID-19 (18). Yang et al., also reported that patients with comorbid COVID-19 and diabetes were more likely to require intensive care and showed a higher fatality rate than patients who did not have diabetes (19). Similarly, the findings of the current study showed that patients who deceased as a result of COVID-19 had significantly higher comorbidity with cardiovascular disease and chronic kidney disease compared to patients who recovered. This is also consistent with previous studies that reported that some comorbidities, including heart disease, can increase patients' risk of COVID-19 infection progression (20).

In summary, our results were consistent with a number of studies to date - Guan et al., who reported that 25% of COVID-19 patients had at least one comorbidity (20), and Yang et al., (19) who reported that, in a small sample of 41 confirmed patients, less than half had underlying diseases, including diabetes, hypertension, and cardiovascular disease. In a systematic review, hypertension had the highest Odds Ratio among death-related comorbidities (21). In a study that analyzed the data from all Iranian hospitals, cardiovascular disease (including hypertension, coronary artery disease, and congestive heart failure) was significantly higher in the deceased group than in those discharged from the hospital (22). Importantly, Guan et al., pointed that fatality rate among patients with any comorbidity was significantly higher than that of other patients (20). This suggests that comorbidities are likely risk factors for adverse outcomes. More research is needed to explore this in more detail and provide much needed confidence in the data, and to confirm any causal relationship between COVID-19 and preexisting comorbidities.

We also found that patients with COVID-19 showed lower oxygen saturation. The number of patients with this symptom at admission was significantly higher in patients who later deceased compared to patients who recovered. Notably, Ottestad (1) argued that one of the symptoms of COVID-19 patients' presentation may be 'silent hypoxia', in which affected patients appear asymptomatic. Consistent with this, several studies reported that many COVID-19 patients were already suffering from pneumonia related to COVID-19 by the time they arrived to the hospital (23-25). It has been argued that the patients may become accustomed and adapted to gradually decreasing levels of oxygen during the slow course of the disease without realizing they were in respiratory distress (23). By the time of admission (due to shortness of breath), the virus had already progressed too far and caused damage to patients’ lungs, with many ending up in critical condition (26). Findings also showed that urban patients had higher mortality rate compared with rural patients. It may be because of failure to identify early cases of COVID-19 in rural areas and higher prevalence of diabetes, hypertension and heart disease in urban living population (27).

Finally, most of the patients who deceased had to be intubated to keep their airway open as they required mechanical ventilation. This was consistent with other studies (24, 26) which reported that patients with COVID-19 who died received invasive mechanical ventilation. Findings also showed that this deceased group of patients were significantly older compared to patients who recovered. Studies from different provinces of Iran also showed that in all study centers, like Tehran (15, 28, and 29), Kashan (30), and Mashhad (31), the
average age of patients who died was significantly higher than those discharged. The similar result was shown in a systematic review (32). This result was also in accordance with the WHO report, indicating that older adults aged 60 years and over were at higher risk of developing severe disease and showed higher mortality rate (22).

5. Conclusion
Our study, showing consistent findings with other similar studies reported globally, highlighted that, in Iran, comorbidities and older age appeared to act as the key factors reported in patients who deceased due to COVID-19 respiratory infection. Older people and people with hypertension, diabetes, kidney disease, and cardiovascular disease should be considered to be the ‘at risk’ group for COVID-19. Given the limited evidence due to its novelty, more adequately powered studies should focus on confirming the association between underlying diseases and poor prognosis of the disease.

Conflicts of Interest
No potential conflicts of interest were reported by the authors.

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