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Clinical characteristics of hospitalized patients with COVID-19: Results from multiple-center experience in Ardabil, Northwest of Iran

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Abstract

Introduction: Since December 2019, coronavirus disease 2019 (COVID-19) has rapidly expanded to cause a worldwide pandemic.

Objectives: We aimed to report the clinical characteristics of infected patients at the first wave in northwest of Iran.

Patients and Methods: In this study, the epidemiological, demographic, clinical, and laboratory data of 1152 confirmed patients with COVID-19 who were admitted to two main hospitals at the first outbreak in northwest of Iran were collected and analyzed.

Results: The most common clinical manifestations at onset were cough (65.8%), dyspnea (40.2%), myalgia (37.8%), and fever (63.4%), loss of appetite (47%), chest pain (38.6%), and headache (49.4%). While the less common were agitation (17.3%), vomiting (22.2%), diarrhea (16.7%), and nausea (24.3%). Laboratory data indicated significant correlation between lymphocyte counts with the severity of the disease based on O₂ saturation.

Conclusion: Overall, assessment the clinical data of COVID-19 patients play a crucial role in understanding the outbreak of novel viral pneumonia, which helps to identify high risk individuals with COVID-19.

Keywords: COVID-19, Clinical characteristics, Infection, Iran

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Introduction

The novel human coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, has been identified in Wuhan, China on December 31, 2019 (1). Due to rapidly spreading global outbreak, COVID-19 has been defined as a pandemic by the Director-General of the World Health Organization (WHO) on March 11, 2020 (2). COVID-19 is listed as the third outbreak of beta corona viruses in the recent century, causing a public health problem of global concern in a short time by human-to-human transmission (3).

Given the potent transmission of COVID-19, it identified as a public health emergency with international concern. Although, the main clinical manifestations of COVID-19 are related to respiratory system (4) patients might occasionally be asymptomatic (5) who are also potential infection sources. Increased pro-inflammatory cytokines level in the serum, like Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV

indicate lung damage and infection severity Assiri. Although, SARS (4) and MERS (6) identified in only around 37 and 27 countries respectively, this pandemic rapidly spread in all over the world. Additionally, Iran was placed among the top-ranking countries challenged with COVID-19 pandemic with high confirmed cases and deaths (7). Several studies confirmed that COVID-19 can induce upper and lower respiratory disease and causes exaggerated immune response in some affected patients. Recently developments in reverse transcription polymerase chain reaction (PCR) for COVID-19 for early detection provides a greater understanding related to the clinical characteristics as well as molecular epidemiology of COVID-19 (8). However, due to the large number of confirmed cases, and the raised number of confirmed cases, COVID-19 is considered as a global concern since the number of affected countries has escalated rapidly in a short period of time (9). While COVID-19 causes infections in the respiratory tract it can infect the digestive

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■ Implication for health policy/practice/research/medical education

To evaluate the clinical characteristics of COVID-19 patients, we conducted a descriptive-analytical study on 1152 patients admitted to the major COVID-19 treatment centers. The most common clinical manifestations such as cough and dyspnea beside the laboratory data we observed significant correlation between lymphocyte counts with the severity of the disease. Overall, assessment the clinical data of COVID-19 patients play a crucial role in understanding the outbreak of novel viral pneumonia.

tract, liver, kidney, neurologic, and cardiovascular (10). A considerable proportion of confirmed COVID-19 patients present with mild symptoms of fever, cough, sore throat, myalgia, and some patients with severe conditions such as multiple organ failure, acute respiratory distress syndrome, pulmonary edema, pneumonia, and leukopenia or lymphopenia (11). Based on the previous studies, a reduction in the absolute value of lymphocytes in most patients (12), indicating that the virus may exerts the infection mainly by acting on lymphocytes, especially T-cells. Damage to T lymphocytes can be found to be a primary factor in exacerbate of patients condition (13). Due to a little information regarding the clinical and epidemiological characteristic of COVID-19 patients in North West of Iran, one of the important focal points in Middle East, the aim of the current study was to describe the clinical characteristics of patients with COVID-19 infection and to compare these characteristics with disease severity.

Patients and Methods

Study design

The university affiliated hospitals in Ardabil have been assigned for control the patients suspected to COVID-19 from March 2020 to May 2020 in Ardabil province, northwest of Iran. All hospitalized cases were monitored based on Iranian National Health guidelines, obtained from the WHO guidelines. Furthermore, both pharyngeal swab and nasopharyngeal specimens were collected with regards to these guidelines based the latest studies on COVID-19.

Patients

In the current descriptive-analytical study, 1152 patients diagnosed with COVID-19 admitted to the major COVID-19 treatment centers in Ardabil, Iran and hospitalized from March 2020 to May 2020 were entered in the study. Diagnosis of COVID-19 patients were conducted based on the National Health Committee guidance and then confirmed by RNA detection of the SARS-CoV-2 in the Ardabil Medical Educational Hospital. All hospitalized cases with confirmed COVID-19 were enrolled and finally, 1152 patients were participated in the final analyses.

Data collection

The epidemiological and clinical data were symptoms at onset of illness, comorbid disease, and vital signs on admission. The laboratory data (white blood cell count, neutrophil count, lymphocyte count, hemoglobin, platelet count, sodium, potassium, lactate dehydrogenase, and C-reactive protein and the chest CT scan of all confirmed COVID-19 patients were collected and analyzed under the support of Ardabil University of Medical Sciences.

Both pharyngeal swab and nasopharyngeal specimens were collected with regards to the WHO guidance. The severity of disease was defined according to the study by Guo et al (14), which contains; shortness of breath, $RR \geq 30$ times/min, and oxygen saturation (Sop_2) (resting state) $\leq 90\%$. Moderate patients were grouped as non-severe cases, while critical cases were grouped as severe individuals in this study. Additionally, the primary chest computerized tomography (CT) scan interpretation was made independently by the pulmonologist or radiologist and the clinical symptoms or the patient's outcome was blind.

Statistical analysis

The collected data was summarized as means (\pm SD: standard deviation). The clinical characteristics of patients were analyzed using unpaired Student's *t* test and chi-square test was used to compare as appropriate. All the statistical analyses were performed by the SPSS software (version 23). Besides, *P* value < 0.05 was considered as indicating statistical significance.

Results

Demographic and clinical characteristics

Of the all hospitalized patients with COVID-19 from March 2020 to May 2020, data of 1152 patients were collected regarding clinical symptoms and outcomes. The demographic and clinical characteristics of the COVID-19 patients are listed in Table 1. A total of 25 (2.7%) were health care workers, having infected cases in family and contact with infected cases was documented in 164 (16.3%) and 244 (24.3%) patients respectively; 726 patients (73.2%) were residents of Ardabil and 266 (26.8%) were from other areas of province.

The confirmed COVID-19 cases were with a mean age of 59 (52.8%) years (range 20–100) consisted of 528 (52.8%) males and 473 (47.3%) females. Moreover, 7.9% of the patients were younger than 30 years of age. Non-severe ($Sop_2 \geq 90$) in 635 (63.0%) patients and severe ($Sop_2 < 90$) in 373 (37.7%) patients were categorized as disease severity.

A number of patients in our study had hypertension 374 (37.1%), diabetes 279 (26.8%), neurologic diseases 68 (6.8%), cancer 21 (2.1%), chronic kidney disease 87 (8.6%), and cardiovascular disease 228 (22.6%) as coexisting medical conditions in addition to COVID-19.

Table 1. Clinical and demographic characteristics of COVID-19 patients in Ardabil, North West of Iran

Variable	Total (%) (n = 11 577)	Non-Severe (n=705)	Severe (n=452)	P value
Age (y)				0.002**
<30	78 (7.9)	49 (7.8)	29 (8.0)	
30-45	204 (20.7)	145 (23.2)	59 (16.3)	
46-60	248 (25.1)	174 (27.8)	92 (25.4)	
≥ 60	457 (46.3)	257 (41.4)	182 (50.3)	
Gender				0.316
Male	528 (52.7)	326 (51.6)	203 (54.9)	
Female	473 (47.3)	306 (48.4)	167 (45.1)	
Education				0.385
Under Diploma	626 (68.3)	417 (69.1)	209 (66.8)	
Diploma	184 (20.1)	121 (20.1)	63 (20.1)	
Bachelor	72 (7.9)	47 (7.8)	25 (8.0)	
MSc	16 (1.7)	9 (1.5)	7 (2.2)	
PhD	15 (1.6)	7 (1.2)	8 (2.6)	
Occupation				0.005**
Non-healthcare worker	916 (97.3)	421 (75.0)	367 (96.1)	
Healthcare worker	25 (2.7)	1136 (24.2)	8 (2.1)	
History of contact with infected cases				0.015*
No	760 (75.9)	487 (76.7)	273 (74)	
Yes	244 (24.3)	148 (23.3)	96 (26.0)	
History of having confirmed COVID-19 patient in the family				0.033*
No	840 (83.7)	539 (84.9)	301 (81.6)	
Yes	164 (16.3)	96 (15.1)	68 (18.4)	
Residency				0.09*
Ardabil	726 (73.2)	473 (75.0)	304 (70.4)	
Non-Ardabil	266 (26.8)	96 (15.1)	126 (29.2)	
Smoking				0.065*
No	881 (87.6)	565 (89.5)	316 (85.2)	
Cigarette	80 (0.8)	45 (7.1)	35 (9.4)	
Hookah	19 (1.9)	13 (2.1)	6 (1.6)	
Addict	26 (2.6)	12 (1.8)	14 (3.8)	
Comorbid Disease				
Hypertension				0.121
No	630 (62.6)	406 (63.9)	224 (60.2)	
Yes	449 (37.1)	257 (35.7)	192 (39.5)	
Diabetes				0.224
No	737 (73.2)	473 (74.3)	264 (71.0)	
Yes	319 (26.8)	172 (25.5)	138 (29.0)	
Cardiovascular disease				0.415
No	779 (77.4)	486 (86.5)	293 (78.8)	
Yes	270 (22.6)	160 (23.5)	110 (21.2)	
Neurogenic disease				0.04*
No	937 (93.3)	595 (93.5)	341 (91.9)	
Yes	68 (6.8)	40 (6.3)	28 (7.5)	
Chronic obstructive pulmonary disease				0.412
No	913 (90.7)	580 (91.7)	333 (89.5)	
Yes	117 (9.1)	64 (8.2)	53 (10.9)	
Chronic kidney disease				0.233
No	920 (91.4)	577 (90.6)	345 (92.7)	
Yes	120 (8.6)	73 (9.4)	47 (7.3)	

Table 1. Continued

Variable	Total (%) (n = 11 577)	Non-Severe (n=705)	Severe (n=452)	P value
Cancer				0.912
No	986 (97.9)	622 (98.0)	364 (97.8)	
Yes	21 (2.1)	13 (2.0)	8 (2.2)	
Symptoms at onset of illness				
Fever				0.04*
No	325 (36.6)	199 (54.7)	96 (32.1)	
Yes	562 (63.4)	195 (45.3)	253 (67.9)	
Cough				0.28
No	307 (34.2)	209 (35.4)	98 (31.8)	
Yes	591 (65.8)	435 (46.6)	290 (68.2)	
Fatigue				0.123
No	631 (75.0)	434 (78.6)	197 (69.9)	
Yes	209 (24.9)	264 (22.2)	380 (30.1)	
Chest pain				0.07
No	489 (61.4)	321 (59.2)	168 (56.9)	
Yes	308 (38.6)	221 (40.8)	87 (34.1)	
Diarrhea				0.02*
No	668 (84.0)	447 (82.0)	221 (87.4)	
Yes	127 (16.7)	98 (18.0)	29 (11.6)	
Nausea				0.01*
No	639 (75.7)	442 (78.2)	197 (70.6)	
Yes	205 (24.3)	123 (21.8)	82 (29.4)	
Vomiting				0.315
No	630 (78.8)	423 (76.8)	207 (79.9)	
Yes	180(22.2)	128 (23.2)	52 (20.1)	
Headache				0.158
No	366 (50.6)	228 (48.6)	138 (54.1)	
Yes	358 (49.4)	241 (51.4)	2 (45.9)	
Myalgia				0.014*
No	544 (62.2)	373 (65.1)	171 (56.6)	
Yes	331 (37.8)	200 (34.9)	131 (43.4)	
Sore throat				0.67
No	679 (86.3)	464 (85.9)	215 (87.1)	
Yes	108 (13.7)	76 (14.1)	32 (13.0)	
Anosemia				0.154
No	696 (89.8)	474 (88.8)	222 (92.1)	
Yes	79 (10.2)	85 (11.2)	49 (7.9)	
Dyspnea				0.001***
No	546 (59.7)	392 (66.2)	154 (47.7)	
Yes	368 (40.2)	652 (33.8)	368 (52.0)	
Agitation				0.024*
No	645 (82.6)	450 (84.3)	195 (78.2)	
Yes	135 (17.3)	84 (15.7)	51 (20.6)	
Loss of appetite				0.004**
No	458 (53.0)	324 (56.4)	134 (46.2)	
Yes	406 (47.0)	350 (43.5)	290 (53.8)	

*P<0.05; **P<0.01; ***P<0.001.

Furthermore, the presence of all coexisting disease was more common in severe patients than among those with non-severe disease. No significant difference was observed in comorbid disease between groups except neurogenic disease ($P=0.04$). In addition, the history of contact with infected cases was different between groups ($P<0.05$).

The most common clinical manifestations at onset were belong to both pulmonary symptoms such as cough (65.8%), dyspnea (40.2%), and extra-pulmonary symptoms including myalgia (37.8%), fever (63.4%), loss of appetite (47%), chest pain (38.6%), and headache (49.4%). While the less common were only extra-pulmonary symptoms such as agitation (17.3%), vomiting (22.2%), diarrhea (16.7%), and nausea (24.3%) (Table 1).

Vital signs of infected patients at admission

Table 2 shows the vital signs of COVID-19 patients on admission. According the patients' vital signs on admission 19 ± 4 had elevated respiratory rate ($>30/\text{min}$). No significant difference was reported between severe and non-severe patients in blood pressure and 120 ± 30 patients had elevated blood pressure. Additionally, the O_2 saturation on admission was less than 90 in 84.35 ± 4.60 patients. The lower mean saturation of O_2 observed among the ICU admitted patients and this was significant ($P=0.001$) and was significantly lower among the deceased patients ($P<0.05$; Table 2). In the case of the blood pressure, only 39.5 % patients had high blood pressure, which were significantly linked to the degree of severity of disease. Vital signs on admission including respiratory rate ($P=0.006$), higher temperature ($P=0.006$) and O_2 saturation ($P=0.001$) were significant between two groups.

Of 150 patients who died, severe patients had higher temperature and higher blood pressure history compared to the dead non-severe cases ($P<0.05$, $P=0.04$ respectively). Although severe patients had unstable hemodynamic, there was any significant different between two groups.

Laboratory findings

Data of laboratory findings were observed in severe and non-severe, the deceased, and living patients with numerous variations (Table 3). Although severe patients showed lower lymphocyte count than non-severe patients, however this correlation was not significant. The present study reported the mean lymphocytes count to be below normal in those severe infected with COVID-19. Most of the patients in severe group had higher levels of C-reactive protein 143 ± 22 (mg/L). The disease had significant influence on laboratory abnormalities (including lymphocytopenia and leukopenia) since more prominent laboratory abnormalities were observed in severe patients. Patients with severe conditions had higher increases in levels of lactate dehydrogenase (850 ± 545 U/L) and lower lymphocyte count ($1014 \pm 605/\mu\text{L}$) compare with non-severe patients ($P=0.009$, $P=0.04$) respectively. The laboratory findings on admission represented CT scans abnormalities in severe patients at the time of admission.

Discussion

During the COVID-19 outbreak, various symptoms and imaging findings leads to the misdiagnosis of the disease especially in the sever cases at the time of admission. Data obtained from the current study from March 2020 up to May 2020, a total number of 1152 of patients were

Table 2. Vital signs at admission of COVID-19 patients in Ardabil, North West of Iran from March 2020 to May 2020

Vital signs on admission	(Non-Severe Mean \pm SD) (n = 705)	Severe (Mean \pm SD)(n = 452)	P value
White blood cell count/ μL	130 \pm 20	110 \pm 30	0.108
Hemoglobin	92.30 \pm 2.28	84.35 \pm 4.60	0.001***
Platelets/ μL	19 \pm 4	23 \pm 6	0.006**
C-reactive protein (mg/L)	93 \pm 10	98 \pm 15	0.300

** $P<0.01$; *** $P<0.001$.

Table 3. Laboratory characteristics of COVID-19 patients in Ardabil, northwest of Iran

Laboratory Findings	Non-Severe (n=705)	Severe (n=452)	P value
White blood cell count/ μL	4.60 \pm 6.68	4.319 \pm 3.74	0.4
Neutrophil count/ μL	38.21 \pm 48.61	35.66 \pm 37.23	0.2
Lymphocyte count/ μL	10.80 \pm 12.25	13.12 \pm 13.70	0.04**
Hemoglobin (g/dL)	14.05 \pm 4.54	13.78 \pm 2.4	0.4
Platelet count/ μL	217000 \pm 98000	189000 \pm 85000	0.05*
Lactate dehydrogenase (U/L)	638 \pm 352	850 \pm 545	0.009
C-reactive protein (mg/L)	1.19 \pm 0.71	1.66 \pm 8.09	0.04*

* $P<0.05$; ** $P<0.01$.

admitted to Ardabil hospitals, in this province with confirmed COVID-19.

We observed the prevalence of COVID-19 is not gender dependent. Another study conducted in Ardabil reported gender difference have less importance as a prognostic factor for death and in the prevalence of COVID-19 (15). Based on several virological findings, it has been reported that some Asian populations may potentially afflicted to COVID-19 than who are lived in other races (16). Furthermore, our results showed that men are more potentially susceptible to COVID-19 than women. In a recent report it has been documented that the male

to female ratio were associated with the contribution of sex hormones and X chromosome related protection, which have a critical role in adaptive and innate immunity (15). However, it may be suggested that the susceptibility of men to disease may have a relationship with their link to work outside the house which is more than women. Furthermore, based on the collecting data which belongs to first of disease simultaneous with the preparation for the New Year in Iranian culture, although women spent more time outside, it has been proposed that they respect to person-to-person contact more than men.

Based on another finding from the current study, we indicated no significant difference in the prevalence of smoking during the first wave of pandemic which consistent with the other study reported lower prevalence of smoke users in COVID-19 patients. Any significant association between smoking and severe condition in COVID-19 patients was observed (17).

Taking aside typical symptoms of the patients into consideration, such as fever, cough, and myalgia our data revealed that symptoms such as abdominal pain, loss of appetite, myalgia, distress, headache, chest pain, weakness, diarrhea, nausea, vomiting are presented in many patients following typical symptoms. Another study in this province reported the most common pulmonary symptoms such as cough and shortness of breath in hospitalized patients (15).

Data from a study in Europe by Lechien et al showed, a significant proportion of patients presented with headache, loss of smell, rhinorrhea and nasal obstruction as the most common symptoms (18). Previously, Bai et al reported atypical symptoms, such as diarrhea and nausea in the patients too (5). Surprisingly, Spinato et al reported that out of 202 confirmed COVID-19 patients, an altered sense of smell or taste in 130 (64.4%) patients was observed (17). These observations can be explained by the proposed theory that different symptoms of disease are several new developed signs that not observed in most patients which may facilitated prevention of the virus spread (7).

In this study we reported high hypertension, diabetes, and cardiovascular disease as the most common coexisting conditions in patients who were died. In a recent study conducted on 138 hospitalized patients, Bai

et al reported this sign as the most common coexisting conditions (5). As mentioned, an overall 15.6% mortality rate was reported among the hospitalized patients with the majority of female hospitalized patients (54 %) and most severe patients were aged over 60 years. This may be due to aging of female population in this study. Other data from previous studies proposed that in this manner such as the high susceptibility to infection in male to female ratio can be associated to the involvement of sex hormones and X chromosome, which plays a fundamental role in adaptive and innate immunity (19). The recent study by Shahriarirad et al indicated that COVID-19 infects men more than women (7).

Aside from the common symptoms of disease, compared with non-intensive care unit (ICU) patients, the most common laboratory abnormalities in our study were lower total lymphocytes and increased lactate dehydrogenase. Although patients who received ICU care had lower total lymphocytes compared to severe patients, the difference was not significant. These data suggest that COVID-19 infection might be due to cellular immune deficiency. We found that patients who had lower O₂ saturation on admission were significantly associated with being severely ill. Furthermore, similar to those previously observed both heart rates and blood pressure were lower in patients who were severely (7). The main reason is derived from the theory that coronavirus affects body systems such as the respiratory system and the cardiovascular system. As previously reported, high levels of myocardial injury biomarkers have been observed in COVID-19 patients' blood samples (10). Another reason for those systems targeted by virus might be related to widely expression of angiotensin-converting enzyme 2 receptors for virus entry in the cardiovascular system and the respiratory system (20). The overall results of vital signs suggest that theses observation at the time of admission play a crucial role in understanding the pandemic.

Some notable limitations in our study either incomplete documentation of the exposure history or laboratory testing of some cases, were due to less timeline for data extraction and training of medical staff who was performed incomplete laboratory testing. The common symptoms of disease such as fever on initial stage of disease makes complicated the diagnosis. Second, it was difficult to assess radiologic data and related data had its own limitations due to incomplete documentation of patients which should be extraction in short time and shortage of trained persons who were medical staff. Therefore, continued observations of the CT of the disease were impossible at hospitalized time. However, due to the incomplete CT records these data were not reported in our study. Finally, the number of infected patients may be much higher than reported here because of limited PCR diagnostic test kits to confirm the cases and involving staff in the hospitals.

Conclusion

In this study on 1152 hospitalized patients, the mean age of patients who were hospitalized, which was 59 (52.8%) years (range 20–100) consisted of 528 (52.8%) males and 473 (47.3 %) females in North West of Iran was reported. Several atypical symptoms which have been developed in patients at the time of admission including weakness, myalgia, agitation, diarrhea, makes the diagnosis difficult. We observed a high significant difference in vital signs in hospitalized severe patients. The current descriptive-analytical study, give rise continuously to understand COVID-19, which should be crucial for the diagnosis, treatment and control of the spreading of the disease. Furthermore, either investigations of more clinical characteristics during hospitalized patients can be developed to resolve this challenge. Finally, improving the identification of clinical features can be effective in combating this challenge.

Limitations of the study

This study was conducted on monitoring the patients at admission. Further studies with following the patients during hospitalization are recommended.

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Authors' contribution

Conceptualization: SM, MD, HGH and ES.

Data collection: SM and LTM.

Methodology: SM and HGH.

Validation: SM, MD, HGH and ES.

Formal analysis: SM and MD.

Investigation: SM and HGH.

Resources: SH and MK.

Data curation: SM, MD, ES.

Writing—original draft preparation: SM, MD and HGH.

Writing—review and editing: SM, MD, HGH and ES.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Ardabil University of Medical Sciences approved this study. The institutional ethical committee at Ardabil University of Medical Sciences approved all study protocols (Ethical code#IR.ARUMS.RWC.1399.006). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D., thesis of Leila Torabi Marjin at this university (Thesis #1003556). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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