

Research Paper

Demographic, Clinical, and Paraclinical Characteristics of the Fourth Surge of the COVID-19 Pandemic in Ardabil Province, Iran



Majid Eterafi¹, Shima Makaremi², Hamidreza Shaker¹, Nasrin Fouladi^{2,3}, Vahid Khaze Shahgoli⁴, Farhad Jeddi⁵, Elham Safarzadeh^{3,6*}

1. Students Research Committee, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
2. Cancer Immunology and Immunotherapy Research Center, Ardabil University of Medical Sciences, Ardabil, Iran.
3. Social Determinants of Health Research Center, Ardabil University of Medical Sciences, Ardabil, Iran.
4. Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
5. Department of Medical Genetics and Pathology, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
6. Department of Microbiology, Parasitology, and Immunology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.



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ABSTRACT

Background: Coronavirus disease-2019 (COVID-19), an infectious disease, has been known as a worldwide pandemic involving many countries, including Iran. Meantime, the analyses of clinical and demographic features of the fourth surge in COVID-19 patients provide a better overview of disease management and mortality reduction.

Objective: This study aimed to identify the effective clinical and demographic hallmarks of the fourth wave of COVID-19 in Ardabil Province, Iran.

Methods: We carried out a population-based analytical cross-sectional study using clinical and demographic characteristics of COVID-19 from February 2021 to May 2021 among confirmed COVID-19 patients who were admitted to the hospital during the fourth surge. Predictors of intensive care unit (ICU) admission and death were evaluated by controlling for intervening variables.

Findings: We evaluated 500 patients, of whom 54.5% were men, and 45.5% were women. Among them, 35.1% of patients had hypertension as the main comorbidity, followed by diabetes (21.4%), cardiovascular disease (8.4%), renal diseases (2.4%), and others. The findings indicated that increasing age has increased mortality among patients with COVID-19. Moreover, our results showed that among the analyzed items, age, sex, and cerebral vascular accident (CVA) were indicated as predictors of ICU admission.

Conclusion: This evaluation demonstrated that old age and comorbidities are two major risk factors for reducing the probability of recovery and increasing admission to the ICU. Therefore, elderly individuals with at least one co-morbidity are at higher risk of becoming infected.

*** Corresponding Author:**

Elham Safarzadeh, PhD.

Address: Department of Microbiology, Parasitology and Immunology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

Phone: +98 (453) 3513419

E-mail: e.safarzadeh@arums.ac.ir

1. Introduction

Over the last two decades, respiratory infectious diseases have been among the most significant global threats and challenges for public health [1]. In December 2019, an emerging coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with an unfamiliar origin, was spreading in the Hubei Province of China. This virus caused a pandemic disease called coronavirus disease-19 (COVID-19). SARS-CoV-2 is considered a global pandemic virus affecting millions of people and resulting in 6.23 million deaths in the world [2]. The viral infection has spread worldwide, prompting the World Health Organization (WHO) to declare a public health emergency of global concern. During the last two decades, coronavirus has caused two large epidemics, first, the SARS coronavirus in 2002-2003, which reported 8,098 confirmed cases and 774 deaths with a 10% mortality rate, and second, the Middle East respiratory syndrome (MERS) coronavirus, which was accompanied by a total of 2,499 laboratory-confirmed cases and 858 deaths with a case fatality rate of around 34.4% between 2012 and 2019 [3].

The manifestations of COVID-19 are characterized by various signs, including mild/asymptomatic to severe and critical forms and death. The typical clinical features included fever (not all), sore throat, cough, headache, breathlessness, fatigue, and myalgia. These conditions can be responsible for severe acute respiratory failure and high mortality rates [4]. Besides, detrimental outcomes and death are more common in older individuals and patients with underlying comorbidities [5]. Therefore, clinicians can identify patients at high risk and require priority therapy to prevent disease progression and unfavorable outcomes by having a better understanding of the possible risk variables in combination with the immunopathology related to COVID-19 severity.

Due to its highly dynamic and unpredictable biological characteristics, which include multiple pandemic surges and developing viral variations that have evolved from the wild type originating in the initial epidemic in China, the COVID-19 pandemic is difficult to prevent. The second and third surges of the continuing pandemic were caused by the B.1.1.7 mutant circulating in the UK, as well as the P.1.5.3. and P1 strains from Africa and Brazil, which are likely to be responsible for the third and fourth surges [6]. The newly discovered SARS-CoV-2 strain B.1.1.7, thought to be 56% more contagious, first appeared in southeast England in November 2020. Therefore, the SARS-CoV-2 virus's B.1.1.7 variation

exhibits greater infectiousness than the wild-type virus, which raises the number of patients in the afflicted areas [7]. Moreover, a new variant, B.1.351, emerged independently of B.1.1.7 and quickly spread in South Africa [8]. Besides, in early January, the novel P.1 SARS-CoV-2 variant was discovered by the Japanese National Institute of Infectious Diseases in passengers returning from Amazonas State, Brazil. According to Coutinho et al. reports, the P.1 variant is approximately 2.6 times more transmissible than the prior circulating variant(s) [9]. The molecular mechanisms underlying the increased transmission and cellular uptake of SARS-CoV-2 variants, including the B.1.1.7 (British), B.1.351 (South African), and P.1 (Brazilian/Japanese) variants are still poorly understood. However, it is interesting to note that the N501Y and D614G mutations are shared by these three variants [7]. This paper was conducted to utilize the clinical manifestations and demographic characteristics of the fourth wave during pandemics to gain more knowledge about clinical management, prevention, and reduction of risks and mortality associated with the COVID-19 pandemic in Ardabil Province, Iran.

2. Materials and Methods

Sample collection and study design

A cross-sectional study was conducted, and demographic and clinical characteristics, along with laboratory findings of 500 COVID-19 patients were collected using the electronic files of the patients and the questionnaires provided by the researcher. These patients were randomly chosen among the 2673 COVID-19 registered cases of patients admitted to Imam Khomeini Hospital in Ardabil from March 21, 2021, to May 21, 2021, the fourth surge of COVID-19 cases in Iran. If the selected patient through random sampling did not meet the inclusion criteria, he/she was replaced by another random sample. Socio-demographic and medical history were obtained using patients' medical records. The required sample size for this study was estimated using the $n = z^2 pq / d^2$ formula, where $z = 1.96$ with a 95% confidence level, $P = 0.33$, $q = 0.67$, and $d = 0.04$.

The main diagnostic methods for COVID-19 confirmation were the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test and computed tomography scan (CT scan). The data were obtained by analyzing the interviews, para-clinical data, clinical evaluation, and taking histories based on interim guidelines from the WHO [10]. The severity of the selected patients' conditions was considered based on their respiratory symptoms, including a respiratory rate (RR) above 30,

O₂ saturation below 93, or blood pressure below 90. All of the cases were enrolled in the current study based on having a history of a positive SARS-CoV-2 PCR nasal swab. All information about current illness symptoms and severity was provided by all participants. Almost all patients stated at least one sign/symptom.

Clinical, laboratory parameters and clinical severity were obtained using questionnaire forms for all involved subjects. To evaluate viral infection by RT-PCR (One-Step RT-PCR Kit, Pishtaz Teb Zaman Diagnostics, Tehran, Iran), nasopharynx samples were provided from clinically suspected patients for COVID-19.

Statistical analysis

Descriptive data were presented as mean±SD for normal distribution. Categorical variables were presented as percentages. Two independent samples were tested by the student t-test. The χ^2 test was performed to compare count data. $P < 0.05$ was considered significant throughout the study.

A regression analysis was performed to determine the predictive role of the studied variables on the probability of death or hospitalization in the intensive care unit (ICU). All variables, that had shown a significant difference between two groups of patients (recovery and death patients, and between ICU hospitalization and non-ICU hospitalization patients) were tested using the binary logistic regression analysis to detect variables predicting ICU hospitalization and death. The dataset analysis was conducted using IBM SPSS statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).

3. Results

Sample characteristics stratified by demographic factors

This present study was conducted on 500 confirmed hospitalized COVID-19 patients during the pandemic period. The study population consisted of 272 men (54.5%) and 228 women (45.5%). Most patients were over the age of 60, and only 0.8% were under the age of 20. Moreover, around 283 individuals (56.7%) were married. Among these, about 81 patients (16.3%) were admitted to the ICU ward, and 419 patients (83.5%) were not admitted to the ICU ward.

Clinical symptoms assessment

In terms of clinical features, the distribution of clinical manifestations in COVID-19 patients was stratified by various clusters based on cardiac and respiratory, neurologic, digestive, and systemic signs. In this context, breathlessness (73.3%) followed by headache (10.8%) and Nausea (15%) were common symptoms among respiratory, nervous, and gastrointestinal symptoms, respectively. As well, cough (47.7%) and fever (26.9%) were usual systemic-related manifestations. Further, the administration and medication status of patients were based on anti-viral (remdesivir [53.3%]), anti-bacterial (meropenem, azithromycin, vancomycin, metronidazole, cefepime, imipenem, and clindamycin [96%]), corticosteroid (serotide, methylprednisolone, and dexamethasone [66.3%]), non-steroidal anti-inflammatory drugs (NSAID) (naproxen [6.2%]).

Association of disease outcomes with clinical and Paraclinical characteristics among patients with COVID-19

In [Table 1](#), we tried to illustrate an overview of ICU, non-ICU patients, and the mortality and recovery rates based on their comorbidities. In this evaluation, the death and recovery rates were different between diverse age groups. The highest rate of ICU admission and the death rate was reported in the age group >60 years. According to this, all patients younger than 20 years had improved, and this trend decreased with age, respectively. Moreover, 23.0% of the female and nearly 11.0% of the male patients were hospitalized in the ICU ward ([Figure 1](#)). Furthermore, our results demonstrated differences in various comorbid diseases among patients. In the case of underlying diseases, hypertension, diabetes mellitus (DM), and cardiovascular disease (CVD) was considered the most common comorbidities. Among these, ICU and non-ICU patients had significantly different rates of chronic obstructive pulmonary disease (COPD) and cerebral vascular accident (CVA). Nevertheless, hypertension, renal diseases (RD), and CVA were significant in the death and recovery group of the study in COVID-19 patients. Besides, differences in the paraclinical variables by participant characteristics are compared in [Table 2](#). According to our results, statistically significant differences were observed between ICU and non-ICU admitted patients regarding white blood cell (WBC), mean corpuscular hemoglobin concentration (MCHC), serum glutamic-oxaloacetic transaminase (SGOT), prothrombin time (PT), partial thromboplastin time (PTT), blood sugar, urea, creatinine, and lactate dehydrogenase (LDH) levels. Moreover, statistically

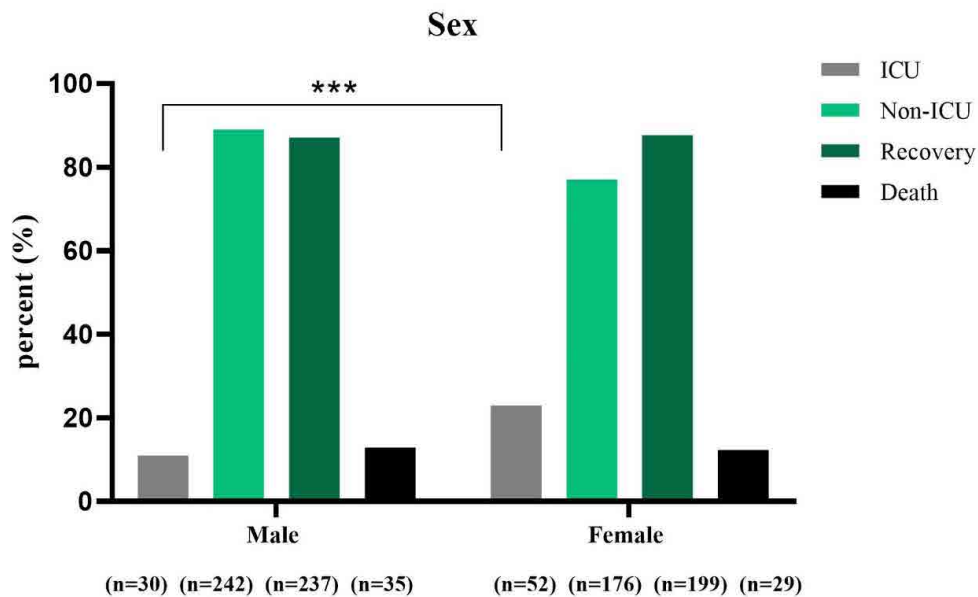


Figure 1. The difference in death and recovery, intensive unit care (ICU) and non-intensive unit care (ICU) admission in terms of sex (***) $P < 0.001$

significant differences were observed between the death and recovery groups of study patients regarding WBC, mean corpuscular volume (MCV), serum glutamic-oxaloacetic transaminase (SGOT), prothrombin time (PT), blood sugar, urea, creatinine, LDH, and creatine phosphokinase (CPK) levels.

Intensive care unit (ICU) admission and death rate associated predictive factors in patients with COVID-19

Among the analyzed items, age, sex, and CVA were indicated as predictors of ICU admission. By controlling the confounding variables in the study, the results

Table 1. Comparison of the frequency of underlying diseases in patients according to the type of hospitalization department and the outcome of the disease

Category	Underlying diseases					P
	ICU	Non-ICU	P	Death	Recovery	
CVD	5(11.9)	37(88.1)	0.405	6(14.3)	36(85.7)	0.735
HTN	34(19.5)	140(80.5)	0.175	29(16.6)	146(83.4)	0.049*
DM	22(20.6)	85(79.4)	0.197	17(15.9)	90(84.1)	0.252
HLP	3(13.0)	20(87.0)	0.648	1(4.3)	22(95.7)	0.220
RD	4(33.3)	8(66.7)	0.111	4(33.3)	8(66.7)	0.029*
COPD	9(39.1)	14(60.9)	0.003*	5(21.7)	18(78.3)	0.178
MI	1(25.0)	3(75.0)	0.644	1(25.0)	3(75.0)	0.454
CVA	5(45.5)	6(54.5)	0.009*	4(36.4)	7(63.6)	0.017*

*Significant differences

Abbreviations: CVA: cerebral vascular accident; CVD: cardiovascular disease; HTN: hypertension; DM: diabetes mellitus; HLP: hyperkeratosis lenticularis perstans; RD: renal diseases; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction

Table 2. Comparison of laboratory findings in patients according to hospitalization department and disease outcome in patients with COVID-19

Variables	Mean±SD/Median (IQR)		P	Mean±SD/Median (IQR)		P
	ICU	Non-ICU		Death	Recovery	
WBC (cells/mm ³)	7166.66±3075.71	5200.00±2600.00	0.000	6783.33±2185.78	5200.00±2700.00	0.000
RBC (million/mm ³)	4.61±0.62	4.78±0.64	0.850	4.47±0.57	4.76±0.65	0.505
HB (g/dl)	12.94±1.75	14.10±3.40	0.069	12.93±2.28	13.90±3.30	0.290
HCT (%)	39.84±5.01	42.30±9.40	0.156	39.08±5.84	42.10±9.00	0.488
MCV (fl)	88.00±5.50	86.54±5.59	0.253	87.00±5.68	86.47±5.45	0.002
MCH (pg)	28.11±1.53	29.00±3.00	0.591	29.00±1.89	29.00±2.00	0.085
MCHC (g/dl)	33.00±1.00	34.00±2.00	0.003	33.00±1.50	33.00±2.00	0.156
PLT (cells/mm ³)	194222.22±71089.34	150000.00±91000.00	0.643	138500.0±61500.0	152000.00±89000.00	0.374
SGOT (IU/L)	61.88±27.22	44.00±30.00	0.000	81.00±51.75	49.00±28.00	0.000
SGPT (IU/L)	40.00±20.98	35.00±25.00	0.723	34.50±29.50	35.00±24.00	0.783
PT (sec)	12.80±1.70	12.50±1.00	0.001	12.55±3.10	12.50±1.00	0.001
INR (Index)	1.00±0.20	1.00±0.10	0.012	1.00±0.20	1.00±0.10	0.011
PTT (sec)	36.44±7.29	32.00±10.00	0.002	33.50±5.08	33.00±10.00	0.109
Blood sugar (mg/dl)	161.22±86.90	109.00±64.00	0.001	96.00±27.75	111.00±68.00	0.006
Urea (mg/dl)	61.00±51.50	37.00±20.00	0.000	113.66±70.50	41.21±17.08	0.000
Creatinine(mg/dl)	1.46±0.99	1.00±0.40	0.048	2.40±1.69	1.00±0.30	0.000
LDH (IU/L)	856.00±395.48	567.59±259.59	0.000	784.83±433.58	545.00±298.00	0.000
CPK (IU/L)	158.88±134.78	94.00±177.00	0.404	277.66±169.37	93.00±146.00	0.012
ESR (mm/hr)	42.44±21.18	37.05±19.87	0.689	45.83±12.57	37.40±20.57	0.813

Abbreviations: ICU: Intensive care unit; WBC: White blood cell; RBC: Red blood cell; HB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelets; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; PT: Prothrombin time; INR: International normalized ratio; PTT: Partial thromboplastin time; LDH: Lactate dehydrogenase; CPK: Creatine phosphokinase; ESR: Erythrocyte sedimentation rate

of the regression analysis showed that decreasing age reduces the probability of the ICU admission rate, and being young has a protective effect on the probability of ICU admission (P=0.02, CI: 0.96-0.99). Moreover, according to our result, the probability of ICU admission for women is 2.52 times higher than for men (P=0.001, CI:1.48-4.27). Among underlying diseases, for the subjects with CVA, the rate of ICU admission was 0.15 times higher than participants without CVA (P=0.009, CI: 0.03-0.62%) (Table 3). The only predictive factor of death in patients was age, young people had a reduced

chance of death, and being young had a protective effect (P<0.001, CI: 0.928-0.968) (Table 4).

4. Discussion

During the recent pneumonia pandemic in January 2020, SARS-CoV-2, known as COVID-19, the seventh human coronavirus, was found in Wuhan, Hubei Province, China. Since the COVID-19 virus spread worldwide, infecting and killing millions of people [11]. This study was conducted on hospitalized cases to identify

Table 3. Variables predicting hospitalization in intensive care unit (ICU) in patients with COVID-19

Variables	B coefficient	Exp (B)	Adjusted (95% CI)		P
			Lower	Upper	
Age	-0.19	0.981	0.965	0.997	0.024*
Sex	0.925	2.522	1.488	4.273	0.001*
CVD	1.068	2.909	0.978	8.655	0.055
HTN	0.357	1.429	0.684	2.987	0.343
DM	-0.223	0.8	0.405	1.581	0.522
HLP	1.016	2.762	0.653	11.688	0.167
RD	-0.785	0.456	0.107	1.941	0.288
COPD	-0.961	0.383	0.140	1.049	0.062
MI	0.380	1.462	0.060	35.313	0.815
CVA	-1.878	0.153	0.037	0.629	0.009*

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Abbreviations: CVA: Cerebral vascular accident; CVD: Cardiovascular disease; HTN: Hypertension; DM: Diabetes mellitus; HLP: Hyperkeratosis lenticularis perstans; RD: Renal diseases; COPD: Chronic obstructive pulmonary disease; MI: Myocardial infarction

Table 4. Variables predicting death in patients with COVID-19

Variables	B Coefficient	Exp (B)	Adjusted (95% CI)		P
			Lower	Upper	
Age	-0.055	0.947	0.928	0.967	0.000*
Sex	-0.110	0.895	0.496	1.615	0.714
CVD	0.611	1.842	0.662	5.124	0.242
HTN	0.068	1.07	0.464	2.470	0.874
DM	-0.131	0.877	0.418	1.842	0.729
HLP	2.503	12.21	0.829	180.021	0.068
RD	-1.335	0.263	0.060	1.163	0.078
COPD	-0.938	0.391	0.114	1.345	0.136
MI	-0.116	0.89	0.054	14.631	0.935
CVA	-1.394	0.248	0.058	1.052	0.059

*Significant differences

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Abbreviations: CVA: cerebral vascular accident; CVD: cardiovascular disease; HTN: hypertension; DM: diabetes mellitus; HLP: hyperkeratosis lenticularis perstans; RD: renal diseases; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction

the effective factors for preventing and lowering severe conditions and mortality in COVID-19 patients based on demographic information. To our knowledge, this cross-sectional study was the first study focusing on hospitalized COVID-19 patients in Ardabil Province, Iran. The results of this study demonstrated that patients with CVA were more likely to be hospitalized in the ICU than individuals without this underlying illness. In the case of gender, significant results were also shown that the probability of ICU admission is higher for women than for men. Besides, older patients were less likely to recover than younger patients and were more likely to be admitted to the ICU.

According to the results, the elderly over 60 years of age constituted the majority of hospitalized patients. Further, the number of old patients admitted to the ICU was higher compared with other age groups. This result was consistent with the outcome of other research that showed that old age was associated with an incremented risk of COVID-19 fatality [12]. Moreover, another study found that older age was correlated with death in hospitalized SARS-CoV-2-infected patients [13]. Therefore, the age factor may have a very effective effect on the rate of recovery of patients and their hospitalization in the ICU. In the case of the sex of patients, a significant association was observed between male and female groups in the rate of ICU admission. The probability of ICU admission is significantly higher for women than for men. However, based on other studies, men were more likely than women to be hospitalized in the ICU [14, 15]. Besides, other research implicated that the mortality rate was higher in men than in women [16-18].

In our study, underlying diseases including hypertension, DM, and CVD were stratified as the most common comorbidities. According to other research, COVID-19 patients with comorbidities, such as hypertension or diabetes are more likely to have a more severe status and progression of the disease [5]. Moreover, a meta-analysis study from Iran illustrated that hypertension (21.1%), DM (16.3%), CVDs (14.0%), and chronic kidney disease (CKD) (5.0%) were the most common comorbidities among the SARS-CoV-2 infected patients [19]. Besides, another research stated that hypertension, DM, and bronchial asthma were the most frequent co-morbidities [20]. Meanwhile, COPD and CVA were significant between ICU and non-ICU patients. Based on the meta-analysis study, the population with COPD is at higher risk of the severe form and worse progression of COVID-19 [21]. The present study demonstrated the underlying disease may be associated with a poor outcome in patients with COVID-19. Nevertheless,

RD and CVA were the most common causes of death in COVID-19 patients in this investigation. Diabetes, hypertension, pneumonia, obesity, immunosuppression, and end-stage kidney disease were the most frequently mentioned reasons in other studies [22]. Another study demonstrated that patients with confirmed COVID-19 and comorbidities, such as hypertension (23.7%) followed by DM (16.2%), coronary heart disease (5.8%), and cerebrovascular disease (2.3%) showed the severe form of the disease [23]. Furthermore, another study reported a similar result, which showed that the occurrence of comorbidities was higher in the critical and severe categories than in the moderate group [24]. Overall, based on previous reports, aged individuals who have chronic health issues, such as diabetes, cardiovascular disease, or lung disease are at a higher risk of both acquiring serious forms of diseases and death. In this evaluation, shortness of breath, headache, and nausea were observed as the main clinical presentations associated with cardiac and respiratory, neurologic, and gastrointestinal signs, respectively. Besides, among the symptomatic manifestation, fever, cough, and lethargy were the most prevalent indicators. Whereas, in Rodriguez-Morales et al.'s study, fever (88.7%), cough (57.6%), and dyspnea (45.6%) were the most common signs [25]. The observed inconsistency may be due to differences in the study population and conditions.

Compared to paraclinical data, patients with higher blood sugar levels had a higher rate of hospitalization in the ICU compared to other patients. Furthermore, people with high blood sugar had a higher mortality rate than those with low blood sugar. This finding is consistent with other studies showing that people with diabetes are at increased risk for mortality and severe COVID-19 disease. Moreover, other laboratory findings, such as LDH and urea concentrations, were significant in the ICU and death groups. Another important finding was that the rate of WBC was significantly higher among patients admitted to the ICU compared to non-ICU patients, as well as mortality rate. This finding supports the previous results that demonstrated the high count of WBC in severe cases of SARS-CoV-2 infection [26]. Therefore, patients with more severe forms of the disease have a higher WBC count. Further, the creatine phosphokinase (CPK) rate in the death group was significantly higher compared to the recovery group. A significant relationship was observed in C-reactive protein (CRP) in the recovery and death groups. Moreover, in a study, elevated CRP and lymphopenia were reported as the most common abnormal laboratory results in patients with COVID-19 [18]. In addition, a retrospective cohort study showed that a CRP level higher than 100 mg/dL during hospitalization may

predict higher odds of hospital death. Specifically, when comparing individuals with high CRP (>101 mg/dl) to those with low CRP (<100 mg/dL), the unadjusted risks of in-hospital mortality were considerably greater [27]. However, no significant correlation was found between creatinine variables in the ICU and non-ICU, or between mortality and creatinine variables. In contrast, a previous study reported an elevated creatinine level in severe COVID-19 old patients [26].

In the case of management and administration of COVID-19 disease, we found that most COVID-19 patients were treated with antibiotics (96%). Moreover, corticosteroids (66.3%) and antiviral drugs (53.3%) were ranked next. Also, remdesivir as an antiviral drug was the only one widely used by patients. These administrations for COVID-19 disease were similar to those in other studies [20].

5. Conclusion

In this study, we determined the demographics and clinical manifestations of admitted COVID-19 patients in Ardabil Province, Iran. Compared to total patients, elderly patients with comorbidities were more likely to be admitted to the ICU and at a higher risk of death than other patients. The current findings suggest that underlying disease and old age are crucial risk factors in the exacerbation of COVID-19 disease. Moreover, a significant percentage of admitted COVID-19 patients have received antibiotics as their main treatment, followed by corticosteroids, and antiviral drugs. Therefore, it can be concluded that age and comorbidity are strongly associated with ICU hospitalization and the death rate of COVID-19 patients. The limitation of the study was the limited population, therefore studies with a larger population are needed for better disease management based on demographic features and clinical indications during the COVID-19 pandemic.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the regional research Ethics Committee of the **Ardabil University of Medical Sciences**, Ardabil, Iran (IR.ARUMS.REC.1400.047).

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Authors' contributions

Conceptualization, reviewing and editing, and project administration: Elham Safarzadeh; Data gathering and resource investigation: Majid Eterafi; Resource investigation, writing- original draft preparation: Shima Makaremi; Data curation, visualization: Farhad Jeddi; Methodology and analysis: Nasrin Fouladi. Analysis: Vahid Khazae; Data gathering: Hamidreza Shaker.

Conflict of interest

The authors declared no conflict of interest.

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