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Investigating the Association between COVID-19 Prognosis and Demographic and Clinical Features, Underlying Diseases, and Drug and Supplement Use in Patients Hospitalized in Zabol, Iran: A Single-Center Retrospective Study

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ABSTRACT

Backgrounds: The primary goal of this study was to identify the potential association between COVID-19 prognosis and demographic and clinical features, underlying diseases, and drug and supplement use in patients admitted to Amir al-Momenin hospital in Zabol.
Materials & Methods: This retrospective study surveyed the electronic health records of 848 COVID-19 patients hospitalized in a tertiary referral hospital in southeastern Iran from the beginning of the COVID-19 outbreak until the end of February 2021. Univariate and multiple analytical tests including unconditional and penalized logistic regressions were used for statistical analysis.
Findings: Out of a total of 848 patients, 371 (43.75%) patients were female, and 477 (56.25%) patients were male. Age, underlying pulmonary and cardiovascular diseases, and loss of consciousness predicted a higher mortality rate. On the contrary, a negative chest X-ray was associated with a lower risk of death.
Conclusion: Identifying predisposing factors of mortality in COVID-19 patients will help physicians provide more intensive care to those at higher risk of death by classifying patients based on risk factors and underlying diseases.

Keywords: COVID-19, Coronavirus, Infection, SARS-CoV-2, Prognosis

CITATION LINKS

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Introduction

Originating in Wuhan, China in December 2019, the latest coronavirus began to spread at an unprecedented pace shortly after the primary reports, causing a global health problem [1, 2]. The lesser common form of pneumonia caused by this newly identified coronavirus resulted in symptoms and mortality rates that differed significantly from those of community-acquired pneumonia. Initially recognized as 2019 novel coronavirus or 2019-nCoV, this strain was later named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses [3]. The misfortunate combination of high infectivity and inaccessibility to any known medical treatment prompted the medical community to adopt repositioning or repurposing of presently approved pharmaceuticals as an alternative solution, enabling healthcare specialists to clinically manage COVID-19 with well-known available drugs [4-6].

An incubation time of 3–7 days has been reported for COVID-19, which may appear as an asymptomatic disease to a critical infection. The main symptoms are fever, sore throat, dry cough, fatigue, and in some cases nasal congestion, rhinorrhea, malaise, and myalgia. In some cases of critical illness, life-threatening symptoms such as ARDS (acute respiratory distress syndrome); septic shock; lymphopenia; cardiac, renal, and hepatic damage; and bleeding disorders have also been reported. As a result of high expression level of ACE-2 receptors in the gastrointestinal tract, specifically the small intestine, gastrointestinal disorders such as pain, anorexia, nausea, vomiting, and diarrhea may be observed [7, 8].

Remdesivir (GS-5734), an RNA-dependent RNA polymerase inhibitor, has been reported to be effective against a broad spectrum of viruses such as MERS (Middle East respiratory syndrome) and SARS (severe acute respiratory syndrome) coronaviruses [9]. Chloroquine and hydroxychloroquine, both antimalarial agents, have been found to exert anti-SARS-CoV-2 activity *in vitro* and have immunomodulatory effects [10, 11]. Given the uncertainty about an appropriate treatment method for COVID-19, the illness was initially inevitably managed at the discretion of clinicians, particularly during the early days of the pandemic [12]. During this period, some medications were accepted in the hospital for symptom-based treatment, such as HIV protease inhibitors (e.g., lopinavir/ritonavir), which were known for their potential activity against other coronaviruses in animal models [13]. Favipiravir, an RNA-dependent RNA polymerase inhibitor, was already known for its therapeutic effects against RNA viruses; thus, it was postulated to be an effective drug to inhibit SARS-CoV-2 as a single-stranded RNA virus. In addition, antibacterial agents from the Macrolide family, such as azithromycin, were anticipated to mitigate superimposed bacterial infection and induce immunomodulatory effects as an adjunct therapy [14, 15]. Anti-interleukin-1 agents, including anakinra and canakinumab, were also proposed for the management of hyper-inflammatory reactions caused by COVID-19, owing to their inhibitory effects on interleukin-1 receptors [16]. Another applied strategy was convalescent plasma therapy, in which plasma collected from recovered patients was used for therapeutic purposes based on the rationale that it might contain anti-SARS-CoV-2 antibodies [8].

The World Health Organization (WHO) has estimated the case fatality rate (CFR) from COVID-19 at 3.8% [17]. In a report of 72314 patients in China, the CFR was reported to be 2.3% [18]. A retrospective cohort study on Iranian patients showed 24.4% in-hospital mortality within 30 days [19]. In another Iranian study, the mortality rate of COVID-19 patients was 17.9%, and about half of these patients were in

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the intensive care unit (ICU) [20]. Studies have shown that diabetes, chronic respiratory diseases, high blood pressure, cardiovascular diseases, chronic kidney diseases, and cancer are the most common co-morbidities in hospitalized COVID-19 patients. In addition, male gender, older age, and underlying diseases have been shown to have a significant relationship with mortality [21, 22]. Also, leukocytosis, high lactate dehydrogenase levels, cardiac injury, hyperglycemia, and high-dose corticosteroid use have been shown to be associated with mortality in patients with severe COVID-19 [23]. Investigating the epidemiological characteristics of COVID-19 and evaluating the underlying diseases of infected patients and the effectiveness of drugs and supplements could help decision-makers, health authorities, and healthcare professionals to take initiatives to reduce the burden of this infectious disease and thereby control this epidemic [24]. Although several studies have recently been conducted to report some epidemiological features of this disease worldwide, few studies have evaluated these important factors in Iranian populations, especially in southeastern Iran. **Objectives:** This study was conducted with the aim of investigating some epidemiological and clinical characteristics of COVID-19 as well as factors related to mortality in a sample of the Iranian population by investigating confirmed COVID-19 cases among all patients admitted to Amir al-Momenin hospital in Zabol, Iran.

Materials and Methods

Study design: This retrospective study was conducted on the electronic health records of 848 COVID-19 patients registered in the hospital information system (HIS) of a tertiary referral hospital in southeastern Iran from the beginning of the COVID-19 outbreak until the end of February 2021. The statistical population included all patients diagnosed with RT-PCR-confirmed COVID-19 and hospitalized in Amir al-Momenin hospital in Zabol, including both recovered and deceased patients.

Data collection: The study was conducted in the hospital following infection control instructions and using personal protective clothing. The archived files of hospitalized COVID-19 patients were reviewed, and their clinical and demographic data were retrieved using the hospital information system. These data included age, gender, underlying medical issues, duration of hospitalization, clinical signs and symptoms on admission, radiological assessment findings, and pharmacological regimens used. A checklist of demographic information, underlying factors, and clinical signs and symptoms was also completed for each participant.

Statistical analysis: Univariate and multiple analytical tests including unconditional and penalized logistic regressions were performed to statistically analyze the association between survival (dependent variable) and demographic variables (independent variables). Age and sex were adjusted for multiple logistic regression. All analyses were performed using Stata software (Version 16, Stata Corp, College Station, Texas, USA), and the significance level was considered to be 0.05.

Findings

A total of 848 COVID-19 patients were included in this study, of whom 169 (19.93%) patients died, and 679 (80.07%) patients survived. The mean age of recovered patients was 50.08 ± 16.90 years, and the mean age of patients who died was 64.94 ± 16.28 years. The sex ratio was roughly equal between decreased and recovered patients. Also, 12% of recovered patients (85 patients) and 37% of decreased persons (61 patients) were rural residents. Moreover, 50% of those who died were hospitalized in the intensive care unit,

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Table 1) Association of demographic and clinical features with COVID-19 mortality by logistic regression analysis (adjusted and unadjusted logistic regression analysis)

Characteristic	OR[a](95% CI)	*P Value*	OR[b](95 % CI)	*P Value*
Demographic				
Age range (years)				
<35	1.00 (Ref)			
35-45	1.50 (0.57-3.94)	.404	1.37 (0.51-3.68)	.532
46-55	3.32 (1.40-7.86)	.006	3.2 (1.28-7.96)	.012
56-65	3.34 (1.43-7.78)	.005	3.04 (1.23-7.5)	.016
>65	4.28 (1.89-9.66)	< .001	3.7 (1.52-9.21)	.004
Sex				
Female	1.00 (Ref)			
Male	0.94 (0.66-1.31)	.721		
Blood type				
O	1.00 (Ref)			
AB	0.94 (0.39-2.30)	.906		
B	1.22 (0.68-2.20)	.497		
A	0.96 (0.59-1.54)	.867		
Comorbidity				
None	1.00 (Ref)			
Smoking	2.87 (1.56-5.27)	.001	2.19 (1.15-4.19)	.4
Mental illness	2.75 (0.91-8.31)	.072	3.17 (0.94-10.5)	.061
Pulmonary disease	1.48 (0.70-3.13)	.299	1.5 (0.48-2.37)	.04
Diabetes	2.86 (1.65-4.95)	< .001	1.51 (0.8-2.84)	.197
Surgrey	1.24 (0.48-3.18)	.654	0.75 (0.27-2.04)	.586
Cancer	2.20 (0.42-11.37)	.345	1.72 (0.311-9.5)	.533
Hypertension	1.48 (0.66-3.34)	.334	0.78 (0.32-1.91)	.593
Cardiovascular disease	2.14 (1.25-3.64)	.005	1.27 (0.69-2.3)	.05
Immunodeficiency	2.40 (0.72-7.98)	.151	1.40 (0.39-4.98)	.6
Hyperlipidemia	0.88 (0.41-1.87)	.744	0.52 (0.22-1.19)	.123
Chest X-ray				
Positive	1.00 (Ref)			
Less than 20% of lung involvement	0.43 (0.25-0.72)	.002	0.41 (0.23-0.69)	.001
Negative	0.24 (0.12-0.50)	< .001	0.24 (0.12-0.51)	.000
Transmission route				
Direct contact	1.00 (Ref)			
Travel	0.70 (0.34-1.46)	.351		

a, crude risk ratio
b, adjusted risk ratio for age and gender

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Table 2) Association of symptoms with COVID-19 mortality based on logistic regression analysis (adjusted and unadjusted logistic regression analysis)

Symptoms	OR[a](95% CI)	*P Value*	OR[b](95 % CI)	*P Value*
Loss of consciousness	1.15 (0.59, 2.25)	.005	1.20 (0.51 , 2.01)	.004
Cough	0.88 (0.59 , 1.31)	.541	0.81 (0.54 , 1.23)	.337
Dyspnea	1.31(0.81 , 2.14)	.264	1.34 (0.82 , 2.20)	.239
Diarrhea	0.89 (0.55, 1.44)	.649	0.86 (0.53 , 1.41)	.574
Headache	0.94 (0.57 , 1.26)	.821	0.95 (0.57 , 1.56)	.846
Myalgia	0.73 (0.42 , 1.26)	.265	0.75 (0.43 ,1.31)	.324
Nausea	0.99 (0.58 , 1.68)	.971	1.00 (0.58 , 1.72)	.988
Weakness	0.89 (0.49 , 1.64)	.730	0.85 (0.46 , 1.57)	.607
Chest pain	0.79 (0.45 , 1.39)	.425	0.83 (0.47 , 1.48)	.541
Loss of smell	0.82 (0.45 , 1.50)	.531	0.89 (0.48 , 1.65)	.730
Fever	1.20 (0.82 1.76)	.326	1.23 (0.83 , 1.81)	.284
Anorexia	1.28(0.63 , 2.57)	.488	0.89 (0.431.83)	.775
Nasal congestion	1.00 (0.43 , 2.34)	.991	1.08 (0.45 , 2.55)	.858

a, crude risk ratio
b, adjusted risk ratio for age and gender

while only 8% of recovered patients (54 patients) were hospitalized in the ICU.

Association between demographic and clinical features, underlying diseases, and drug and supplement use and COVID-19 mortality based on univariate logistic regression analysis: The results of simple logistic regression analysis without adjusting confounders showed that age, cigarette smoking, diabetes, and cardiovascular diseases increased the risk of death. In addition, patients with a negative chest X-ray had a higher chance of survival than those with a positive chest X-ray (Table 1). Patients who referred to the hospital with symptoms such as decreased level of consciousness and shortness of breath had a higher risk of death, whereas patients who presented to the hospital with early symptoms of diarrhea and muscle pain had a lower risk of death (Table 2). Regarding the prescribed drugs, fewer deaths were observed among people using vitamin C, vitamin D, thiamine, omega-3, calcium citrate, vitamin B complex, zinc, naproxen, aspirin, famotidine, loperamide, melatonin, cefazolin, atorvastatin, nasal cannula, acetylcysteine, bromhexine, expectorant, dextromethorphan, budesonide/formoterol, budesonide, diphenhydramine, dexamethasone, and doxycycline. However, more deaths were observed among people using gabapentin, methadone, fentanyl, dopamine, heparin, enoxaparin, methylprednisolone, aminophylline, ipratropium bromide, ipratropium/salbutamol, salbutamol, and ceftriaxone (Table 3).

Association between demographic and clinical features, underlying diseases, and drug use and COVID-19 mortality based on multiple logistic regression analysis: Possible confounding variables in the multiple regression model were analyzed, and the findings are presented in the tables. The risk of death was 3.7 times higher in patients over 65 years of age compared

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Table 3) Association between drug and supplement use and COVID-19 mortality (adjusted and unadjusted logistic regression analysis)

Drugs and Supplements	OR[a](95% CI)	*P Value*	OR[b](95 % CI)	*P Value*
Colchicine	1.26 (0.58, 2.71)	.554	1.27 (0.58 , 2.74)	.541
Vitamin C	0.14 (0.09 , 0.21)	< .001	0.13 (0.09 , 0.21)	< .001
Vitamin D	0.11 (0.08 , 0.17)	< .001	0.11 (0.08 , 0.17)	< .001
Thiamine	0.08 (0.01, 0.60)	.014	0.07 (0.01 , 0.58)	.013
Omega 3	0.26 (0.13 , 0.50)	< .001	0.25 (0.13 , 0.49)	< .001
Calcium citrate	0.28 (0.15 , 0.52)	< .001	0.28 (0.15 ,0.53)	< .001
B complex	0.50 (0.34 , 0.73)	< .001	0.50 (0.34 , 0.73)	< .001
Zinc	0.19 (0.11 , 0.32)	< .001	0.19 (0.11 , 0.32)	< .001
Acetaminophen	0.72 (0.51 , 1.01)	.063	0.73 (0.52 , 1.03)	.082
Acetaminophen codeine	1.50 (0.93 , 2.42)	.090	1.51 (0.93 , 2.43)	.088
Naproxen	0.47 (0.31 , 0.69)	< .001	0.46 (0.31 , 0.69)	< .001
Gabapentin	2.65 (1.63 , 4.32)	< .001	2.66 (1.63, 4.34)	< .001
Methadone	3.86 (1.67 , 8.93)	.002	3.83 (1.65 , 8.86)	.002
Dopamine	240.71 (51.86,4281.82)	< .001	241.81 (52.04,4303.11)	< .001
Heparin	1.48 (1.03 , 2.12)	.030	1.50 (1.04 , 2.15)	.027
Enoxaparin	7.58 (2.50 , 22.93)	< .001	7.75 (2.55 , 23.54)	< .001
Aspirin	0.46 (0.32 , 0.66)	< .001	0.45 (0.31 , 0.65)	< .001
Famotidine	0.23 (0.16 , 0.33)	< .001	0.23 (0.16 , 0.32)	< .001
Pantoprazole	0.71 (0.44 , 1.15)	.172	0.73 (0.45 , 1.17)	.201
Loperamide	0.50 (0.30 , 0.83)	.007	0.51 (0.30 , 0.84)	.009
Methylprednisolone	1.99 (1.38 , 2.87)	< .001	1.98 (1.37 , 2.87)	< .001
Alprazolam	0.74 (0.50 , 1.11)	.158	0.75 (0.50 , 1.13)	.176
Diazepam	3.04 (0.67 , 13.75)	.147	3.16 (0.69 , 14.35)	.136
Melatonin	0.27 (0.16 , 0.45)	< .001	0.26 (0.16 , 0.45)	< .001
Cefazolin	0.17 (0.05 , 0.56)	.004	0.17 (0.05 , 0.57)	.004
Atorvastatin	0.38 (0.26 , 0.55)	< .001	0.38 (0.26 , 0.55)	< .001
Nasal cannula	0.28 (0.18 , 0.42)	< .001	0.28 (0.18 , 0.43)	< .001
Aminophylline	3.67 (2.12 , 6.36)	< .001	3.72 (2.14 , 6.46)	< .001
Montelukast	0.16 (0.21 , 1.20)	.076	0.15 (0.02 , 1.17)	.072
Acetylcysteine	0.15 (0.05 , 0.42)	< .001	0.15 (0.05 , 0.41)	< .001

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Table 3) Association between drug and supplement use and COVID-19 mortality (adjusted and unadjusted logistic regression analysis)

Drugs and Supplements	OR[a](95% CI)	*P Value*	OR[b](95 % CI)	*P Value*
Bromhexine	0.53 (0.36 , 0.78)	.001	0.52 (0.35 , 0.76)	.001
Expectorant	0.31 (0.18 , 0.52)	< .001	0.32 (0.19 , 0.54)	< .001
Dextromethorphan	0.42 (0.28 , 0.64)	< .001	0.43 (0.28 , 0.65)	< .001
Ipratropium bromide	3.79 (1.85 , 7.76)	< .001	3.71 (1.80 , 7.64)	< .001
Ipratropium/Salbutamol	3.60 (2.47 , 5.27)	< .001	3.58 (2.45 , 5.24)	< .001
Salbutamol	3.37 (2.20 , 5.15)	< .001	3.43 (2.24 , 5.27)	< .001
Budesonide/ Formoterol	0.31 (0.11 , 0.87)	.027	0.31 (0.11 , 0.87)	.027
Budesonide	0.12 (0.01 , 0.95)	.045	0.12 (0.01 , 0.95)	.044
Fluticasone/Salmeterol	1.61 (0.78 , 3.32)	.189	1.66 (0.80 , 3.42)	.170
Diphenhydramine	0.63 (0.41 , 0.97)	.036	0.65 (0.42 , 0.99)	.049
Nicotin gum	1.07 (0.35 , 3.27)	.901	1.11 (0.36 , 3.42)	.847
Nicotin patch	1.45 (0.71 , 2.95)	.300	1.43 (0.70 , 2.91)	.323
Fentanyl	8.29 (2.05 , 33.51)	.003	7.87 (1.93 , 32.02)	.004
Azithromycin	1.19(0.67,2.11)	.535	1.29(0.72,2.31)	.381
Remdesivir	1.21(0.76,1.93)	.417	1.16(0.72,1.87)	.527
Favipiravir	0.64(0.37,1.09)	.105	0.62(0.36,1.07)	.088
Interferon	1.07(0.61,1.85)	.806	1.04(0.59,1.82)	.877
Dexamethasone	0.61(0.42,0.88)	.009	0.61(0.42,0.89)	.011
Sofosbuvir/Daclatasvir	0.97(0.63,1.50)	.916	0.99(0.64,1.53)	.979
Hydroxychloroquine	1.14(0.71,1.83)	.572	1.15(0.71,1.86)	.549
Doxycycline	0.65(0.43,0.99)	.049	0.67(0.44,1.02)	.068
Lopinavir	1.006(0.68,1.47)	.975	1.01 (0.68,1.49)	.952
Tocilizumab	0.76(0.43,1.33)	.344	0.76(0.43,1.35)	.358
Oseltamivir	1.09(0.68,1.74)	.717	1.01 (0.63,1.63)	.948
Ceftriaxone	1.62(1.06,2.47)	.024	1.60(1.04,2.46)	.030

a, crude risk ratio
b, adjusted risk ratio for age and gender

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to those under 35 years of age (adjusted risk ratio: 3.70, 95% CI: 1.52-9.21). Accordingly, the risk of death in patients aged 35 to 45 years was 1.37 times higher than in people under 35 years old (adjusted risk ratio: 1.37, 95% CI: 0.51-3.68). In addition, the risk of death in patients aged 45-55 years was 3.2 times higher than in participants younger than 35 years (adjusted risk ratio: 3.2, 95% CI: 1.28-7.96) (Table 1).

Investigating the underlying comorbidities of patients with COVID-19 indicated that the risk of death in participants with lung and heart diseases was about 1.5 and 1.27-fold compared to those without these diseases, respectively. No significant association was observed between COVID-19 survival and other comorbidities. In the radiological assessment of the lungs by chest X-ray, it was found that the risk of death was lower in patients with a negative chest X-ray (non-involvement of the lungs) (0.24 fold) compared to those with a positive chest X-ray (0.41 fold) (Table 1).

Symptoms such as decreased level of consciousness predicted a higher mortality rate (Table 2). Regarding the prescribed drugs, fewer deaths were observed among people using vitamin C, vitamin D, thiamine, omega-3, calcium citrate, vitamin B complex, zinc, naproxen, aspirin, famotidine, loperamide, melatonin, cefazolin, atorvastatin, nasal cannula, acetylcysteine, bromhexine, expectorant, dextromethorphan, budesonide/formoterol, budesonide, diphenhydramine, dexamethasone, and doxycycline. However, more deaths were observed among people using gabapentin, methadone, fentanyl, dopamine, heparin, enoxaparin, methylprednisolone, ipratropium bromide, ipratropium/salbutamol, salbutamol, aminophylline, and ceftriaxone (Table 3).

Discussion

The present study aimed to investigate the association between COVID-19 mortality and demographic and clinical factors, underlying diseases, and prescribed drugs in a population of COVID-19 patients admitted to Amir al-Momenin hospital in Zabol.

The results showed that the mortality rate was significantly higher in patients over 65 years old compared to those under 35 years old ($p< .004$). Of the 848 COVID-19 patients, 93 (10.93%) participants were under 35 years of age, of whom seven (7.53%) patients died. Also, 294 (34.67%) participants were over 65 years old, of whom 76 (25.85%) patients died. Based on these results, age was positively associated with COVID-19 mortality. Studies have confirmed that COVID-19 mortality is associated with age. Zheng et al. (2020) in their investigation of 161 COVID-19 patients reported an average age of 45 years for COVID-19 mortality [25]. A systematic review by Rodriguez-Morales et al. (2020) concluded that the mean age of COVID-19 patients was 51.97 years based on the results of 18 studies [26]. Therefore, older age is considered as a risk factor for poor clinical outcome in the case of COVID-19. Of the 848 patients surveyed in this study, 371 (43.75%) patients were female, and 477 (56.25%) patients were male. Among all investigated cases, 169 cases of death were registered, of whom 76 (44.97%) cases were female, and 93 (55.03%) cases were male. Chen et al. (2020) found that men were slightly more susceptible to contracting COVID-19 than women [27]. However, studies by Li et al. (2020) and Du et al. (2020) on deceased patients have shown that susceptibility to contracting COVID-19 is relatively higher among women, which is not in agreement with the results of the present study [23, 28].

It was found that patients with at least one underlying disease were at higher risk of death compared to those without any underlying disease. Lung and heart diseases

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increased the risk of death by 1.5 and 1.27 times, respectively. Li et al. reported that most deceased patients had at least one underlying disease, and comorbidities such as hypertension, heart diseases, and diabetes were more prevalent in deceased patients [23]. Since older people are more vulnerable to mortality, and existing underlying diseases are more common in this age group, the risk of death is anticipated to increase among these cases, which was confirmed in the present study [18]. In another study, preliminary investigations showed that people with underlying diseases were at higher risk of COVID-19-associated complications and mortality. Roughly 50% of hospitalized patients with suspected COVID-19 had other chronic diseases as well. In addition, about 40% of hospitalized patients with confirmed SARS-CoV-2 infection had cardiovascular or cerebrovascular diseases [18]. Another study demonstrated that the three major predictors of COVID-19 mortality were male sex, old age (>60), and underlying diseases including diabetes, hypertension, chronic respiratory disease, and cancer [29]. The results of a study on 128 hospitalized adults with COVID-19 showed that 49% suffered from hypertension, 48.3% from chronic respiratory disease, and 28.3% from diabetes. Based on the results, most of the patients who referred to the hospital were elderly and had at least one underlying disease [30].

In terms of chest X-ray findings, 67.18% of patients had lung involvement, and 83.13% of deceased patients were included in this category. In addition, 18.36% of participants had lung involvement below 20%, a category in which 11.45% of deceased patients were included. Lastly, 14.45% of admitted patients had no lung involvement, which included 5.42% of deceased patients as well. Considering the time of referring to the hospital after the onset of initial symptoms, deceased patients had an average referral delay of 8.1 days with an average oxygen saturation of 90.3%, while recovered patients had an average referral delay of 4.71 days with an average oxygen saturation of 93.4%. Therefore, an inclination to overlook the serious nature of the disease was observed in deceased patients, which ultimately resulted in severe lung involvement and increased mortality. A systematic review based on the results of 35 studies demonstrated that the presence of consolidation on chest X-ray, hypoxemic respiratory failure, and lower oxygen saturation during hospitalization were the risk factors for death [31].

Regarding the prescribed drugs, fewer deaths were observed among people using vitamin C, vitamin D, thiamine, omega-3, calcium citrate, vitamin B complex, zinc, naproxen, aspirin, famotidine, loperamide, melatonin, cefazolin, atorvastatin, nasal cannula, acetylcysteine, bromhexine, expectorant, dextromethorphan, budesonide/formoterol, budesonide, diphenhydramine, dexamethasone, and doxycycline. However, more deaths were observed among people using gabapentin, methadone, fentanyl, dopamine, heparin, enoxaparin, methylprednisolone, ipratropium bromide, ipratropium/salbutamol, salbutamol, aminophylline, and ceftriaxone. The most important drugs used in the treatment of severe COVID-19 cases in Zabol Amir al-Momenin hospital included dexamethasone, favipiravir, remdesivir, tocilizumab, interferon, sofosbuvir/daclatasvir, lopinavir, and oseltamivir. Among these drugs, only dexamethasone was able to reduce the mortality rate. Despite many studies on the effectiveness of antiviral drugs in the treatment of COVID-19, the effectiveness of these drugs in the treatment of severe cases of this disease has not yet been proven [32]. Dexamethasone is a corticosteroid drug used in a broad spectrum of conditions because of its anti-inflammatory and immunosuppressive effects. In a ran-

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domized trial, 6 mg of dexamethasone was used orally or intravenously to reduce the progression of respiratory failure and death in patients with COVID-19; in this study, 2,104 patients were treated with dexamethasone (test group), while 4,321 patients received the same regimen minus dexamethasone (control group). Overall, 482 patients (22.9%) in the test group and 1,110 patients (25.7%) in the control group died within 28 days. Generally, the use of dexamethasone led to a lower mortality rate among patients who received mechanical ventilation or oxygen alone, while no such effects were reported for patients who did not receive respiratory support. The results of this study are consistent with the present study results [33].

In the present study, the risk of death in patients who referred with symptoms of decreased level of consciousness was 1.2 times higher than in those without these symptoms. Regarding the clinical symptoms at the time of admission, fever was the most common symptom in all patients, followed by shortness of breath. The prevalence of diarrhea was significantly higher in patients who recovered, while decreased level of consciousness was more frequent in patients who died (p< .05). Wu et al. (2020) found that the most common clinical symptoms of COVID-19 patients were fever and cough [34]. Another study reported that the most common complaints were fever and cough, followed by muscle pain and fatigue [35]. However, some investigations have reported the prevalence of dyspnea (shortness of breath) among most patients. Du et al. (2020) showed that early onset of dyspnea may indicate a poor prognosis of the disease [28].

In the present study, decreased level of consciousness was significantly more prevalent among deceased patients. The obtained results are in agreement with those of another research by Wang et al. (2020), who compared ICU and none-ICU hospitalized patients [36]. By examining the clinical signs and symptoms of deceased patients, it was revealed that they had more severe conditions at the time of admission. Blood oxygen saturation data showed that the SpO_2 value was less than 93% in most of them. The most frequently reported symptoms in deceased patients were shortness of breath and impaired consciousness. Thus, examining and observing patients' clinical symptoms may help physicians identify factors that may negatively impact prognosis.

This study has some limitations. First, all of our cases were hospitalized, which is a bias to outpatients. Thus, the results could be overestimated, and further studies are needed to provide a standardized approach for accurate and acceptable guidelines. Second, post-discharge follow-up was not performed in this study; thus, we were not able to include post-discharge deceased cases. Third, another limitation of the present study was the absence of some clinical and laboratory data in the archived files of hospitalized COVID-19 patients.

Conclusion

In this study, the results demonstrated that old age, pulmonary diseases, cardiovascular diseases, and loss of consciousness predicted a higher mortality rate. On the contrary, a negative chest X-ray was associated with a lower risk of death. Due to the fact that elderly patients, especially those with underlying diseases, are more susceptible to contracting poor-prognosis COVID-19, it is necessary to take precautionary measures for this group. Also, it is important to conduct further studies on new cases of COVID-19 caused by new SARS-CoV-2 variants.

Availability of data and materials: The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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