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Clinical characteristics and outcomes of COVID-19 in people living with HIV in 2021 in Fars, Iran: a hospital-based study

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Abstract

Introduction: Human immunodeficiency virus (HIV) is considered a risk factor for COVID-19. This study described the COVID-19-related clinical characteristics and outcomes of people living with HIV (PLHIV) in Fars province, Iran.

Material and methods: This was a cross-sectional study, including 95 PLHIV who were hospitalized due to COVID-19. Quantitative variables were described with mean and standard deviations, and qualitative variables were defined with frequency and percentage. Logistic regression analysis was used for modeling. Analyzes were performed using IBM SPSS v. 24 software, with a *p*-value less than 0.05 considered significant.

Results: The mean age of patients was 54.4 ± 17.5 years, out of whom 17 (17.8%) died. Mortality among males and females was not considerably different, while mortality in patients under 40 years and patients with a history of underlying diseases were 21.4% and 20.9%, respectively. The most common symptoms of COVID-19 were respiratory distress (47.4%), cough (34.7%), and fever (32.6%), and the most underlying diseases included diabetes mellitus (18.9%), chronic kidney disease (11.6%), and heart disease (10.5%).

Conclusions: These findings indicate that PLHIV have a significantly higher risk of mortality when hospitalized due to COVID-19. The study also suggests that the immune response and comorbidities play a crucial role in determining the outcomes of COVID-19 in HIV-infected patients.

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Introduction

SARS-CoV-2, the agent of coronavirus 2019, has created a significant burden of morbidity and mortality worldwide [1]. Older age, high blood pressure, diabetes mellitus, obesity, etc., are known risk factors for more severe infection and worse prognosis in patients with COVID-19 [2]. In addition, immune deficiencies were identified as a risk factor for disease exacerbation. Therefore, human immunodeficiency virus (HIV)-infected individuals with low CD4+ T cell counts or those with untreated HIV are known to be at risk of developing severe COVID-19 [3, 4].

According to the World Health Organization, about 37.7 million people were living with HIV worldwide in 2020. Of these, about 73% had access to antiretroviral therapy and approximately 16% of all people living with HIV (PLHIV) did not know about their HIV-positive status [5]. In 2018, about 4,400 new HIV infections and 2,600 acquired immune deficiency syndrome (AIDS)-related deaths were reported in Iran. Also, the estimated total number of HIV patients in 2018 was about 61,000, of which nearly 21,600 (36%) were aware of the disease and 12,400 (20%) had access to antiretroviral therapy [6].

PLHIV infected with COVID-19, especially those with a history of comorbidity, are at higher risk of severe course of COVID-19, which create additional health burdens [7, 8]. Previous studies demonstrated that most PLHIV who were infected with COVID-19 had a history of at least one underlying condition, and the most common underlying conditions included high blood pressure [4, 9-11], diabetes mellitus [7, 10], and cardiovascular diseases [4]. Moreover, some research reported fever as the most common symptom [9]. Numerous studies suggested that the clinical symptoms and outcomes of COVID-19 (severity or death) in HIV-positive patients were not significantly different from non-HIV-infected individuals [1, 12, 13]. However, hospitalization and more severe clinical manifestations of COVID-19 were observed more in HIV-positive individuals [3, 14, 15].

Awareness of the complex interaction between HIV and coronavirus infection is essential in developing new strategies for better management of COVID-19 in HIV-infected patients. It is also important to understand the mechanism of COVID-19 in the human body and the role of the immune system response in severity, progression, and outcomes of the disease. In this current study, we described the clinical characteristics and outcomes of PLHIV who were hospitalized due to COVID-19.

Material and methods

This was a cross-sectional study among 95 PLHIV who were hospitalized due to COVID-19. Data were obtained from the Medical Care Monitoring Center (MCMC) system of Shiraz University of Medical Sciences in Fars province in 2021. This system collects daily data from hospitals in times of crisis. Demographic information included age, gender, nationality, and type of referral to the hospital. In addition, clinical data regarding underlying diseases, ward of patient hospitalization, close contact, intubation, PO_2 saturation, O_2 therapy, high-resolution computed tomography (HRCT) of the lungs result, smoking, and opium use were documented.

Quantitative variables were described with mean and standard deviation, and qualitative variables were defined with frequency and percentage. Shapiro-Wilk test was used to determine normality of quantitative variables, while logistic regression analysis was applied for modeling. Analyzes were performed using IBM SPSS 24 software, with a p-value less than 0.05 considered significant. This study was approved by the Ethics Committee of Shiraz University of Medical Sciences, with the ethics code of IR.SUMS.REC.1399.1165.

Results

The mean age of patients was 54.4 ± 17.5 years, and the mean age of women was 56.8 ± 19.2 years (more than men). Out of the 95 patients included, 17 (17.9%) died and 78 (82.1%) were discharged. In addition, the mean onset of symptoms and duration of hospitalization were 5.3 ± 6.1 and 6.7 ± 5.8 days, respectively. The mortality of patients under 40 and with a history of underlying diseases was 21.4% and 20.9%, respectively. The mortality of hospitalized patients in intensive care unit (ICU) was 37.5%, higher than hospitalization of patients in other wards. In addition, the mortality of patients without any findings on HRCT of the lungs was 40%. The detailed demographic and clinical characteristics are provided in Table 1. The most common symptoms of COVID-19 disease were respiratory distress (47.4%), cough (34.7%), and fever (32.6%) (Figure 1A). Furthermore, 52.2% of patients had underlying diseases, and the most common underlying diseases were diabetes mellitus (18.9%), chronic kidney disease (11.6%), and heart disease (10.5%) (Figure 1B). The modeling results showed that the mortality among males and females was not considerably different (p = 0.913) (Table 2).

Discussion

In the present study, PLHIV who were hospitalized due to COVID-19 disease were investigated in terms of clinical characteristics and outcomes of COVID-19, showing that 17.9% of them died. A study reported that 2.1% of total COVID-19 cases died in Iran until September 2021 [16]. Data on the prognosis and outcomes of COVID-19 in PLHIV is limited and with conflicting results [8, 17, 18]. A systematic review showed that 11.1% of PLHIV died because of COVID-19 outcomes [19], while in another study in the UK, HIV-positive status was related to amplified mortality [15]. Inconsistent with our study, Eybpoosh *et al.* [12] in Iran demonstrated that HIV infection decreased the risk of death among COVID-19 cases.

Likewise, mortality in patients that refer to the hospital by an ambulance was higher than in patients referred by

Table 1. Demographic and clinical characteristics of hospitalized HIV-infected patients with COVID-19 (n = 95)

Variable		Total, *n* (%)*	Mortality, *n* (%)
Demographic			
Age group			
	< 40	28 (29.5)	6 (21.4)
	40-59	29 (30.5)	4 (13.8)
	≤ 60	38 (40.0)	7 (18.4)
Gender			
	Male	57 (60.0)	10 (17.5)
	Female	38 (40.0)	7 (18.4)
Nationality			
	Iranian	88 (92.6)	16 (18.2)
	Non-Iranian	7 (7.4)	1 (14.3)
Clinical			
Type of referring to hospital			
	By himself	57 (60.0)	6 (10.5)
	By ambulance	38 (40.0)	11 (28.9)
Hospitalization ward			
	ICU	16 (16.8)	6 (37.5)
	Non-ICU	79 (83.2)	11 (13.9)
Close contact			
	Yes	20 (21.1)	5 (25.0)
	No	75 (78.9)	12 (16.0)
Intubation			
	Yes	12 (12.6)	8 (66.7)
	No	83 (87.4)	9 (10.8)
PO_2 saturation			
	< 93%	60 (63.2)	14 (23.3)
	≤ 93%	35 (36.8)	3 (8.6)
O_2 therapy			
	Yes	15 (30.6)	5 (33.3)
	No	34 (69.4)	4 (11.8)
HRCT of the lungs			
	Without findings	10 (14.7)	4 (40.0)
	With findings	58 (85.3)	9 (15.5)
Smoking			
	Yes	13 (13.7)	4 (30.8)
	No	77 (81.1)	13 (16.9)
Opium use			
	Yes	20 (21.1)	4 (20.0)
	No	70 (73.7)	13 (18.6)
Underlying diseases**			
	Yes	47 (52.2)	9 (20.9)
	No	43 (47.8)	8 (17.0)
Total	95	17	17.9

**Some variables with missing values.*
***Diabetes, hypertension, chronic liver disease, heart disease, chronic kidney disease, chronic blood disease, pulmonary disease, chronic nervous disorders, cancer.*

themselves. It might be due to the severity of the disease in patients referred by ambulance [5].

The mortality in patients in the ICU ward (37.5%) was higher than in non-ICU-admitted cases. Ceballos *et al.* [4] found a significant relationship between ICU admission and death, though some other research suggested that mortality in PLHIV was not related to ICU admission [20, 21].

In our results, patients without abnormal findings on HRCT of the lungs demonstrated higher level of mortality (40%) compared with those with abnormal findings on HRCT (15.5%), whereas some studies reported worse findings on chest CT in COVID-19 patients who died of this disease [22, 23]. One reason might be that HIV-infected patients have low inflammatory response because of a compromised immune system, therefore it is possible that in patients without signs (abnormal findings), an increased number of deaths was observed. The other reason may be the cellular immunity that is reduced in these patients, but the inflammatory phenomenon in the lungs seen on HRCT of COVID-19 patients seems mostly due to the humeral immunity. Also, the effect of antibodies can be a reason for increased mortality in patients with HRCT of the lungs without abnormal findings [24, 25], although this may not be significant.

The mortality in smoking patients (30.8%) was more than that in non-smokers (16.9%), which is in line with Alqahtani *et al.* study [26].

The average age of patients was 54.4 years, consistent with a research conducted in Spain in 2020, showing the average age of patients of 53.3 years [7]. A WHO study from 2021 with data obtained from 37 countries on demographics, clinical presentation, clinical outcomes, and risk factors among PLHIV who have been hospitalized for suspected or confirmed COVID-19, reported the mean age of patients of 45.5 years [17].

The results of this study demonstrate that the most common symptoms of COVID-19 were respiratory distress (47.4%), cough (34.7%), and fever (32.6%), while Baluku *et al.* [19] presented fever (73.8%) and cough (57.3%) as the most common symptoms of COVID-19. Vizcarra *et al.* [7] in 2020 showed that cough (71%) was the most common symptom of the disease.

PLHIV (52.2%) who were hospitalized due to COVID-19 had underlying diseases, and the most common included diabetes mellitus (18.9%), chronic kidney diseases (11.6%), and chronic cardiac diseases (10.5%). In a systematic review study, 65.3% of patients had at least one comorbidity, and the most common were hypertension (26.4%), hyperlipidemia (15.3%), and diabetes mellitus (9.7%) [19]. Vizcarra *et al.* study [7] conducted in Spain reported that 63% of cases had comorbidity, mostly hypertension and diabetes mellitus. Another study showed that hypertension (33.2%) and diabetes mellitus (22.7%) were the most common underlying conditions among PLHIV hospitalized with COVID-19 [17]. Nasreddine *et al.* [2] revealed that the most common comorbidities were hypertension (34%) and diabetes mellitus (13%), while in general, 9% of patients died. In the study

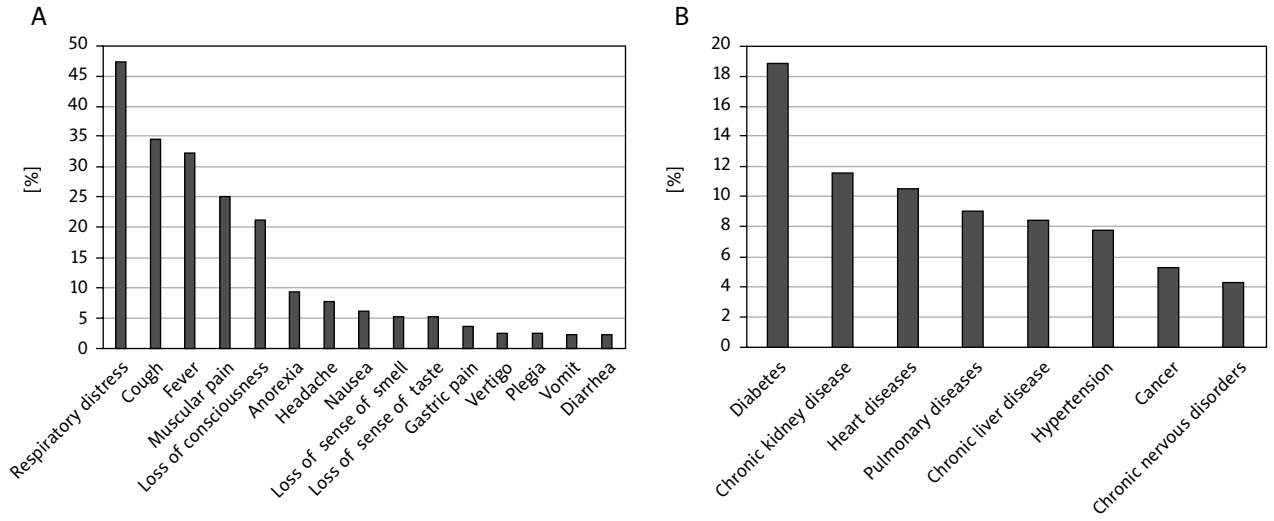

Figure 1. A) Percentage of COVID-19 disease symptoms in HIV-infected patients. **B**) Percentage of underlying diseases in HIV-infected patients with COVID-19 (some cases had more than one sign, symptom, or underlying disease)

by Ceballos *et al.* [4], the mean age of HIV-positive patients co-infected with COVID-19 was 44 years, the most common comorbidity was hypertension (16.7%), and the most common symptom was cough (69.4%). ICU admission was required for 22% of cases and hospital mortality was 13.9%.

The mean duration of hospital stay was 6.7 days and ICU admission was required for 16.8% of patients. Another study showed that the average duration from admission to death or discharge was 9.5 days and 23.1% of patients died [17]. In a study conducted in Belgium in 2021 [2], the median length of hospital stay of PLHIV who were hospitalized due to COVID-19 disease was 6 days, and ICU admission was required for 15% of patients; these results are similar with the present research.

The strength of this study is the utilization of data from a province in southern Iran, and data recording is very accurate and precise. However, the limitation of this study is the lack of laboratory data, including HIV RNA level, CD4+ T lymphocyte count, clinical category, and antiretroviral treatment status. The study assessed HIV-confirmed cases, and we suggest that further studies with larger HIV-positive cohorts, considering PLHIV's immune system and antiretroviral therapy status should be performed.

Table 2. Logistic regression on the association between demographic and clinical variables with death among hospitalized HIV-infected patients due to COVID-19

Variable	Logistic regression	
	p-value	OR (95% CI)
Age in years		
> 40	Ref.	–
40-59	0.762	1.20 (0.35-4.09)
≤ 60	0.613	0.70 (0.18-2.69)
Gender		
Female	Ref.	–
Male	0.913	1.06 (0.36-3.08)
Underlying diseases		
No	Ref.	–
Yes	0.637	1.29 (0.44-3.70)

Conclusions

The mortality rate among PLHIV who were hospitalized due to COVID-19 disease in Iran until September 2021 was 17.9%, which is significantly higher than the overall mortality rate of COVID-19 cases in the country of 2.1%. Among COVID-19 patients, those with normal HRCT findings (without abnormal findings) had a higher mortality rate (40%) compared with those with abnormal HRCT findings (15.5%). The observed inflammatory phenomenon in the lungs of COVID-19 patients on HRCT scans, seems mostly attributed to the humoral immunity and the effect of antibodies. In contrast, PLHIV have compromised cellular immunity, which might contribute to their higher mortality rate when infected with COVID-19. The presence of comorbidities appears to be a contributing factor to hospitalization among PLHIV due to COVID-19, which may explain the higher mortality rate in this population.

In summary, the findings indicate that PLHIV have a significantly higher risk of mortality when hospitalized due to COVID-19 compared with the general population in Iran. Also, the study suggests that the immune response and underlying health conditions (comorbidities) play a crucial role in determining the outcomes of COVID-19 in these patients. However, it is important to note that these conclusions are based on data available until September 2021 and

may not represent the current situation. Further research and data collection are necessary to verify and update these conclusions.

Disclosures

1. Institutional review board statement: The protocol of this study was approved by the Ethical Committee of Shiraz University of Medical Sciences with the ethics code of IR.SUMS.REC.1399.1165.
2. Assistance with the article: We would like to thank the Shiraz University of Medical Sciences.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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