

Clinical features, severity, and outcomes of patients with COVID-19 infection: A follow-up study

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Abstract

Few epidemiological investigations explored disease outcomes in patients with COVID-19 in Iraqi Kurdistan. The association of clinical and epidemiological characteristics of COVID-19 patients with outcomes was examined in this study. Patients who were diagnosed with COVID-19 from a private clinic were followed up until recovery or death between 15th August and 20th October 2020. The mean age of the COVID-19 patients was 47.12 (6-90 years). Fatigue (76.15%), myalgia (66.53%), fever (65.33%), cough (62.53%), sweating (58.52%), and headache (56.11%) were the most prevalent symptoms. Most of the patients had mild sever-

ity (350, 70.14%) followed by moderate (74, 14.83%), severe (46, 9.22%), and critical (29, 5.81%). The case fatality rate (CFR) was 5.41% (n=27) and was significantly increased with increasing severity; mild (0.0%), moderate (1.35%), severe (10.87%), and critical (72.41%; P<0.001). The patients with the critical and severe situations were significantly older; medians: 67 vs 55 years compared to those patients with moderate and mild situations; medians: 51 vs 45 years; P<0.001. The patients who died were significantly older compared to recovered patients; medians: 65 vs 46 years; P<0.001, respectively. The disease severity was the only factor to predict mortality in patients with COVID-19 disease. Concerning the severity, being older, having anorexia, fatigue, pleurisy, diarrhea, fever, sweating, shortness of breath, and being male were determined to be predictors of severity in COVID-19 patients. The incidence rate of severe/critical conditions was significantly increased with increasing age. The older age was determined to be a predictor for higher mortality.

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Introduction

The novel coronavirus infection called COVID-19 was originated in China in 2019.¹ The outbreak was spread to other countries and regions, including Iraqi Kurdistan.² Worldwide, by 28 April 2021 the total reported confirmed and dead cases of COVID-19 were 148,329,348 and 3,128,962 deaths, respectively.³ World Health Organization (WHO) has expressed deep concern about the spread and severity of this pandemic.⁴ The initial confirmed cases in Iraqi Kurdistan were among those individuals who returned from Iran in February 2020. Following that time, the Kurdistan Regional Government (KRG) released preventive measures for travelers and the general population. In this regard, public and private schools and universities were closed in response to this outbreak, and a curfew was imposed from March 13 until April 23, 2020. The individuals arriving from an epidemic area were quarantined for at least 14 days.⁵

The viral agent of this disease is not completely understood yet.⁶ The common clinical characteristics of the COVID-19 disease are fever, shortness of breath, dry cough, and pneumonia.⁷ The disease has different severity from mild to critical illnesses. The severe form of the disease is developed in patients with some risk factors such as old age (≥ 65 years), smokers, and coexisting medical conditions.⁸ The median incubation period of the COVID-19 disease is 5-6 days; but, it takes up to 24 days.⁹ The disease transmission may occur in the early stages of the disease, but the infectivity period is not completely understood.¹⁰ The prevention of the disease is important to the overall control of the disease owing to great epidemiological concerns. The different degrees of abnormalities are found in the laboratory findings e.g. leukopenia, leukocytosis, lymphopenia etc.¹¹

The diseases have various demographic and anthropometric

characteristics in different geographic locations¹² and these differences could affect clinical outcomes. We need to analyze data from different geographic areas to find out the specific treatment plan and optimize resource allocation. In this regard, we aimed to examine the association of clinical and epidemiological characteristics with outcomes in COVID-19 patients.

Materials and Methods

Study design and patients

In this follow-up study, the patients who were diagnosed with the COVID-19 disease by a pulmonologist from a private clinic were followed up until recovery or death. The patients had different severities, including mild, moderate, severe, and critical. The patients with severe and critical conditions were admitted to the hospital and were followed up from the hospitals. The patients were diagnosed at the private clinic in Erbil city in Iraqi Kurdistan between 15th August and 20nd October 2020. The pulmonologist diagnosed the COVID-19 cases based on the WHO *interim guidance* for COVID-19¹³ and local guidelines of the Ministry of Health.¹⁴ The patients were included in this study regardless of disease severity, coexisting medical conditions, and socio-demographic aspects. The severity of the disease was determined.¹⁴ The patients of both gender diagnosed with COVID-19 were eligible to include in this study.

Diagnosis and Measures

The general and clinical features of the patients were recorded in a pre-designed questionnaire. The diagnosis of the disease was made and the severity of the disease is rated as mild, moderate, severe, or critical.¹⁴

Statistical analysis

Incidence rates of symptoms, disease severity, outcomes of patients with COVID-19 were determined in number and percentage. The case fatality rate in patients with different severities and characteristics and association of outcomes with symptoms was examined in the Pearson Chi-squared test. The role of disease severity, symptoms, and general characteristics on outcomes of COVID-19 patients was examined in the binary logistic regression model. The statistical calculations were performed by JMP Pro 14.3.

Table 1. Case fatality rate in patients with different severities.

Severity and outcomes (n=499)	Outcomes		P
	Recovered	Death	
Disease severity			
Mild	350 (100)	0 (0.0)	<0.01
Moderate	73 (98.65)	1 (1.35)	
Severe	41 (89.13)	5 (10.87)	
Critical	8 (27.59)	21 (72.41)	
Symptoms			0.40
Asymptomatic	30 (100)	0 (0.0)	
Symptomatic	442 (94.24)	27 (5.76)	
Gender			0.11
Male	234 (92.86)	18 (7.14)	
Female	238 (96.36)	9 (3.64)	

Pearson chi-squared test was performed for statistical analyses.

Ethical considerations

The approval and guarantee to publish the data were obtained from the College of Medicine of Hawler Medical University in Iraqi Kurdistan.

Results

The mean age of the COVID-19 patients was 47.12 (Sta. deviation: 15.76) between 6 and 90 years and were males (252, 50.50%) and females (247, 49.50%), pregnant (5, 1.00%). Fatigue (76.15%), myalgia (66.53%), fever (65.33%), cough (62.53%), sweating (58.52%), and headache (56.11%) were the most prevalent symptoms in patients with COVID-19 (Figure 1).

Most of the COVID-19 patients had mild severity (350, 70.14%) followed by moderate (74, 14.83%), severe (46, 9.22%), and critical (29, 5.81%). Accordingly, 27 patients (5.41%) died and 472 (94.59%) were recovered from the disease (Figure 2).

The study showed that CFR was significantly increased with increasing severity; mild (0.0%), moderate (1.35%), severe (10.87%), and critical (72.41%; $P < 0.001$). But, the mortality was not associated with being symptomatic or asymptomatic ($P = 0.40$) with no significant difference between male and female patients ($P = 0.11$, Table 1).

The patients with the critical and severe situation were significantly older; medians: 67 vs 55 years compared to those patients with moderate and mild situations; medians: 51 vs 45 years; $P < 0.001$. In addition, the patients who died of the COVID-19 were

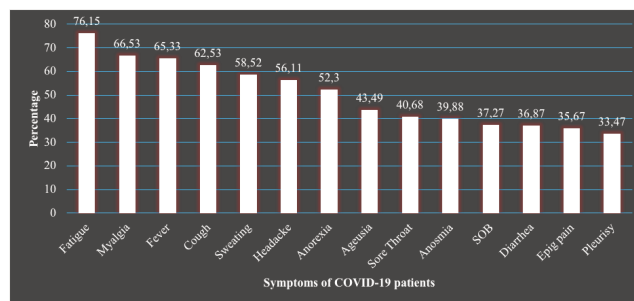


Figure 1. Incidence rates of symptoms in patients with COVID-19.

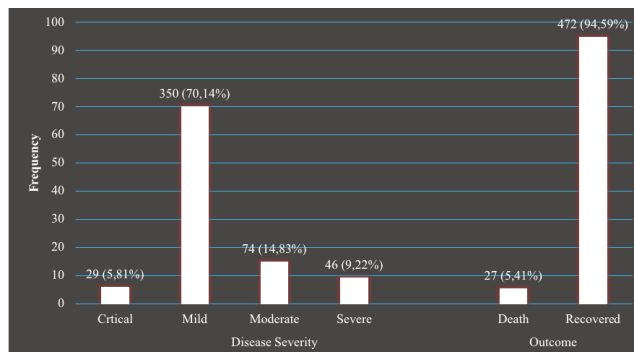


Figure 2. Disease severity and outcomes of patients with Covid-19.

significantly older compared to recovered patients; medians: 65 vs. 46 years; $P < 0.001$, respectively (Figure 3).

The study found that the patients who had cough at presentation; 7.4% vs 2.1%; $P = 0.012$; shortness of breath (10.8% vs 2.2%; $P < 0.001$); fatigue (7.7% vs 2.9%; $P = 0.019$), diarrhea (8.2% vs 3.8%; $P = 0.038$) were more likely to die of the COVID-19.

The multivariate analysis through nominal logistic regression showed that disease severity is the only factor to predict mortality in patients with COVID-19 disease. The odds ratios of CFR were 446449807 (0 for moderate/mild); 10.44 (0.60-181.63; for severe/moderate; and 82.91 (9.17-749.55, for critical/severe). Concerning the severity, being older, having anorexia, fatigue, pleurisy, diarrhea, fever, sweating, shortness of breath, and being male were determined to be predictors of severity in COVID-19 patients (Table 2).

Discussion

The mean age of the COVID-19 patients was 47.12 between 6 and 90 years. Fatigue, myalgia, fever, cough, sweating, and headache were the most prevalent symptoms. The most prevalent severity of the disease was mild followed by moderate, severe, and critical. The CFR was significantly increased with increasing severity and age. The patients with the critical and severe situation were significantly older; medians: 67 vs 55 years compared to those patients with moderate and mild situations; medians: 51 vs 45 years. The patients who had cough; shortness of breath; fatigue and diarrhea were more likely to die of the COVID-19. The disease severity was the only factor to predict the mortality in patients with COVID-19 disease.

The median age was lower compared to studies from Italy

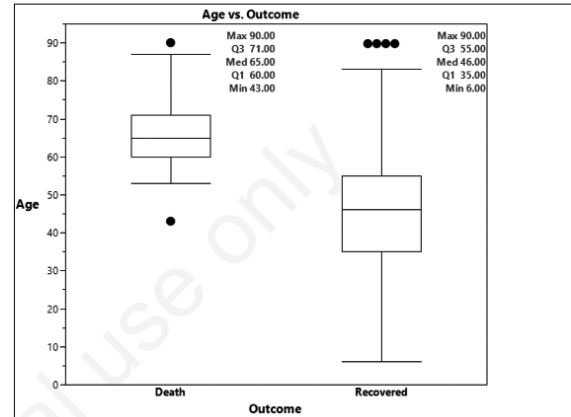
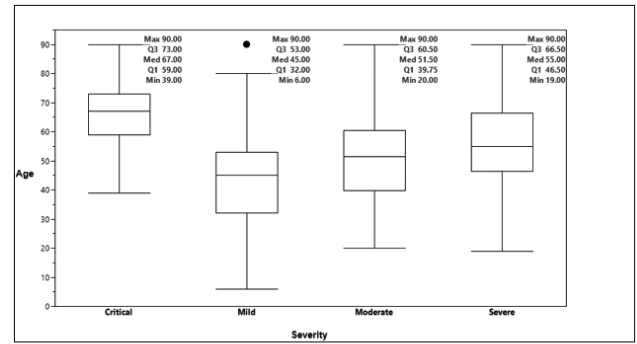


Figure 3. Comparisons of age in patients with different outcomes and severities.

Table 2. Role of disease severity, symptoms, and general characteristics on outcomes of COVID-19 patients

Controlling factors (n=499)	Dependent variable: Outcomes OR (95% CI)	P	Dependent variable: Severity Outcome
Severity		<0.01	Outcome
Moderate/ Mild	446449807 (no lower-upper range)		
Severe/ Moderate	10.44 (0.60-181.63)		
Critical/ Severe	82.91 (9.17-749.55)		
Anorexia	8.68 (0.86-87.55)	0.05	0.011
Age	1.06 (0.99-1.12)	0.06	<0.01
Epigastric pain	0.23 (0.04-1.34)	0.09	0.90
Fatigue	483756045 (0 to .)	0.14	0.01
Pleurisy	0.26 (0.03-1.97)	0.17	0.01
Diarrhea	3.10 (0.48-19.94)	0.21	0.01
Myalgia	0.19 (0.01-3.69)	0.26	0.63
Ageusia	0.34 (0.04-3.10)	0.33	0.86
Fever	0.35 (0.03-4.63)	0.42	0.04
Cough	0.39 (0.02-8.41)	0.55	0.17
Sore Throat	0.52 (0.06-4.67)	0.56	0.42
Anosmia	2.08 (0.14-31.90)	0.60	0.66
Sweating	1.57 (0.21-11.93)	0.66	0.04
SOB	1.53 (0.17-14.00)	0.71	0.01
Headache	1.23 (0.17-8.97)	0.84	0.23
Sex (male/Female)	0.89 (0.16-4.87)	0.89	0.01

Nominal logistic regression was performed for statistical analysis. Point: The odds ratio was measured as per unit change in regressor.

(65.0 between 18 and ≥ 75 years),¹⁵ China (47.0 between 0 and ≥ 65 years),¹⁶ and (56.0 between 18 and 87 years),¹⁷ and the United States (63.0 between 0 and 107 years).¹⁸

In this study, the incidence rates of severe and critical COVID-19 patients were 9.22% and 5.81%, respectively. It was linked with the increasing age group. It is well documented in the literature that worse outcomes are associated with increasing age.^{16,19} Overall, increasing age is associated with impaired immunity and there is an increased prevalence of comorbid diseases such as diabetes mellitus and hypertension. The different rates of severe/critical conditions were reported in the literature, for instance, 15.74%.¹⁶ The studies have reported that COVID-19 patients with severe/critical conditions are older with different median years, 7 years in China.¹⁶

This study reveals that 6.01% of the patients were asymptomatic upon visiting a medical doctor. Usually, few asymptomatic patients visit the hospitals for medical care. Fatigue, myalgia, fever, cough, sweating, and headache were the most prevalent symptoms. Concerning the severity, being older, having anorexia, fatigue, pleurisy, diarrhea, fever, sweating, shortness of breath, and being male were determined to be predictors of severity in COVID-19 patients. The patients who had cough; shortness of breath; fatigue, diarrhea were more likely to die of the COVID-19. The literature has reported that fever and cough on admission are the most prevalent symptoms in COVID-19 patients. Guan *et al.*¹⁶ reported that 43.8% and 88.7% had fever on admission and during hospitalization, respectively and 67.8% had cough. In addition, the patients with coexisting illnesses were more likely to have severe disease compared to non-severe patients, 38.7% vs 21.0%, respectively.¹⁶ Similar findings were reported in other parts of the world in terms of symptoms.^{15,20} A meta-analysis confirmed that fever and cough are the most frequent symptoms.²¹ A meta-analysis of 148 articles of 24,410 adults with confirmed COVID-19 from 9 countries reported that fever (78%), cough (57%), and fatigue (31%) are the most prevalent symptoms.

The CFR was 5.41% among 499 patients who were followed up and included in this study. The CFR rate was significantly increased with increasing age and disease severity. The CFRs are different based on the coexisting chronic conditions, clinical features, and epidemiological factors. A meta-analysis of 148 articles reported a 7% mortality rate.²² The early findings reported from China revealed that CFR is 1.4% in laboratory-confirmed COVID-19 patients¹⁶ and 24.0% in Italy.¹⁵ The Italian study reported that patients aged older than 65 years, history of coronary artery disease, active cancer as independent factors related to increased mortality risk. Zhou *et al.*¹⁷ performed a multivariable regression and showed that in-hospital mortality is associated with older age, d-dimer greater than 1 $\mu\text{g/mL}$ on admission, and higher Sequential Organ Failure Assessment score.

The disease severity was the only predictor of mortality in COVID-19 patients. Old age was determined to be the predictor of severity in this study. Some other factors have been reported to be predictors of mortality. For example, Ciceri *et al.*¹⁵ reported that through multivariable analysis that older age, coronary artery disease, cancer, low lymphocyte count, and high RALE (Radiographic Assessment of Lung Edema) score as factors independently associated with an increased risk of mortality. Other investigations have reported that older age and the presence of comorbidities are associated with an increased mortality rate in COVID-19 patients.^{17,20,23} We confirmed the previously published findings in patients from China,²⁴ United States,¹⁸ and Italy.¹⁵ They reported that older age, coexisting medical conditions such as coronary artery disease, history of hypertension, diabetes, COPD,

and chronic renal failure, and cancer are related to increased mortality. We back the effect of chronic diseases on increased mortality to their effect on immunity.²⁵ The current findings give us the utmost importance to reduce the burden of the general health system, targeting the efforts for sufficient screening of the patients at risk. The role of age in immune system suppression must not be ignored in this disease. The countries with higher infection rates have an older population compared to countries with low infection rates,²⁶ France and Italy compared to Iraq and Saudi Arabia, respectively. Older adults and patients with coexisting medical conditions are more likely to have a severe-even deadly-coronavirus infection.²⁷ Therefore, the high infection and mortality rates in high-income countries could be due to aging and accordingly low immunity level. A recent study reported that the crude mortality rate has been increased by increasing consumption of sugar-sweetened beverages and decreased by increasing fruit consumption and beans and legumes.²⁸

Except for the insufficient age-related micronutrient, the nutritional status of the population has a role in the overall development of the SARS-CoV-2 infection, the clinical status, and outcomes. Therefore, the individuals need the maintenance of host macro- and micronutrient status to avoid the COVID-19 infection.²⁹

Older individuals have less ability to respond to immune challenges and pathogens, antigens, and mitogens.³⁰ Besides, the older persons have reduced the production of T cells in the involved thymus. Accordingly, this decreases the function of mature lymphocytes in secondary lymphoid tissues.³¹

Implications and limitations

The main strong point of this study is that we tried to include as much as possible the patients with sufficient information that allowed us to present a clearer picture of clinical features of the COVID-19 in this region. The predictors reported in this study could assist clinicians to determine at an early stage patients with COVID-19 with poor prognosis. However, the study was not exempt from the limitations. We could not record the radiological and laboratory-based information of this large study. Anyhow, we suggest that a large study of radiological and laboratory-based information be performed in a multi-center investigation.

Conclusions

This study showed that patients with COVID-19 have a low incidence rate of severe/critical status in Iraqi Kurdistan. The incidence rate of severe/critical conditions was significantly increased with increasing age. We found that older COVID-19 patients were more likely to have severe/critical status and a high rate of CFR. Old age was determined to be the only factor that predicted higher mortality.

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