

Time from symptom onset to severe COVID-19 and risk factors among patients in Southern Ethiopia: a survival analysis Journal of International Medical Research 50(8) 1–12 © The Author(s) 2022 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/03000605221119366 journals.sagepub.com/home/imr



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Abstract

Objective: This study aimed to assess the time to severe coronavirus disease 2019 (COVID-19) and risk factors among confirmed COVID-19 cases in Southern Ethiopia.

Method: This two-center retrospective cohort study involved patients with confirmed COVID-19 from 1 October 2020 to 30 September 2021. Kaplan–Meier graphs and log-rank tests were used to determine the pattern of COVID-19 severity among categories of variables. Bivariable and multivariable Cox proportional regression models were used to identify the risk factors of severe COVID-19.

Results: Four hundred thirteen patients with COVID-19 with a mean age of 41.9 ± 15.3 years were involved in the study. There were 194 severe cases (46.9.1%), including 77 (39.6%) deaths. The median time from symptom onset to severe COVID-19 was 8 days (interquartile range: 7–12 days). The risk factors for severe COVID-19 were age >65 (adjusted hazard ratio [AHR] = 2.65, 95% confidence interval [95%CI]: 1.02, 3.72), cough (AHR = 1.59, 95%CI: 1.39, 2.84), chest pain (AHR = 1.47, 95%CI: 1.34, 2.66), headache (AHR = 2.04, 95%CI: 1.43, 2.88), comorbidity (AHR = 1.3, 95%CI: 1.01, 2.04), asthma (AHR = 1.6. 95%CI: 1.04, 2.24), and symptom onset to admission more than 5 days (AHR = 0.48, 95%CI: 0.34, 0.68).

Conclusion: Patients with symptoms and comorbidities should be closely monitored.

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Keywords

COVID-19, severe, risk factor, comorbidity, survival analysis, Southern Ethiopia

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Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by the novel coronavirus. It was first detected in Wuhan, China in December 2019 and has since spread worldwide. COVID-19 was declared a pandemic by the World Health Organization (WHO) on 11 March 2020.¹ According to the WHO daily report on 27 July 2021, the global burden of COVID-19 reached 194,608,040 confirmed cases and 4,170,155 deaths within 1 year. Africa has reported 4,813,735 confirmed cases, of which 3,512,473 have recovered, and 113.646 have died.² African countries have a lower incidence of illnesses and deaths compared with European and American countries. This may be attributed to a limited testing capacity, underreporting, and a younger population.

COVID-19 is usually asymptomatic, and approximately 80% of asymptomatic cases improve without specialized medical care. However, pneumonia and acute severe respiratory failure occur in a considerable number of patients with COVID-19.³

Studies indicate that the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurs primarily through close contact with infected people via secretions or respiratory droplets.^{4–7} The severity of infectious diseases is a crucial feature to consider. Fatality rates help with determining the severity of an illness, identifying at-risk individuals, and assessing healthcare quality.⁸

COVID-19 mortality rates are continuing to increase globally. However, data on the determinants of mortality in patients with COVID-19 are limited. Predicting mortality is crucial for identifying risk factors and developing treatments.⁹ A systematic review performed to assess the risk factors associated with COVID-19 mortality revealed that patients with hypertension, coronary artery disease, and diabetes had higher mortality rates. Those who died had elevated troponin, alanine transferase, C-reactive protein, creatinine, interleukin 6, and d dimer and lower albumin levels than those who survived.¹⁰

According to the WHO, patients with mild infections typically recover within 2 weeks, whereas those with serious illnesses usually recover within 3 to 6 weeks. Therefore, determining the duration of severe COVID-19 disease in different contexts and settings is crucial for developing preventive measures and optimizing treatment options.¹¹ Accordingly, this study aimed to investigate the risk factors of severe COVID-19 in Southern Ethiopia using survival analysis.

Methods

Study design and settings

This hospital-based retrospective cohort study was conducted from 1 October 2020 to 30 September 2021 at two COVID-19 treatment centers. The two COVID-19 treatment centers were established within the hospital for the management of COVID-19 cases. According to the admission criteria of COVID-19 cases in Ethiopia, an emergency department and a resuscitation department treat severe or critical cases of COVID-19. Asymptomatic cases (patients with mild and moderate infection) without life-threatening comorbidities are managed at home. Before the start of the study, ethical approval was obtained from the Institutional Review Board of Dilla University, College of Medicine and Health Science (reference number: duirb/007/22-01). This study was conducted through a review of medical records. Therefore, the need for informed patient consent was waived.

Population and samples

This two-center retrospective observational study included patients with COVID-19 who were admitted to the two collaborative COVID-19 treatment centers. The study population included all patients hospitalized with COVID-19 from 1 October 2020 to 30 September 2021. Patients with incomplete baseline information, such as the date of admission, or incomplete data for outcome variables were excluded from the study.

The sample size was calculated using a double population proportion formula by considering the level of significance $(\alpha = 0.05)$, proportion of severe cases = 0.32, and proportion of mild cases = 0.67¹² The calculated sample size was 400. Finally, 5% of the sample size was added considering the likelihood of medical chart incompleteness for the variable of interest. Therefore, the final sample size was 420. The simple random sampling (table of random numbers) technique was used to select patients with COVID-19 from the admission registry. The reporting of this study conforms to STROBE guidelines.13

Definitions

• Non-severe COVID-19 cases: Defined as the absence of any criteria for severe or critical COVID-19.

- Severe COVID-19 cases: Patients with shortness of breath, respiratory rate >30 breaths/minute, resting blood oxygen saturation <93%, and PaO2/ FiO2 <300 mm Hg. Cases with radiographic findings of pneumonia progressing more than 50% in 24 to 28 hours were considered severe.¹⁴
- **Censoring**: Represents patients with mild and moderate disease.
- **Time to event or censoring**: Time between the date of symptom onset of COVID-19 to the development of severe COVID-19 or censoring (in days).

Data collection, procedures, and data quality control

We extracted the data from the registration logbook of COVID-19 forms and medical cards of patients. Data collection included patient's age, sex, place of residence, date of admission, date of symptom onset, reported signs and symptoms, clinical characteristics, comorbidities reported by the patients, home medications, and treatments (including oxygen therapy and mechanical ventilation).

Trained health professionals working in the treatment centers extracted the data. The primary outcome of COVID-19 severity was confirmed by reviewing the chart during data collection. The completeness of each questionnaire was checked by the supervisor daily.

Data management and statistical analysis

Demographic and epidemiological categorical variables were expressed as frequencies and percentages. For normal and nonnormally distributed continuous variables, the mean with the standard deviation (SD) and median with the interquartile range (IQR) were used, respectively. Shapiro– Wilk tests were used to assess the normality of continuous variables. Kaplan–Meier curves were used to determine the pattern of COVID-19 disease severity among different categories of variables. A log-rank test was performed to determine if there were statistically significant differences among groups of covariates at a 5% level of significance. Univariable and multivariable Cox proportional hazard regression analyses were carried out to identify the association between COVID-19 severity and risk factors. Univariable analysis was performed at a 25% level of significance to screen independent variables used in the multivariable Cox proportional hazard regression model. In multivariable Cox proportional hazard regression analysis, the 95% confidence interval (CI) for the adjusted hazard ratio (AHR) was calculated, and variables with a p-value <0.05 were considered statistically associated with COVID-19 severity during admission. The proportional hazard assumption was assessed using a global goodnessof-fit test. Data were analyzed with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Demographic and clinical characteristics of patients

A total of 413 patients with PCR-confirmed COVID-19 were included. Seven patient

cards were excluded from the study because their charts were lost. The mean \pm SD age of patients was 41.9 \pm 15.3 years. The majority of patients (245, 59.3%) were men, and 213 (51.6%) patients had a rural residence (Table 1).

Presenting symptoms and comparison between severe and non-severe cases

All patients had one or more symptoms of COVID-19 at admission. The most common symptoms, which occurred mainly in severe cases, were as follows: 331 (80.1%) patients had a fever, 308 (74.6%) had a cough, 230 (55.7%) had chest pain, and 255 (61.7%) had a headache. On admission, chest computed tomography abnormalities were detected, including 287 (69.5%) cases of bilateral infiltration and 91 (22.0%) cases of unilateral infiltration (Table 2).

Among all enrolled patients with COVID-19, 77 (18.649%) died during hospitalization, and the rest recovered and were discharged. The median time from symptom onset to hospital admission (diagnosis) was 4 days (IQR: 3–5 days) for all cases, 4 days (IQR: 3–5 days) for severe cases, and 4 days (IQR: 2–5 days) for non-severe cases. The median time from

Table 1. Socio-demographic characteristics of the study population.

Variable	Response	Total (n = 413)	Non-severe cases (n = 219)	Severe cases (n = 194)
Sex	Men	245 (59.3)	4 (57.6)	104 (42.4)
	Women	168 (40.7)	78 (46.4)	90 (53.6)
Age	≤24	33 (8.0)	27 (81.8)	6 (148.2)
0	25-39	182 (44.1)	113 (62.1)	69 (37.9)
	40–64	160 (38.7)	69(43.I)	91 (59.9)
	≥65	38 (9.2)	10 (26.3)	28 (73.7)
Mean age \pm standard deviation		41.9 ± 15.3	37.7 ± 13.5	46.7 ± 15.7
Place of residence	Rural	213 (51.6)	112 (52.6)	101 (47.4)
	Urban	200 (48.4)	107 (53.5)	93 (46.5)
Smoking history	Yes	48 (11.7)	16 (33.3)	32 (66.7)
	No	365 (88.4)	203 (55.6)	162 (44.4)

		Total	Non-severe	Severe
Variable	Response	(n = 413)	(n = 219)	(n = 194)
Fever	No	82 (19.9)	26 (31.7)	56 (68.5)
	Yes	331 (80.1)	193 (58.3)	138 (41.7)
Cough	No	105 (25.4)	76 (72.4)	29 (27.6)
-	Yes	308 (74.6)	143 (46.4)	165 (53.6)
Sore throat	No	203 (49.2)	109 (53.7)	94 (46.3)
	Yes	210 (50.8)	110 (52.4)	100 (47.6)
Dyspnea	No	208 (50.4)	139 (66.8)	69 (32.3)
	Yes	205 (49.6)	80 (39.0)	125 (61.0)
Chest pain	No	183 (44.3)	125 (68.3)	58 (31.7)
	Yes	230 (55.7)	94 (40.9)	136 (59.1)
Headache	No	158 (38.3)	102 (64.6)	56 (35.4)
	Yes	255 (61.7)	117 (45.9)	138 (54.1)
Hemoptysis	No	295 (71.4)	179 (60.7)	116 (39.3)
	Yes	118 (28.6)	40 (33.9)	78 (66.1)
Runny nose	No	356 (86.2)	199 (55.9)	157 (44.1)
	Yes	57 (13.8)	20 (35.1)	37 (64.9)
Diarrhea	No	332 (80.4)	178 (53.6)	154 (46.4)
	Yes	81 (19.6)	41 (50.6)	40 (49.4)
Chest CT findings	Normal	35 (8.5)	31 (88.6)	4 (11.4)
	Bilateral	287 (69.5)	146(50.9)	141 (49.1)
	Unilateral	91 (22.0)	42 (46.2)	49 (53.3)
PR		114 (101, 129)	128 (107, 134	110 (96, 118)
RR		29 (27, 31)	29 (27, 32)	28 (28, 30)
Temperature		38.5 (38.1, 39)	38.3 (38, 39)	38.5 (38, 39.1)
DBP		80 (70, 100)	70 (70, 90)	90 (70, 100)
Time from symptom of to admission, days	onset	4 (3, 5)	4 (2, 5)	4 (3, 5)
Time from symptom of to severe disease, d		8 (5, 13)	9 (4, 15)	8 (7, 12)
Length of hospitalizati		15 (10, 20)	16 (12, 18)	12 (9, 22)
Death		77 (18.64)	0 (0.0)	77 (100)

Table 2. Symptoms at hospital admission and comparison between severe and non-severe cases.

Continuous variables are reported as the mean (standard deviation) or median (interquartile ranges) as appropriate. CT, computed tomography; PR, pulse rate; RR respiratory rate; DBP, diastolic blood pressure.

symptom onset to severe disease was 8 days (IQR: 7–12; mean 8.4 ± 3.6 days). The median length of hospital stay in the two treatment centers was 15 days (IQR: 10–20 days). The length of hospital stay in patients with severe disease was 12 days (IQR: 9–22 days), which was longer than that for the non-severe cases (Table 2).

Pre-existing history of comorbidities and comparison between non-severe and severe cases

Among patients, 205 (49.6%) had a history of one or more pre-existing comorbidities. The most common was hypertension in 114 (27.6%), followed by diabetes mellitus in 89 (21.5%), ischemic heart disease in 76 (18.4%), and asthma in 65 (15.7%) (Table 3).

Comparison of severity experience

The duration from symptom onset to severe disease was plotted using Kaplan–Meier survival estimates for selected variables. The results showed that there was no significant difference in the median duration between those residing in rural and urban areas (Figure 1). A log-rank test was used to assess the difference in severe COVID-19 experience among groups of variables. There was a statistically significant difference in the median duration between difference (all p < 0.05) (Table 4).

Risk factors for severe COVID-19

Bivariable Cox regression analysis was conducted to identify factors associated with the severity of COVID-19. Except for the place of residence, all variables were significantly associated with the severity of COVID-19 (all p < 0.05). To adjust for other factors and confirm prognostic

factors, all variables with p < 0.25 in the bivariable Cox regression model were included in the multivariable Cox proportion regression step-down reduction model. Except for the place of residence, all variables were selected for multivariable Cox regression analysis. Age >65 (AHR = 2.65, 95%CI: 1.02, 3.72), cough (AHR = 1.59, 95%CI: 1.39, 2.84), chest pain (AHR = 1.47, 95%CI: 1.34, 2.66) headache (AHR = 2.04, 95%CI: 1.43, 2.88), comorbidity (AHR = 1.3, 95%CI: 1.01, 2.04), asthma (AHR = 1.6. 95%CI: 1.04, 2.24), and time from symptom onset to admission (AHR = 0.48, 95% CI: (0.34, 0.68) werefound to be significantly associated with the severity of COVID-19 (all p < 0.05).

The presence of cough was identified as a variable that predicted the severity rate of COVID-19 cases. The estimated risk of severe COVID-19 for cases with cough at admission was higher than that for patients without cough on admission (AHR = 1.59, 95%CI: 1.39, 2.84, p = 0.01). Similarly, the presence of any type of comorbidity determined the severity of COVID-19. The risk of severe disease for patients with any type

 Table 3. Frequency of patients with comorbidities admitted to the hospital and comparison between severe and non-severe patients.

Variable	D	Total	Non-severe	Severe
variable	Response	(n = 413)	(n = 219)	(n = 194)
Comorbidities	No	208 (50.4)	137 (65.9)	71 (34.1)
	Yes	205 (49.6)	82 (40.0)	123(60.0)
Hypertension	No	299 (72.4)	191 (63.9)	108 (36.1)
	Yes	114 (27.6)	28 (24.6)	86 (75.4)
Diabetics	No	324 (78.5)	190 (58.6)	134 (41.4)
	Yes	89 (21.5)	29 (32.6)	60 (67.4)
lschemic heart disease	No	337 (81.6)	144 (42.7)	193 (57.3)
	Yes	76 (18.4)	22 (28.6)	54 (71.4)
Chronic kidney disease	No	384 (93.0)	206 (53.6)	178 (46.4)
	Yes	29 (7.0)	13 (44.8)	16 (55.2)
Asthma	No	348 (84.3)	209 (60.1)	139 (39.9)
	Yes	65 (15.7)	10 (15.4)	55 (84.6)
Stroke	No	365 (88.4)	194 (53.2)	171 (46.8)
	Yes	48 (11.6)	25 (52.I)	23 (47.9)

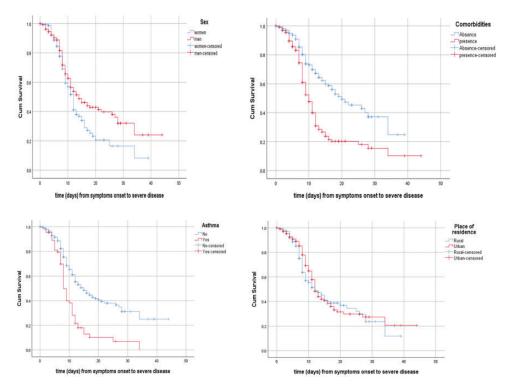


Figure 1. Risk factors for severe coronavirus disease 2019 (COVID-19) by univariable Kaplan–Meier survival analysis.

of comorbidity was 1.3 times higher than that for patients without a comorbidity (AHR = 1.3, 95%CI: 1.01, 2.04, p = 0.03). The estimated risk of severe disease for patients with a time from symptom onset to admission longer than 5 days was 52% (AHR = 0.48, 95%CI: 0.34, 0.68, p = 0.01) lower than that for the other group (Table 5).

After fitting the multivariable Cox proportional hazard model, the proportional hazard assumption was assessed using a global goodness-of-fit test (chi2=18.14; probability >chi2=0.068). The results indicated that the model fitted the data well.

Discussion

This study aimed to assess the duration from symptom onset to severe COVID-19 and the risk factors for severe disease at two COVID-19 treatment centers in Southern Ethiopia. Assessing this outcome as an indicator of clinical improvement from the disease is important as measuring the duration from symptom onset to the severe stage assists in deciding hospital capacity in terms of oxygen facility arrangement and organizing intensive care units with supplemental oxygen systems. This ensures maximum capacity to provide better care to patients in treatment centers.

COVID-9 remains a major cause of hospitalization and mortality worldwide. The common methods of human-to-human transmission include direct contact and airborne transmission through aerosols, such as during medical procedures.¹⁵

The COVID-19 pandemic triggered a race to develop a vaccine to build herd immunity and reduce the harmful effects

Variable	Category	Median duration in days (95%CI)	Log-rank test, p-value	
All		9 (8, 11)	-	
Sex	Men	9 (7.85, 10.15)	0.02	
	Women	10 (8.53, 11.47)		
Age	≤24		0.001	
	25–39			
	40–64			
	\geq 65			
Place of residence	Rural	8 (7.45, 8.55)	0.452	
	Urban	12 (11.0, 13.1)		
Smoking history	No	8 (6.8, 9.20)	0.003	
	Yes	10 (9.08, 10.9)		
Fever	No	13 (11.5, 14.5)	0.001	
	Yes	9 (8.45, 9.55)		
Cough	No	16 (9.0, 22.9)	0.001	
-	Yes	9 (8.4, 9.60)		
Headache	No	13 (8.83, 17.2)	0.001	
	Yes	9 (8.4, 9.6)		
X-Ray	Normal	, , ,	0.001	
	Unilateral	(9.69, 2.30)		
	Bilateral	8 (7.20, 8.80)		
Comorbidity	No	13 (10.5, 15.5)	0.001	
	Yes	9 (8.4, 9.60)		
Hypertension	No	12 (10.7, 13.3)	0.001	
	Yes	8 (7.30, 8.70)		
Diabetic	No	10 (6.90, 11.1)	0.009	
	Yes	9 (7.5, 10.4)		
Time (days) from symptom onset to admission	≤4	8 (7.60, 8.40)	<0.001	
	5	13 (11.25, 14.7)		

Table 4. Duration from symptom onset to severe COVID-19 by different factors.

of COVID-19. The WHO approved various COVID-19 vaccine subtypes, and many countries have approved the use of the following vaccines as of 16 May 2021: Pfizer in 85, Moderna in 46, Oxford/AstraZeneca in 101, and Janssen in 41.¹⁶ However, vaccine-resistant and vaccine-hesitant populations have proven to be major obstacles to these government-sponsored vaccination programs.¹⁷

The treatment of COVID-19 cases is based on the severity of clinical manifestations. Patient isolation and close observation, including monitoring oxygen saturation, are essential in every case. If the patient develops refractory hypoxemia, then nitric oxide inhalation, neuromuscular blocker administration, and endotracheal intubation are initiated. Mechanical ventilation using extracorporeal membrane oxygenation is needed in severe cases.¹⁸

In this study, the overall median time from symptom onset to severe COVID-19 was 8 days (IQR 5–13 days), with a mean of 10.24 ± 7.2 days. The estimated median number of days from the onset of COVID-19 symptoms to intensive care unit admission was 9 in Singapore (IQR: 3–12 days),¹⁹

Variable	Category	CHR (95%CI)	p-value	AHR (95%CI)	p-value
Sex	Male	1.38 (1.04, 1.84)	0.025	1.34 (0.94, 1.81)	0.05
	Female	I		I Í	
Age	≤24	I		I	
-	25–39	0.18 (0.07, 0.44)	0.001	0.36 (0.13, 0.91)	0.03
	40–64	0.33 (0.21, 0.52)	0.001	0.45 (0.27, 0.75)	0.06
	>64	3.46 (1.39, 4.93)	0.021	2.6 (1.02, 3.72)	0.01
Place of residence	Rural	I		_	-
	Urban	1.11 (0.83, 1.47)	0.46		
Smoking history	No	I			
	Yes	1.82 (1.24, 2.66)	0.02	1.29 (0.15, 1.92)	0.16
Fever	No	I		I Í	
	Yes	1.3 (0.95, 1.78)	0.09	1.28 (0.93, 1.78)	0.13
Cough	No	I		1	
6	Yes	2.3 (1.57, 3.46)	0.01	1.59 (1.39, 2.84)	0.01
Headache	No	I		I	
	Yes	2.2 (1.61, 3.02)	0.01	2.04 (1.43, 2.88)	0.01
Chest pain	No	I		I	
	Yes	2.81 (2.05, 3.84)	0.01	1.47 (1.34, 2.66)	0.01
Sore throat	No	I		I	
	Yes	0.89 (0.67, 1.18)	0.04	1.14 (0.85, 1.53)	0.05
Dyspnea	No	I		I	
	Yes	1.86 (1.4, 2.5)	0.01	0.72 (0.53, 0.98)	0.03
Hemoptysis	No	I		I	
	Yes	1.6 (1.20, 2.14)	0.01	1.24 (1.09, 2.03)	0.05
Comorbidity	No	I		I	
	Yes	1.44 (1.33, 2.59)	0.01	1.3 (1.01, 2.04)	0.03
Hypertension	No	I		I	
	Yes	2.36 (1.76, 3.14)	0.01	1.3 (0.88, 1.96)	0.08
Asthma	No	I		I	
	Yes	2.34 (1.71, 3.21)	0.01	1.6 (1.04, 2.24)	0.03
Diabetics	No	I		I	
	Yes	1.71 (1.26, 2.32)	0.01	0.92 (0.63, 1.34)	0.07
Symptom onset to admission	<4 days	I		I	
	\geq 5 days	0.52 (0.37, 0.72)	0.01	0.48 (0.34, 0.68)	0.01

Table 5. Multivariable Cox proportional hazard regression analysis of the median time of severe COVID-19 and its predictors.

CHR, crude hazard ratio; AHR, adjusted hazard ratio; CI, confidence interval.

9 in China (IQR: 3-12 days),²⁰ and 10 in Italy (IQR: 6-14),²¹ which are higher than that in our study.

In our study, the estimated median time from symptom onset to hospitalization was 4 days (IQR: 3–5), with a mean of 4.3 days (95%CI: 4.03, 4.54). This finding was consistent with a previous systematic review and meta-analysis, in which the estimated mean number of days from the onset of COVID-19 symptoms to the first clinical visit was 4.92 (95%CI: 3.95, 5.9).²²

In this two-center study, the length of stay in the COVID-19 treatment center was 15 days (IQR: 10–20 days). The median length of stay for patients in the non-severe group was 16 days (IQR: 12–18 days), and that for the severe group

was 12 days (IQR: 9–22 days). This finding is similar to the result reported from India (16 days).²³ However, the result of this study is higher than the 6 days reported in Saudi Arabia,²⁴ 7 days in Peru,²⁵ and 8.5 days in the Mediterranean.²⁶ This variation might be due to differences in the type of health facilities.

Based on the findings of this study, the risk factors associated with the severity of COVID-19 included being male, age >60 years, smoking history, cough, headache, chest pain, sore throat, presence of comorbidity, asthma, and >5 days from symptom onset to admission, which were consistent with some study findings from China.^{27–30}

Patients with a history of cough at admission were 1.6 times (AHR = 1.6, 95% CI: 1.4, 2.7) more likely to develop severe COVID-19 compared with those who had no history of cough. Fever is also an indication of serious disease and an active immune response of the body to infection. Therefore, having symptoms of cough and fever may imply that the patient has competent immunity that is fighting the infection, resulting in a favorable disease outcome.

In multivariable Cox proportional hazard regression analysis, the presence of a comorbidity (AHR = 1.3, 95%CI: 1.01, 2.04) was found to be a significant determinant of COVID-19 severity, which was consistent with previous reports.^{31–33} Moreover, this study did not find that diabetes was associated with the prognosis of severe COVID-19, which was in-line with a previous study.³⁴

Our study showed that the risk of severe COVID-19 for patients admitted to the treatment centers >5 days after symptom onset was 85% (AHR = 0.48, 95%CI: 0.34, 0.68) lower than that for patients who were admitted to the hospital within 5 days of symptom onset.

The limitations to this study are as follows. This retrospective observational study collected data by chart review and integrated hospital management system data recorded by the two hospital treatment centers. In addition, our study could not assess important variables, such as body mass index and respiratory system compliance, which may have a significant association with disease severity. A lack of complete laboratory investigations and lost patient charts are also limitations.

Conclusion

Our study found that the risk factors for the development of severe COVID-19 included age >65 years, cough, headache, chest pain, comorbidities, asthma, and time from symptom onset to admission >5 days. These are helpful to predict and prevent severe cases of COVID-19. Therefore, patients with symptoms and comorbidities should be closely monitored.

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Author contributions

GS: Conceived and designed the study, conducted statistical analysis and result interpretation, and prepared the manuscript. BM: conceived and designed the study and conducted result interpretation. AB: Conducted the statistical analysis and result interpretation. All authors read and approved the manuscript.

Declaration of conflicting interest

The authors declare that they have no competing interests.

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