



Incidence of Death and Its Predictors of COVID-19 in Amhara Region, Ethiopia: A Retrospective Follow Up Study

Anteneh Mengist Dessie¹, Zelalem Animut², Almaw Genet³, Chalachew Yenew¹

¹Department of Public Health, College of Health Sciences, Debre Tabor University, Debre Tabor, Ethiopia; ²Department of Public Health, Fahoba Health and Business College, Debre Markos, Ethiopia; ³Department of Public Health, College of Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia

Correspondence: Chalachew Yenew, Tel +251945563008, Email Chalachewyenew50@gmail.com

Background: Risk factors associated with COVID-19 incidence of death would aid to notify the most favorable management strategies, hang about undecided, Moreover, studies regarding this issue are limited in Ethiopia and no region-wise study is conducted. Hence, the study investigated the COVID-19 incidence of death and its predictors in the Amhara regional state, Ethiopia.

Methods: A facility-based retrospective survey was conducted at all Amhara regional state COVID-19 treatment centers from 13 March 2020, through 13 January 2022. Epidata version 3.1 and STATA version 14 were used for data entry and analysis, respectively. Linearized survey analysis in a stratified Cox regression model was fitted to identify independent risk factors. P-value with 95% CI for hazard ratio was used for testing the significance at alpha 0.05.

Results: A total of 28,533 study participants were analyzed in this study. Of these, 2873 (11.2%) died and 25,660 (88.8%) were recovered from COVID-19. The death rate was 11.78 per 1000 person-days of observation with a median survival time of 32 days with IQR [12, 44]. Patients with co-morbidities (AHR = 1.54: 95% CI: 1.51–1.55), patients with age <5-year (AHR = 1.69: 95% CI: 1.78–1.81) and patients with age 60+ years (AHR = 2.91: 95% CI: 1.79–3.99), patients with asymptomatic diseases condition (AHR = 1.15: 95% CI: 1.01–1.19), and being male (AHR = 1.22: 95% CI: 1.18–1.27) were independent significant risk factors of death from COVID-19.

Conclusion: A relatively high incidence of death from COVID-19 was found in this study. Significant risk factors were identified as patients with age <5 years, patients with age 60+ Years, being male, patients having at least one comorbid condition, and patients with asymptomatic disease conditions. These factors should be taken into consideration for a strategy of quarantining and treating COVID-19 patients.

Keywords: incidence of death, predictors, COVID-19, cox regression model

Introduction

Coronavirus disease 2019 (COVID-19), a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) infection, was declared a global pandemic in early 2020 (1). The pandemic has affected almost all nations in the world.¹ There were more than 592.7 million confirmed COVID-19 cases and about 6.4 million deaths worldwide as of August 11, 2022.² Human-to-human transmission (measured by population density) and air pollution-to-human transmission (airborne viral infectivity) are two ways that contribute to COVID-19 transmission dynamics.³ Both COVID-19 transmission modes are important in low-income nations like Ethiopia, and in these settings, higher transmissibility is anticipated due to larger household sizes, overcrowding, and inadequate water and sanitation, which will affect the adoption of recommended preventive measures.⁴ Ethiopia is exceptionally vulnerable to the spread of the pandemic due to its relatively fragile health systems, limited infrastructure, population mobility and connectedness, and susceptibility to social and political unrest.⁵

The COVID-19 pandemic is a human tragedy that occurred in this era. It poses an unprecedented social, economic, political, and health crisis starting from its outbreak, unlike any since the end of the Second World War. To reduce the humanitarian and economic impacts of the pandemic, countries introduced various degrees of response measures. Whereas these measures have been there, the cases and their impact have increased since the first case was identified.⁶ The socio-economic impacts being felt across Ethiopia already are wide-range and serious, with the potential to become severe, depending on the combination of the pandemic's trajectory, the effects of countermeasures, and underlying and structural factors.⁷

It is anticipated that the pandemic may have a profound case fatality rate in low and middle-income countries (LMICs) including Ethiopia. This hypothesis was supported by the high prevalence of communicable diseases, such as human immunodeficiency virus (HIV), tuberculosis, malaria, and other neglected infectious diseases in LMIC.^{8,9} Moreover, non-communicable diseases are also being identified with increasing frequency in these settings which will result in the high case fatality rate of COVID-19.⁸

Substantial knowledge has now accumulated regarding the acute clinical presentations, path physiological changes observed, and prognosis of COVID-19 patients. However, there is considerable variation in the estimates of the death rate of COVID-19 in a systematic review reported early in the pandemic.¹⁰ Similarly, the report of the WHO-China Joint Mission on COVID-19 indicated that the COVID-19 death rate significantly varies among different regions of China.¹¹ Studies in different parts of the world including Ethiopia also show various figures for the prevalence and incidence of death from COVID-19 ranging from 1.7% to 32%^{12–16} and 0.2 to 18 per 1000 person-days,^{12,15–17} respectively. As the study indicated, various factors including age, sex, preexisting co-morbidities, presence of symptoms at presentation, corticosteroid therapy, and time from onset to hospitalization determine the death rate.^{16–18}

Although the mortality rate of COVID-19 also varies among patients and settings, studies conducted around the world are majorly outside of Ethiopia. Studies regarding this issue are limited in Ethiopia, and no region-wise study that enrolled a large sample size has been conducted in Amhara regional state, Ethiopia. Hence, knowing the evidence on the determinant factors associated with the mortality rate of COVID-19 in Ethiopia including the study region will be crucial to strengthen the Government of Ethiopia's capacity to be prepared to respond to the COVID-19 outbreak such as to avail Medical Supplies and Equipment (Case management, IPC), Preparedness, Capacity Building, and Training, and for Quarantine, Isolation, and Treatment Centers establishment and Project Implementation and Monitoring. Therefore, this study aimed to assess the incidence of death and risk factors of COVID-19 among patients admitted to the Amhara regional state COVID-19 treatment center, Ethiopia.

Methods and Materials

Sample and Data

The participants in this study included all cases (28,533 patients) who tested positive for COVID-19 and were admitted to any of the Amhara regional state COVID-19 treatment centers (Gondar Hospital, Boru Meda Hospital, Tibebe Gion hospital, Debre Birhan Hospital, Debark hospital, Debre Markos hospital, Injibara hospital, Kobo hospital, Tefera Hailu hospital, and Dessie hospital) from 13 March 2020, through 13 January 2022. Amhara region is the country's second most populous region with 16 administrative zones and 238 districts. According to the regional report of the Amhara Health Bureau, the region has 98 hospitals, 917 health centers, 3725 health posts, 1346 private health facilities, and 60,482 health workforces by the start of 2022. Patients with incomplete outcome variables and lacking important baseline information such as date of admission, death, transfer, or discharge, were excluded. A facility-based retrospective survey data were retrieved between 1 and 30 February 2022. Trained health professionals who have been working in the treatment centers extracted the data from the registration logbook and patient's medical cards.

Measures of Variables

The outcome variable was the incidence of death of COVID-19; the time in days from the patient was diagnosed positive for COVID-19 and admitted to the treatment center until the occurrence of the outcome (event/censored). The event was the death of COVID-19 and censored were those patients who have not developed an event (recovered and/or transferred

out). Explanatory variables were age, sex, disease condition, and co-morbidity (Cases with comorbidities are those of COVID-19 patients with one or more coexisting medical illness/s).

Data Analysis Procedure

Epidata version 3.1 and STATA version 14 were used for data entry and analysis, respectively. Linearized survey analysis in a stratified cox regression model was fitted to identify independent risk factors. P-value with 95% CI for hazard ratio was used for testing the significance at alpha 0.05.

Results

Demographic and Clinical Characteristics of Patients

A total of 28,533 patients were included in the study. The mean age of the patient was 40.00 with an SD of ± 1.725 . Among COVID-19 admitted patients, 63.58% were males, and 7615 (26.69%) were under the age category of 25–34 years (Table 1).

Outcome Status

Of the total 28,533 population, 2873 (11.2%) died and 25,660 (88.8) were recovered from covid-19 in Amhara regional state COVID-19 treatment centers (Figure 1).

Factors Associated with the Incidence of Death from COVID-19

The incidence of death was 11.78 per 1000 person-days of observation with a median survival time of 32 days with IQR [12, 44]. Patients with age <5-year (AHR = 1.69; 95% CI: 1.78–1.81), 15–24 (AHR = 1.23; 95% CI: 1.01–1.79), 25–34 (AHR = 1.14; 95% CI: 1.06–1.19), 35–44 (AHR = 1.49; 95% CI: 1.39–1.59), 45–59 (AHR = 1.51; 95% CI: 1.30–1.69), and 60+ years (AHR = 2.91; 95% CI: 1.79–3.99) had a higher hazard of death than those aged 5 to 14 years. The death hazard of being male is 1.22 times (AHR = 1.22; 95% CI: 1.18–1.27) greater than being female. The death hazard of patients without signs and symptoms of COVID-19 is 1.15 times (AHR = 1.15; 95% CI: 1.01–1.19) greater than patients with signs and symptoms. The death hazard of patients with related diseases or comorbidities is 1.54 times (AHR = 1.54; 95% CI: 1.51–1.55) greater than that without related diseases (Table 2).

Table 1 Demographic and Clinical Characteristics of COVID-19 Patients Admitted to the Amhara Region COVID-19 Treatment Centers, Ethiopia from March 13, 2022 Through January 13, 2022 (N=28,533)

Variables	Category	Frequency	Percent (%)
Age	<1-year	271	0.95
	1–4	827	2.9
	5–14	858	3.01
	15–24	5516	19.33
	25–34	7615	26.69
	35–44	3862	13.54
	45–59	5785	20.27
	60+	3799	13.31
	Sex	Female	10,391
Male		18,142	63.58
Disease-condition	Asymptomatic	26,243	91.97
	Symptomatic	2290	8.03
Comorbidities	No	18,231	63.89
	Yes	10,302	36.11

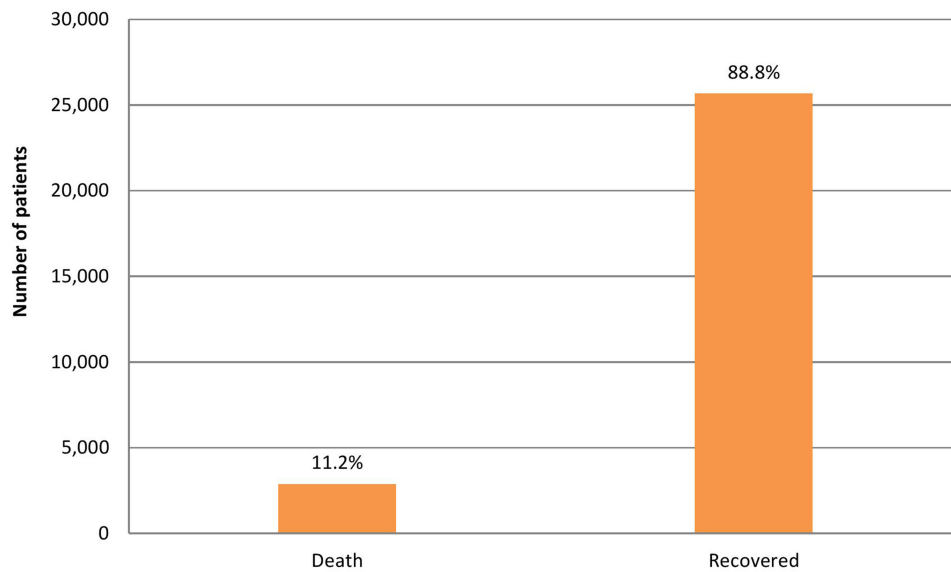


Figure 1 Outcome status of COVID-19 patients admitted to Amhara region COVID-19 treatment centers, Ethiopia from March 13, 2022 through January 13, 2022 (N=28,533).

Discussion

The pandemic of COVID-19 emerged as a public health problem and has resulted in increased anxiety, death, and deterioration of health with high case fatalities among elders and people who had co-morbidities.^{12,19} This multicenter facility-based retrospective follow-up study of hospitalized patients with COVID-19 was used to determine the incidence of death from COVID-19 and identify its predictors in the Amhara region, Ethiopia.

The current study found an incidence of death of 11.78 per 1000 person-days with a median survival time of 32 days with IQR [12, 44]. This finding is comparable to the previous study conducted among COVID-19 cases hospitalized at

Table 2 Linearized Survey Analysis in the Stratified Cox Regression Model for Risk Factors of Incidence of COVID-19 Patients Admitted to Amhara Region COVID-19 Treatment Centers, Ethiopia from March 13, 2022 Through January 13, 2022 (N=28,533)

Variable	CHR (95% CI)	AHR (95% CI)	P-value
Age categories			
<5-Year	1.70(1.58–1.83)	1.69(1.78–1.81)	0.001
5–14-Year	Reference		
15–24-Year	1.10(1.03–1.89)	1.23(1.01–1.79)	0.01
25–34-Year	1.15(1.06–1.24)	1.14(1.06–1.19)	0.001
35–44-Year	1.51(1.40–1.63)	1.49(1.39–1.59)	0.001
45–59-Year	1.55(1.35–1.78)	1.51(1.30–1.69)	0.001
60+-Year	2.79(1.89–3.81)	2.91(1.79–3.99)	0.001
Sex			
Female	Reference		
Male	1.25(1.23–1.29)	1.22(1.18–1.27)	0.001
Disease’s condition			
Asymptomatic	1.16(1.10–1.21)	1.15(1.01–1.19)	0.001
Symptomatic	Reference		
Comorbidities			
No	Reference		
Yes	1.54(1.53–1.56)	1.54(1.51–1.55)	0.001

Abbreviations: AHR, Adjusted Hazard Ratio; CHR, Crude Hazard Ratio; CI, Confidence Interval.

Bokoji Hospital COVID-19 treatment center with a 6.35 incidence of death per 1000 person-days¹⁵ and the finding from tertiary care hospital in the Harari region with an incidence death of 16.2 per 1000 person-days.¹⁶ This might be due to the similar socio-cultural and socio-economic status of both study settings with Amhara regional states. In addition to these, similar strategies and regulations are implemented across the country. However, the prevalence of death from COVID-19 in this study (11.2%) was so much higher than the finding of studies from china 2.84%,²⁰ South Korea 1.1%,²¹ and Iran 1.8%.²² It is expected that the impact of the COVID-19 outbreak in Ethiopia is to be far reaching and more catastrophic than in high-income countries. This might be due to concurrent co-morbidity among the general population, population size, and status of health systems and health workforce, which both have low resilience to external shocks and have insufficient critical care capacities.²³

In this study, different predictors showed an association with the incidence of death among hospitalized COVID-19 patients. Patients with comorbidities, patients with asymptomatic disease conditions, being male, patients with age <5 years, and patients with age 60+ years were independent significant risk factors for death rate in hospitalized COVID-19 patients. The death hazard of children under five years old and older patients aged 60 years and above is higher than patients in the age group of 5–14 years. This finding is consistent with previous studies done in South Central, Ethiopia,¹⁸ the United States,²⁴ and England.²⁵ This could be because the body's immune defense system is weak in this age group as well as older persons were more prone to severe disease or chronic diseases that hampered their health.

This study also revealed that males were at a greater risk of death than females. This finding is supported by previous studies conducted in Sub-Saharan African countries.²⁶ This might be due to gender being closely related to behavioral, social, and biological factors. For instance, the immune system, genetics, sex hormones, and the microbiome could contribute to lower COVID-19 death rates among women. On the other hand, greater health-harming behaviors among men (ie, smoking) contribute to the development of non-communicable diseases.²⁷ Patients who had co-morbidities also have a greater risk of death than their counterparts which is supported by studies from tertiary care hospitals in the Harari region,¹⁶ Italy,²⁸ and Mexico.²⁹ These could be due to the co-existence of COVID-19 patients with these comorbidities are more prone to acquire severe health condition that leads to immunosuppressive effect and low treatment outcomes, in case of these deaths could be exacerbated due to cytokine storm and an acute hyperinflammatory response formation.³⁰

The death hazard of patients without signs and symptoms has a greater risk than patients with signs and symptoms. The finding is supported by a study conducted in Korea which concluded that the most potent predictor for patient mortality in initially asymptomatic patients.³¹ This might be because patients who develop signs and symptoms have the chance to have an early visit to a health facility to get treatment than those who do not develop signs and symptoms. In addition, initially symptomatic patients were more likely to receive ICU care compared to initially asymptomatic patients.³¹ Early diagnosis and treatment of their disease help the patients not to develop complications; which decreases the death of COVID-19. It may also relate to the immunity status of these asymptomatic individuals. Immunosuppressed patients may present with not exhibiting any symptoms due to the decreased detrimental inflammatory responses and they are at a high risk of dying from COVID-19.³²

Conclusions

In conclusion, a relatively high incidence of death from COVID-19 was found in this study. Significant risk factors were identified as patients with age <5 years, patients with age 60+ years, being male, patients having at least one comorbid condition, and patients with asymptomatic disease conditions. This implies, that to reduce the burden of death from COVID-19, these factors should be taken into consideration for a strategy of quarantining and treating COVID-19 patients. It is important to consider special interventions and care for those patients who have comorbidity and are extremely aged. In addition, public health interventions for better practice of simple COVID-19 prevention mechanisms like wearing a mask, covering coughs and sneezes, keeping physical distance, and hand washing might contribute to reducing the burden of death from COVID-19 in the Amhara region, Ethiopia. Though this study analyzed a large sample size and enrolled all cases of COVID-19 who were admitted to any of Amhara regional state treatment centers, it is not without a limitation. Thus, the finding should be interpreted with caution by assuming the limitation that the study was conducted based on patient's secondary data, where it is impossible to address detailed individual level variables, which

precluding detailed analyses of factors that may affect the hazard of death from COVID-19. Further large scale studies with a strong design are needed to examine more individual level variables.

Abbreviations

AHR, Adjusted Hazard Ratio; CHR, Crude Hazard Ratio; CI, Confidence Interval; COVID-19, Coronavirus disease 2019; LMICs, Low and Middle-Income Countries; RNA, Ribonucleic Acid; SARS-CoV2, Severe Acute Respiratory Syndrome Coronavirus 2.

Data Sharing Statement

Data are available from the corresponding author upon reasonable request.

Ethics Approval

Ethical approval was obtained from the Institutional Review Board (IRB) of the College of Medicine and Health Sciences; at Bahir Dar University. A formal letter of cooperation was written to each treatment center and permission was obtained from the treatment center administration. It is a retrospective study of medical records and personal identifiers were not used on the data collection checklist. So, the IRB waived the requirement for informed consent. The study complies with the principle of the declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is, in the conception, proposal writing, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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