Survival status and predictors of mortality among mechanically ventilated COVID-19 patients in Addis Ababa COVID-19 Care Centers, Ethiopia: A survival analysis [version 1; peer review: awaiting peer review]

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Abstract

Background: The COVID-19 pandemic has caused stress on the health care system of many countries worldwide. To accommodate the growing number of critically ill patients requiring mechanical ventilation, hospitals expanded and tried to meet overwhelming demands. Despite this, outcomes of patients after mechanical ventilation were devastating, with high mortality rates. Therefore, this study investigated the survival status and predictors of mortality among mechanically ventilated COVID-19 patients.

Methods: A retrospective cohort study was applied on the patient charts of 496 critically ill and mechanically ventilated COVID-19 patients at intensive care units of Addis Ababa COVID-19 Care Centers from September 2020 to October 2021. Data were collected using a data extraction checklist and entered into Epi data manager. Then, data were transferred to STATA V-14 for cleaning and analysis. The cox-proportional hazard regression model was used for analysis. Covariates with p-value ≤0.20 in the bivariate analysis were fitted to multivariate analysis after the model fitness test. Finally, statistical significance was decided at p-value <0.05, and hazard ratios were used to determine the strength of associations.

Results: Of the 496 patients, 63.3% had died. The incidence rate of mortality was 56.7 (95% CI: 50.80, 63.37) per 1,000 person-days of observation, with 5534 person-day observations recorded. Advanced age (>60 years old) (adjusted hazard ratio (AHR)=1.86; 95% CI: 1.09, 3.15) and being invasively ventilated (AHR=2.02; 95% CI: 1.25, 3.26) were associated with increased risk of mortality. Furthermore, presence of diabetes (AHR=1.50; 95% CI: 1.09, 2.08), shock (AHR=1.99; 95% CI: 1.12, 3.52), and delirium (AHR=1.60; 95% CI: 1.05, 2.44) were
significantly associated with increased mortality.

**Conclusions:** Clear directions are needed in the recommendation of non-invasive versus invasive ventilation, especially among elderly patients. The controversy of when to intubate (early versus late) needs to be clarified as well. Early detection and prompt management of shock is paramount.

**Keywords**
Mechanical ventilator, COVID-19, Mortality, predictors, Ethiopia

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*This article is included in the Emerging Diseases and Outbreaks gateway.*

*This article is included in the Coronavirus collection.*

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**Author roles: Nega G:** Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Software, Validation, Visualization, Writing – Original Draft Preparation; **Sibhat M:** Conceptualization, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Mekonnen A:** Formal Analysis, Funding Acquisition, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – Review & Editing; **Techane T:** Conceptualization, Formal Analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**Grant information:** The author(s) declared that no grants were involved in supporting this work.

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**How to cite this article:** Nega G, Sibhat M, Mekonnen A and Techane T. **Survival status and predictors of mortality among mechanically ventilated COVID-19 patients in Addis Ababa COVID-19 Care Centers, Ethiopia: A survival analysis [version 1; peer review: awaiting peer review]** F1000Research 2022, 11:1329 https://doi.org/10.12688/f1000research.124586.1

**First published:** 16 Nov 2022, 11:1329 https://doi.org/10.12688/f1000research.124586.1
Introduction

Coronavirus disease 2019 (COVID-19), a contagious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) (One), imposed public health challenges within a short period.\(^1\) Over the past two years, the COVID-19 pandemic caused stress on the health care system of many countries in the world. Hospitals were overcrowded, and many lives were lost worldwide. As of 29\(^{th}\) June 2022, about 545.2 million confirmed COVID-19 cases were reported globally, of which 6,334,728 have died, and around 12 billion people received vaccination (One).

In the first few months of the pandemic, 13.8% of the total confirmed cases were severe, and 5% were critically ill.\(^1\) Severe respiratory failure was reported as the most common cause of death.\(^2\) According to the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) report, the world’s largest database, of all confirmed COVID-19 cases, 20% required intensive care unit (ICU) or highly dependent unit (HDU) admission during their illness.\(^3\)

The mechanism of COVID-19 infection remains puzzling yet. It is hypothesized that it may affect the pulmonary, cardiac, nervous, hepatic, renal and the coagulation system.\(^4\)\(^-\)\(^6\) COVID-19 can lead to different health consequences, including cardiomyopathy, shock, acute coronary syndrome, lung fibrosis, myocarditis, acute kidney injury, thromboembolism and arrhythmias.\(^7\)\(^-\)\(^9\)

Because of acute respiratory distress syndrome (ARDS) and diffuse parenchyma injury, about 60-90% of patients admitted to the ICU demand respiratory support with mechanical ventilators.\(^10\)\(^-\)\(^12\) Mechanical ventilation (MV) is the medical term for artificial ventilation where machines are used to assist or replace spontaneous breathing either invasively or non-invasively. Invasive mechanical ventilation (IMV) is a method of ventilation that involves inserting a plastic/metal tube into the patient’s airway. IMV is performed in the ICU or emergency room to meet the patient’s oxygen demands. Conversely, non-invasive ventilation (NIV) is breathing support administered through a face mask, nasal mask, or a helmet without tracheal intubation.\(^13\)\(^-\)\(^15\)

In the earliest stages of the pandemic, early intubation was encouraged over NIV due to the fear of increased viral transmission from aerosolization.\(^14\)\(^,\)\(^15\) Lately, almost all studies conducted to investigate the outcome of mechanically ventilated patients reported devastating figures (mortality rate as high as 97%). Nonetheless, the proportion of mortality was even higher among invasively ventilated patients,\(^16\)\(^-\)\(^18\) and NIV was associated with a significant survival benefit.\(^19\)\(^-\)\(^21\) On the other hand, it was hypothesized that COVID-19 might not cause classic ARDS that question the use of mechanical ventilation in such patients.\(^22\)\(^,\)\(^23\)

Healthcare interventions undertaken in the initial times of the pandemic in line with community mobilization and considerable government commitment played a significant role to limit the number of new cases and deaths due to COVID-19. The pandemic resulted in remarkable economic crisis, especially in low and middle-income countries. This damage is estimated to take years to recover.\(^24\)

The number of incident cases, severity of the disease, and fatality rate in Ethiopia were lower than in the rest of the world in the earliest periods. Nonetheless, the COVID-19 infectivity, severity, and fatality rate have reached to peak after then. At present, it imposes an additional impact on the country’s overburdened healthcare and socio-economic issues.\(^25\)

Therefore, in this study, we aimed to assess survival status and predictors of mortality of mechanically ventilated COVID-19 patients admitted to the ICU settings.

Methods

A retrospective cohort study was employed. Recordings of patients admitted to the ICU settings of the COVID-19 Care Centers in Addis Ababa, Ethiopia starting from September 2020 to October 2021 were reviewed retrospectively. There were three major COVID-19 Care Centers in Addis Ababa. Despite considerable resource delimitations, Millennium COVID-19 Care Center (MCCC) was recognized as an organized and relatively well-equipped COVID-19 care center compared to other centers countrywide. The center is the largest COVID-19 treatment center in the country, with a capacity of greater than 1,000 admission beds. It serves patients with confirmed mild, moderate, and critically ill COVID-19 infection in different treatment units, including outpatient departments, emergency service, wards, HDU, and ICU service (>40 ICU beds). Until November 2021, an overall 6,211 patients were admitted to the center. Of those, 1,537 were diagnosed with severe and critical illness, demanding ICU services. Among those who were admitted to the ICU settings of MCCC, 722 were admitted to the ICU from September 2020 to October 2021. Data collection was conducted from January 23, 2022, to March 07, 2022. We have taken efforts to minimize potential sources of bias by setting and following thoroughly predetermined research plans, performing analysis by different team members independently, and receiving critics and reviews from external peers. The study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies.\(^25\)
All COVID-19 infected patients admitted to the ICU and received mechanical ventilation support at Addis Ababa COVID-19 care centers were the source population. The study population included recordings of all patients admitted to the ICU and received respiratory support with a mechanical ventilator at the Millennium COVID-19 Care Center from September 2020 to October 2021. The lists of medical records were obtained from the COVID-19 registry and the liaison office reports. Recordings of patients deceased in the therapeutic center were considered events, whereas recordings of patients who discharged alive, weaned off from mechanical ventilator, and transferred out, were considered censored cases. Patient recordings with complete information were included in the study. The details of participant recruitment procedures were described in the flowchart (Figure 1).

Operationalization of terms and measurements
An event was considered when a patient died while on mechanical ventilation. Time to event or censor refers to the time to occurrence of an event (death) or other outcomes measured from ICU admission to the date that the event or censor occurred. Censored were those cases discharged alive from the ICU, transferred to other institutions, or weaned off to mechanical ventilators. Mechanical ventilation refers to providing artificial respiratory support using a ventilator machine either invasively (IMV) or non-invasively (NIV). The follow-up was started when the patient was put on a mechanical ventilator for respiratory support and ended when the patient was weaned off from a machine, transferred out from ICU while on MV, or died while receiving MV support, and was measured in days.

Data collection tools and procedure
The data extraction checklist was developed from the WHO COVID-19 guideline, mechanical ventilation protocols, and related literature. Before the actual study, recordings of all ICU mechanically ventilated patients were roughly reviewed (extracted) to identify the study subjects using medical record numbers (MRN) obtained from the ICU admission and discharge registration book. Then, all charts that fulfilled the inclusion criteria were reviewed, and relevant data were extracted. The data extraction tool comprised socio-demographic, disease-related, ventilator-related, and management-related variables. Data collectors and supervisors were recruited and trained on the data collection requirements. The checklist was pretested on 5% of randomly selected charts at MCCC to check its clarity and consistency. Accordingly, variables not recorded in the patient recordings were excluded from the extraction checklist. The pretest data was not included in the actual analysis. During data collection, each filled checklist was crosschecked and revised daily by the investigator for completeness. Hence, incomplete tools and missing information were managed at the
spot during the data collection procedure by cross-checking and communicating with the data collector at the end of each day.

**Data processing, analysis, and presentation**

After completion of data collection, the data was coded and entered into EpiData Manager 4.4.2.1 and exported to Stata 14 (an open-access alternative that can perform an equivalent function is Rstudio) for data cleaning and analysis. Then, an exploratory analysis was conducted to determine the level of missing values, influential outliers, and data distribution. The data were described using frequency tables, percentages, graphs, and means with standard deviations or medians with interquartile ranges based on the nature of data. A Kaplan-Meier curve was constructed to compare survival differences and to estimate the median survival time. Life tables were used to estimate cumulative probabilities of death at different time intervals.

Bivariate analysis was conducted using the Cox-proportional hazard model to determine the association between each independent variable with the outcome variable (death). Accordingly, variables with a p-value of ≤0.20 were considered for further analysis (multivariate analysis) to identify the net effect of each variable on mortality. The proportional hazard model assumption was checked using a global test (Schoenfeld residuals) (p=0.877). Besides, model fitness was checked using Cox-Snell residuals, and the graph showed the model fits the data well (Figure 2). Finally, statistical significance was declared at p≤0.05, and the strength of associations was summarized using an adjusted hazard ratio (AHR) with 95% confidence intervals.

**Ethical consideration**

The study was conducted after granting ethical approval (Reference=PM23/799; dated 06/12/2021) from the Saint Paul’s Hospital Millennium Medical College institutional review board (IRB). After approval, the IRB provided a waiver of patient consent since the study was conducted by chart review. Accordingly, permission for data collection was received from hospital directors on behalf of patients to get full access to patient recordings. Data coding and aggregate reporting were used so that names and other personal identifiers were not stated throughout the study process to ensure anonymity and confidentiality.

**Results**

Overall, 722 COVID-19 infected patients were admitted to ICU settings in the Millennium COVID-19 care center from September 2020 to October 2021. Consequently, 496 (n=496) mechanically ventilated patients with complete records were incorporated for analysis.

**Description of socio-demographic characteristics of study participants**

The study finding showed that more than 70% (350/496) of study participants were male. On the other hand, 79% of male patients and 60% of female patients died in the ICU. The mean age of participants was 59 years (SD=14.5), and only one-fourth of the study subjects were below the age of 50 years. The proportion of death was 41.5% (59/142) among patients below 50 years of age. In contrast, about 80% (n=200) of patients aged 65 years and over died during the follow-up period (Table 1).
Based on the findings, more than 55% (276/496) of patients were admitted to the center after seven days of symptom onset. The median time from symptom onset to hospital admission was eight days (IQR=3). Drastically, more than 75% of the cases were found to be hypoalbuminemic (<3.25g/dl) with a mean albumin level of 2.38g/dl (SD=1.32) at admission (Table 2). The findings also revealed that 314 patients had at least one chronic medical illness, of which 78.7% (247/314) have died. Conversely, 36.8% (67/182) of patients who did not have any chronic illness ended up with death due to COVID-19 infection. Diabetes mellitus (DM) (47%, n=496) and hypertension (HTN) (43%, n=496) were the most frequently recorded comorbidities. The proportion of death was much higher among those having DM (84.5%, n=233) and HTN (81.3%, 214) compared to patients who were free of DM (44.5%, n=263) and HTN (49.6%, n=282) (Table 2).

**Table 1.** Overall presentation of continuous variables using numeric measures among mechanically ventilated COVID-19 patients at Addis Ababa COVID-19 Care Centers, Ethiopia, 2022 (N=496).

| Continuous variable | Statistical measure | Mean  | SD    | Median | IQR  | 1st quartile | 3rd quartile | Min.  | Max. |
|---------------------|---------------------|-------|-------|--------|------|--------------|--------------|-------|------|
| Age (in years)      |                     | 59.25 | 14.48 | 60     | 21   | 49           | 70           | 24    | 88   |
| Days of Sx onset    |                     | 7.38  | 2.76  | 8      | 3    | 6            | 9            | 1     | 27   |
| SPO2 at baseline    |                     | 88    | 51.34 | 86     | 6    | 82           | 88           | 56    | 92   |
| Baseline albumin    |                     | 2.38  | 1.32  | 2.3    | 1.9  | 1.4          | 3.25         | 0.52  | 5.62 |
| Average PIP         |                     | 30.97 | 4.48  | 32     | 6    | 28           | 34           | 16    | 40   |
| Average PEEP        |                     | 10.50 | 1.64  | 10     | 2    | 10           | 12           | 6     | 14   |
| Average FiO2        |                     | 87.46 | 13.89 | 90     | 17.5 | 82.5         | 100          | 50    | 100  |
| Days on MV          |                     | 10.69 | 5.43  | 10     | 7    | 7            | 14           | 1     | 39   |
| WBC at the end      |                     | 17.82 | 4.72  | 19     | 9.5  | 12.5         | 22           | 9     | 26   |
| Cr at the end       |                     | 2.54  | 1.65  | 2.6    | 2.9  | 0.8          | 3.7          | 0.2   | 8.8  |

Abbreviations: SD, standard deviation; IQR, inter quartile range; Sx, symptom; SPO2, oxygen saturation; PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure; FiO2, fraction of inspired oxygen; MV, mechanical ventilator; WBC, white blood cell; Cr, creatinine.

**Table 2.** Distribution of comorbidities among mechanically ventilated COVID-19 patients at Addis Ababa COVID-19 Care Centers, Ethiopia, 2022 (N=496).

| Independent variables | Categories | Outcome status | Died, n (%) | Censored, n (%) | Total, n (%) |
|-----------------------|------------|----------------|-------------|-----------------|-------------|
| Comorbidities         | No         |                | 67 (36.8)   | 115 (63.2)      | 182 (36.7)  |
|                       | Yes        |                | 247 (78.7)  | 67 (21.3)       | 314 (63.3)  |
| DM                    | No         |                | 117 (44.5)  | 146 (55.5)      | 263 (53)    |
|                       | Yes        |                | 197 (84.5)  | 36 (15.5)       | 233 (47)    |
| HTN                   | No         |                | 140 (49.6)  | 142 (50.4)      | 282 (56.9)  |
|                       | Yes        |                | 174 (81.3)  | 40 (18.7)       | 214 (43.1)  |
| CKD                   | No         |                | 273 (61.8)  | 169 (38.2)      | 442 (89.1)  |
|                       | Yes        |                | 41 (75.9)   | 13 (24.1)       | 54 (10.9)   |
| Cardiac               | No         |                | 286 (62.2)  | 174 (37.8)      | 460 (92.7)  |
|                       | Yes        |                | 28 (77.8)   | 8 (22.2)        | 36 (7.3)    |
| Asthma                | No         |                | 254 (59.9)  | 170 (40.1)      | 424 (85.5)  |
|                       | Yes        |                | 60 (83.3)   | 12 (16.7)       | 72 (14.5)   |
| COPD                  | No         |                | 263 (60)    | 175 (40)        | 438 (88.3)  |
|                       | Yes        |                | 51 (87.9)   | 7 (12.1)        | 58 (11.7)   |
| HIV/AIDS              | No         |                | 196 (41.9)  | 272 (58.1)      | 468 (94.3)  |
|                       | Yes        |                | 18 (64.3)   | 10 (35.7)       | 28 (5.7)    |
Table 2. Continued

| Independent variable | Categories | Died, n (%) | Censored, n (%) | Total, n (%) |
|----------------------|------------|-------------|-----------------|--------------|
| Smoking status       | No         | 204 (54.5)  | 170 (45.5)      | 374 (75.4)   |
|                      | Yes        | 110 (90.16) | 12 (9.83)       | 122 (24.6)   |

Abbreviations: DM, diabetes mellitus; HTN, hypertension; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome.

Description of COVID-19 management and ventilator-related variables

After commencing artificial ventilation, patients remain on a mechanical ventilator for a median of 10 days (IQR=7). In-line with this, more than 55% (174/314) of deaths were recorded within the first 10 days of MV initiation (Table 1). According to the study result, 315 (63.5%) patients were intubated. Pressure regulated volume control (PRVC) was the most widely used (63.5%, n=315) mode of ventilation for intubated patients. An overall 181 (36.5%) patients were ventilated only with the non-invasive method of ventilation, of which 29 (16%) died. In opposition, 285 (90.5%, n=315) deaths were recorded among patients who received invasive ventilator support. The study results also showed that 71.8% (356/496) of study subjects developed ICU complications. All 496 (100%) study subjects took antibiotics, steroid therapy, and thromboprophylaxis (Table 3).

Table 3. Distribution of management-related characteristics among mechanically ventilated COVID-19 patients at Addis Ababa COVID-19 Care Centers, Ethiopia, 2022 (N=496).

| Independent variable | Categories | Died, n (%) | Censored, n (%) | Total, n (%) |
|----------------------|------------|-------------|-----------------|--------------|
| Method of ventilation | NIV        | 29 (16)     | 152 (84)        | 181 (36.5)   |
|                      | IV         | 285 (90.5)  | 30 (9.5)        | 315 (63.5)   |
| Mode of ventilation  | PRVC       | 178 (89)    | 22 (11)         | 200 (40.3)   |
|                      | PCV        | 74 (92.5)   | 6 (7.5)         | 80 (16.1)    |
|                      | VCV        | 33 (94.3)   | 2 (5.7)         | 35 (7.1)     |
|                      | CPAP       | 29 (16)     | 152 (84)        | 181 (36.5)   |
| Vasopressor use      | No         | 23 (15.8)   | 123 (84.2)      | 146 (29.4)   |
|                      | Yes        | 291 (83.1)  | 59 (16.8)       | 350 (70.6)   |
| Hemodialysis         | No         | 312 (63.2)  | 182 (36.8)      | 494 (99.6)   |
|                      | Yes        | 2 (100)     | 0 (0)           | 2 (0.4)      |
| Complication         | No         | 13 (9.3)    | 127 (90.7)      | 140 (28.2)   |
|                      | Yes        | 301 (84.5)  | 55 (15.4)       | 356 (71.8)   |
| Chest tube inserted  | No         | 219 (56.7)  | 167 (43.3)      | 386 (77.8)   |
|                      | Yes        | 95 (86.4)   | 15 (13.6)       | 110 (22.2)   |
| Reason for Chest tube insertion | Pneumothorax | 92 (86.8) | 14 (13.2) | 106 (21.4) |
|                      |            | 3 (75)      | 1 (25)          | 4 (0.8)      |
| AKI                  | No         | 49 (24.6)   | 150 (75.4)      | 199 (40.1)   |
|                      | Yes        | 265 (89.2)  | 32 (10.8)       | 297 (59.9)   |
| Sepsis/HAI           | No         | 13 (9.3)    | 127 (90.7)      | 140 (28.2)   |
|                      | Yes        | 301 (84.5)  | 55 (15.4)       | 356 (71.8)   |
| Electrolyte imbalance| No         | 20 (13.5)   | 128 (86.5)      | 148 (29.8)   |
|                      | Yes        | 294 (84.5)  | 54 (15.5)       | 348 (70.2)   |
| Delirium             | No         | 40 (20.1)   | 159 (79.9)      | 199 (40.1)   |
|                      | Yes        | 275 (92.6)  | 23 (7.4)        | 297 (59.9)   |
Comparison of survival status using Kaplan Meier curve
The Kaplan-Meier survival curve decreases stepwise and crosses the survival function at a survival probability of 0.5 (50%) (Figure 3).

Survival function and incidence rate of mortality
The overall mortality rate among mechanically ventilated COVID-19 patients was 63.3% (95% CI: 59.1, 67.6). Among 182 (36.7%) patients who were considered censored, 170 (93.4%) patients were weaned off from mechanical ventilators, and the rest 12 (6.6%) were transferred to other institutions. The total person-time observation was 5534 person-days. The incidence rate of mortality among mechanically ventilated COVID-19 infected patients was 56.7 (95% CI: 50.80, 63.37) per 1000 person-days of observation. The median survival time was found to be 13 days (95% CI: 8.0, 18.0). Thus, 50% of participants could remain on mechanical ventilation for up to 13 days of follow-up. The cumulative probabilities of mortality at the end of 7, 14, 21, and 28 days were 0.24, 0.72, 0.95, and 0.98 consecutively (Table 4).

Table 3. Continued

| Independent variable | Categories | Died, n (%) | Censored, n (%) | Total, n (%) |
|----------------------|------------|-------------|----------------|-------------|
| Shock                | No         | 24 (14.8)   | 138 (85.2)     | 162 (32.7)  |
|                      | Yes        | 290 (86.8)  | 44 (13.2)      | 334 (67.3)  |
| Coagulopathy         | No         | 102 (40.5)  | 150 (59.5)     | 252 (50.8)  |
|                      | Yes        | 212 (86.9)  | 32 (13.1)      | 244 (49.2)  |

Abbreviations: NIV, non-invasive ventilation; IV, invasive ventilation; PRVC, pressure regulated volume control; PCV, pressure control ventilation; VCV, volume control ventilation; CPAP, continuous positive airway pressure; AKI, acute kidney injury; HAI, hospital-acquired infections.

Figure 3. Overall Kaplan-Meier curve for mechanically ventilated COVID-19 patients at Addis Ababa COVID-19 Care Centers, Ethiopia, 2022 (N=496).

Table 4. Life table of mechanically ventilated COVID-19 patients at Addis Ababa COVID-19 Care Centers, Ethiopia, 2022 (N=496).

| Time interval, months | Beginning, total number | Death, total number | Cumulative failure, Probability (95% CI) |
|----------------------|-------------------------|---------------------|----------------------------------------|
| 0–7                  | 496                     | 120                 | 0.24 (0.21–0.28)                        |
| 7–14                 | 376                     | 237                 | 0.72 (0.68–0.76)                        |
| 14–21                | 139                     | 115                 | 0.95 (0.93–0.97)                        |
| 21–28                | 24                      | 14                  | 0.98 (0.96–0.99)                        |
| Covariate Category | Outcome variable | CHR (95% CI) | Sig. CHR | AHR (95% CI) | Sig. AHR |
|--------------------|-----------------|--------------|----------|--------------|----------|
| Death              | Death Censored  | 1            | 1        | 1            | 1        |
| Age                | ≤40 years       | 1            | 1        | 1            | 1        |
|                    | 41-60 years     | 1            | 1        | 1            | 1        |
|                    | >60 years       | 1            | 1        | 1            | 1        |
| Comorbidities      | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| DM                 | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| HTN                | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| CHD                | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| COPD               | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| Albumin at baseline| <3.4 g/dl       | 1            | 1        | 1            | 1        |
|                    | ≥3.4 g/dl       | 1            | 1        | 1            | 1        |
| Method of ventilation| NIV            | 1            | 1        | 1            | 1        |
|                    | >10 cmH2O       | 1            | 1        | 1            | 1        |
|                    | >35 cmH2O       | 1            | 1        | 1            | 1        |
| Shock after admission| No             | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| Coagulopathy       | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| AKI after admission| No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |
| Delirium in ICU    | No              | 1            | 1        | 1            | 1        |
|                    | Yes             | 1            | 1        | 1            | 1        |

*Statistically significant at a 95% uncertainty interval in the multivariable analysis.

Abbreviations: CHR, crude hazard ratio; AHR, adjusted hazard ratio; CI, confidence interval; DM, diabetes mellitus; HTN, hypertension; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; AKI, acute kidney injury; ICU, intensive care unit.
Predictors of death among mechanically ventilated COVID-19 patients

After determining the nature of the data, the Kaplan-Meier curve and life tables were used for data description. Then, a log-rank statistic test was used to compare the survival difference between groups. Afterward, a bivariate analysis was conducted, and variables to be included in the final model for multivariable analysis were identified. Accordingly, patient's age, comorbidities, shock, albumin, peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), DM, chronic kidney disease (CKD), chronic obstructive pulmonary diseases (COPD), method of ventilation, coagulopathy, acute kidney injury (AKI) and delirium after admission were transferred for further analysis. However, sepsis, length of stay on MV, electrolyte level, and smoking status were excluded since they violate the proportional hazard assumptions with the value of less than 0.05 during the Schoenfield residual test.

In the multivariable analysis, advanced age, invasive ventilation, DM, delirium, and shock were found to be independent predictors of mortality among mechanically ventilated COVID-19 infected patients at a 95% confidence level (Table 5).

Discussion

This study was conducted to determine survival status and predictors of mortality among COVID-19 patients who were mechanically ventilated. The incidence rate of mortality among mechanically ventilated COVID-19 patients was 56.7 (95% CI: 50.80, 63.37) per 1000 person-days of observation. The median survival time was found to be 13 days (95% CI: 8.0, 18.0). Older age (>60yrs), having DM, shock, and delirium while on MV were reported as predictors of mortality among mechanically ventilated COVID-19 patients. Moreover, being invasively ventilated was significantly associated with an increased mortality.

The overall mortality rate among mechanically ventilated COVID-19 patients was 63.3% (95% CI: 59.1, 67.6). The incidence rate of mortality among COVID-19 patients was 56.7 (95% CI: 50.80, 63.37) per 1000 person-days of observation with a total of 5534 person-day observations. This finding was much higher than reports of previous studies conducted in Belgium, 55%, 13 Norway, 21%, 29 Singapore, 9.1%, 44 Kuwait, 45.6%, 30 and Saudi Arabia, 32.1%. 31 The possible rationale might be that previous studies used a small sample size and included mild and moderate cases, unlike the current study, which considered only critically ill patients. Besides, a significant delay in admission after symptom onset and shorter duration of stay on a mechanical ventilator (median=10 days) in our study could inflate the mortality rate compared to earlier studies 13,31,32 since literature evidenced an inverse relationship between the length of stay and chance of mortality. 19,33 Furthermore, the difference in the level of readiness to halt the pandemic would also result in this discrepancy. ICU services require intensive resources in terms of equipment, medications, skilled professionals, space, and time, which is challenging for developing nations like Ethiopia. Here in Ethiopia, medical supplies, including lifesaving medications, were scarce. 25,34

Conversely, a study conducted in Pakistan reported a higher ICU mortality rate (77%). 19 The possible justification could be that the Pakistan study was conducted in the earliest waves of the pandemic, where countries lack readiness and inconsistent management protocols that might significantly influence patient outcomes. Furthermore, a shorter duration of follow-up and a small sample size applied can contribute to this discrepancy. 19

Patients aged above 60 years were 1.86 times at an increased hazard of death compared to their counterparts (AHR=1.86; 95% CI: 1.09, 3.15). This finding was conformable with reports of several studies conducted abroad. 19,29,31,32,35,36 The possible justification could be physiological responses decline with advanced age, which weakens host defense in acute infections resulting in an increased risk of complications and adverse health outcomes. 32 On the contrary, previous studies suggested that elders have increased differential gene expression for an inflammatory condition, with a reduction in type I interferon beta. This is because the innate host response to viral infections is stronger in elders than in younger age groups. 38

Furthermore, the hazard of death among diabetic patients was 50% (AHR=1.50; 95% CI: 1.09, 2.08) higher than those who were not diagnosed with DM. Results of former studies conducted in Brazil and Norway were in agreement with this finding. 29,30,40 This is because diabetic patients have immune suppression that makes them susceptible to severe infections. Hence, the COVID-19 virus might rapidly replicate and invade the lung parenchyma easily. Moreover, this immune-compromised state can expose patients to superimposed infections such as hospital-acquired or superimposed pneumonia and sepsis. 40 Diabetic patients also have elevated levels of pro-inflammatory markers. 40

The hazard of death was two-folds higher among invasively ventilated (intubated) patients compared to their counterparts (AHR=2.02; 95% CI: 1.25, 3.26). This was in line with previous study findings. 19,20,32,54 This can be multifactorial. First, in most scenarios, intubation is considered if NIV is unsuccessful, which could increase the chance of refractory hypoxia. 42 Second, intubated patients were highly prone to ventilator-associated complications, including
pneumothorax, ventilator-associated pneumonia, increased risk of sepsis, and sedation inadequacy or excess.\textsuperscript{43} Third, unlike those non-invasively ventilated, intubated patients can not complain of any discomfort or inconvenience such as pain and are solely dependent on the skill and commitment of health personnel. Previous studies also agreed that more than half of patients who fulfilled intubation criteria survived with just NIV and avoided invasive ventilation, whereas clinical outcomes and mortality among invasively ventilated patients were devastating.\textsuperscript{20,41}

Additionally, a diagnosis of shock while on artificial ventilation also showed a statistically significant association with mortality of critically ill COVID-19 patients. Mechanically ventilated patients who developed shock had a twofold (AHR=1.99; 95% CI: 1.12, 3.52) increased risk of death due to critical COVID-19 illnesses compared to their counterparts. We could not find any research that reported the effect of shock on the mortality of COVID-19 patients who needed MV support. The scientific rationale could be that shock can result in hypoperfusion and hypoxemia. To add fire to the chaff, the pressure support (specially PEEP) can compromise tissue perfusion by indirectly counteracting venous return and cardiac output,\textsuperscript{44–46} making shock management arduous. As a result, hypoperfusion of vital organs could lead to multi-organ failure and hypo-function, thus, ending up in death.

On the other hand, the risk of death among patients who developed delirium in the ICU compared to their counterparts was 60% higher (AHR=1.60; 95% CI: 1.05, 2.44). This might be due to the effect of delirium on patient-ventilator interaction. Patients with delirium usually have asynchrony, especially during NIV support. Furthermore, delirious patients would fight with the ventilator machine, which could increase peak airway pressure. Sequentially, this will lead to an increased risk of pulmonary barotrauma (pneumothorax). On the other hand, delirious patients require an extra dose of sedation to maintain synchrony, exposing them to unintended drug adverse effects and an unrousable state. Consequently, all these factors can deteriorate the patient’s condition and result in death.

The study considered censored observations. Besides, in addition to baseline information, follow-up data were used to estimate patient characteristics, which enabled a more accurate investigation of the effects of these variables. Conversely, this study also has its limitations. First, there was considerable delay in ICU admission and mechanical ventilation support from symptom onset. Hence, there might be an overestimation of the mortality rate. Second, we did not evaluate the effect of some important variables such as procalcitonin, troponin, serum ferritin, d-dimer, lactate dehydrogenase, and interleukin-6 that showed statistically significant association in the previous studies conducted abroad due to lack of access for these laboratory tests.

**Conclusions**
The study finding showed a high incidence of mortality among critically ill COVID-19 patients who were supported with mechanical ventilators. Older age (>60 years), invasive means of mechanical ventilation, having DM, and ICU complications such as shock and delirium were independent predictors of death among mechanically ventilated COVID-19 patients. Clear directions are needed in the recommendation of non-invasive versus invasive ventilation, especially among elderly patients. The controversy of when to intubate (early versus late intubation dilemma) needs to be clarified as well. Early detection and prompt management of shock is paramount, especially considering that most intubated patients develop shock immediately after intubation and are due to sepsis.

**Data availability**
**Underlying data**
Figshare: DATASET for Survival status and predictors of mortality among mechanically ventilated COVID-19 patients in Addis Ababa COVID-19 Care Centers, Ethiopia. \url{https://doi.org/10.6084/m9.figshare.21126178}.

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

**Reporting guidelines**
Figshare: STROBE checklist for ‘Survival status and predictors of mortality among mechanically ventilated COVID-19 patients in Addis Ababa COVID-19 Care Centers, Ethiopia’. \url{https://doi.org/10.6084/m9.figshare.20870908}.

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

**Acknowledgments**
The authors would like to thank data collectors, supervisors, hospital staff, and administrators for their unreserved efforts and commitment. The authors also appreciated Saint Paul’s Hospital Millennium Medical College for chasing this chance and covering the data collection costs.
Characteristics of and important lessons from COVID-19: a review. Int. Med. 2020; 48(7): 434–448. PubMed Abstract; Publisher Full Text

3. Wiersinga WJ, Rhodes A, Cheng AC, et al.: Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19) (2): 465. PubMed Abstract; Publisher Full Text

4. Grasselli G, Zangrillo A, Zanella A, et al.: Clinical characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020; 323(13): 1229–1242. PubMed Abstract; Publisher Full Text

5. Costa IBSS, Bittar CS, Rízk SI, et al.: Association of home noninvasive positive pressure ventilation with clinical outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA. 2020; 323(5): 455–465. PubMed Abstract; Publisher Full Text

6. de Terwaeghe C, Sorgente A, Tortora R, et al.: Mortality Rate and Predictors among Patients with COVID-19 Related Acute Respiratory Failure Requiring Mechanical Ventilation: A Retrospective Single Centre Study. J. Crit. Care Med. 2021; 7(1): 21–27. PubMed Abstract; Publisher Full Text

7. Phua J, Weng L, Ling L, et al.: Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir. Med. 2020; 8(S6): 506–517. PubMed Abstract; Publisher Full Text

8. McGann F, Humphries RS, Lee JH, et al.: Aerosol generation related to respiratory interventions and the effectiveness of a personal ventilation hood. Crit. Care Resusc. 2020; 22(3): 212–220. PubMed Abstract

9. Wang Y, Lu X, Li Y, et al.: Clinical course and outcomes of 344 intensive care patients with COVID-19. Am. J. Respir. Crit. Care Med. 2020; 11(1): 1430–1434. PubMed Abstract; Publisher Full Text

10. Quah P, Li A, Phua J: Mortality rates of patients with COVID-19 in the intensive care unit: a systematic review of the emerging literature. Crit. Care. 2020; 24: 1–4. PubMed Abstract; Publisher Full Text

11. Zhou F, Yu T, Du R, et al.: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395(10229): 1054–1062. PubMed Abstract; Publisher Full Text

12. Rahim F, Amin S, Noor M, et al.: Mortality of Patients With Severe COVID-19 in the Intensive Care Unit: An Observational Study From a Major COVID-19 Receiving Hospital. Cureus. 2020; 12(10).

13. Daniel P, Mecklenburg M, Massiah C, et al.: Noninvasive positive pressure ventilation versus endotracheal intubation in treatment of COVID-19 patients requiring ventilatory support. Am. J. Emerg. Med. 2021; 43: 103–108. PubMed Abstract; Publisher Full Text

14. Hua J, Qian C, Luo Z, et al.: Invasive mechanical ventilation in COVID-19 patient management: the experience with 469 patients in Wuhan. Crit. Care. 2020; 24(1): 1–3. PubMed Abstract; Publisher Full Text

15. Santos MM, Lucena EE, Lima KC, et al.: Survival and predictors of deaths of patients hospitalised due to COVID-19 from a retrospective and multicentre cohort study in Brazil. Epidemiol. Infect. 2020: 148. PubMed Abstract; Publisher Full Text

16. Tu Y, Yang P, Zhou Y, et al.: Risk factors for mortality of critically ill patients with COVID-19 receiving invasive ventilation. Int. J. Med. 2021; 43: 1–8. PubMed Abstract; Publisher Full Text
43. Haribhai S, Mahboobi SK: Ventilator Complications. StatPearls. Treasure Island FL: © 2022: StatPearls Publishing LLC; 2022.

44. Zhou L, Cai G, Xu Z, et al.: High positive end expiratory pressure levels affect hemodynamics in elderly patients with hypertension admitted to the intensive care unit: a prospective cohort study. BMC Pulm. Med. 2019; 19(1): 1–9.

45. Courmand A, Motley HL, Werko L, et al.: Physiological studies of the effects of intermittent positive pressure breathing on cardiac output in man. American Journal of Physiology-Legacy Content. 1947;

46. Pinsky MR: The hemodynamic consequences of mechanical ventilation: an evolving story. Intensive Care Med. 1997; 23(5): 493–503.

47. Sibhat M: DATASET for Survival status and predictors of mortality among mechanically ventilated COVID-19 patients in Addis Ababa COVID-19 Care Centers, Ethiopia. figshare. [Dataset]. 2022.
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