Cohort Study

ANNALS OF MEDICINE & SURGERY

OPEN

Survival status and predictors of mortality among COVID-19 patients admitted to intensive care units at COVID-19 centers in Addis Ababa, Ethiopia: a retrospective study

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Introduction: Worldwide, including in Ethiopia, there is an increased risk of coronavirus disease 2019 (COVID-19) disease severity and mortality. This study aimed to assess the survival status and predictors of mortality among COVID-19 patients admitted to the intensive care unit.

Methods: This study included 508 COVID-19 patients retrospectively who were under follow-up. The work has been reported in line with the STROCSS (strengthening the reporting of cohort, cross-sectional and case–control studies in surgery) criteria. The data were collected through a systematic sampling from patients' charts. Kaplan–Meier survival curves and logrank test, and Cox's regression analyses were conducted to check the difference among categories of covariates and to identify predictors of mortality, respectively.

Results: All patient charts were reviewed and the information was recorded. The average age (mean + SD) of these patients was 62.1 + 13.6 years. Among study participants, 422 deaths occurred and the mortality rate was 64.1 per 1000 person-days. The median survival time was 13 days [interquartile range (IQR): 10–18]. The significant predictors for this survival were: Age > 45 years [adjusted hazard ratio (AHR) = 4.34, 95% CI: 2.46–7.86], Diabetes mellitus (AHR = 1.37, 95% CI: 1.05–1.77), Hypertension (AHR = 1.39, 95% CI: 1.09–1.79), Renal disease (AHR = 1.86, 95% CI: 1.01–3.43), Hypotension (AHR = 1.71, 95% CI: 1.28–2.27), Electrolyte treatment (AHR = 0.78, 95% CI: 0.63–0.97).

Conclusion: The median survival of COVID-19 patients after their admission was 13 days, and predictors for this time were advanced age, preexisting comorbidities (like diabetes mellitus, hypertension, and renal disease), hypotension, and electrolyte therapy.

Keywords: COVID-19, Cox's regression, Ethiopia, SARS-COV-2, survival analysis

Introduction

Numerous human communicable diseases have developed and spread over time, posing a long-standing problem for scientists. One of these illnesses is coronavirus disease 2019 (COVID-19), which is characterized as an infection that causes severe acute respiratory syndrome and has become an emergency[1,2]. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) novel strain type that caused this infection was discovered in the China peninsula of Wuhan in December 2019[1–7].

In March 2020, the World Health Organization (WHO) declared the outbreak of a global pandemic and threat to public health[8]. Since its outbreak, COVID-19 has caused ~459 million illnesses and more than 6.6 million deaths in the world, and more than 258 thousand deaths in Africa as well as more than 7500 mortalities in Ethiopia[2,3,9]. It is still a serious health issue that kills thousands of people every day across the globe[9–11]. Several studies have been carried out to comprehend the public

HIGHLIGHTS

- The mortality rate in this study was higher (83.1%) than in different world findings.
- The incidence mortality rate was high with a 13-day median survival time of patients after their admission.
- Older age (> 45 years), preexisting comorbidities (diabetes mellitus, hypertension, and chronic obstructive pulmonary disease), complications related to coronavirus disease 2019 (COVID-19) (acute kidney injury and hypotension), and high creatinine levels were found to be significant predictors for the survival of COVID-19 patients.
- Patients who received electrolyte treatment had good outcomes than patients who did not.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2023) 85:2368–2378

Received 17 February 2023; Accepted 1 May 2023

Published online 10 May 2023

http://dx.doi.org/10.1097/MS9.0000000000000803

health effects of COVID-19, which is continuously increasing disease severity and mortality risk worldwide, including in Ethiopia[5,7,12–14].

The incidence, severity, and mortality of COVID-19 disease are higher in patients with risk factors like advanced age, male sex, and comorbidities like hypertension, diabetes, chronic respiratory disease, heart disease, cancer, and a variety of laboratory test abnormalities. Therefore, these are the main factors that have been reported and strongly influence the risk of dying from COVID-19[13,15–18].

Infiltrates in both lungs, acute respiratory distress syndrome (ARDS), intubation, sepsis, intensive care unit (ICU) admission, and a longer median length of hospital stay were all more prevalent in the COVID-19 patients who passed away in hospitals[19]. Patients with hypotension and hypoxemia on COVID-19 had noticeably worse outcomes. The mortality of COVID-19 patients with hypotension and hypoxemia was correlated with age, temperature, troponin, and blood glucose[11].

According to a different study, the survival and mortality of COVID-19 patients varied depending on several measurements at the time of admission, including elevated levels of cardiac troponin, creatinine, interleukin, D-dimer, and decreased albumin[15]. Patients who also have end-organ damage, acute inflammation, or cardiometabolic disease are more likely to die from COVID-19 infection and need more aggressive treatment[15,20].

Based on another study, the increased COVID-19 disease severity and/or mortality associated with numerous preexisting comorbidities (cardiovascular disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, chronic kidney disease), hypoxemia, specific computed tomography findings indicative of extensive lung involvement, acute kidney disease, elevated levels of leukocytes, blood urea nitrogen, erythrocyte sedimentation rate, lymphocytopenia, severity, and hospital admission[5,12,13,17,20–24].

According to a study conducted in Ethiopia, the presence of fever, history of smoking, drinking, comorbidity, decreased oxygen saturation, and low lymphocyte count are all predictors of mortality[25]. The severity of the clinical manifestation of COVID-19 disease varies; patients with severe symptoms like pneumonia quickly progressing to ARDS, multiorgan failure, and death can present with no symptoms or only mild symptoms[2,26]. There have been at least 1.4 times more deaths attributed to COVID-19, according to estimates from the World Mortality Dataset of deaths in various nations, which is indicative of the daily death of COVID-19 that is available online and updated daily[9,27,28].

Ethiopia is sixth in Africa and second in Sub-Saharan Africa in terms of the number of cases and deaths that have been reported, with an overall case fatality rate (CFR) of about 1.5% compared to the 2.2% in the rest of the world[9]. Over 75% of patients admitted under COVID-19 require intranasal oxygen supplementation[2]. The CFR among hospitalized patients varies by age, ranging from 0.3 per 1000 cases for patients between the ages of 5 and 17 to 304.9 per 1000 cases for patients over the age of 85. The duration of viral clearance among COVID-19 patients who have been admitted, however, varies with populations' age structure, presence of comorbidity, and quality of healthcare. Remdesivir treatment, however, improves the duration of viral clearances in hospitalized patients[1,2,8,29].

Patients with COVID-19 have a different average survival time in the ICU and emergency rooms of hospitals. In central Florida's ICU, the survival time of survivors compared to nonsurvivors was 14 [interquartile range (IQR) 7–24] and 9.5, respectively (IQR 6–11)[30] and in the Democratic Republic of the Congo's Kinshasa Medical Center, patients with COVID-19 had a cumulative survival rate of 86.9%, 65.0%, and 19.9% at 5, 10, and 20 days, respectively, with increased deterioration at hospitals. The median survival time for the entire group was 12 days at the emergency department[19,26]. According to a study from eastern Ethiopia, the median survival time was 44 days with IQR (28–74)[1].

The most important aspect of the patient's prognosis is optimized support because there is no specific antiviral therapy. Patients with symptoms and comorbidities must receive special attention during interventions to further lower mortality and recovery times at the treatment facility[1]. Remdesivir and corticosteroids are currently the most promising COVID-19 treatments, though additional research may be required to confirm their efficacy[31].

To maintain the advancements made in ensuring longer and healthier lives, timely and effective health policies are essential, as are interventions to reduce the potential direct and indirect effects of COVID-19 on life expectancy due to excess mortality for populations of different ages, especially among older adults. The assessment of survival and predictors of mortality of COVID-19 is crucial[32,33].

Several studies have shown how COVID-19 affects public health globally, including in Ethiopia, where it continues to cause disease severity and mortality risk. Even though COVID-19 patients admitted to ICU Centers have a high mortality rate, studies on the survival status and its predictors of mortality among COVID-19 patients are scarce worldwide, including in our country Ethiopia.

Materials and methods

The study design and period

The work has been reported in line with the STROCSS 2021 guideline: Strengthening The Reporting Of the Cohort Studies in Surgery[34]. The institution-based retrospective cohort study was conducted at COVID-19 Centers in Ethiopia from 5 May to 20 July 2022. During this period, patients' information was retrieved from charts of patients who were admitted and received care at COVID-19 ICU Centers from 13 March 2020 to 31 December 2021.

Study area and population

All randomly selected charts of COVID-19 patients admitted to the ICU of selected COVID-19 centers from 13 March 2020 to 31 December 2021 were included in the study.

Sample size determination

The sample size was determined using the single population proportion formula under the assumptions of $\alpha = 0.05$, power = 0.8, the proportion of the survival group = 0.81, and the proportion of deceased patients = 0.19[1]. Hence, the calculated sample size was 317. However, by considering to add a 10% of incomplete medical records of patients, the minimum required sample size became 349. To increase the precision of the result, the investigators included all 508 charts of COVID-19 patients admitted and their treatment outcomes were identified before 31 December 2021, at both COVID-19 centers.

Sampling procedure

Currently, two active COVID-19 centers have been selected. After that, the medical record numbers of COVID-19 ICU centers were isolated from the computer registration liaison office. Then, from the isolated medical record numbers in each Center, a systematic random sampling technique was applied to select the records. Finally, the selected medical charts based on the records were reviewed.

Variables of the study

The outcome variable used in this study was the survival status of COVID-19 patients whereas predictor variables were age, sex, occupation, support, residency; hypertension, diabetes mellitus, chronic obstructive pulmonary disease, alcohol consumption, smoking, renal disease, cardiac disease, creatinine, complete blood count (CBC), coagulation profile, computed tomography (CT) scan angiography, chest X-ray, glutamic–oxaloacetic transaminase (GOT), glutamic–pyruvic transaminase (GPT), blood urea nitrogen (BUN), antibiotics, remdesivir, hydrocortisone, dexamethasone, asthmatic treatment (aminophylline and salbutamol), electrolyte, and antipsychotic/sedation.

Operational definitions of variables

(1) Incidence density rate of survival – it was computed by dividing the number of events by the total follow-up time in person-days observation.
(2) Time to death – the number of days it takes from admission until a patient has died of COVID-19 (that can be measured by using incidence density rate and median survival time).
(3) Survival status – the status of the patients at the end of the follow-up period (event or censored).
(4) Censored – patients who lost to follow-up and those who did not develop the outcome of concern (death) during the follow-up period.
(5) Follow-up time: from the time of hospitalization until an event occurred.
(6) Event – the occurrence of death due to COVID-19 at the time of hospital stay from 13 March 2020 to 31 December 2021.

Data collection tool and procedure

A data abstraction format was adapted from different literatures[10–13,15,19–22,25,31,35]. Based on the study's goals, four parts of data abstraction checklists (sociodemographic, clinical, laboratory, and treatment-related) data were collected from medical records. Data collectors and supervisors received a 1-day training on the importance of the study, the truthfulness with which the checklist should have been completed, and ethical considerations in order to standardize the data collection. Following that, all study participants' records were chosen in accordance with the eligibility requirements, and all pertinent data from patient records were retrieved. Then, using a structured data extraction format, they extracted from the patient charts all pertinent variables which satisfy the objective of the study. The diagnosis of COVID-19 served as the starting point for the retrospective follow-up, and the dates of discharge, transfer to another facility, and death served as the endpoints.

Data quality assurance

Pretest was performed on 5% of the study samples at the COVID-19 center to ensure the accuracy of the data, and corrections were made based on any errors discovered during the verification process to guarantee that the data abstraction format complied with the study objectives. Daily during the data collection process, the completeness of the collected data was verified on-site. Throughout the data management, storage, cleaning, and analysis processes, all completed data collection forms were checked for accuracy and consistency. The principal investigator randomly chose a sample of medical records and compared them for similarity to assess consistency.

Data processing and analysis

The retrieved and extracted data were entered, coded, and cleaned by using Epi Data version 4.2 before being exported to STATA 14 for further analysis. Schoenfeld's residual test was used to verify Cox's proportional hazard regression model's essential premise. The data were presented using descriptive and inferential statistics. The sociodemographic characteristics and the clinical characteristics of the study participants' survival status were summed up using descriptive statistics like the mean and median of survival time.

The result was divided into two categories: censored and event. The logrank test was used to compare the survival curves among categorical predictors, and the Kaplan–Meier survival curve was used to estimate survival time. To find predictors of death among COVID-19 patients, bivariate Cox's regression was conducted, and variables with a P value less than 0.25 were added to the multivariable Cox's regression analysis. The significant predictors of mortality of COVID-19 patients were reported using hazard ratios with a 95% confidence interval and P values less than 0.05.

Results

Sociodemographic characteristics and preexisted comorbidity status of study participants

In this study, all charts of the 508 patients were used in the analysis; hence, the mean age of patients with its standard deviation was 62.1 + 13.6 years. About half, 267 (52.6%), of patients were male. The majority of the patients, 500 (98.4%), were from the city. The leading source of referral of 195 (38.4%) patients was health centers. Almost all patients, 504 (99.2%), had a positive record of social support. Few patients, 34 (6.7%) and 74 (14.2%) had a history of smoking and alcohol drinking, respectively. Nearly half of them, 245 (48.2%), had a history of medical problem before they suffered from COVID-19 infection. Of patients who had a history of medical problems, the majority, 230 (93.9%), of them had one to two medical comorbidities. Regarding the clinical status of the patients at admission, 476 (93.7%) of them were in critical condition and admitted to ICU. Among events, 396 (93.8%) and 26 (6.2%) were critical and semicritical at the time of their admission, respectively (Table 1).

Table 1

Sociodemographic characteristics and clinical status of COVID-19 patients ($n = 508$)

Variables	Category	Number (%)	Survival status, *n* (%)	
			Censored	Event
Sex	Male	267 (52.6)	45 (52.3)	222 (52.6)
	Female	241 (47.4)	41 (47.7)	200 (47.4)
Residency	Addis Ababa	500 (98.4)	85 (98.8)	415 (98.3)
	Out of Addis Ababa	8 (1.6)	1 (1.2)	7 (1.7)
Social support	Yes	504 (99.2)	84 (97.7)	420 (99.5)
	No	4 (0.8)	2 (2.3)	2 (0.5)
Source of referral	Health center	195 (38.4)	34 (39.5)	161 (38.2)
	Hospital	168 (33.1)	20 (23.3)	148 (35.1)
	Private facility	145 (28.5)	32 (37.2)	113 (26.8)
Smoking status	Yes	34 (6.7)	2 (2.3)	32 (7.6)
	No	474 (93.3)	84 (97.7)	390 (92.4)
Alcohol drinking status	Yes	72 (14.2)	3 (3.5)	69 (16.4)
	No	436 (85.8)	83 (96.5)	353 (83.6)
History of the medical problem before COVID-19 infection	Yes	245 (48.2)	5 (5.8)	240 (56.9)
	No	263 (51.8)	81 (94.2)	182 (43.1)
Number of medical comorbidities	No comorbidity	263 (51.8)	81 (94.2)	182 (43.1)
	1-2 comorbidities	230 (45.3)	4 (4.7)	226 (53.6)
	≥ 3 comorbidities	15 (3.0)	1 (1.2)	14 (3.3)
History of the medical problem before COVID-19 diagnosis	Diabetes mellitus	104 (20.5)	3 (3.5)	101 (23.9)
	Hypertension	116 (22.8)	2 ((2.3)	114 (27.0)
	HIV/AIDS	17 (3.3)	1 (1.2)	16 (3.8)
	Heart disease	35 (6.9)	0 (0.0)	35 (8.3)
	COPD	58 (11.4)	0 (0.0)	58 (13.7)
	Cancer	4 (0.9)	0 (0.0)	4 (1.0)
	Asthma	17 (3.3)	1 (1.2)	16 (3.8)
	Kidney disease	11 (2.2)	0 (0.0)	11 (2.6)
Clinical status at admission time	Critical	476 (93.7)	80 (93.0)	396 (93.8)
	Semicritical	32 (6.3)	6 (7.0)	26 (6.2)
Patient admitted to	ICU	476 (93.7)	81 (94.2)	395 (93.6)
	HDU	32 (6.3)	5 (5.8)	27 (6.4)

COPD, chronic obstructive pulmonary disease; HDU, high dependent unit; ICU, intensive care unit.

Clinical and laboratory characteristics of COVID-19 patients

Of all COVID-19 patients, the majority of them, 506 (99.6%), developed COVID-19-related medical complications. Of COVID-19-related medical complications, the majority, 493 (97%), of them developed three and above medical comorbid complications. At the average time, the mean of oxygen concertation of patients was 80.5 + 5.2. In addition, at the average time, the mean pulse rate, respiration rate, blood pressure, and random blood sugar were 104.5 + 18 beats/min, mean respiration rate 35.5 + 7.9 RR/min, 122.9 + 25.2/77.3 + 19.7 mmHg, and 147.3 + 97.6 mg/dl respectively. Among patients with the event, 413 (97.9%) of them had three and above medical comorbidity complications due to COVID-19 infections. Of patients who died, acute kidney disease 57.6%, hypertension 78.9%, diabetes mellitus 58.1%, asthmatic problem 70.4%, and stress/psychosis 96.0% were common comorbidities. Based on the laboratory finding for patients with the event, common predictors were leukocytosis 175 (41.5%), lymphocytopenia 47(11.6%), high creatinine 187 (44.3%), high GOT 180 (42.7%), high GPT 174 (41.2%), low prothrombin time (PT) test 100 (23.7%), low partial thromboplastin (PTT) time 88 (20.9%), and high BUN 94 (22.3%) (Table 2).

Treatment-related characteristics of COVID-19 patients

Of all COVID-19 patients, 508(100%) were put on oxygen therapy by mechanical ventilation, unfractionated heparin (UFH), and antibiotics. The majority of the patients, 497 (97.8%), were taking either hydrocortisone or dexamethasone, and 493(97%) took antipsychotic (haloperidol)/sedation (diazepam). More than half of the patients, 68.7%, used asthmatic treatment (aminophylline or salbutamol) and 57.5% took electrolytes (potassium chloride). A small number of patients, 91 (17.9%), have got chance of remdesivir treatment (Fig. 1).

Survival status of COVID-19 patients

Five hundred eight patients admitted to COVID-19 ICU centers have followed for 6584 days with a minimum of 3 days to a maximum of 27 days with an overall median survival day of 13 days (95% CI: 12.4–13.6) or 13 days with an IQR of 10–18. Overall, during the entire cohort, 86 (16.9%) were censored and 422 (83.1%) died. The overall incidence density rate of death for this study was found to be 64.1 per 1000 person-days observation (95% CI: 58.3–70.5). The incidence rate of death for female patients was higher as compared to male patients (64.8 vs. 63.5 deaths per 1000 persons-day observations). The probability of survival at 3, 6, 11, 16, 21, and 26 days were 99.8%, 90.4%, 62.8%, 33.6%, 8.8%, and 3.8%, respectively (Fig. 2).

Time to death of COVID-19 patients

A logrank test (Mantel–Cox) was conducted to assess the existence of any significant differences in survival time among the different categories of predictor variables. Based on this test result, sex, social support, smoking history, history of (HIV/AIDS, heart disease, cancer, and asthmatic problem), COVID-related medical complications, leukopenia, lymphocytopenia, and hemoglobin were statistically significant ($P < 0.05$). This indicates that there was a statistically significant difference among and between categories of predictor variables. This evidenced that there is a significant difference in the survival probability of patients among different categories (Table 3).

According to this study, the median time to death of COVID-19 patients with a history of one to two medical comorbidities before COVID-19 infection was 12 days (95% CI: 11.4–12.6), which was lower than the median time to death of patients with three or more medical comorbidities which is 15 days (95% CI: 12.2–17.8) (Fig. 3).

This study shows that those patients who were admitted with a critical condition at the time of admission have a less median survival of 13 days (95% CI: 12.5–13.5) when compared with patients admitted with semicritical conditions, which had 16 median survival days (95% CI: 12.8–19.2) (Fig. 4).

The cumulative failure of COVID-19 patients was low on the third day of admission, which increases as follow-up time increases to 27 days. At the end of the 6th day of hospital stay, the

Table 2

Clinical and laboratory characteristics of COVID-19 patients (*n* = 508)

Variables	Category, mean + SD	Number (%)	Survival status, *n* (%)	
			Censored	Event
Average vital signs registered from admission to the outcome	Mean oxygen saturation (%)	80.5 + 5.2	82 + 4.9	80 + 6.6
	Mean pulse rate (beats/min)	104.5 + 18.0	96.7 + 7.2	107.4 + 22.3
	Mean respiration rate (RR/min)	33.5 + 7.9	32.2 + 3.6	33.8 + 9.5
Mean blood pressure (mmHg)	Systolic	122.9 + 25.1	106.9 + 21.2	125.3 + 28.7
	Diastolic	77.3 + 19.7	68.8 + 12.4	79.0 + 21.7
	Mean random blood sugar (mg/dl)	147.3 + 97.6	113.6 + 57.6	153.2 + 114.3
COVID-19-related complications	Yes	506 (99.6)	84 (97.7)	422 (100)
	No	2 (0.4)	2 (2.3)	0 (0.0)
Numbers of COVID-19-related complications	No complication	2 (0.4)	2 (2.3)	0 (0.0)
	One to two complications	13 (2.6)	4 (4.7)	9 (2.1)
	Three and above complications	493 (97.0)	80 (93.0)	413 (97.9)
COVID-19-related medical complications after admission	Acute kidney injury	252 (49.6)	9 (10.5)	243 (57.6)
	Hypertension	359 (70.7)	26 (30.2)	333 (78.9)
	Diabetes mellitus	285 (56.1)	40 (46.5)	245 (58.1)
	Asthmatic problem	334 (65.7)	47 (54.7)	297 (70.4)
	Stress/psychosis	485 (95.5)	80 (93.0)	405 (96.0)
	Other[a]	22 (4.3)	1 (1.2)	21 (5.0)
Laboratory and imaging predictors	Leukocytosis (10^3/μl)	190 (37.4)	15 (17.4)	175 (41.5)
	Leukopenia (10^3/μl)	8 (1.6)	0 (0.0)	8 (1.9)
	Lymphocytopenia (10^3/μl)	50 (9.4)	1 (1.2)	49 (11.6)
	Low hemoglobin (g/dl)	48 (9.4)	1 (1.2)	47 (11.1)
	Low creatinine (mg/dl)	59 (11.6)	3 (3.5)	56 (13.3)
	High creatinine (mg/dl)	193 (38.0)	6 (7.0)	187 (44.3)
	High GOT	182 (35.8)	2 (2.3)	180 (42.7)
	High GPT	176 (34.6)	2 (2.3)	174 (41.2)
	Low PT test	101 (19.9)	1 (1.2)	100 (23.7)
	Low PTT time	90 (17.7)	2 (2.3)	88 (20.9)
	Low INR	60 (11.8)	0 (0.0)	60 (14.2)
BUN (mg/dl)	Low BUN	15 (3.0)	0 (0.0)	15 (3.6)
	High BUN	97 (19.1)	3 (3.5)	94 (22.3)
CT scan	Yes	59 (11.6)	3 (3.5)	56 (13.3)
	Massive lung involvement (*n* = 59)	41 (64.5)	3 (3.5)	38 (9.0)
	Chest X-ray	56 (11.0)	5 (5.8)	51 (12.1)

[a]Septic shock, pneumonia.

BUN, blood urea nitrogen; CT, computed tomography; GOT, glutamic–oxaloacetic transaminase; GPT, glutamic–pyruvic transaminase; INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time.

failure was 9.6%, and at the end of 11 days, 31.2%, which increases to 96.2% at the end of 26 days of follow-up (Fig. 5).

Predictors for the survival of COVID-19 patients

Cox's proportional hazard regression model was used to analyze the association between the survival time of patients and predictor variables. Predictor variables were analyzed for association with the outcome variable, and those variables associated with a *P* value less than 0.25 were included in the multivariable Cox's regression model. In the multivariable Cox's regression analysis, eight predictor variables had a significant association with the survival of COVID-19 patients.

The result of multivariable Cox's regression analysis showed that COVID-19 patients who were 45–54 years of age had three times the hazard to die (adjusted hazard ratio (AHR) = 2.72, 95% CI: 1.42–5.03), 55–64 age had more than four times hazard to die (AHR = 4.53, 95% CI: 2.47–8.32), 65–74 age interval had six times hazard to die (AHR = 5.81, 95% CI: 3.10–10.89), and 75 or older age had five times hazard to die (AHR = 5.06, 95% CI: 2.65–9.67) than those age group of 35–44 years. The hazard of dying for those COVID-19 patients with preexisted diabetes mellitus and hypertension was 1.4 times (AHR = 1.37, 95% CI: 1.05–1.77) and 1.39 times (AHR = 1.39, 95% CI: 1.09–1.79) higher than those patients without diabetes mellitus and hypertension, respectively. Patients with preexisted renal disease were almost two times more likely hazard of death (AHR = 1.86, 95% CI: 1.01–3.43) than those patients without renal disease. Having the preexisted comorbidity of chronic obstructive pulmonary disease (COPD) increases the hazard of death by 1.64 times (AHR = 1.64, 95% CI: 1.21–2.22) compared to the counterpart.

Regarding COVID-19-related medical complications, those who developed acute kidney injury had a 1.5 times more likely hazard of dying than those without acute kidney injury (AHR = 1.50, 95% CI:1.21–1.86). Similarly, hypotension increases the hazard of death more likely by 1.7 times than patients with no comorbidity complications of hypotension (AHR = 1.71, 95% CI: 1.28–2.27).

Furthermore, patients who had a higher-than-normal range of creatinine level (> 1.3 mg/dl) had a 1.5 times higher hazard of dying (AHR = 1.51, 95% CI: 1.17–1.94) than patients with a

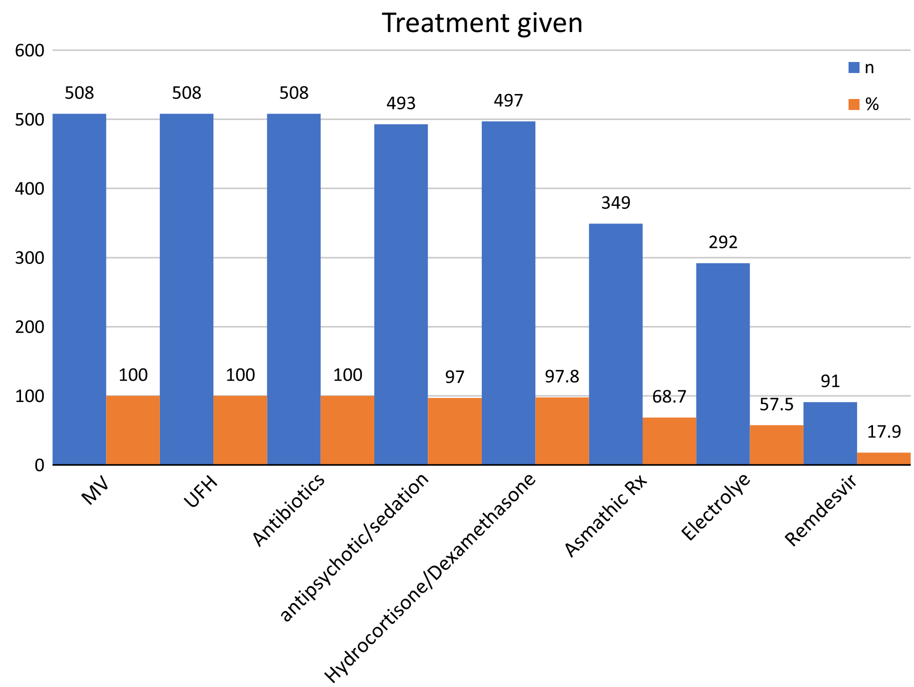

Figure 1. Treatment characteristics of coronavirus disease 2019 (COVID-19) patients. MV, mechanical ventilation; UFH, unfractionated heparin.

normal range of creatinine level. COVID-19 patients who received electrolyte treatment were 22% less likely to die than patients who had not received the electrolyte treatment (AHR = 0.78, 95% CI: 0.63–0.97) (Table 4).

Proportional hazard assumption test

For the interpretation and use of fitted proportional hazard models, it is essential to test the proportional hazard assumption. Because of this, global testing and goodness-of-fit (GOF) tests, specifically Schoenfeld's residuals proportional hazard assumption tests, were used in this work. The outcomes showed that each variable in the model met the proportional hazard (PH) assumptions ($P > 0.05$) and global for Cox's proportional hazard (P value $= 0.673 > 0.05$), according to the findings in Table 5.

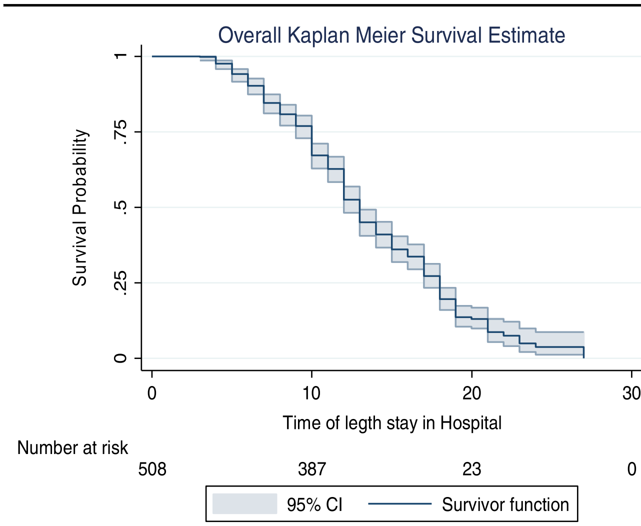

Figure 2. Overall Kaplan–Meier survival estimate of coronavirus disease 2019 (COVID-19) patients.

Discussion

The management and care of COVID-19 patients, particularly those who had a high vulnerability to death, depend heavily on the estimation of the median time to death and the identification of predictors of mortality. In this study, COVID-19 patients admitted to ICU centers were evaluated to determine the incidence density rate of death and to identify factors that predict the survival of patients. The mortality rate in this study was 422 (83.1%), which was higher than the rates in studies conducted in other nations such as Spain (30.7%)[10], Italy (26%)[36], France (20%)[35], the United States (35.4%)[37], and the United Kingdom (29.3–41.4%)[38]. This variation could be the result of a different level of care at the facility, a different study period, or an infection wave.

In the current study, there were 64.1 deaths per 1000 person-days of observation among COVID-19 patients during the study period. This result is significantly different than the study carried out in the eastern region of Ethiopia, which was 16.2 per 1000 person-days of observation[1]. Differences in the characteristics of the study participants and the study environment might be the cause of the discrepancy between the two findings.

In this study, the overall follow-up period, which ranged from 3 to 27 days, the probability of survival for COVID-19 patients was high on the 3rd day of admission (99.8%), but it started to decline as the follow-up period gets longer to a maximum of 27 days. The failure rate was 9.6% at the end of the 6th day of the hospital stay, 31.2% at the end of the 11th day, and 96.2% at the end of the 26-day follow-up. This shows that as a patient's hospital stay lengthens, their chance of survival shortens. This result

Table 3

Median survival time and logrank test for equality of survivor functions ($n = 508$)

Variables	Category	Median survival time to death in days (95% CI)	Logrank test (*P*)
Age	35–44	22 (21.6–23.7)	0.000
	45–54	16 (0.16.1–17.9)	
	55–64	12 (10.7–13.3)	
	65–74	12 (11.3–12.7)	
	≥ 75	12 (11.3–12.7)	
Alcohol consumption	Yes	12 (11–13)	0.029
	No	13 (12.3–13.7)	
Preexisting medical problem before COVID-19 diagnosis	Yes	12 (11.3–12.7)	0.000
	No	15 (13.5–16.5)	
History of DM before COVID-19 diagnosis	Yes	11 (9.9–12.1)	0.000
	No	13 (12.1–13.9)	
History of hypertension before COVID-19 diagnosis	Yes	12 (11–13)	0.000
	No	13 (12.2–13.8)	
History of COPD before COVID-19 diagnosis	Yes	12 (11.1–12.9)	0.000
	No	13 (12.3–13.7)	
History of kidney disease before COVID-19 diagnosis	Yes	10 (7.9–12.1)	0.046
	No	13 (12.4–13.6)	
Acute kidney disease due to COVID-19 complication	Yes	12 (11.4–12.6)	0.000
	No	14 (12.3–15.7)	
Hypertension due to COVID-19 complication	Yes	12 (11.4–12.6)	0.000
	No	15 (13.4–16.4)	
Asthmatic problem due to COVID-19 complications	Yes	12 (11.5–12.5)	0.037
	No	14 (12.6–15.6)	
Any other complications due to COVID-19	Yes	11 (8.7–13.3)	0.049
	No	13 (12.4–13.6)	
Leukocytosis	Yes	13 (12.1–13.9)	0.002
	No	13 (12.3–13.7)	
Creatinine	Normal	14 (12.3–15.7)	0.000
	Low	13 (11.5, 14.5)	
	High	12 (11.3–12.7)	
GOT	Normal	13 (12–14)	0.000
	High	12 (11.1–12.9)	
GPT	Normal	13 (12–13)	0.000
	High	12 (11.1–12.9)	
PT time	Normal	13 (12.4–13.6)	0.000
	Low	11 (9.8–12.2)	
	High	14 (10.7–17.3)	
PTT	Normal	13 (12.4–13.6)	0.006
	Low	10 (8.7–11.3)	
	High	13 (11–15)	
INR	Normal	13 (12.4–13.6)	0.022
	Low	12 (10.3–13.7)	
Overall		13 (12.4–13.6)	

COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; GOT, glutamic–oxaloacetic transaminase; GPT, glutamic–pyruvic transaminase; INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time.

is consistent with a study conducted in Congo that found that the likelihood of survival declines as hospital stay lengthens[26].

The median survival time of patients during the cohort of follow-up was 13 days (95% CI: 12.4–13.6), or 13 days with an interquartile range of 10–18 days in the current study. This research was almost identical to that conducted in the eastern region of Ethiopia, where it was discovered that the median survival time before death was 14 days[39], Brazil 12 days[4], and the study done at Kinshasa Medical Center of the Democratic Republic of Congo at the emergency department 12 days[26]. However, this finding was greater than the finding from a study done at Leon Spain Hospital, which was 11 days[40], Italy 8 days[16], and New York city 9 days[41]. The reason for the discrepancy of this finding with that of Leon Spain, Italy, and New York city might be due to the sociodemographic characteristic of the study participants, the hospital bed coverage, and other health coverages. Almost the age of the COVID-19 patients admitted at both centers was relatively an older age and they had lifestyle-related comorbidities. In addition, the median survival time of this study was less than that of a study conducted in Indonesia, which was 18 days, on average[13], China 25 days[42], and Germany 25 days[43]. This might be the result of the disparity in healthcare standards between low-income and high-income nations in the COVID-19 case, including the scarcity of ventilator machines, among other things.

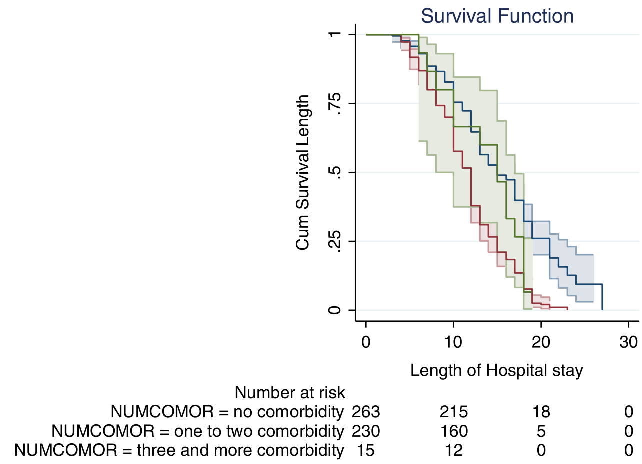

Figure 3. The Kaplan–Meier (KM) survival curves compare the median survival time with different medical comorbidities.

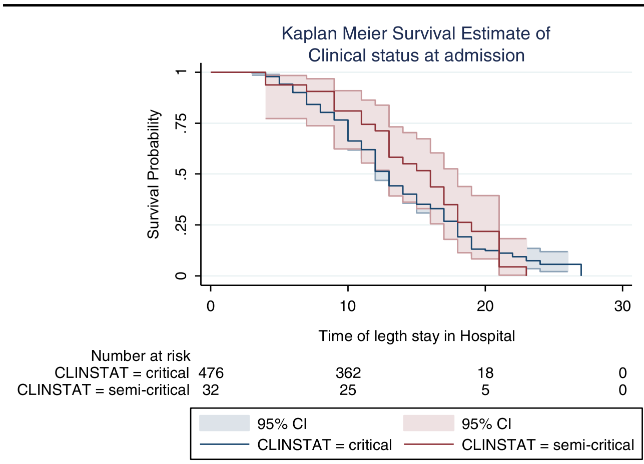

Figure 4. The Kaplan–Meier (KM) survival curves compare time to death with clinical status at admission.

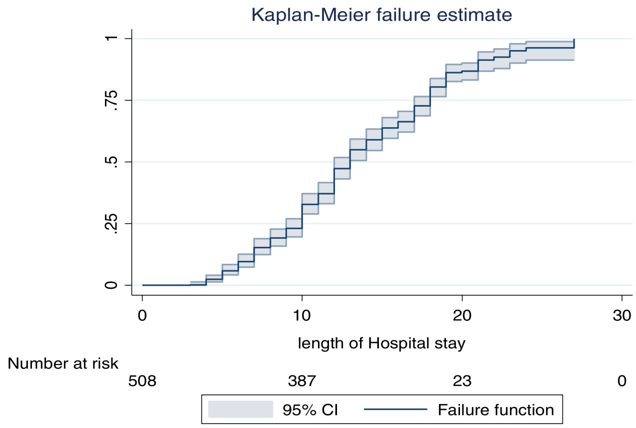

Figure 5. The Kaplan–Meier (KM) failure curves among coronavirus disease 2019 (COVID-19) patients.

Age was discovered to be a significant predictor for survival of COVID-19 patients in this study. According to the results of multivariable Cox's regression analysis, the risk of death for COVID-19 patients was three times higher for those aged 45–54, four times higher for those aged 55–64, six times higher for those aged 65–74, and five times higher for those aged 75 or older than for those in the age group of 35–44. The risk of dying from COVID-19 increases with age. Therefore, this finding emphasizes the need for prompt medical attention for older individuals who have COVID-9 infections. The results were consistent with numerous studies conducted in nations including Saudi Arabia, Iran, the United States, China, the Netherlands, Spain, and Ethiopia[5,10–12,15,20,23,24,44]. The likelihood of death in older adults was likely increased by their susceptibility to multiple organ failure and comorbidities. Additionally, a recent study found that COVID-19 puts older adults at a higher risk of mortality for four main reasons the presence of asymptomatic systemic inflammation in the absence of significant disease, a suppressed immune system, and type-I interferon response as a result of persistent inflammation, downregulation of the ACE2 receptor, as well as biological ageing[43].

Patients with COVID-19 who have at least one comorbid condition have a higher risk of dying than patients without comorbid conditions. The risk of death for those with diabetes mellitus and hypertension is increased by 1.4 times. Patients with COVID-19 compared to those without diabetes mellitus and/or high blood pressure. This finding is pretty close to the study done in different countries like Italy[16,45], Iran[24], France[46], and the systematic review done in China[15], and India[47]. This might be since being diabetic is directly associated with low immune function, thus increasing the risk of both bacterial and viral infections including COVID-19, consequently poor outcomes. This finding highlights that the importance of timely monitoring and greater conservative management for those individuals with comorbidities.

Similarly, several studies were done in different parts of the world: Island[17], northwest of Ethiopia[23], Swiss[32], and Congo[26]; in this study, renal disease and COPD were others preexisted predictors of COVID-19 mortality. When compared to their counterparts, COPD and renal disease both increase the risk of death by 1.6 and 2 times, respectively. This may be due to the fact that one of the most frequent immediate causes of death in COVID-19 patients is COPD, which has been found to be associated with a higher risk for poor outcomes. This is probably because these patients typically have decreased lung function in addition to other comorbidities[29,43]. Existing renal disease may increase the likelihood of end-organ damage and put patients at a much higher risk of dying in the hospital[48].

Those who developed kidney injury had a 1.5 times greater risk of dying from COVID-19-related medical complications than those who did not develop kidney injury. The kidney cells are infected by the virus itself. The new coronavirus can attach to kidney cells, invade, and replicate inside them, potentially causing damage to the tissues. The heart, lungs, and other systems are impacted by vital kidney functions. Because of this, kidney damage that develops in COVID-19 patients is a fatal progression

Table 4

Bivariate and multivariable Cox's regression analysis ($n = 508$)

Variables	Category	CHR (95% CI)	AHR (95% CI)	*P*
Age	35–44	1.00	1.00	
	45–54	3.31 (1.82–6.02)	2.72 (1.42–5.03)	0.001
	55–64	6.41 (3.60–11.39)	4.53 (2.47–8.32)	0.000
	65–74	8.42 (4.75–14.93)	5.81 (3.10–10.89)	0.000
	≥ 75	8.07 (4.54–14.35)	5.06 (2.65–9.67)	0.000
Alcohol consumption	Yes	0.76 (0.59–0.99)	1.04 (0.76–1.42)	0.819
	No	1.00	1.00	
Preexisted medical problem before COVID-19 diagnosis				
Diabetes mellitus	Yes	1.60 (1.28–2.01)	1.37 (1.05–1.77)	0.020
	No	1.00	1.00	
Hypertension	Yes	1.62 (1.30–2.01)	1.39 (1.09–1.79)	0.050
	No	1.00	1.00	
Renal disease	Yes	1.76 (0.97–3.21)	1.86 (1.01–3.43)	0.048
	No	1.00	1.00	
COPD	Yes	0.63 (0.47–0.83)	1.64 (1.21–2.22)	0.002
	No	1.00	1.00	
COVID-19-related medical complications after admission to centers				
Acute kidney injury	Yes	1.75 (1.44–2.12)	1.50 (1.21–1.86)	0.000
	No	1.00	1.00	
Hypotension	Yes	2.03 (1.60–2.56)	1.71 (1.28–2.27)	0.000
	No	1.00	1.00	
Hypertension	Yes	1.47 (1.21–1.79)	1.72 (0.89–2.33)	0.091
	No	1.00	1.00	
Baseline laboratory markers				
Leukocytosis	Yes	1.33 (1.10–1.62)	1.11 (0.90–1.39)	0.336
	No	1.00	1.00	
Creatinine level	Normal	1.00	1.00	
	Low	1.66 (1.23–2.24)	1.52 (0.89–2.08)	0.090
	High	1.77 (1.44–2.18)	1.51 (1.17–1.94)	0.001
GOT	Normal	1.00	1.00	
	High	1.63 (1.34–1.98)	1.28 (0.81–2.02)	0.293
PT coagulation time	Normal	1.00	1.00	
	Low	1.50 (1.20–1.88)	1.12 (0.75–1.65)	0.589
PTT	Normal	1.00	1.00	
	Low	1.38 (1.09–1.74)	0.88 (0.61–1.26)	0.474
Remdesivir treatment	Yes	1.00	1.00	
	No	0.77 (0.61–0.99)	0.99 (0.76–1.30)	0.963
Electrolyte treatment	Yes	1.00	1.00	
	No	0.67 (0.55–0.82)	0.78 (0.63–0.97)	0.024

AHR, adjusted hazard ratio; CHR, cumulative hazard ratio; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; GOT, glutamic–oxaloacetic transaminase; PT, prothrombin time; PTT, partial thromboplastin time.

Table 5

Schoenfeld's residual test for assessing proportional hazards model assumptions

Variables	ρ	χ^2	df	P
Age	0.01954	0.17	1	0.6758
Smoking history	− 0.01698	0.13	1	0.7203
Alcohol consumption	− 0.03471	0.55	1	0.4584
Preexisted DM	0.04892	1.15	1	0.2839
Preexisted hypertension	0.02698	0.34	1	0.5617
Preexisted HIV/AIDS	− 0.03872	0.66	1	0.4162
Preexisted COPD	0.00232	0.19	1	0.9584
Preexisted renal disease	0.03156	0.45	1	0.5044
Acute renal failure due to COVID-19 complications	− 0.04472	0.89	1	0.3445
Hypotension due to COVID-19	− 0.06619	2.04	1	0.1532
Hypoxemia due to COVID-19	0.02689	0.33	1	0.5656
Asthmatic problem due to COVID-19	0.03818	0.68	1	0.4110
Any other complications due to COVID-19	− 0.08626	3.49	1	0.0617
Leukocytosis	− 0.02082	0.20	1	0.0617
Leukopenia	− 0.05127	1.20	1	0.2727
Lymphocytopenia	− 0.02501	0.31	1	0.5763
Hemoglobin level	0.00794	0.03	1	0.8618
Creatinine level	− 0.02591	0.31	1	0.5795
GOT level	− 0.05376	1.45	1	0.2278
GPT level	0.06795	2.25	1	0.1333
PT coagulation time	0.00520	0.01	1	0.9070
PTT coagulation time	− 0.00831	0.03	1	0.8562
INR time	− 0.03809	0.71	1	0.4009
Remdesivir treatment	0.03153	0.46	1	0.4992
Electrolyte treatment	− 0.04637	1.01	1	0.3159
Global test		23.21	27	0.6730

COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; GOT, glutamic–oxaloacetic transaminase; GPT, glutamic–pyruvic transaminase; PT, prothrombin time; PTT, partial thromboplastin time.

of the illness. This study is supported by global findings done in Spain[10], Italy[49], and China[15].

As different literature revealed in this finding, hypotension increases the hazard of dying by 1.7 times more than patients with no comorbidity complications of hypotension. Hypotension is the most prevalent complication among dying COVID-19 patients. Hypotension is the factor that aggravates the status of COVID-19 patients and consequences poor outcomes[11,15].

Furthermore, compared to patients with a normal range of creatinine level, patients with a higher-than-normal range of creatinine level (> 1.3 mg/dl) had a 1.5 times higher risk of dying. This suggests that a rise in creatinine levels might be regarded as a sign of poor outcomes. To identify these patients and provide them with specialized care, early creatinine screening is crucial upon admission. This will lower the risk of death from COVID-19. This result is consistent with a China study that found a high creatinine baseline level was a predictor of mortality[48,50].

Patients who received electrolyte treatment had a 22% lower risk of passing away than patients who did not. There is a poor outcome among COVID-19 patients when blood serum electrolyte decreases, according to the literature[51]. Hospitalized and intensive care patients are more likely to experience fluid and electrolyte disturbances[52]. Body fluid volume and electrolyte concentrations can be used to assess disease status and disease progression because fluid and electrolyte disturbances can be seen in COVID-19. To determine timely and appropriate corrective actions, it is preferable to measure electrolytes at initial presentation and serially monitor them throughout hospitalization.

Conclusions

This study tried to assess the survival status of COVID-19 patients and to identify associated predictors with the survival time of patients. Hence, the incidence mortality rate was high with 13-day median survival time of patients after their admission. Older age (> 45 years), preexisting comorbidities (diabetes mellitus, hypertension, and chronic obstructive pulmonary disease), complications related to COVID-19 (acute kidney injury and hypotension), and high creatinine level were found to be significant predictors for the survival of COVID-19 patients.

Strength and limitation

To properly identify predictors of mortality and control confounding effects, the study used advanced analysis techniques. The data, however, were derived retrospectively from patient medical records, and some significant factors, such as laboratory markers (CRP level, albumin, cardiac markers dimer, IL-6, lactate dehydrogenase, and serum ferritin) that were significant predictors of COVID-19 mortality in other studies, were either not recorded at all or were recorded insufficiently and were therefore excluded from the analysis.

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Yekatit 12 Hospital Medical College with Protocol number: 124/22 and permission from Eka Kotobe and St. Peter Specialized hospitals to review the record of patients.

Consent

Permission from the centers to review the record of patients was obtained. The privacy and confidentiality of the information were obtained by principal investigators.

Sources of funding

None.

Author contribution

A.B. and K.H.: study conception and design; A.B.: data collection; A.B. and K.H.: data analysis and interpretation; A.B.: drafting of the article; A.B., K.H., A.T., and G.W.: critical revision of the article.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: researchregistry8866.

3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

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Data availability statement

The data set used and/or analyzed during the study can be obtained from the corresponding author upon reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgments

Our deepest gratitude goes to Yekatit 12 Hospital and Medical College. We would also like to thank Eka Kotobe Hospital and St. Peter Specialized Field Hospital staff.

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