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Incidence and predictors of mortality among COVID-19 patients admitted to treatment centers in North West Ethiopia; A retrospective cohort study, 2021

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ABSTRACT

Background: Currently, coronavirus disease 2019 (COVID-19) is the leading cause of death and the rate of mortality is rapidly increasing over time. There is a paucity of information regarding the incidence and predictors of mortality among COVID-19 patients from low-income countries, particularly in Ethiopia.

Objective: To assess incidence and predictors of mortality among COVID-19 patients admitted to treatment centers in North West Ethiopia.

Methods: An institution-based retrospective cohort study was conducted among 552 laboratory-confirmed COVID-19 cases at Debre Markos University and Tibebe Ghion Hospital COVID-19 treatment centers in North West Ethiopia from March 2020 to March 2021. Data were collected from patients’ medical records using a structured data extraction tool. Cox-proportional hazards regression models was fitted to identify significant predictors of mortality.

Result: The overall mortality rate of COVID-19 was 4.7, (95 % CI: 3.3–6.8) per 1000 person day observations. Older age (AHR: 4.9; 95% CI: 1.8, 13.5), rural residence (AHR: 0.18; 95% CI: 0.05, 0.64), presence of hypertension (AHR: 3.04; 95% CI: 1.18, 7.8), presence of diabetes mellitus (AHR: 8.1; 95% CI: 2.9, 22.4) and cardiovascular disease (AHR: 5.2; 95% CI: (1.69, 16.2) were significantly associated with mortality.

Conclusions: The rate of mortality among hospitalized COVID-19 patients in this study was low. COVID-19 patients from urban residences, older patients, and patients with comorbidity have a high risk of death. These high risk groups should be prioritized for COVID-19 vaccinations, and early screening and appropriate intervention should be established on presentation to health facility.

1. Background

Coronavirus is one of the major pathogens that mainly target the respiratory system of humans. Previous outbreaks of coronaviruses were recorded in history as Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) (GeoPoll, 2020). The coronavirus disease 2019 (COVID-19) remains the worst global public health challenge starting from March 2020, the day it was declared as a pandemic (Cucinotta & Vanelli, 2020). According to the Worldometer report, the COVID-19 is affecting more than 220 countries. More than 170 million cases and 3.5 million deaths happened due to COVID-19 (Du et al., 2020; Worldometer, 2021). The new coronavirus identified as the cause of the acute respiratory disease since the end of December 2019, later labeled as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization (WHO) is a different strain of coronavirus from SARS and MERS coronaviruses. The difference is genetic make-up, clinical presentations, case fatality, and the rate of spread across the world. SARS-CoV2, the virus that causes COVID-19, has become the newest virus to cause global health fear (Chen et al., 2020; Nuwagira and Muzoora, 2020).

Death due to COVID-19 is defined as a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case or a

Abbreviations: COVID-19, Coronavirus Disease 2019; DMU, Debre Markos University; ICU, Intensive Care Unit; RT-PCR, Real-Time Reverse Transcriptase-Polymerase Chain Reaction; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; TGH, Tibebe Ghion Hospital WHO: World Health Organization.

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death due to COVID-19 may not be attributed to another disease (WHO, 2020). Currently, COVID-19 is the 12th leading cause of global death and the 6th leading cause of death in developed countries (Kirenga & Byakika-Kibwika, 2021). United States of America (USA) is the region where the highest death rate due to COVID-19 was observed followed by India and Mexico (Dyer, 2021). The incidence rate of mortality due to COVID-19 was 61.4 per 1,000,000 Korean (Lai et al., 2020), and a global result of systematic review and meta-analysis showed the burden of mortality due to COVID-19 was 18.8% (Noor & Islam, 2020).

A study conducted on the African continent showed that the continent accounts for only 3% of the global COVID-19 related mortality (Samboye et al., 2021). However, the number of confirmed cases in Africa is increasing rapidly (Kirenga & Byakika-Kibwika, 2021). If the spread of the disease is not well managed, its impact on the African economy will be extensive. Africa’s already fragile health systems, coupled with a high burden of COVID-19 would cost the continent greatly. The speed with which countries can detect, report, and respond to outbreaks can be a reflection of their wider institutional capacity (Ikhaq, Riaz, Bashir, & Uja, 2020; Olapegba et al., 2020). A preliminary report of WHO from 21 African countries showed that 66% reported inadequate critical care capacity, 24% reported burnout among health workers and 15 countries reported low oxygen production which is crucial for severely ill COVID-19 patients (Lawal, 2021).

Studies reported that being elderly, and having co-morbidities such as Diabetes Mellitus, hypertension, and lung disease were found to be factors increasing the risk of mortality due to COVID-19 (Albitar, Balouze, Ooi, & Ghadzi, 2020; Noor & Islam, 2020). The coexistence of chronic non-communicable disease with COVID-19 is the major contributing factor for the increased severity and mortality from COVID-19 (Prado-Galbarro, Sanchez-Piedra, Gamiño-Arroyo, & Cruz-Cruz, 2020; Muniyappa & Gubbi, 2020; Corrao et al., 2020). Similar studies identified that kidney disease, late presentation to health facilities, dementia, and reduced peripheral oxygen saturation were factors that are positively associated with COVID-19 mortality (Becerra-Munoz et al., 2021; García-Possada et al., 2021).

According to the Ministry of Health Ethiopia, the number of infected cases has surpassed 273,678 and more than 4000 deaths due to COVID-19 were reported (Worldometer, 2021). In a developing country like Ethiopia, where trained human resources and equipment for the treatment of COVID-19 are scarce, the rate of death is under-reported. The government of Ethiopia has declared a state of emergency to stop the spread of the disease. These include the implementation of staying home, banning social gatherings, closure of schools, and avoiding close spread of the disease. These factors were implemented to keep the spread of the disease low and to manage the burden of mortality due to COVID-19 (WHO, 2022). Despite all these efforts done by the government, still, the rate of death is rapidly increasing over time. However, there is paucity of information regarding the incidence and predictors of mortality among COVID-19 patients from low-income countries, particularly in Ethiopia. Therefore, this study aimed to assess incidence and predictors of mortality among COVID-19 patients admitted to treatment centers in North West Ethiopia.

2. Methods

2.1. Study area and period

This study was conducted in Debre Markos University (DMU) and Tibebe Ghion Hospital (TGH) COVID-19 treatment centers. These centers are found in Debre Markos and Bahir Dar towns; 299 and 565 kilometers far from North West of Addis Ababa respectively. Data extraction was conducted from April to May 2021 among records of patients admitted from March 2020 to March 2021.

2.2. Study design

A one-year institution-based retrospective cohort study design was employed.

2.2.1. Source population

All laboratory-confirmed COVID-19 patients who were admitted to DMU and TGH COVID-19 treatment centers.

2.2.2. Study population

Laboratory confirmed COVID-19 patients who were admitted to DMU and TGH COVID-19 treatment centers whose records were available.

2.3. Eligibility criteria

2.3.1. Inclusive criteria

COVID 19 patients who were 18 years or older and admitted to the treatment centers during the study period.

2.3.2. Exclusion criteria

COVID-19 patients with incomplete medical records (patients with unknown outcomes) were excluded from the study.

2.3.3. Sample size determination and sampling procedure

To calculate sample size, the general formula for time to event data was used in STATA version 14 by considering proportional hazard assumption, the equal allocation between two groups in log-rank method (0.5) by taking ICU admission (AHR = 1.38) as a predictor from the previous study conducted on survival and predictors of deaths of patients due to COVID-19 in Brazil (Santos, 2020).

Sample size = \[ \frac{\text{Number of event (E)}}{\text{Probability of event (PE)}} \]

where Number of event = \[ \frac{(1.96)^2 + (\beta/2)^2}{\text{HR}^2} \]

and the probability of event is calculated as 1- (π1S1 (t) + π2S2 (t)).

The sample size of the study was determined by considering the following parameters:

- \( Z_{α/2} = 1.96 \) at \( α = 0.05 \) significance level
- \( Z_β = 0.8 \) power
- \( π_1 = π_2: \) proportion of population allocated to the exposed and non-exposed group = 0.5
- \( HR: \) Hazard Ratio = 1.38
- \( S_1 (t): \) Survival function at time \( t_1 = 0.5 \)
- \( S_2 (t): \) Survival function at time \( t_2 = 0.38 \)

And hence the sample size for this study was determined as 552. A total of 1272 COVID-19 patients were treated in the treatment centers (449 from DMU and 823 from TGH) during the study period. Proportional allocation of samples was made for each treatment center and patients were selected (195 from DMU and 357 from TGH) using a simple random sampling technique using medical record numbers as a sampling frame.

2.4. Variables of the study

2.4.1. Dependent variable

- Time to death

2.4.2. Independent variables

- Socio-demographic variables: (age, sex, marital status, residence, and occupation)
- Comorbidity: (Hypertension, asthma, HIV/AIDS, tuberculosis)
- Admission signs: include headache, coma, fever, vomiting, diarrhea, chest pain, cough, throat pain, runny nose, signs of respiratory distress.
2.4.3. Operational definition

- **Vital signs:** Heart rate, respiratory rate, blood pressure, temperature, O₂ saturation

2.5. Data collection tools and procedures

Patients’ medical records which were registered from March 1, 2020, to March 31, 2021, were retrieved using a data extraction checklist adapted from different studies (Khamis et al., 2021; Abraha et al., 2021; van Halem et al., 2020; Santos, 2020; Tolossa, et al., 2021; Zhou et al., 2020). The data extraction checklist consists of socio-demographic factors (age, sex, marital status, residence, and occupation), co-morbidity, vital signs (heart rate, respiratory rate, blood pressure, body temperature, ) and clinical signs at admission (see supportive file). All selected medical records were retrieved and a death certificate was supplemented for events.

2.6. Data quality assurances

The training was given for data collectors and supervisors about the objective of the study and the method of data collection. A pretest was done on 5% of the sample size to keep consistency and modification of the checklist was done (items that are not available from patients’ medical records were omitted from the checklist). Close supervision was provided during the data collection process.

2.7. Data processing and analysis

Data were entered using Epi-Data version 3.1 and analysis was done using STATA 14 statistical software. Data were cleaned and edited before analysis. Descriptive statistics were computed and cross-tabulation was used for categorical data. The outcome of each participant was dichotomized into censored or event. The Life table, the Kaplan Meier survival curve, and log-rank test were used to measure the strength of association and a p-value.<ref>

2.8. Ethical considerations

Ethical clearance was obtained from the institutional review board (IRB) of Bahir Dar University, college of medicine and health sciences (Ref. No. 087/2021). A formal letter was submitted to DMU and TGH treatment centers and permission was assured. As secondary data were used, informed consent from patients was not required. All information collected from patients’ cards was kept strictly confidential and names and medical record numbers of the patients were not included in the checklist.

3. Results

3.1. Socio-demographic characteristics of COVID-19 patients

This study included a total of 552 laboratory-confirmed COVID-19 cases hospitalized at DMU and TGH treatment centers. The mean age of participants was 41 ± 13 years ranging from 18 to 87 years and more than half of the participants were males (Table 1).

3.2. Clinical characteristic of COVID-19 patients

Majority of COVID-19 patients (94%) presented with at least one clinical sign at admission. Of the total participants, 95%, 84%, and 40% had normal body temperature, heart rate, and respiratory rate respectively. Eight percent of COVID-19 cases had one or more comorbidity at admission (Table 2).

3.3. The incidence rate of mortality among COVID-19 patients

From 552 study participants, 29 (5.3%) of patients developed an event and the rest 523 (94.7%) patients were censored observations. The lowest and the highest length of follow-up were 1 and 30 days respectively, and the total person-time risk was 6155 person day observations. Twenty percent of mortality occurred with the first day of admission and 76% of deaths occurred within the first week of hospitalization. The overall mortality rate of COVID-19 was 4.7, (95% CI: 3.3–6.8) per 1000 person day observations. The mortality rate among male and female patients was 6.8 and 2.4 per 1000 person day observations respectively.

### Table 1

| Variable      | Category | Outcome | Total frequency (%) |
|---------------|----------|---------|---------------------|
| Age (years)   |          | Died (frequency) | Censored (frequency) |
| 18–44         |          | 2       | 367                 |
| 45–64         |          | 12      | 129                 |
| 65+           |          | 15      | 27                  |
| Sex           |          | Male    | 22                  |
|               |          | Female  | 7                   |
| Residence     |          | Urban   | 26                  |
|               |          | Rural   | 3                   |
| Marital status|          | Single  | 4                   |
|               |          | Married | 21                  |
|               |          | Widowed | 4                   |
| Occupation    |          | Gov’t employed | 14                  |
|               |          | Self-employed |                  |
|               |          | Farmer  | 3                   |
|               |          | Student | 2                   |
|               |          | Housewife | 0                   |
|               |          | Other   | 2                   |

From Table 1, we can see that the highest morality rate was among patients aged 65+ years, male, rural residents, single status, unemployed, and with no occupation.
The rates of mortality among urban and rural residents were 7.3 and 1.2 per 1000 person day observations respectively. Older patients (≥65 years) had a higher rate of mortality (38.9) as compared to younger ones (<65 years) (2.4) per 1000 person day observations.

The mortality rate of COVID-19 patients varied across different categories of clinical characteristics of patients. The incidence of mortality among patients presented with and without comorbidity was 61.8 and 0.9 per 1000 person day observations respectively. In addition, patients who had respiratory distress at admission revealed a higher mortality rate (37) than their counterparts (0.5) per 1000 person day observations.

3.4. Survival status of COVID-19 patients

The Kaplan-Meier survival curve was used to estimate the survival status of COVID-19 patients. The curve tends to decrease slowly in the first twenty days and sustained thereafter indicating that the majority of deaths occurred within the first 10 days (Fig. 1). The cumulative survival probability of COVID-19 patients at 10 days of admission was 95% and at the end of the follow-up period was 87%. The log-rank test at a 5% significance level was used to compare the survival status of COVID-19 patients. The log-rank test estimate together with the Kaplan-Meier survival curve revealed that the survival pattern of mortality among COVID-19 patients was varied significantly with age, sex, and co-morbidity (Figs. 2–4).

3.5. Predictors of mortality among COVID-19 patients

Socio-demographic predictors (age, sex, residence), clinical signs at admission (fever and chest pain), and co-morbidity (hypertension, diabetes mellitus, asthma, HIV, and cardiovascular disease) were selected through the stepwise backward elimination approach at a p-value of ≤0.25 level of significance in the bivariable Cox regression model. In the final multivariable Cox regression model, ten predictors were analyzed and five predictors (age, residence, hypertension, diabetes mellitus, and cardiovascular disease) were significantly associated with mortality at a p-value of 0.05 levels of significance.

After adjusting other covariates, the age of COVID-19 patients was an independent socio-demographic predictor of mortality. Older COVID-19 patients (≥65 years) were 4.9 times more likely to die as compared to their counterparts (AHR: 4.9; 95% CI: 1.8, 13.5). The mortality rate of COVID-19 patients from the rural residences was decreased by 82% as compared to those patients from urban residences (AHR: 0.18; 95% CI: 0.05, 0.64). The risk of mortality among COVID-19 patients with hypertension was 3 times higher than those without hypertension (AHR: 3.0; 95% CI: 1.2, 7.4).

### Table 2
Clinical characteristics of COVID-19 patients in North West Ethiopia, 2021.

| Variable                | Category   | Outcome              | Total frequency (%) |
|-------------------------|------------|----------------------|---------------------|
| Admission sign          | Yes        | 28                   | 490                 | 518(93.8) |
|                         | No         | 1                    | 33                  | 34(6.2)  |
| Temperature (°C)        | 35-37.4    | 10                   | 517                 | 527(95.5) |
|                         | 37.5-38.4  | 15                   | 4                   | 19(3.4)  |
|                         | ≥38.5      | 4                    | 2                   | 6(1.2)   |
| Heart rate              | 60-100     | 14                   | 451                 | 465(84.2) |
|                         | >100       | 15                   | 72                  | 87(15.8) |
| Respiratory rate        | 12-20      | 1                    | 221                 | 222(40.2) |
|                         | ≥21        | 28                   | 302                 | 330(59.8) |
| Oxygen saturation (%)   | <90        | 29                   | 52                  | 81(14.7) |
|                         | ≥90        | 0                    | 471                 | 471(85.3) |
| Comorbidity             | Yes        | 24                   | 22                  | 46(8.3)  |
|                         | No         | 5                    | 501                 | 506(91.7) |

### Table 3
Clinical features and co-morbidities of COVID-19 patients in North West Ethiopia, 2021.

| Variable                  | Frequency (n = 552) | Percentage (%) |
|---------------------------|---------------------|----------------|
| Signs                     |                     |                |
| Headache                  | 430                 | 77.9           |
| Respiratory distress      | 82                  | 14.9           |
| Fever                     | 298                 | 54.0           |
| Cough                     | 572                 | 67.4           |
| Client pain               | 311                 | 56.3           |
| Throat pain               | 119                 | 21.6           |
| Runny nose                | 61                  | 11.1           |
| Diarrhea                  | 64                  | 11.6           |
| Vomiting                  | 12                  | 2.2            |
| Goma                      | 8                   | 1.5            |
| Co-morbidities            |                     |                |
| Hypertension              | 21                  | 3.8            |
| Retroviral infection      | 15                  | 2.7            |
| Diabetes mellitus         | 22                  | 4.0            |
| Cardiovascular disease    | 18                  | 3.3            |
| Asthma                    | 10                  | 1.8            |
| Others                    | 6                   | 1.1            |

Others include tuberculosis and neurological disease. Some patients had multiple features at admission.
3.04; 95% CI: 1.18, 7.8). COVID-19 patients who had diabetes mellitus have 8 times the higher hazard of mortality as compared to patients without diabetes mellitus (AHR: 8.1; 95% CI: 2.9, 22.4). The rate of mortality among patients admitted with cardiovascular disease was 5 times higher as compared to those patients who had no cardiovascular disease during admission (AHR: 5.2; 95% CI: (1.69, 16.2) (Table 4).

3.6. Proportional Hazard (PH) assumption and model goodness of fit

The Cox Proportional Hazard assumption was tested both graphically and statistically for each covariate all of which holds the assumption. The overall model fitness for the final model was checked using the Cox-Snell residual graph which indicates that the model fitted to the data adequately (Fig. 5).

4. Discussion

This study provided comprehensive evidence on the incidence as well as predictors of mortality among COVID-19 patients admitted to treatment centers in North West Ethiopia. The study demonstrated that the incidence rate of mortality among COVID-19 patients admitted in treatment centers in North West Ethiopia was 4.7 per 1000 person day observations or 5.2%. This finding is approximately similar to the studies conducted among hospitalized COVID-19 patients in South Korea (7.4%) (Acharya, Lee, Lee, Lee, & Moon, 2020) and Wuhan China (3.7%) (Zhang et al., 2020), 4.3% (Wang, Bo, & Hu, 2020) university hospitals. This could be due to the relative similarity of the clinical characteristics of study participants included in the studies. However, the current finding is lower than the study done at Millennium COVID-19 Care Center, Addis Ababa, Ethiopia in which the incidence of mortality was 10.5% (Leulseged et al., 2021). This finding is also lower than

Table 4
Multivariable Cox regression analysis of mortality among COVID-19 patients in North West Ethiopia, 2021.

| Covariate               | Category | CHR(95%CI) | AHR(95%CI) | P-value |
|-------------------------|----------|------------|------------|---------|
| Age (years)             | <65      | 1          | 4.9(1.8-13.5) | 0.002*  |
|                         | ≥65      | 15.3       | (7.3-31.7)  |         |
| Sex                     | Male     | 1          |            |         |
|                         | Female   | 0.32       | (0.13-0.77) | 0.6     |
| Residence               | Urban    | 1          |            |         |
|                         | Rural    | 0.15       | (0.04-0.52) | 0.008*  |
| Fever                   | Yes      | 4.1(1.6-9.9)| 2.3(0.74-7.3)| 0.14    |
|                         | No       | 1          |            |         |
| Chest pain              | Yes      | 1.3        | (0.65-2.94)| 0.29    |
|                         | No       | 1          | (0.22-1.57)|         |
| Hypertension            | Yes      | 11.1       | (5.1-24.4)| 0.02*   |
|                         | No       | 1          | (1.18-7.8)|         |
| Diabetes mellitus       | Yes      | 35.1       | (16.8-73.5)| < 0.001*|
|                         | No       | 1          | (2.9-22.4)|         |
| Asthma                  | Yes      | 10.2       | (3.5-29.4)| 0.37    |
|                         | No       | 1          | (0.48-6.95)|         |
| HIV                     | Yes      | 3.7(1.1-12.5)| 0.3(0.04-2.2)| 0.25    |
|                         | No       | 1          | (1.69-16.2)|         |
| Cardiovascular disease  | Yes      | 17.6       | (7.6-40.8)| 0.004*  |
|                         | No       | 1          | (1.69-16.2)|         |

CHR: Crude Hazard Ratio; AHR: Adjusted Hazard Ratio.
* Statistically significant at 0.05.
4.1 Limitation of the study

As the study used secondary data, it did not include biomedical profiles and medication-related variables which could be potential predictors of mortality. In addition, although the adjusted analysis was used, potential confounders could be considered as a limitation.

5. Conclusions

The rate of mortality among hospitalized COVID-19 patients in this study was low as compared to findings of other studies (Bepouka et al., 2020; Wang B et al., 2020; Kim et al., 2020; Leulseged et al., 2021). COVID-19 patients from urban residences, older patients, and patients with hypertension, diabetes mellitus, and cardiovascular disease have a high risk of death. Patients with advanced age (≥65 years), hypertension, diabetes mellitus, and cardiovascular disease need careful observation and early intervention of cases is crucial to prevent the potential COVID-19 related mortality. In addition, these high-risk groups should be prioritized for COVID-19 vaccinations, and early screening and appropriate intervention should be established on presentation to health facilities. [34].

Authors’ contributions

BM and ZA conceived, designed and performed formal the analysis of the study; ZA collected the clinical information; BM and TT wrote the original draft of the manuscript and all authors reviewed, read and approved the final manuscript.

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Ethics approval and consent to participate

Ethical clearance was obtained from the institutional review board (IRB) of Bahir Dar University, college of medicine and health sciences (Ref. No. 987/2021). A formal letter was submitted to DMU and TGH treatment centers and permission was assured. As secondary data were used, informed consent from patients was not requested. All information collected from patient’s cards was kept strictly confidential and names and medical record numbers of the patients were not included in the checklist.

Consent for publication

Not applicable

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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