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Research Article

Assessment of Factors Affecting Time to Recovery from COVID-19: A Retrospective Study in Ethiopia

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Background. The average duration of recovery from COVID-19 and influencing factors, which would help inform optimal control strategies, remain unclear. Moreover, studies regarding this issue are limited in Ethiopia, and no region-wise studies were conducted. Hence, this study aimed to investigate the median recovery time from COVID-19, and its predictors among patients admitted to Amhara regional state COVID-19 treatment centers, Ethiopia. *Methods*. A facility-based retrospective follow-up study was conducted at Amhara regional state COVID-19 treatment centers from 13 March 2020 through 30 March 2021. Data were entered using EpiData version 3.1, and STATA version 14 was used for analysis. A Kaplan–Meier curve was used to estimate survival time, and the Cox regression model was fitted to identify independent predictors. *P* value with 95% CI for the hazard ratio was used for testing the significance at alpha 0.05. *Results*. Six hundred twenty-two cases followed, and 540 observations developed an event at the end of the follow-up. The median time to recovery was 11 days with an interquartile range of 9–14 days. Most of the patients were recovered from COVID-19 between days seven and fourteen. In the first six days of admission, only 4.2% of cases had recovered, but by day 14, 73.8% had recovered. Patients without comorbid illness/s were faster to recover than their counterparts (AHR = 1.44 : 95% CI: 1.10, 1.91) and those who have signs and symptoms on admission (AHR = 0.42 : 95% CI: 0.30, 0.60) and old-aged (AHR = 0.988; 95% CI: 0.982, 0.994) took longer to recover. *Conclusion*. In conclusion, a relatively short median recovery time was found in this study. Significant predictors for delayed recovery from COVID-19 were older age, presence of symptoms at admission, and having at least one comorbid condition. These factors should be placed under consideration while developing a strategy for quarantining and treating COVID-19 patients.

1. Introduction

Coronavirus disease 2019 (COVID-19), the disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, was declared a global pandemic in early 2020 [1]. The pandemic has affected almost all major nations in the world. There were more than 447.8 million confirmed COVID-19 cases and about 6 million deaths worldwide as of March 07, 2022 [2]. At the same time, in Ethiopia, since the first case of COVID-19 was confirmed on 13 March, 2020, 468, 966 confirmed cases and 7,476 deaths were recorded [3].

The COVID-19 pandemic is a human tragedy that occurred in this era. It poses an unprecedented social, economic, political, and health crisis starting from its outbreak, unlike any after Second World War. Countries implemented various response measures to mitigate the pandemic's humanitarian and economic effects. However, these measures have been there, cases and their impact have increased since the first case was identified [4]. The socioeconomic impacts being felt across Ethiopia already are wide-range and high level, with the potential to become severe, depending on the pandemic's trajectory, the effects of countermeasures, and underlying and structural factors [5].

Substantial knowledge has now accumulated regarding the acute clinical presentations, pathophysiological changes observed, and prognosis of COVID-19 patients. However, there is considerable variation in the estimate of recovery time from COVID-19. Early in the pandemic, a systematic review reported that the average duration of recovery time was 19 days [6]. On the other hand, the report of the WHO-China joint mission on COVID-19 indicated that the estimated recovery time is two weeks for patients with mild infection and 3 to 6 weeks for those with serious illnesses [7]. The average time to recover from the disease ranges from 5 to 36 days in Indian states [8]. Studies in different parts of the world, including Ethiopia, show various figures of median recovery time from 8 to 31 days [9–17]. As studies indicated, factors such as age, sex, comorbid illness/s, presence of symptoms at presentation, corticosteroid therapy, and time from onset to hospitalization determine the duration of recovery time of COVID-19 [9–14, 18].

Although the median time to recovery from COVID-19 varies among patients and settings, all studies conducted worldwide are almost outside Ethiopia, particularly Amhara regional state. Hence, knowing the median duration of viral ribonucleic acid (RNA) shedding and identifying factors associated with the time taken of shedding among COVID-19 patients in this area, Amara regional state, will be crucial in formulating preventive measures and optimizing treatment options. Therefore, this study aimed to investigate the recovery time from SARS-CoV-2 infection and its predictors among COVID-19 patients admitted to Amhara region COVID-19 treatment centers, Amhara, Ethiopia.

2. Materials and Methods

2.1. Study Design, Period, and Settings. An institution-based retrospective cohort study was conducted at Amhara regional state COVID-19 treatment centers from 13 March, 2020, to 30 March, 2021. In Amhara regional state, there are 8 COVID-19 treatment centers. These are Gondar University, Tibebe Gion hospital, Debre Birhan-Tebasi health center, Borumeda hospital, Debre Markos University, Injibara University, Kobo hospital, and Dessie hospital. The data were retrieved between May 1 and 30, 2021.

2.2. Study Participants. Patients who tested positive for COVID-19 and admitted to any of the COVID-19 treatment centers in Amhara regional state from 13 March, 2020, to 30 March, 2021, with a definite outcome (event or censored) and whose chart is available during the data collection period have participated in this study. Patients with incomplete outcome variables and lacking baseline information, such as date of admission, death, and transfer/discharge, were excluded from the study.

2.3. Sample Size Determination and Sampling Procedure. We used STATA version 14 statistical software to calculate the minimum required sample size. Sample size calculation for the survival analysis (log-rank test comparing two survival rates) was used by considering the presence of fever as the major predictor variable (14) and taking survival probability among nonexposed = 0.158, hratio = 1.29, wdprob = 0.1, alpha = 0.05, and power = 0.8. Finally, the minimum sample size required to conduct this study was 622. Then, the sample was proportionally allocated for each COVID-19 treatment center, and a simple random sampling technique was employed to select study participants in each treatment center.

2.4. Study Variables. The outcome variable was time to recovery from COVID-19; the number of days between the first rRT-PCR positive test for SARS-CoV-2 and the occurrence of the outcome (event/censored). The event was recovery from COVID-19 (those who have had two consecutive negative rRT-PCR results for the virus from a throat swab in 24 hours) and censored were those patients who have not developed an event (death, transferred out, and complete follow-up without an event). Explanatory variables were age, sex, marital status, residence, symptoms at admission, severity, comorbidity, and type of comorbidity. Cases with comorbidity are those COVID-19 patients with one or more coexisting medical illness/s. We use the WHO classification to determine COVID-19 severity. COVID-19 infection is classified as mild if there are no signs of pneumonia or hypoxia and as moderate or severe if there is a clinical and radiological indication of pneumonia. Then, if SpO2 was ≥90% on room air, it was classified as moderate and severe if the respiratory rate was ˃30 breaths/minute or SpO2 was <90% on room air.

2.5. Data Collection Tools and Procedures. The data extraction tool was prepared based on COVID-19 patient medical cards. It consists of sociodemographic-related variables, factors related to comorbidity, and symptoms at presentation. Trained health professionals who have been working in the treatment center extracted the data from the registration logbook and patient's medical cards.

2.6. Data Management and Analysis. Data entered using EpiData version 3.1, and STATA version 14 was used for analysis. Survival probability was estimated using the Kaplan–Meier survival curve. Survival experience of different groups in a categorical covariate compared using the log-rank test. Cox proportional hazards regression model fitted to identify potential predictors of time to recovery from COVID-19 after checking the proportional hazard assumption using the Schoenfeld residuals test. We used adjusted HR with 95% CI to test significance, and statistical significance was declared when it was significant at a 5% level (P value <0.05). Model adequacy was checked using Cox Snell residual graph.

3. Results

3.1. Sociodemographic Characteristics of Patients. The median age of the patients was 41 years old with an IQR of 54 − 31 = 23. Around two-thirds, 348 patients (55.9%) were

male. Regarding marital status and residence, 409 patients (65.8%) were married and 375 (60.3%) were urban residents (Table 1).

3.2. Clinical Characteristics of Patients. Almost all the patients ($n = 585$; 94.1%) experienced signs and symptoms at the time of presentation. The commonest presenting symptom was headache ($n = 444$, 75.9%) followed by cough ($n = 421$, 71.9%). The least common signs and symptoms observed were a runny nose and vomiting (Figure 1). Most of the patients ($n = 343$; 55.1%) had mild COVID-19 severity at admission and the rest had moderate ($n = 218$; 35.1%) and severe ($n = 61$; 9.8%) disease at presentation. One-fourth of the study participants had at least one or more comorbidity (Table 2).

3.3. Time of Recovery from COVID-19. The cohort of 622 COVID-19 patients contributed 6892 person-days at risk throughout the study. Five hundred forty observations (86.82%) developed an event (recovery). The remaining 18 (3.00%) had not recovered at the time of the last contact, 58 (9.32%) died of COVID-19, and 7 (1.13%) transferred out. The median recovery time of COVID-19 was 11 days with an IQR of 9–14 days. The overall incidence rate of recovery was 7.84 per 100 (95% CI: 7.20, 8.52) person-day observations. The Kaplan–Meier survival curve indicated that most patients recovered from COVID-19 between days seven and fourteen (Figure 2). In the first 06 days after admission, only 4.2% of cases had recovered, but within 14 days, 73.8% had recovered. The log-rank test for equality of survival function shows a significant difference in recovery rate among groups classified by their symptom status, COVID-19 severity, and comorbid illness (all P values <0.05). However, no difference was observed among groups classified by their sex and residence.

3.4. Predictors of Recovery Time from COVID-19. Based on the results of the bivariable analysis at a 25% level of significance and the significant variables identified from the literature, the following variables were included in the final Cox regression model: age, residence, comorbid illness/s, presence of symptom at admission, and COVID-19 severity. Only the age of patients, presence of signs and symptoms during admission, and comorbid illness/s found to have a statistically significant association with recovery time in the final multivariable Cox regression model.

Accordingly, the rate of achieving recovery among symptomatic patients was 58% (AHR = 0.42 : 95% CI: 0.30, 0.60) lower than patients who were asymptomatic at presentation. Likewise, for every one-point increase in age of the patient, hazard of being recovered from COVID-19 was decreased by 1.2% (AHR = 0.988; 95% CI: 0.982, 0.994). After adjusting for the above-listed variables, patients without any comorbid illness/s were 44% (AHR = 1.44 : 95% CI: 1.10, 1.91) faster to recover than their counterparts (Table 3).

Table 1: Sociodemographic characteristics of COVID-19 patients admitted to Amhara region COVID-19 treatment centers, 2021 ($n = 622$).

Variable	Category	Frequency	Percentage
Age	<25	52	8.36
	25–64	497	79.90
	≥65	73	11.74
Sex	Male	348	55.95
	Female	274	44.05
Residence	Urban	375	60.29
	Rural	247	39.71
Marital status	Married	409	65.76
	Not married	213	34.24

3.5. Model Goodness of Fit. The adequacy of the fitted model was assessed by using a Cox Snell residual plot for each uncensored observation. Finally, the graph of the Nelson–Aalen cumulative hazard function and the Cox Snell residuals variable were compared with the hazard function on the diagonal line. The hazard function follows a 45° slope close to the baseline, which indicates that the model fitted the data well (Figure 3).

4. Discussion

This study demonstrates the time to recovery from COVID-19, and its predictors among COVID-19 patients admitted to Amhara regional state COVID-19 treatment centers. Accordingly, it pointed out that the median recovery time of COVID-19 was 11 days. This median recovery time was lower than a study in Italy (24 days) [17] and previous studies done in Ethiopia; Millennium COVID-19 care center, Eka Kotebe general hospital, and Wollega University referral hospital with a median recovery time of 16, 19, and 18 days, respectively [9, 11, 14]. The possible reason for the observed discrepancy between the studies might be variation in study setting and time. Relatively better care and treatment were given to the patients recently than before. The time variability between the start and end of the follow-up will also explain this difference in recovery time [17]. Patients diagnosed negative for COVID-19 and discharged from hospital are considered the end point of a follow-up in a study from western Ethiopia. As a result, waiting until the patient discharged from the hospital may result in a lengthy recovery period in the study. However, the median duration of recovery in this study is consistent with the previous study findings from Israeli (13.2 days) [19], Singapore (12 days) [20], Guangzhou (12 days) [10], and Jiangsu and Anhui (11 days) [21].

In this study, one of the significant predictors of delayed recovery was older age. Several studies also reported that older age was an independent risk factor that can delay the recovery time of COVID-19 patients [10, 14, 22–25]. It might be due to older age causing numerous biological changes in the immune system, which increase susceptibility to infectious diseases. Not only do these changes determine infection susceptibility but also disease progression and clinical outcomes [26]. In addition, it might also be because there will be degeneration of pulmonary function among

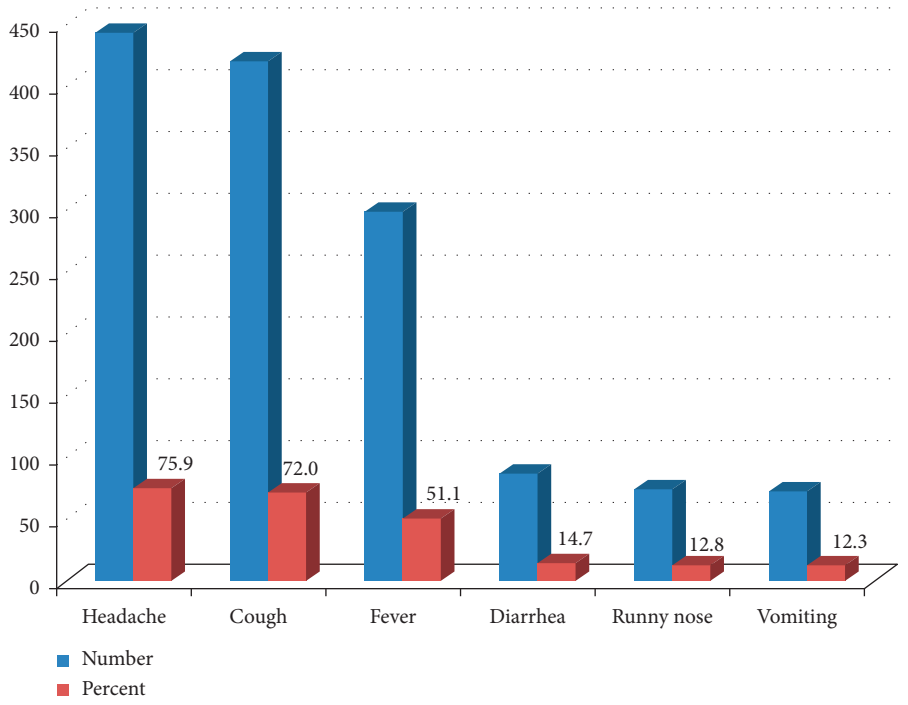

Figure 1: Signs and symptoms observed in the study participants at Amhara region COVID-19 treatment.

Table 2: Baseline clinical features of COVID-19 patients admitted to Amhara region COVID-19 treatment centers, 2021 ($n = 622$).

Variable	Category	Frequency	Percentage
Symptom status	Have ≥1 symptom	585	94.05
	Have no symptom	37	5.95
COVID-19 severity	Mild	343	55.14
	Moderate	218	35.05
	Severe	61	9.81
Comorbidity	Yes	156	25.08
	No	466	74.92
Hypertension ($n = 156$)	Yes	52	33.33
	No	104	66.67
Diabetes mellitus ($n = 156$)	Yes	53	33.97
	No	103	66.03
Asthma ($n = 156$)	Yes	23	14.74
	No	133	85.26

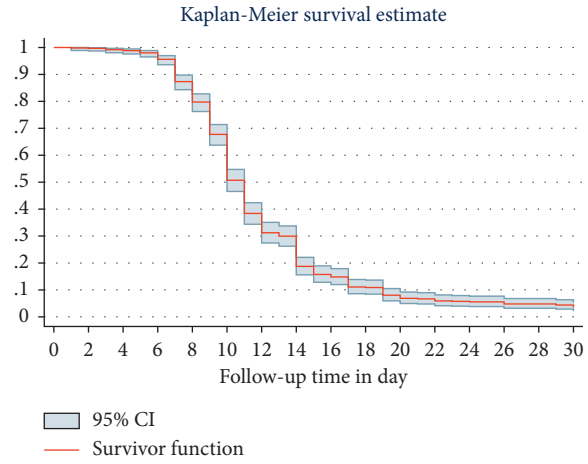

Figure 2: Overall Kaplan–Meier survival curve with 95% confidence interval (CI).

elders, which contributes to severe COVID-19 cases and delays in recovery time.

This study also revealed that duration of recovery time from COVID-19 was significantly affected by the symptom status of the patient at presentation. Symptomatic patients showed a relatively delayed recovery time compared to asymptomatic patients. It is consistent with studies conducted before [11, 13, 14, 23]. This could be because usually COVID-19 patients who have no symptoms are in a stage of mild COVID-19 severity, which results in fast recovery from the disease. Moreover, pulmonary insufficiency will be there when the patient has a high respiratory rate which may result from high temperature. This pulmonary insufficiency will be a cause for a slower recovery rate.

Furthermore, having a comorbid illness has been linked to a longer recovery time in this study, as it has been in other studies [9, 14, 21, 23, 27]. Since comorbidities are a well-known phenomenon in the elderly population, the observed association between comorbid illness and delayed recovery could be the effect of becoming older. The occurrence of comorbid illness/s among the elderly is not uncommon in the field of global public health. This comorbid condition, combined with getting older, is linked to a higher risk of poor functional status and adverse events in response to diagnostic and therapeutic procedures like multiple medications, which often leads to a delay in recovery. However, in this study, factors found significant determinants of recovery time in other studies,

Table 3: Multivariable Cox proportional hazards analysis of predictors of time to recovery from COVID-19 in Amhara region COVID-19 centers, 2021 ($n = 622$).

Variables	Survival status		Crude hazard ratio (CRH) (95% CI)	Adjusted hazard ratio (AHR) (95% CI)
	Recovered	Censored		
Age	All as continues variable		0.99 (0.98, 0.99)	0.988 (0.982, 0.994)*
Residence				
Rural	223	24	1.13 (0.95, 1.34)	1.186 (0.997, 1.411)
Urban	317	58	1	1
Symptom status at admission				
Have ≥1 symptom	506	79	0.49 (0.33, 0.67)	0.421 (0.296, 0.603)*
Have no symptom	34	3	1	1
Comorbid illness/s				
Yes	78	78	1	1
No	462	4	1.62 (1.27, 2.07)	1.441 (1.089, 1.906)*
COVID-19 severity				
Mild	341	2	1.83 (1.13, 2.95)	1.146 (0.677, 1.940)
Moderate	181	37	1.66 (1.02, 2.70)	1.211 (0.728, 2.016)
Severe	18	43	1	1

*Significant at $P < 0.05$.

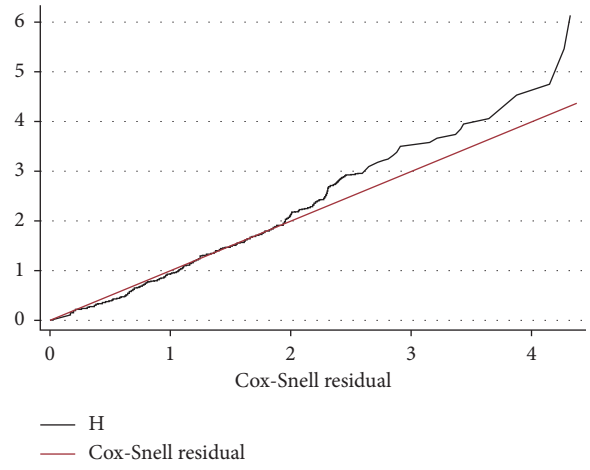

Figure 3: Cox Snell residual test for overall adequacy of the model.

such as sex and disease severity, showed no significant association.

4.1. Limitation of the Study. Even though the study is multicenter and uses an advanced statistical model for analysis, limitations concerning the design and data will be there. First, demographic characteristics were incomplete because of the retrospective study design. Second, those patients excluded from the study, who have incomplete outcome variables and lack baseline information, could influence the regression results significantly. Finally, professionals usually use self-reports to record comorbidity on the patient's charts, and it was considered comorbidity in the collection and analyses of this study.

5. Conclusions and Recommendations

In conclusion, a relatively short median recovery time was found in this study. Older age, presence of symptoms at admission, and having at least one comorbid condition were independently associated with prolonged recovery from COVID-19. Hence, to improve the recovery rate from COVID-19, it is better to give different interventions and care for those patients who have comorbidities and are old aged. Medical decisions get more complicated and challenging as people get older and have comorbidities. Yet, there is no different guideline for COVID-19 management among elders with comorbidity. Therefore, health planners should organize an expert group to formulate the guiding principles for clinical management of COVID-19 among elders with comorbidity via considering the complexity and feasibility of the treatment plan. In addition, these factors should be placed under consideration while developing a strategy for quarantining and treating COVID-19 patients. However, this finding should interpret with caution, and further large-scale studies with a cohort design are needed to confirm this finding.

Abbreviations

AHR: Adjusted hazard ratio
CHR: Crude hazard ratio
CI: Confidence interval
COVID-19: Coronavirus disease 2019
RNA: Ribonucleic acid
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Data Availability

Data are available from the corresponding author upon reasonable request.

Ethical Approval

The authors obtained ethical approval from Bahir Dar University, College of Medicine and Health Sciences Institutional Review Board (IRB). Formal letter of cooperation

was written to each treatment center and permission obtained from the treatment center administrations. Besides, the data collection checklist did not include personal identifiers.

Conflicts of Interest

The author reports no conflicts of interest in this work.

Authors' Contributions

All the authors made a significant contribution to the work reported. Their contribution was either in the conception, proposal writing, data acquisition, analysis, or interpretation stages. All took part in drafting, revising, or critically reviewing the manuscript and gave final approval of the version to be published.

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