Clinical Characteristics and Treatment Outcomes of COVID-19 Patients at Eka Kotebe General Hospital, Addis Ababa, Ethiopia

Dawit Kebede Huluka, 1* Eyob Kebede Etissa, 2 Sebrina Ahmed, 3 Hiluf Abate Abule, 1 Nebiyu Getachew, 1 Sisay Abera, 3 Abebaw Bekele Seyoum, 3 Hiruy Araya, 3 Tsegaye Gebreyes Hundie, 3 Bethlehem Tadesse Anteneh, 3 Getachew Demoz Gebremedhin, 3 Yonas Gebregziabher, 3 Rediet Yitagesu Tefera, 3 Addisu Birhanu Tereda, 3 Yohannes Feleke, 1 Yonathan Abebe, 1 Tewodros Haile Gebremariam, 1 Hanan Yusuf Ahmed, 1 Wondwossen Amogne, 1 Deborah A. Haisch, 4 Charles B. Sherman, 5 and Neil W. Schluger⁶

¹College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia; ²East African Training Initiative, Addis Ababa, Ethiopia; ³Eka Kotebe Hospital, Addis Ababa, Ethiopia; ⁴Weill Cornell Medical College, New York, New York; ⁵Warren Alpert School of Medicine, Brown University, Providence, Rhode Island; ⁶Westchester Medical Center, New York Medical College, New York, New York

Abstract. Data from much of Africa are still scarce on the clinical characteristics, outcomes of treatment, and factors associated with disease severity and mortality of COVID-19. A cross-sectional study was conducted at Eka Kotebe General Hospital, Ethiopia's first COVID-19 treatment center. All consecutive symptomatic SARS CoV-2 RT-PCR positive individuals, aged 18 and older, admitted to the hospital between March 13 and September 16, 2020, were included. Of the total 463 cases, 319 (68.9%) were male. The median age was 45 years (interquartile range 32–62). The most common three symptoms were cough (69%), shortness of breath (SOB; 44%), and fatigue (37%). Hypertension was the most prevalent comorbidity, followed by diabetes mellitus. The age groups 40 to 59 and \geq 60 were more likely to have severe disease compared with those < 40 years of age (adjusted odds ratio [aOR] = 3.45, 95% confidence interval [CI]: 1.88–6.31 and aOR = 3.46, 95% CI: 1.91–6.90, respectively). Other factors associated with disease severity included the presence of any malignancy (aOR = 4.64, 95% CI: 1.32–16.33) and SOB (aOR = 3.83, 95% CI: 2.35–6.25). The age group \geq 60 was significantly associated with greater in-hospital mortality compared with those < 40 years. In addition, the presence of any malignancy, SOB, and vomiting were associated with higher odds of mortality. In Ethiopia, most COVID-19 patients were male and presented with cough, SOB, and fatigue. Older age, any malignancy, and SOB were associated with disease severity; these factors, in addition to vomiting, also predicted mortality.

INTRODUCTION

As of December 2, 2021, there were more than 261 million COVID-19 cases and 5.2 million verified COVID-19 deaths worldwide. In Africa, there were approximately 8.8 million cases and 224,000 deaths. Most who contract the virus are asymptomatic, but the majority of symptomatic patients will have mild to moderate respiratory disease. On the other hand, older individuals and those with comorbidities can become severely ill and require medical attention. However, people of any age can become extremely ill or die of the disease. 1-3

In the initial WHO-China Joint Mission on Coronavirus Disease 2019 and according to a comprehensive overview and meta-analysis, the most common disease symptoms are fever, cough, fatigue, sputum, dyspnea, myalgia, chest tightness/pain, sore throat, headache, diarrhea, nasal congestion/rhinorrhea, nausea/vomiting, abdominal discomfort, and hemoptysis. In most individuals, COVID-19-related comorbidities include hypertension (HTN), diabetes mellitus (DM), and cardiovascular disease. Some researchers have reported additional comorbidities of endocrine disorders, gastrointestinal ailments, chronic liver disease, and chronic obstructive pulmonary disease (COPD).^{4–8}

Older age; comorbidities such as DM, HTN, cardiovascular illness, and chronic respiratory disease, and the symptom of shortness of breath (SOB) have been identified as predictors of disease severity and mortality. 9–20 Others have reported risk factors for disease severity to be male gender, low oxygen

saturation (SpO₂), two or more comorbidities, malignancy, chronic kidney disease (CKD), human immunodeficiency virus (HIV), obesity, smoking, cough, fever, and fatigue. ^{9,10,17,18,20}

COVID-19 mortality has been associated with decreased SpO₂, CKD, malignancy, HIV/AIDS, and fever.^{9,15,21} Others report male gender, greater sequential organ failure assessment, and previous and current tuberculosis.^{15,21,22}

As of this writing, it has been 1.5 years since the first case was reported in Ethiopia. As of December 2, 2021, 371,272 cases and 6,771 deaths had been reported in the nation. Only a few studies have been published from Ethiopia on the clinical features, illness severity, treatment, and outcomes. This study aimed to describe the clinical manifestations, treatment, outcomes, and factors related to severity and mortality at Eka Kotebe Hospital, Ethiopia's pioneer COVID-19 treatment facility.

METHODS

Study design and setting. This cross-sectional retrospective study was undertaken in Eka Kotebe General Hospital, the first COVID-19 treatment center in Addis Ababa. It was initially established as an extension of the Amanuel General Hospital until April 2020 when it became a stand-alone federal hospital. It has a bed capacity of approximately 400, with 40 beds dedicated to intensive care services, 16 of which are for patients requiring mechanical ventilation (such as critically sick COVID-19 patients). Patients of all levels of severity (mild to critical COVID-19) were admitted to the hospital. It is staffed by more than 130 nurses, 90 general practitioners, three anesthesiologists, three emergency physicians, two internists, one pulmonary and critical care subspecialist, two obstetrics and gynecology physicians, two surgeons,

^{*}Address correspondence to Dawit Kebede Huluka, College of Health Sciences, Addis Ababa University, P.O. Box 2380, Addis Ababa, Ethiopia. E-mail: dndrda97@gmail.com

COVID-19 IN ETHIOPIA 253

Table 1
Baseline characteristics, comorbidities, and admission symptoms of respondents in Eka Kotebe Hospital

Variables	n (%)
Age (median: 45, IQR: 32-62) < 40	177 (90 (
< 40 40–59	177 (38.2 147 (31.7
≥ 60	139 (30.0
Sex	100 (00.0
Male	319 (68.9
Female	144 (31. ⁻
Comorbidities and symptoms	
Comorbidity	
Yes	189 (40.8
No	274 (59.2
Hypertension	110 (04 (
Yes No	112 (24.2 351 (75.8
Type 2 diabetes mellitus	331 (73.0
Yes	96 (20.7
No	367 (79.3
Chronic cardiac disease	,
Yes	27 (5.8)
No	436 (94.2
Chronic lung disease	
Yes	21 (4.5)
No	442 (95.5
Malignancy	
Yes	19 (4.1)
No HIV/AIDS	444 (95.9
Yes	11 (2.4)
No	452 (97.6
Chronic kidney disease	402 (07.0
Yes	8 (1.7)
No	455 (98.3
Obesity	`
Yes	6 (1.4)
No	413 (98.6
Chronic liver disease	
Yes	2 (0.4)
No Courab	461 (99.6
Cough Yes	212 (69 (
No	313 (68.6 150 (32.4
Shortness of breath	130 (32.5
Yes	204 (44.
No	259 (55.9
Fatigue/malaise	200 (00.0
Yes	171 (36.9
No	292 (63. ⁻
Fever	,
Yes	162 (35.0
No	301 (65.0
Headache	
Yes	131 (28.3
No	332 (71.
Myalgia	440 (00 (
Yes	110 (23.8
No	353 (76.2
Arthralgia	400 (00)
Yes	109 (23.5
No	354 (76.5
Loss of appetite	00 /10 /
Yes No	89 (19.2
NO Sore throat	374 (80.8
Yes	65 (14.0
No	398 (86.0
Chills	230 (00.0
Yes	40 (8.6)
No	423 (91.4

(continued)

Table 1 Continued

Continue	tu .
Variables	n (%)
Vomiting	
Yes	31 (6.7)
No	432 (93.3)
Abdominal pain	, ,
Yes	29 (6.3)
No	434 (93.7)
New loss of smell	,
Yes	26 (5.6)
No	434 (94.4)
New loss of taste	` ,
Yes	22 (4.8)
No	437 (95.2)
Diarrhea	,
Yes	19 (4.1)
No	441 (95.9)
Nausea	(,
Yes	17 (3.7)
No	444 (96.3)
Rhinorrhea	(,
Yes	17 (3.7)
No	446 (96.3)
	. 10 (00:0

IQR = interquartile range.

three psychiatrists, two radiologists, and two pediatricians. Nine of these senior physicians are academic staff at the College of Health Sciences, Addis Ababa University, and they have been working in the hospital since April 2020.

Study period. The study took place from March 13, 2020, through September 16, 2020.

Study population. All consecutive symptomatic SARS CoV-2 Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) positive were included.

Inclusion criteria. Regardless of data completeness, all COVID-19 patients aged 18 and older were included. Only those who were symptomatic and those with positive RT-PCR on admission or who turned positive after admission were included.

Exclusion criteria. Asymptomatic cases and those with SARS CoV-2 RT-PCR-negative test results who were admitted to the hospital early in the pandemic when it was serving as both an isolation and a quarantine center.

Sample size. All cases meeting the inclusion criteria during the study period were included.

Operational definitions.

- COVID-19 patient: An individual who had a positive RT-PCR irrespective of symptoms.
- Asymptomatic COVID-19: Individuals who had a positive RT-PCR with no symptoms suggestive of COVID-19.
- Symptomatic COVID-19: Individuals who had a positive RT-PCR with one or more of the symptoms suggestive of COVID-19 including fever, cough, headache, myalgia, arthralgia, loss of smell/taste sensation, vomiting, and diarrhea.
- Mild disease: A symptomatic COVID-19 case with no radiologic finding who did not require oxygen and had a normal hemodynamic status.
- Moderate disease: A symptomatic COVID-19 case with radiographic evidence of infiltrates or pneumonia and SpO₂ > 90%
- Severe disease: A COVID-19 case with SpO₂ < 90% irrespective of symptoms or radiographic findings.

254 HULUKA AND OTHERS

Table 2
Laboratory findings and clinical management of study participants in Eka Kotebe Hospital

Variables		n (%)
Oxygen therapy	Yes	231 (49.9)
	No	232 (50.1)
Noninvasive positive pressure ventilation	Yes	26 (5.6)
	No	437 (94.4)
Invasive ventilation	Yes	37 (8.0)
	No	426 (92.0)
Prone ventilation	Yes	149 (32.2)
	No	314 (67.8)
Tracheostomy inserted	Yes	8 (1.7)
	No	455 (98.3)
Chloroquine administered	Yes	38 (8.2)
	No	425 (91.8)
Antibiotics	Yes	290 (62.6)
0	No	173 (37.4)
Steroids	Yes	109 (23.5)
Decelo le Caracilla de la con-	No	354 (76.5)
Prophylactic anticoagulant	Yes	201 (43.4)
Full does entire equilant	No Yes	262 (56.6)
Full dose anticoagulant	nes No	60 (13.0) 403 (87.0)
Vocantagor required	Yes	, ,
Vasopressor required	No	32 (6.9) 431 (93.1)
ALC ($N = 404$)	< 1,000	140 (34.7)
ALC (IV = 404)	< 1,000 ≥ 1,000	264 (65.3)
AST $(N = 356)$	< 37	220 (61.8)
A01 (W = 000)	< 37 ≥ 37	136 (38.2)
ALT ($N = 360$)	= 67 ≤ 63	292 (81.1)
7121 (11 333)	- 63 > 63	68 (18.9)
Length of stay (median, IQR) (15, 14-21)	, 00	00 (10.0)
Length of stay (days)	≤ 15	255 (55.1)
- J	> 15	208 (44.9)
		()

ALC = absolute lymphocyte count; ALT = alanine transaminase; AST = aspartate transaminase; IQR = interguartile range.

- Critical COVID: A COVID-19 case requiring mechanical ventilation or hemodynamic support. This includes patients with acute respiratory distress syndrome, acute renal failure, and septic shock.
- Disease severity: Nonsevere COVID-19 (mild to moderate cases) and severe COVID-19 (severe or critical cases).
- Chronic lung diseases included preexisting COPD and bronchial asthma.

Data collection and quality assurance. A structured questionnaire was used to collect data on demographics, clinical manifestations, comorbidities, laboratory values, inpatient medications, treatments (including invasive mechanical ventilation and kidney replacement therapy), and outcomes (including length of stay, discharge, readmission, and mortality) of the study subjects. Trained physician data clerks collected data from the chart. The questionnaire was tested, and revisions were made before data collection started.

Data analysis. The collected data were coded, entered into CSPro software, and exported to SPSS version 26 for analysis. Categorical variables were presented using frequency and percentages, whereas continuous variables were reported as medians with interquartile ranges (IQRs). For categorical variables, the chi-square or Fisher exact test for expected frequency < 5 in univariate analysis was used to make a comparison between groups. An independent t test for continuous variables was performed to compare the means of two independent groups for normally distributed and the Mann-Whitney U test for nonnormally distributed numeric data. To determine the predictor of disease severity

(nonsevere versus severe) and COVID-19 outcome (alive or dead during hospital stay), a binary logistic regression model was used independently. In the univariate analysis, variables with P < 0.1 were used to identify potential significant factors for the final models. A binary logistic regression model was well fitted to identify predictor variables Hosmer and Lemeshow goodness of fit test P = 0.126 and P = 0.055 for disease severity and mortality outcome respectively. Adjusted odds ratio (aOR) with a 95% confidence interval (CI) and P value < 0.05 was used as statistically significant.

Source of funding and ethical consideration. This study was supported by the East African Training Initiative. Ethical clearance was obtained from the Institutional Review Board of Eka Kotebe General Hospital (ref. no. Yek/150/5/9). All data managers and collectors received the same training on maintaining confidentiality.

RESULTS

A total of 463 laboratory-confirmed symptomatic COVID-19 patients met the inclusion criteria; 319 (68.9%) were male. The median age was 45 years (IQR: 32–62); 38.2% (n = 177) of subjects were younger than 40 years. Cough (n = 313, 68.6%), SOB (n = 204, 44.1%), fatigue/malaise (n = 171, 36.9%) fever (n = 162, 35.0%), and headaches (n = 131, 28.3%) were the most common symptoms. Comorbidities were present in 189 (40.8%) of the participants. HTN (N = 112, 24.2%), DM (n = 96, 20.7%), and chronic cardiac diseases (n = 27, 5.8%) were the most prevalent comorbidities (Table 1).

An absolute lymphocyte count (ALC) < 1,000/mm³ was seen in 140 (34.7%) subjects, aspartate transaminase (AST) > 37 u/L (reference range up to 37) in 136 (38.2%), and alanine transaminase (ALT) > 63 u/L (up to 63 reference range) in 68 (18.9%). Antibiotics (n = 290, 62.6%), corticosteroid (n = 109, 23.5%), chloroquine (n = 38, 8.2%), prophylactic anticoagulation (n = 201, 43.4%), full-dose anticoagulation (n = 60, 13.3%), and vasopressor support (n = 32, 6.9%)were administered to study subjects. Oxygen therapy was provided to 231 (49.9%), prone ventilation (either awake or with mechanical ventilation) to 149 (32.2%), invasive mechanical ventilation to 37 (8.0%), and noninvasive positive pressure ventilation to 26 (5.6%) patients. Tracheostomy was done for eight (1.7%) study participants. One hundred seventy-eight patients (38.4%) had severe and critical disease, and the remaining 285 (61.6%) had mild or moderate severity. The median duration of hospital stay was 15 days (IQR: 14-21). Case fatality was 11.4% (53 of 463) (Table 2).

A chi-square test result revealed a statistically significant difference in disease severity across patient groups based on age, gender, presence of any comorbidities, HTN, DM, chronic cardiac disease, chronic lung disease, malignancy, CKD, cough, SOB, fatigue/malaise, headache, and new loss of smell sensation (P < 0.05). A statistically significant proportion of patients aged ≥ 60 years had severe disease (45.0% versus 20.7%, P < 0.001) compared with nonsevere disease, whereas a statistically significant proportion of patients aged younger than 40 years had nonsevere disease (53.3% versus 14.0%, P < 0.001) compared with severe disease. A significantly higher proportion of patients having any comorbidity or HTN, DM, chronic cardiac disease, chronic

 $\mathsf{T}_{\mathsf{ABLE}}\,3$ Demographic, comorbidity, and symptom characteristics; comparison based on disease severity and factors associated

	,		,		,			
		Severity	ity					
Characteristics	All patients	Nonsevere (mild and moderate) ($n = 285$)	Severe (severe and critical) $(n = 178)$	P value	aOR (95% CI)	P value	aOR (95% CI)	P value
in years (median,	45 (32–62)		55 (45–67)	0.001	*		*	
Age < 40	177 (38.2)		25 (14.0)	0.00				•
40-59	147 (31.7)	٠.	73 (41.0)		5.998 (3.522-10.215)	0.001	3.445 (1.882-6.307)	0.000
09 ∧	139 (30.0)	ಲ	80 (45.0)		8.244 (4.802–14.153)	0.001		*000.0
Sex n (%) Male	319 (68.9)	206 (72.3)	113 (63.5)	0.047	0.667 (0.447–0.995)	0.047	0.841 (0.507–1.395)	0.503
Female	144 (31.1)	79 (27.7)	65 (36.5)		-		-	
Comorbidity	189 (40.8)	77 (27.0)	112 (62.9)	0.001	4.584 (3.069–6.846)	0.001	1.233 (0.552–2.754)	0.610
Hypertension	112 (24.2)	41 (14.4)	71 (39.9)	0.000	3.949 (2.527–6.172)	0.001		0.177
Type 2 diabetes mellitus	96 (20.7)	37 (13.0)		0.001	3.323 (2.086–5.293)	0.001	1.559 (0.792–3.070)	0.199
Chronic cardiac disease	27 (5.8)	10 (3.5)	17 (9.6)	0.007	0.344 (0.154-0.770)	0.009	0.950 (0.358-2.519)	0.917
Chronic lung disease	21 (4.5)	7 (2.5)	14 (7.9)	0.007	3.390 (1.341–8.572)	0.010		0.295
Malignancy	19 (4.1)	7 (2.5)	12 (6.7)	0.024	2.871 (1.108–7.436)	0.030	4.641 (1.319–16.337)	0.017*
HIV/AIDS	11 (2.4)	6 (2.1)		0.756				
Chronic kidney disease	8 (1.7)	1 (0.4)		9000	11.626 (1.418–95.305)	0.022	3.084 (0.340–27.990)	0.317
CLD	2 (0.4)	1 (0.4)	1 (0.6)	0.736				
Cough	313 (67.6)	179 (62.8)	134 (75.3)	0.005	1.803 (1.189–2.736)	900.0	1.122 (0.664–1.896)	0.666
Shortness of breath		82 (28.8)	122 (68.5)	0.001	5.393 (3.589-8.104)	0.001	3.831 (2.347–6.252)	*000.0
Fatigue/malaise	171 (36.9)	88 (30.9)	83 (46.6)	0.001	1.956 (1.328–2.880)	0.001	1.456 (0.883–2.401)	0.141
Fever	162 (35.0)	93 (32.6)		0.178				
Headache	131 (28.3)	95 (33.3)		0.002	0.507 (0.326-0.788)	0.003	0.630 (0.367-1.084)	0.095
Myalgia	110 (23.8)	63 (22.1)		0.290				
Arthralgia	109 (23.5)	63 (22.1)	46 (25.8)	0.356				
Loss of appetite	89 (19.2)		41 (23.0)	0.100				
Sore throat	65 (14.0)	45 (15.8)	20 (11.2)	0.170				
Chill	40 (8.6)	20 (7.0)	20 (11.2)	0.119				
Vomiting		16 (5.6)	15 (8.4)	0.239				
Abdominal pain		17 (6.0)		0.737				
New loss of smell	26 (5.6)	21 (7.4)		0.038	0.363 (0.134-0.982)	0.046	0.497 (0.146–1.699)	0.265
New loss of taste	22 (4.8)	17 (6.0)		0.120				
Diarrhea	19 (4.1)	14 (4.9)		0.267				
Nausea	17 (3.7)	4	4 (2.2)	0.198				
Runny nose (rhinorrhea)	17 (3.7)	13 (4.6)	4 (2.2)	0.198				
aOR = adjusted odds ratio; CI = confidence interval; CLD = chronic liver disease; IQR =	rval; CLD = chronic liver d	isease; IQR = interquartile range.	oi oi					

256 HULUKA AND OTHERS

lung disease, malignancy, CKD, cough, SOB, and fatigue/malaise had severe disease (Table 3).

Age, malignancy, and SOB were significantly associated with COVID-19 severity in the multivariable binary logistic regression. The odds of having severe disease compared with nonsevere disease are 3.4 and 3.6 times greater in the 40 to 59 and 60 and older age groups than for patients younger than 40 years (aOR = 3.44, 95% Cl: 1.88–6.31, P < 0.0001) and (aOR = 3.63, 95% Cl: 1.91–6.90, P < 0.0001), respectively. The odds of having severe COVID-19 were 4.6 times higher in patients with the presence of malignancy (aOR = 4.64, 95% Cl: 1.32–16.33, P = 0.017). The presence of SOB also increased the odds of having severe disease (aOR = 3.83, 95% Cl: 2.35, 6.25, P < 0.0001) (Table 3).

The median age in those who died was older than in those who survived (61 versus 43 years, P < 0.0001), and fewer patients died in the age group below 40 than above 60 years (13.2 versus 60.4%, P < 0.0001). On univariate analysis HTN, DM, the presence of any comorbidity, malignancy, chronic liver disease (CLD), SOB, loss of appetite, vomiting, AST \geq 37 u/L were significantly associated with in-hospital mortality whereas headache, loss of appetite and ALC count > 1,000/mm³ were found to decrease mortality (Table 4).

Patients aged 60 and older had a 3.9-fold increased risk of mortality compared with patients younger than 40 (aOR = 3.94, 95% CI: 1.44–10.78, P=0.008). After adjusting for covariates, age, malignancy, SOB, and vomiting were significantly associated with mortality in the multivariable binary logistic regression. Patients with malignancy were 9 times (aOR = 9.03, 95% CI: 2.46–33.09, P<0.001) more likely to die. Patients with SOB had a 2.3 times (aOR = 2.34, 95% CI: 1.15–4.75, P=0.019) higher risk of mortality than those without. Patients with vomiting had a more than 3-fold higher odds of death compared with those who did not (aOR = 3.04, 95% CI: 1.13–8.26, P=0.028) (Table 4).

DISCUSSION

This study investigated the clinical manifestations, treatment, outcomes, and factors related to the severity and mortality of COVID 19 in patients admitted to a COVID-19 specialty hospital in Addis Ababa, Ethiopia, in the prevaccine era. In our treatment center, more than two-thirds of participants were male. The median age was 45 years with 30% of study participants \geq 60 years of age. Cough, SOB, fatigue/malaise, fever, and headaches were the most common symptoms. HTN, DM, and chronic cardiac diseases were the most frequent comorbidities. Overall, age \geq 60 years, malignancy, and SOB were found to be significant predictors of disease severity; these factors, in addition to vomiting, also predicted mortality.

The reported rate of bacterial superinfection has been variable ranging from 8% in earlier clinical studies to 32% from autopsy reports. A recent more objective study based on bronchoalveolar lavage samples within 48 hours of hospitalization revealed 21% of superinfection. However, in our study, three out of five patients received antibiotics. This practice was predicated on the universal recommendation of antibiotic use in moderate to critical disease conditions in the previous national guidelines. ^{28,29}

More than half of the patients received anticoagulants, prophylactic or therapeutic, in accordance with the observed benefit of these medications in COVID-19, particularly those

with severe disease.³⁰ Slightly less than a quarter of patients were given corticosteroids, in contrast to current evidence that steroids have a survival advantage in severe to critical COVID-19.³¹ This underuse of steroids was due, in part, to the discretion of the managing team before publication of the interim report of the RECOVERY trial.

HTN, DM, and chronic cardiac disease were the most prevalent comorbidities. This finding is consistent with results from previous Ethiopian reports 12,32 and other studies done in Africa, China, Brazil, and the United States. 9,14 In multivariable analyses, HTN and DM were not associated with disease severity. This is in contrast to most studies. Another local study by Abraha et al. also found no association between HTN and severity of disease. However, DM, was associated with disease severity.32 COVID-19 in-hospital mortality was not associated with HTN or DM in multivariable analyses, similar to previous reports from Ethiopia, Saudi Arabia, Brazil, the U.S.-Mexico border, and the United States. 9,14 HTN did not also increase risk for death in the largest COVID registry from United Kingdom.33 Further, HIV/AIDS was not associated with disease severity or mortality in our study. This finding agrees with other Ethiopian published reports 32,34,35 and those from other areas of Africa, Europe, China, and the United States. 9,15,21

Age was significantly associated with disease severity and in-hospital mortality, which was similar to the findings of other Ethiopian, African, and international studies. $^{1,9-11,13,14,16,20,21,32,33,35-38}$ Proposed explanations include the physiological aging process, particularly the increased prevalence of frailty, age-related decline in lung function, comorbidities, and a weakened immune system. 39,40 More than half of our study participants were <50 years of age. Our age distribution was similar to other treatment centers in Ethiopia 32,34,35 and data from other sub-Saharan countries, $^{41-43}$ but younger than study populations reported from Europe, North America, and China. 44 This variation could be due to the generally younger population of the African continent and greater hospital admissions in the region early during the pandemic for those with mild COVID-19 disease.

Patients with malignancy had adjusted odds ratio (aOR) 4.6 times greater for severe disease and 9 times greater for mortality compared with nonsevere disease. These findings are consistent with those of another Ethiopian study by Hiluf et al. from Tigray.³² It might be because of weakened immunity from the malignancy itself or from the immunosuppressive drugs used to treat the condition. The presence of SOB was associated with more than 3-fold increased odds of severe disease compared with nonsevere disease, and the risk of death was 2.3 times higher. This is in accordance with previously published studies. 9,11-13,18,20 It might be because SOB occurs late in the course, usually in the inflammatory stage of the disease when mortality is high. Vomiting was also significantly associated with an increased likelihood of mortality. This is consistent with a report from Iraq that showed a poor prognosis in those with concomitant respiratory symptoms. 45 However, it is contrary to reports from the United States. 46-48

There are several study limitations. The lack of comprehensive laboratory findings prohibited us from including them in the final model as possible predictors of disease outcome. The cross-sectional nature of the study design made it difficult to establish a cause-effect relationship between

 $\mathsf{T}_{\mathsf{ABLE}}\,4$ Demographic, comorbidity, and symptom characteristics; comparison based on disease outcome and factors associated

	3 l	٠٠٠٠ ((· · · - · · · · · · · · · · ·				
		Out	Outcome					
Characteristics	All patients	Death $(n = 53)$	Alive $(n = 410)$	P value	aOR (95% CI)	P value	aOR (95% CI)	P value
Age in years (median, IQR)	45 (32–62)	61 (47–70)	43 (31–60)	< 0.0001				
Age < 40		7 (13.2)	170 (41.5)	< 0.0001	-		-	
40–59	147 (31.7)	14 (26.4)	133 (32.4)		2.556 (1.003–6.513)	0.049	1.463 (0.519,4.121)	0.471
09 ∧∣	139 (30.0)	32 (60.4)	107 (26.1)		7.263 (3.096–17.041)	0.000	3.935 (1.437–10.779)	0.008*
Sex, n (%) Male		31 (58.5)	288 (70.2)	0.082	0.597 (0.332-1.072)	0.084	0.955 (0.484-1.885)	0.894
Female	144 (31.1)	22 (41.5)	122 (29.8)		,—		-	
Comorbidity	189 (40.8)	36 (67.9)	153 (37.3)	0.000	3.557 (1.932–6.550)	0.000	0.905 (0.315-2.606)	0.854
Hypertension	112 (24.2)	23 (43.4)	89 (21.7)	0.001	2.765 (1.530–4.997)	0.001	1.198 (0.472–3.043)	0.704
Type 2 diabetes mellitus		19 (35.8)	77 (18.8)	0.004	2.417 (1.308–4.464)	0.005	1.880 (0.816-4.331)	0.138
Chronic cardiac disease	27 (5.8)	5 (9.4)	22 (5.4)	0.218	•			
Malignancy		7 (13.2)	12 (2.9)	0.003	5.047 (1.893–13.459)	0.001	9.028 (2.463-33.092)	*1000
HIV/AIDS	11 (2.4)	1 (1.9)		1.000	•			
Chronic kidney disease	8 (1.7)	3 (5.7)	5 (1.2)	0.052	4.860 (1.127–20.952)	0.034	1.659 (0.317-8.678)	0.549
Chronic lung disease	21 (4.5)	5 (9.4)	16 (3.9)	0.069	2.565 (0.899–7.315)	0.078	1.838 (0.539–6.266)	0.331
CLD	2 (0.4)	2 (2.8)	0.0) 0	0.013	1.299E+10 (0.000)	0.999	,	
Cough	313 (67.6)		271 (66.1)	0.054	1.958 (0.978–3.923)	0.058	1.411 (0.642–3.103)	0.391
Shortness of breath		37 (69.8)	167 (40.7)	0.000	3.365 (1.813–6.247)	0.000	2.336 (1.148-4.752)	0.019*
Fatigue/malaise	171 (36.9)	24 (45.3)		0.181				
Fever	162 (35.0)	21 (39.6)	141 (34.4)	0.452				
Headache	131 (28.3)	8 (15.1)	123 (30.0)	0.023	0.415 (0.190-0.906)	0.027	0.542 (0.230-1.279)	0.162
Myalgia		12 (22.6)	98 (23.9)	0.839				
Arthralgia			99 (24.10)	0.394				
Loss of appetite		16 (30.2)	73 (17.8)	0.031	1.996 (1.054–3.781)	0.034	1.329 (0.631–2.797)	0.454
Sore throat	65 (14.0)	3 (5.7)	62 (15.1)	0.062	0.337 (0.102–1.114)	0.074	0.503 (0.141–1.794)	0.290
Chill	_	4 (7.5)		1.000				
Vomiting		9 (17.0)	22 (5.4)	0.005	3.607 (1.564–8.322)	0.003	3.049 (1.126–8.255)	0.028*
Abdominal pain		5 (9.4)		0.359				
New loss of smell	26 (5.6)	1 (1.9)		0.341				
New loss of test	22 (4.8)	1 (1.9)	21 (5.1)	0.494				
Diarrhea	_	1 (1.9)		0.711				
Nausea		3 (5.7)	14 (3.4)	0.428				
ninorrhe		1 (1.9)	16 (3.9)	0.707				
ALC $(n = 404)$ < 1,000	140 (34.7)	34 (66.7)	106 (30.0)	0.000				
ΛΙ	264 (65.3)	17 (33.3)	247 (70.0)					
AST ($n = 356$) < $\frac{37}{2}$	220 (61.8)	13 (28.9)	207 (66.6)	0.000				
	136 (38.2)	32 (71.1)	104 (33.4)					
ALT $(n = 360)$ ≤ 63	292 (81.1)	34 (73.9)	258 (82.2)	0.182				
> 63	68 (18.9)	12 (26.1)	56 (17.8)					
Incle = TIV: tailoo of codamil at iloade = OIV	o +rapeaminasor ACT - a	Ol . Sedimesact states	opacy olitical protati — aC					

ALC = absolute lymphocyte count; ALT = alanine transaminase; AST = aspartate transaminase; IQR = interquartile range.

the various factors and disease severity or treatment outcome. Being a single-center and hospital-based study, the findings may not be generalizable.

In conclusion, in Ethiopia, most COVID-19 patients were male and presented with cough, SOB, and fatigue. Older age, any malignancy, and SOB were associated with disease severity; these factors, in addition to vomiting, also predicted mortality.

Received December 6, 2021. Accepted for publication March 16, 2022.

Published online July 5, 2022.

Acknowledgments: We extend our heartfelt gratitude to Eka Kotebe Hospital for giving us the ethical clearance to undertake this study. We are also so grateful to the East African Training Initiative, sponsored by Vital Strategies and the Swiss Lung Foundation, for funding the data collection. The American Society of Tropical Medicine and Hygiene has waived the Open Access fee for this article due to the ongoing COVID-19 pandemic.

Financial support: This study was supported by the East African Training Initiative.

Authors' addresses: Dawit Kebede Huluka, Sebrina Ahmed, Hiluf Abate Abule, Nebiyu Getachew, Yohannes Feleke, Yonathan Abebe, Tewodros Haile Gebremariam, Hanan Yusuf Ahmed, and Wondwossen Amogne, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia, E-mails: dndrda97@gmail.com, amisub7575@ gmail.com, hilufabate@gmail.com, neboneba@gmail.com, yohannes feleke91@gmail.com, zidgich@gmail.com, drtewodroshaile@gmail. com, hananyusufahmed@gmail.com, and wonamogne@yahoo.com. Eyob Kebede Etissa, East African Training Initiative, Addis Ababa, Ethiopia, E-mail: eyobke@gmail.com. Sisay Abera, Abebaw Bekele Seyoum, Hiruy Araya, Tsegaye Gebreyes Hundie, Bethlehem Tadesse Anteneh, Getachew Demoz Gebremedhin, Yonas Gebregziabher, Rediet Yitagesu Tefera, Addisu Birhanu Tereda, Eka Kotebe Hospital, Addis Ababa, Ethiopia, E-mails: sisayabera21@gamil.com, abex4397@gmail. com, hiruya6@gmail.com, tsegayegebreyes@yahoo.com, bethlehem. tadesse.anteneh@gmail.com, getudm@gmail.com, yonasgebregziab her1@gmail.com, yitagesuredi@gmail.com, and addisbirae@gmail. com. Deborah A. Haisch, Weill Cornell Medical College, New York, NY, E-mail: dah2020@med.cornell.edu. Charles B. Sherman, Warren Alpert School of Medicine, Brown University, Providence, RI, E-mail: cbsherman@gmail.com. Neil W. Schluger, Westchester Medical Center, New York Medical College, New York, NY, E-mail: neil.schluger@

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC-BY) License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

REFERENCES

- Huang C et al., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395: 497–506.
- World Health Organization, 2021. Corona Virus Disease 19 (COVID-19) Pandemic. Available at: https://www.who.int/ emergencies/diseases/novel-coronavirus-2019?gclid=CjwKCAjw zaSLBhBJEiwAJSRokrB3MPgON1vmtgMy0UEUkVHK5h6lnWB SBV9TNYCBtrRS6Rin83M1khoCuFEQAvD_BwE. Accessed October 16, 2021.
- World Health Organization, 2021. Coronavirus Disease (COVID-19). Available at: https://www.who.int/health-topics/ coronavirus#tab=tab_1. Accessed October 16, 2021.
- Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, Khare S, Srivastava A, 2020. Clinical features of COVID-19 and factors associated with severe clinical course: a systematic review and meta-analysis. SSRN. doi: 10.2139/ssrn.3566166.
- Wong CKH, Wong JYH, Tang EHM, Au CH, Wai AKC, 2020. Clinical presentations, laboratory and radiological findings,

- and treatments for 11,028 COVID-19 patients: a systematic review and meta-analysis. *Sci Rep 10:* 19765.
- Olumade TJ, Uzairue LI, 2021. Clinical characteristics of 4499 COVID-19 patients in Africa: a meta-analysis. J Med Virol 93: 3055–3061.
- Fu L et al., 2020. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and metaanalysis. J Infect 80: 656–665.
- World Health Organization, 2020. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Available at: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf. Accessed October 14, 2021.
- Cervantes J, Sureen A, Galura G, Dodoo C, Dwivedi AK, Bashashati M, Zuckerman M, Meza A, 2021. Factors associated with COVID-19 severity and mortality among Hispanic patients living on the USA–Mexico border. *J Investig Med.* doi: 10.1136/jim-2020-001667.
- Khan A, Althunayyan S, Alsofayan Y, Alotaibi R, Mubarak A, Arafat M, Assiri A, Jokhdar H, 2020. Risk factors associated with worse outcomes in COVID-19: a retrospective study in Saudi Arabia. East Mediterr Health J 26: 1371–1380.
- Maru EH et al, 2020. Predictors of death in severe COVID-19 patients at millennium COVID-19 care center in Ethiopia: a case–control study. medRxiv. doi: 10.1101/ 2020.10.07.20205575.
- Leulseged TW et al, 2020. Characteristics and outcome profile of hospitalized African COVID-19 patients: the Ethiopian context. medRxiv. doi: 10.1101/2020.10.27.20220640.
- Du R-H et al., 2020. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J 55: 2000524.
- Cummings MJ et al., 2020. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 395: 1763–1770.
- Osibogun A et al., 2021. Outcomes of COVID-19 patients with comorbidities in southwest Nigeria. PLoS One 16: e0248281.
- Mohammed M et al., 2021. Risk factors associated with mortality among patients with novel coronavirus disease (COVID-19) in Africa. J Racial Ethn Health Disparities 8: 1267–1272.
- Li X, Zhong X, Wang Y, Zeng X, Luo T, Liu Q, 2021. Clinical determinants of the severity of COVID-19: a systematic review and meta-analysis. *PLoS One 16*: e0250602.
- Fouda Mbarga N et al., 2021. Clinical profile and factors associated with COVID-19 in Yaounde, Cameroon: a prospective cohort study. PLoS One 16: e0251504.
- Geng M-J et al., 2021. Risk factors for developing severe COVID-19 in China: an analysis of disease surveillance data. Infect Dis Poverty 10: 48.
- Soares RCM, Mattos LR, Raposo LM, 2020. Risk factors for hospitalization and mortality due to COVID-19 in Espírito Santo State, Brazil. Am J Trop Med Hyg 103: 1184–1190. doi: 10.4269/ajtmh.20-0483.
- Jassat W et al., 2021. Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study. Lancet HIV 8: e554–e567.
- Zhou F et al., 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet 395*: 1054–1062. doi: 10.1016/ S0140-6736(20)30566-3.
- Worldometer, 2021. Coronavirus: Ethiopia. Available at: https:// www.worldometers.info/coronavirus/country/ethiopia/. Accessed October 8, 2021.
- Africa WHO, 2020. First Case of COVID-19 Confirmed in Ethiopia. Available at: https://www.afro.who.int/news/first-casecovid-19-confirmed-ethiopia. Accessed October 16, 2021.
- Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, Soucy J-PR, Daneman N, 2020. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect 26: 1622–1629.
- Clancy CJ, Schwartz IS, Kula B, Nguyen MH, 2021. Bacterial superinfections among persons with coronavirus disease 2019: a comprehensive review of data from postmortem studies. Open Forum Infect Dis 8. doi: 10.1093/ofid/ofab065.

COVID-19 IN ETHIOPIA 259

- Pickens CO et al., 2021. Bacterial superinfection pneumonia in patients mechanically ventilated for COVID-19 pneumonia. Am J Respir Crit Care Med 204: 921–932. doi: 10.1164/rccm. 202106-1354OC.
- Federal Ministry of Health, Ethiopia, 2020. National Comprehensive Covid19 Management Handbook, 1st ed. Available at; https://covidlawlab.org/wp-content/uploads/2020/06/National-Comprehensive-COVID19-Management-Handbook. pdf. Accessed October 14, 2021.
- Federal Ministry of Health, Ethiopia, 2020. National Comprehensive COVID 19 Clinical Management Handbook for Ethiopia, 2nd ed. Available at: https://www.afro.who.int/news/first-case-covid-19-confirmed-ethiopia. Accessed October 14, 2021.
- The REMAP-CAP, ACTIV-4a, and ATTACC Investigators, 2021. Therapeutic anticoagulation with heparin in critically ill patients with COVID-19. N Engl J Med 385: 777–789.
- The RECOVERY Collaborative Group, 2020. Dexamethasone in hospitalized patients with COVID-19. N Engl J Med 384: 693–704.
- Abraha HE et al., 2021. Clinical features and risk factors associated with morbidity and mortality among patients with COVID-19 in northern Ethiopia. Int J Infect Dis 105: 776–783.
- Williamson EJ et al., 2020. Factors associated with COVID-19related death using OpenSAFELY. Nature 584: 430–436.
- Abdela SG, Abegaz SH, Demsiss W, Tamirat KS, van Henten S, van Griensven J, 2020. Clinical profile and treatment of COVID-19 patients: experiences from an Ethiopian treatment center. Am J Trop Med Hyg 104: 532–536.
- Leulseged TW et al., 2020. COVID-19 disease severity and determinants among Ethiopian patients: a study of the millennium COVID-19 care center. medRxiv. doi: 10.1101/2020.10. 09.20209999.
- Gupta S et al., 2020. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. JAMA Intern Med 180: 1436–1447.
- Li X et al., 2020. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 146: 110–118.

 Leulseged TW et al., 2021. Factors associated with development of symptomatic disease in Ethiopian COVID-19 patients: a case-control study. BMC Infect Dis 21: 759.

- Ho FK et al., 2020. Is older age associated with COVID-19 mortality in the absence of other risk factors? General population cohort study of 470,034 participants. PLoS One 15: e0241824.
- Bonanad C et al., 2020. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. J Am Med Dir Assoc 21: 915–918.
- Nachega JB et al., 2020. Clinical characteristics and outcomes of patients hospitalized for COVID-19 in Africa: early insights from the Democratic Republic of the Congo. Am J Trop Med Hyg 103: 2419–2428. doi: 10.4269/ajtmh.20-1240.
- Morton B et al., 2021. Distinct clinical and immunological profiles of patients with evidence of SARS-CoV-2 infection in sub-Saharan Africa. Nat Commun 12: 3554.
- Bakamutumaho B et al., 2021. Severe COVID-19 in Uganda across two epidemic phases: a prospective cohort study. Am J Trop Med Hyg 105: 740–744.
- Richardson S et al., 2020. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 323: 2052–2059.
- Sulaiman T, Algharawi AA, Idrees M, Alzaidy RH, Faris K, Cullingford G, Rasheed J, 2020. The prevalence of gastrointestinal symptoms among patients with COVID-19 and the effect on the severity of the disease. *JGH Open 4*: 1162–1166.
- Nobel YR, Phipps M, Zucker J, Lebwohl B, Wang TC, Sobieszczyk ME, Freedberg DE, 2020. Gastrointestinal symptoms and coronavirus disease 2019: a case-control study from the United States. *Gastroenterology* 159: 373–375.e2.
- Ramachandran P, Onukogu I, Ghanta S, Gajendran M, Perisetti A, Goyal H, Aggarwal A, 2020. Gastrointestinal symptoms and outcomes in hospitalized coronavirus disease 2019 patients. *Dig Dis* 38: 373–379.
- Livanos AE et al., 2020. Gastrointestinal involvement attenuates COVID-19 severity and mortality. medRxiv. doi: 10.1101/2020. 09.07.20187666.