BMC Global and Public Health

RESEARCH

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In-hospital trends of non-communicable disease mortality during the pandemic for patients without COVID-19 at a regional referral hospital in southwestern Uganda

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Abstract

Background Non-communicable diseases (NCDs) represent a growing health burden in sub-Saharan Africa, especially in Uganda. The COVID-19 pandemic presented significant challenges for the Ugandan healthcare system, though changes in hospital admissions and outcomes for adults with NCDs and without COVID-19 infection remain unknown. We evaluated trends of NCD-related in-hospital mortality among patients without COVID-19 in a large regional referral hospital in Uganda from March 2019 through August 2021.

Methods Between March 1, 2019, and August 31, 2021, we conducted a chart review of Ugandan adults who carried a history of or were admitted for an NCD to Mbarara Regional Referral Hospital. Based on mortality trends, we broke admissions into three periods: Pre-Pandemic (March 1, 2019, to May 31, 2020), Early Pandemic (June 1, 2020, to March 31, 2021), and Late Pandemic (April 1, 2021, to August 31, 2021), and calculated admission and mortality rates for the most common NCD diagnoses. A multivariable logistic regression model was fitted for a primary outcome of in-hospital mortality.

Results Of 3777 total individuals, 1655 were admitted Pre-Pandemic, 1423 in the Early Pandemic, and 699 in the Late Pandemic. We found a five-fold increase in mortality in the Early Pandemic period compared to the Pre-Pandemic and Late Pandemic periods (15.4 vs 2.9 vs 2.4, $p < 0.001$). Factors associated with increased odds for in-hospital mortality included admission during the Early Pandemic period (odds ratio [OR] 5.59; 95% CI 3.90, 8.02; $p < 0.001$), admission with hypotension (OR 2.13; 95% CI 1.40, 3.24; $p < 0.001$), admission diagnosis of malignancy (OR 1.79; 95% CI 1.06, 3.01; $p = 0.028$) and stroke (OR 1.75; 95% CI 1.06, 2.88; $p = 0.028$), and each unit increase in SOFA score (OR 1.41; 95% CI 1.30, 1.52; $p < 0.001$). Length of stay greater than 7 days was associated with decreased odds of in-hospital mortality (OR 0.56; 95%CI 0.40, 0.79; $p = 0.001$).

Conclusions NCD-associated in-hospital mortality was high in the early COVID-19 pandemic period. Disruptions in longitudinal NCD care that occurred due to the pandemic may have been contributory, though this requires

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further investigation. Future work should focus on NCD care for hospitalized individuals in resource limited settings and developing more resilient systems of NCD care.

Keywords Non-communicable disease, Uganda, COVID-19 pandemic, Hospital care

Background

Non-communicable diseases (NCDs) comprise a growing health burden in sub-Saharan Africa with deaths from NCDs projected to outpace infectious causes by 2030 [1, 2]. NCDs account for over one-third of disability-adjusted life years (DALYs) in low-income countries and represent up to 30% of hospitalizations, with heart failure a leading cause of in-patient mortality in Uganda with rising rates of chronic kidney disease, stroke and cancer [3–7]. In Uganda, 33% of deaths were attributed to NCDs in 2016 and health facilities are inadequately equipped to properly manage NCDs [8–10].

The COVID-19 pandemic had a global impact on healthcare systems particularly in low- and middle-income countries (LMICs) that already had struggling healthcare infrastructure. From March 18, 2020, through June 2, 2020, and from June 6, 2021, through July 30, 2021, Uganda instituted country-wide socio-geographical movement restrictions where transportation and social services were severely limited, and businesses and institutions were temporarily closed [11]. This disruption led to loss of jobs, income [12, 13] and to a 10–17% decrease in hypertension and diabetes outpatient visits, though the impact on NCD-related hospitalizations and mortality remains unknown [14–16]. Moreover, access to essential medications was severely limited during this period, and the already limited clinical resources were repurposed towards COVID-19 care [17, 18].

In March 2020, in preparation for the impacts of lockdowns, the Ugandan Ministry of Health created a national committee to ensure continuity of essential health services, but significant disruptions in care delivery remained, especially early in the COVID-19 pandemic [19, 20]. Trends of NCD-related in-hospital mortality of patients without COVID-19, before, during, and after lockdowns are limited, with cross-sectional studies showing an overall decrease in hospital utilization and mortality after the start of country-wide lockdowns in 2020 [15, 21]. We have previously shown that patients with NCDs in Uganda had limited access to affordable medication during the pandemic [18]. However, no studies in Uganda have looked specifically at in-hospital outcomes for individuals with NCDs and without COVID-19. Not only are NCD patients particularly susceptible to disruptions in longitudinal care, looking at those without COVID-19 will evaluate the effects of the pandemic on the health system. Here, we describe the trends of NCD-related in-hospital mortality among patients without COVID-19 in a large regional referral hospital in Uganda from March 2019 through August 2021.

Methods

Study setting and population

This study took place at Mbarara Regional Referral Hospital (MRRH), a publicly operated tertiary care hospital in Mbarara, Uganda. MRRH is a 600-bed teaching hospital affiliated with Mbarara University of Science and Technology that serves the southwestern region of Uganda with a catchment area of 6–8 million people offering both medical and surgical subspecialty services. Medical services are provided free of charge by policy, although frequent stockouts of medications and sundries require individuals to pay for much of their care out of pocket since there is no universal health insurance.

The time-period covered by the chart review began in March 2019, a year prior to the COVID-19 pandemic to August 2021. Our study period was centered on the lockdown period in Uganda that initially lasted from March 18, 2020, and August 8, 2020, followed by May 10, 2021, to June 22, 2021 [22]. The two lockdown periods coincided with the first and second waves of COVID-19 cases in Uganda (Fig. 1).

Study design and data collection

We conducted a retrospective manual chart review of all individuals admitted to the medical ward at MRRH during the study period. We included all individuals 18 years and older who carried a history of or were admitted for an NCD. We defined NCDs as non-infectious cardiovascular, endocrine, renal, gastrointestinal, pulmonary, hepatic, neurologic, hematologic, dermatologic, and mental health disease in addition to malignancy and acute poisoning. We excluded individuals that tested positive for COVID-19 or tested negative but were deemed high risk for COVID-19 per Ugandan COVID-19 test protocols, as these patients were admitted to the COVID-19 ward rather than the general medical ward.

Trained reviewers abstracted individual data including demographics (age, sex, district of residence, occupation, level of education, smoking and alcohol use), comorbid conditions (history of cardiovascular, renal, and lung diseases, stroke, heart failure, malignancy,

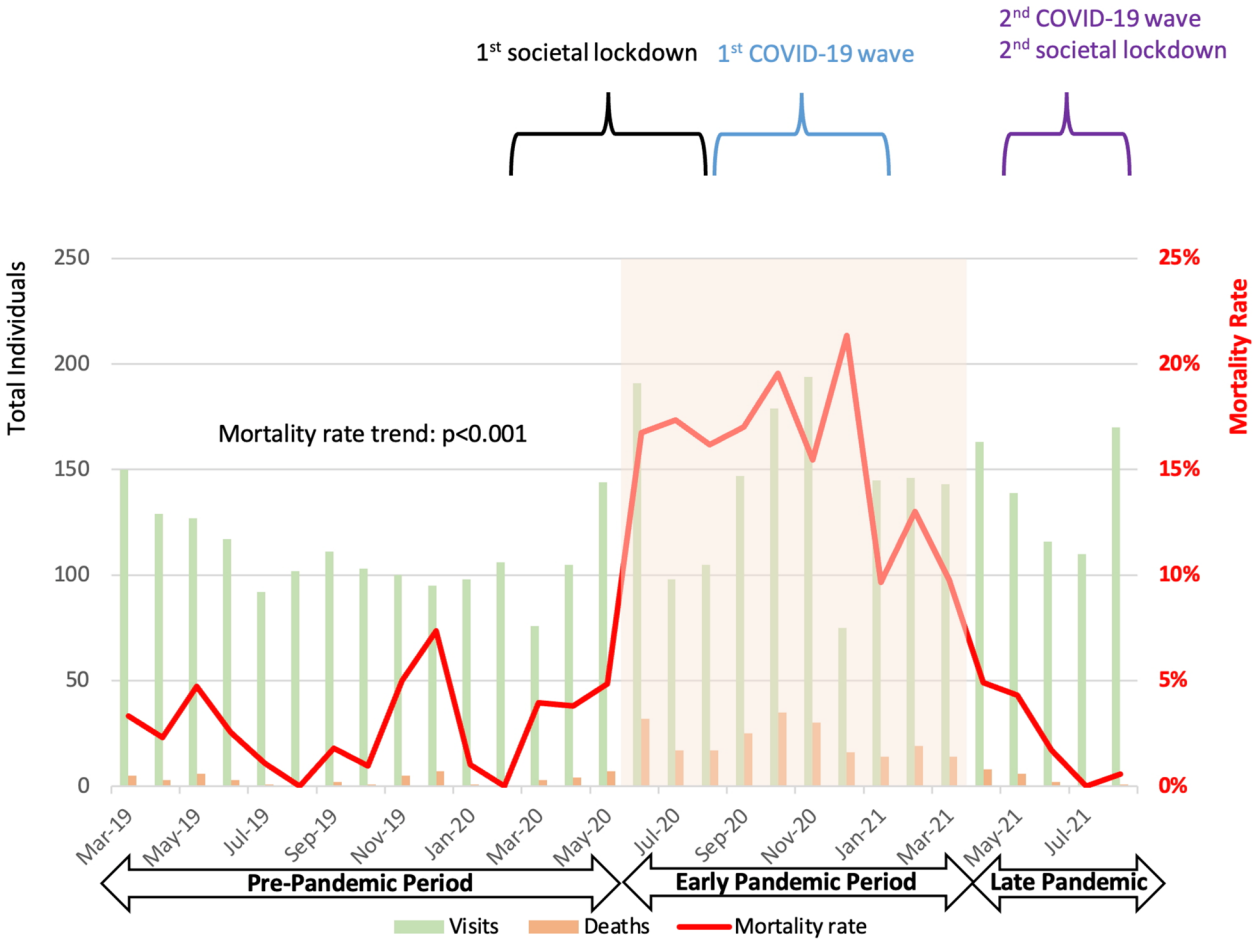

Fig. 1 Trends in in-hospital mortality at Mbarara Regional Referral Hospital from March 2019 through August 2021. Ugandan societal lockdowns occurred March 18, 2020, to August 8, 2020, and May 10, 2021, to June 22, 2021. The first wave of COVID-19 cases occurred approximately between August 1, 2020, and January 31, 2021, and the second wave occurred approximately between May 1, 2021, and August 31, 2021

human immunodeficiency virus [HIV]), medications (prior to admission, received during admission, and prescribed upon discharge), clinical data (vital signs and laboratory values on day of admission), and clinical outcomes (discharge, in-hospital death, transfer to the intensive care unit [ICU], transfer to outside facilities). Reviewers were all medical school students. We also recorded alcohol-related admissions, which were defined as acute alcohol intoxication, alcohol withdrawal, or acute alcoholic hepatitis without evidence of cirrhosis. At discharge, individuals often leave the hospital with the results of their laboratory and radiology results to keep for their records and there are often no retained copies of this data in the hospital. Additionally, labs often cost money for patients at MRRH, and there are many patients who do not get laboratory testing done during a hospital admission [23]. We defined "labs drawn during admission" as those individuals with laboratory values in the patient chart during data collection.

Statistical analysis

We categorized patient admissions and in-hospital mortality rate, overall and stratified by calendar month, to visually evaluate changes in admission and mortality patterns; changes were assessed using the Jonckheere-Terpstra test for trend [24]. From this graphical analysis, three time periods were identified based on differing levels in mortality rate: "Pre-pandemic" was defined as March 1, 2019, through May 31, 2020; "Early Pandemic" was defined as June 1, 2020, through March 31, 2021; and "Late Pandemic" was defined as April 1, 2021, through August 31, 2021 (Fig. 1).

We summarized baseline characteristics including by timing relative to the COVID-19 pandemic. Comparisons were made among individuals admitted during the "Pre-Pandemic," "Early Pandemic," and "Late Pandemic"

periods noted above using one-sided ANOVA tests and Pearson's chi-square tests for continuous variables and categorical variables, respectively.

For the most common admission diagnoses, we calculated total admissions per diagnosis and compared admission rates between "Early Pandemic," "Pre-Pandemic," and "Late Pandemic" periods using Pearson's chi-square tests. Admission rates were calculated by dividing total admissions of a particular diagnosis during a particular period by the total admissions during a particular period. Mortality rates were calculated by dividing total deaths of a particular diagnosis during a particular period by the total deaths during a particular period. Given that the mortality rate in the Pre-Pandemic and Late Pandemic eras were similar, we aimed to understand changes that occurred during the Early Pandemic period. For these common diagnoses, disease-specific mortality rates were calculated as deaths by admission diagnosis divided by total visits of the admission diagnosis. We compared disease specific mortality rates separately between Pre-Pandemic, Early Pandemic, and Late Pandemic using Pearson's chi-square tests.

Logistic regression models fitted with the outcome of in-hospital mortality were used to determine factors associated with mortality. Univariable regression models were used to determine crude estimates for each exposure variable. A multivariable regression model was fitted with all exposure variables while assessing for possible confounding [25]. Exposure variables included age, sex, admission time period, ICU admission, length of stay (LOS) of less or more than one week, past medical history (including HIV serostatus), distance of home from the hospital, admission diagnosis, and clinical severity. Potential interaction between significant variables was explored. We evaluated disease severity using two clinical severity scores (Sequential Organ Failure Assessment [SOFA] [26] and the Charlson Comorbidity Index [CCI] [27]). Clinical severity was also evaluated using past medical history (i.e., history of cardiovascular, renal, and lung diseases, stroke, heart failure, malignancy, and HIV), and the presence of hypotension (systolic blood pressure [SBP] < 90 mmHg) or hypertensive urgency (SBP > 180 mmHg) on admission. Given the retrospective nature of this work, the fact that patients often took test results home without a copy left in the chart, and that we analyzed paper charts where paper could fall out, there was likely some missing laboratory and radiological data that we cannot quantify. Variables in the regression model were evaluated for co-linearity using uncentered Variance Inflation Factor (VIF). A VIF score of 10 was used as a cut-off, with none meeting criteria. Missing data were treated as missing using listwise deletion, and variables were not included if they included significant missing data (greater than or equal to 10%) [28]. All data were analyzed using Stata IC 16.0 (StataCorp LLC, College Station, TX, USA).

Results

In-hospital mortality rate

Total admissions to the medical ward, total in-patient mortality, and in-patient mortality rate plotted against the three pandemic periods are shown in Fig. 1. In the Pre-Pandemic period, mortality fluctuated by month, but remained 8% or lower, peaking in December 2019. During the Ugandan societal lockdown (March 18, 2020 through June 2, 2020), there was an increase in mortality with especially high rates between June 1, 2020 (17%) and March 31, 2021 (10%), peaking at 21% in December 2020 (Fig. 1). Mortality returned to Pre-Pandemic period levels in April 2021 (5%) and remained below 5%. The observed trend in mortality rate was statistically significant (trend $p < 0.001$). In total, 284 (7.5%) of individuals died during hospitalization (Table 1).

Comorbidities

Overall, 3777 admissions were recorded for individuals admitted to the medical ward at MRRH with an NCD diagnosis between March 1, 2019, and August 31, 2021 (Table 1). The mean age was 50 years (standard deviation (SD) ± 20), and 1859 (49.3%) were women. Medical comorbidities were previously diagnosed in 1894 (50.2%) of individuals: hypertension ($n = 861$, 22.8%), diabetes ($n = 465$, 12.3%), heart failure ($n = 248$, 6.6%), chronic kidney disease (CKD) ($n = 154$, 4.1%), chronic obstructive pulmonary disease (COPD) or asthma ($n = 115$, 3.0%), mental health disorder ($n = 73$, 1.9%), malignancy ($n = 37$, 1.0%), and stroke ($n = 33$, 0.9%).

Differences in comorbidities, admission diagnosis, length of stay, and morbidity by period

In evaluating the three time periods, 1,655 (43.8%) admissions took place in the Pre-Pandemic period, 1423 (37.7%) visits in Early Pandemic period, and 699 (18.5%) visits in Late Pandemic period. As shown in Table 1, we observed a significant increase in the number of individuals with a past medical history of hypertension (344 [20.8%] vs 349 [24.5%] vs 163 [24.1%], $p = 0.03$) and HIV (200 [12.2%] vs 168 [11.9%] vs 115 [16.6%], $p = 0.001$). The mean length of stay was significantly different across the time periods with shortest length of stay during the Early Pandemic period (6.7, SD 8.1; $p = 0.02$). Mortality was highest in the Early Pandemic period (219 [15.4%], $p > 0.001$), as was the mean SOFA score (1.3 [SD 1.7], $p < 0.001$), mean CCI

Table 1 Patient demographic and clinical characteristics. Demographic and clinical characteristics of individuals admitted at MRRH during three periods identified by differing mortality rates

	Overall	Pre-Pandemic: Mar 1, 2019–May 31, 2020	Early Pandemic: June 1, 2020–March 31, 2021	Late Pandemic: April 1, 2021–August 31, 2021	*p*-value
Total, *N* (%)	3777	1655 (43.8)	1423 (37.7)	699 (18.5)	
Age, years mean, (SD)	49.6 (20.1)	49.4 (20.4)	50.2 (20.1)	48.8 (19.6)	0.28
Women, *n* (%)	1859 (49.3)	838 (50.7)	704 (49.5)	317 (45.4)	0.06
Past medical history, *n* (%)					
Hypertension	861 (22.8)	344 (20.8)	349 (24.5)	168 (24.1)	**0.03**
Diabetes	465 (12.3)	185 (11.2)	192 (13.5)	88 (12.6)	0.15
Heart failure	248 (6.6)	123 (7.4)	84 (5.9)	41 (5.9)	0.17
Kidney disease	154 (4.1)	73 (4.4)	58 (4.1)	23 (3.3)	0.46
COPD/asthma	115 (3.0)	55 (3.3)	35 (2.5)	25 (3.6)	0.25
Liver disease	73 (1.9)	29 (1.8)	35 (2.5)	9 (1.3)	0.14
Mental health	41 (1.1)	19 (1.2)	16 (1.1)	6 (0.9)	0.81
Malignancy	37 (1.0)	15 (0.9)	16 (1.1)	6 (0.9)	0.78
Stroke	33 (0.9)	18 (1.1)	12 (0.8)	3 (0.4)	0.29
HIV serostatus, *n* (%)					**0.001**
Positive	482 (12.9)	200 (12.2)	168 (11.9)	115 (16.6)	
Negative	1177 (31.5)	496 (30.3)	485 (34.4)	196 (28.3)	
Unknown	2078 (55.6)	939 (57.4)	758 (53.7)	381 (55.1)	
Length of hospital stay days, mean, (SD)	7.0 (7.8)	7.1 (7.7)	6.7 (8.1)	7.7 (7.3)	**0.02**
Transfer to outside facility, *n* (%)	31 (0.8)	19 (1.2)	5 (0.4)	7 (1.0)	**0.04**
In-hospital mortality, *n* (%)	284 (7.6)	48 (2.9)	219 (15.4)	17 (2.4)	**< 0.001**
distance from hospital, km mean (SD)	43.8 (52.7)	43.6 (53.5)	45.8 (51.9)	40.1 (52.5)	0.07
SOFA, mean (SD)	1.1 (1.6)	1.0 (1.6)	1.3 (1.7)	1.1 (1.6)	**< 0.001**
CCI, mean (SD)	2.0 (1.8)	2.0 (1.8)	2.2 (1.8)	2.0 (1.9)	**0.02**
Labs drawn during admission, *N* (%)	1235 (33.0)	475 (29.0)	510 (36.1)	250 (35.9)	**< 0.001**

Significant values ($p < 0.05$) are indicated in bold

SD standard deviation, *COPD* chronic obstructive pulmonary disease, *HIV* human immunodeficiency virus, *SOFA* Sequential Organ Failure Assessment, *CCI* Charlson Comorbidity Index

(2.2 [SD 1.8], $p = 0.02$) and the number of individuals with labs drawn during hospitalization (510 [36.1%], $p < 0.001$).

The most common admission diagnosis was heart failure (532, 14.1%), followed by malignancy (355, 9.4%), stroke (341, 9.0%), gastrointestinal bleed (229, 6.1%), CKD (227, 6.0%), diabetes (204, 5.4%), cirrhosis (196, 5.2%), alcohol-related admission (152, 4.0%), acute poisonings (179, 4.7%), hypertension (110, 2.9%), and COPD/asthma (110, 2.9%) (Table 2). Admission diagnoses for major NCDs changed across the periods and was significant for malignancy (147 [8.9%] vs 125 (8.8%] vs 37 [5.3%], $p = 0.009$), stroke (116 [7.0%] vs 172 [12.1%] vs 58 [8.3%], $p < 0.001$), GI bleed (130 [7.9%] vs 56 [3.9%] vs 43 [6.2%], $p < 0.001$), cirrhosis (79 [4.8%] vs 91 [6.4%] vs 26 [3.7%], $p = 0.02$), and hypertension (62 [3.8%] vs 31 [2.2%] vs 17 [2.4%], $p = 0.025$).

Disease-specific mortality for each common diagnosis rose during the Early Pandemic period, as compared to both the Pre-Pandemic and Late Pandemic periods (Table 2). The increase in disease-specific mortality across the periods was significant for heart failure (10 [4.0%] vs 31 [15.9%] vs 1 [1.2%], $p < 0.001$), malignancy (7 [4.8%] vs 25 [20.0%] vs 0 [0%], $p < 0.001$), stroke (4 [4.3%] vs 38 [22.1%] vs 3 [5.2%], $p < 0.001$), gastrointestinal bleeding (2 [1.5%] vs 6 [10.7%] vs 0 [0%], $p = 0.006$), CKD (2 [2.2%] vs 19 [19.8%] vs 1 [2.6%], $p < 0.001$), and cirrhosis (1 [1.3%] vs 22 [24.2%] vs 3 [11.5%], $p < 0.001$).

Factors associated with in-hospital mortality

In multivariable analysis of all individuals (Table 3), factors that were associated with increased odds of in-hospital mortality included admission during the Early Pandemic period (odds ratio [OR] 5.59; 95%CI 3.90, 8.02; $p < 0.001$), admission with hypotension (OR 2.13; 95%CI 1.40, 3.24; $p < 0.001$), admission diagnosis of malignancy (OR 1.79; 95%CI 1.06, 3.01; $p = 0.028$) or stroke (OR 1.75;

Table 2 Changes of NCD-related hospitalization between the Early Pandemic, Pre-Pandemic, and Late Pandemic periods

Admission diagnosis	Total	Pre-pandemic	Early pandemic	Late pandemic	*p*-value
Total admissions (%)	3777 (100)	1655 (43.8)	1423 (37.7)	699 (18.5)	.0157
Total deaths (%)	284 (7.5)	48 (2.9)	219 (15.4)	17 (2.4)	**< 0.001**
Heart failure (%)					
Admissions	532 (14.1)	250 (15.1)	195 (13.7)	87 (12.5)	0.207
Deaths	42 (8.0)	10 (4.0)	31 (15.9)	1 (1.2)	**< 0.001**
Malignancy (%)					
Admissions	309 (8.2)	147 (8.9)	125 (8.8)	37 (5.3)	**0.009**
Deaths	32 (10.4)	7 (4.8)	25 (20.0)	0	**< 0.001**
Stroke (%)					
Admissions	346 (9.2)	116 (7.0)	172 (12.1)	58 (8.3)	**< 0.001**
Deaths	42 (13.3)	5 (4.3)	38 (22.1)	3 (5.2)	**< 0.001**
GI bleed (%)					
Admissions	229 (6.1)	130 (7.9)	56 (3.9)	43 (6.2)	**< 0.001**
Deaths	8 (3.5)	2 (1.5)	6 (10.7)	0	**0.006**
CKD (%)					
Admissions	227 (6.0)	93 (5.6)	96 (6.8)	38 (5.4)	0.330
Deaths	22 (9.7)	2 (2.2)	19 (19.8)	1 (2.6)	**< 0.001**
Diabetes (%)					
Admissions	204 (5.4)	82 (5.0)	92 (6.5)	30 (4.3)	0.064
Deaths	16 (7.8)	3 (3.7)	12 (13.0)	1 (3.3)	0.053
Cirrhosis (%)					
Admissions	196 (5.2)	79 (4.8)	91 (6.4)	26 (3.7)	**0.020**
Deaths	26 (13.3)	1 (1.3)	22 (24.2)	3 (11.5)	**< 0.001**
Alcohol-related (%)					
Admissions	152 (4.0)	60 (3.6)	59 (4.2)	33 (4.7)	0.446
Deaths	7 (4.6)	1 (1.7)	4 (6.8)	2 (6.1)	0.334
Attempted suicide by poisoning (%)					
Admissions	179 (4.7)	91 (5.5)	57 (4.0)	31 (3.4)	0.139
Deaths	8 (4.5)	3 (3.3)	4 (7.0)	1 (3.2)	0.625
Hypertension (%)					
Admissions	110 (2.9)	62 (3.8)	31 (2.2)	17 (2.4)	**0.025**
Deaths	9 (8.2)	3 (4.8)	5 (16.1)	1 (5.9)	0.172
COPD/asthma (%)					
Admissions	110 (2.9)	53 (3.2)	36 (2.5)	21 (3.0)	0.535
Deaths	3 (2.7)	1 (1.9)	2 (5.6)	0	0.584

Significant values ($p < 0.05$) in bold

GI gastrointestinal, *CKD* chronic kidney disease, *COPD* chronic obstructive pulmonary disease

95%CI 1.06, 2.88; $p = 0.028$), and each unit increase in SOFA score (OR 1.41; 95%CI 1.30, 1.52; $p < 0.001$). LOS of more than 7 days was associated with decreased odds of in-hospital mortality (OR 0.56; 95%CI 0.40, 0.79; $p = 0.001$).

Discussion

In this study of trends of in-hospital mortality due to NCDs before and during the COVID-19 pandemic at a regional referral center in Uganda, we found that NCD-associated mortality significantly increased early in the COVID-19 pandemic. This period of increased mortality overlapped with both Uganda's first societal lockdown and the first wave of COVID-19 cases in Uganda. Individuals admitted during this time were sicker with higher SOFA scores, had more comorbidities per the CCI, and had shorter lengths of stay. These results were not specific to select diagnoses; rather, we found that in-hospital mortality was increased for the most common NCD diagnoses we encountered. In multivariable regression, we found that being admitted during the Early Pandemic period and illness severity were significantly associated

Table 3 Variables associated with in-hospital mortality. Logistic regression findings of variables associated with in-hospital mortality for all individuals

Variable		In-hospital mortality % (*n*/*N*)	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Demographics						
Age, years (per year)			1.01 (1.00, 1.02)	**< 0.001**	1.01 (0.99, 1.02)	0.381
Sex	Female	7.0 (130/1859)	Ref		Ref	
	Male	8.0 (153/1915)	1.16 (0.91, 1.48)	0.227	1.14 (0.84, 1.55)	0.388
History of alcohol use	No	7.1 (157/2202)	Ref		Ref	
	Yes	8.3 (118/1426)	1.18 (0.92, 1.51)	0.204	1.22 (0.86, 1.71)	0.260
History of cigarette use	No	7.5 (214/2845)	Ref		Ref	
	Yes	7.6 (59/774)	1.01 (0.75, 1.37)	0.925	0.83 (0.56, 1.22)	0.332
Distance from hospital (km)	<= 20	6.1 (80/1310)	Ref		Ref	
	> 20	8.3 (204/2467)	1.39 (1.06, 1.81)	**< 0.001**	1.27 (0.92, 1.76)	0.142
HIV status	Negative	7.6 (250/3294)	Ref		Ref	
	Positive	7.0 (34/483)	0.92 (0.64, 1.34)	0.669	1.06 (0.66, 1.68)	0.818
Clinical Factors						
Length of stay (days)	<= 7	8.4 (211/2527)	Ref		Ref	
	> 7	5.2 (63/1207)	0.60 (0.45, 0.81)	**0.003**	0.56 (0.40, 0.79)	**0.001**
SOFA (per unit of score)			1.51 (1.42, 1.60)	**< 0.001**	1.41 (1.30, 1.52)	**< 0.001**
CCI (per unit of score)			1.23 (1.15, 1.30)	**< 0.001**	1.12 (0.97, 1.29)	0.122
Hypotension (SBP < 90 mmHg) on admission	No	6.6 (228/3483)	Ref		Ref	
	Yes	19.1 (56/294)	3.36 (2.44, 4.62)	**< 0.001**	2.13 (1.40, 3.24)	**< 0.001**
Hypertensive urgency (SBP > 180 mmHg)	No	7.2 (243/3389)	Ref		Ref	
	Yes	10.6 (41/388)	1.53 (1.08, 2.17)	0.017	1.45 (0.93, 2.25)	0.100
Labs drawn during admission	No	4.9 (124/2512)	Ref		Ref	
	Yes	13.0 (160/1235)	2.87 (2.24, 3.66)	**< 0.001**	1.80 (1.30, 2.50)	**< 0.001**
ICU transfer	No	7.5 (277/3717)	Ref		Ref	
	Yes	14.3 (5/35)	2.07 (0.80, 5.38)	0.135	1.32 (0.39, 4.51)	0.657
Period of admission	Pre pandemic	2.9 (48/1655)	Ref		Ref	
	Early pandemic	15.4 (219/1423)	6.09 (4.42, 8.40)	**< 0.001**	5.59 (3.90, 8.02)	**< 0.001**
	Late pandemic	2.4 (17/699)	0.83 (0.48, 1.46)	0.527	0.96 (0.52, 1.75)	0.890
Admission diagnosis						
Heart failure	No	7.5 (242/3245)	Ref		Ref	
	Yes	7.9 (42/532)	1.06 (0.76, 1.50)	0.723	1.29 (0.77, 2.15)	0.336
Malignancy	No	7.3 (252/3468)	Ref		Ref	
	Yes	10.4 (32/309)	1.47 (1.00, 2.17)	0.050	1.79 (1.06, 3.01)	**0.028**
Stroke	No	6.9 (238/3431)	Ref		Ref	
	Yes	13.3 (46/346)	2.06 (1.47, 2.88)	**< 0.001**	1.75 (1.06, 2.88)	**0.028**
GI bleed	No	7.8 (276/3548)	Ref		Ref	
	Yes	3.5 (8/229)	0.43 (0.21, 0.88)	**< 0.001**	0.67 (0.27, 1.65)	0.385
CKD	No	7.4 (262/3550)	Ref		Ref	
	Yes	9.7 (22/227)	1.35 (0.85, 2.13)	**< 0.001**	1.03 (0.56, 1.88)	0.925
Diabetes	No	7.5 (268/3573)	Ref		Ref	
	Yes	7.8 (16/204)	1.05 (0.62, 1.77)	0.857	1.31 (0.64, 2.66)	0.461
Cirrhosis	No	7.2 (258/3581)	Ref		Ref	
	Yes	13.3 (26/196)	1.97 (1.28, 3.03)	**0.002**	1.66 (0.84, 3.31)	0.147
Alcohol-related admission	No	7.6 (277/3625)	Ref		Ref	
	Yes	4.6 (7/152)	0.58 (0.27, 1.26)	0.169	0.77 (0.32, 1.82)	0.547
Poisoning	No	7.7 (276/3598)	Ref		Ref	
	Yes	4.5 (8/179)	0.56 (0.27, 1.15)	0.118	0.77 (0.31, 1.90)	0.565

Table 3 (continued)

Variable		In-hospital mortality % (*n*/*N*)	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Hypertension	No	7.5 (275/3667)	Ref		Ref	
	Yes	8.2 (9/110)	1.10 (0.55, 2.20)	0.789	1.68 (0.69, 4.13)	0.254
COPD	No	7.6 (281/3667)	Ref		Ref	
	Yes	2.7 (3/110)	0.34 (0.11, 1.07)	0.065	0.71 (0.21, 2.44)	0.585
Past medical history						
Hypertension	No	7.1 (207/2916)	Ref		Ref	
	Yes	8.9 (77/861)	1.29 (0.98, 1.69)	0.072	1.02 (0.70, 1.47)	0.912
Diabetes	No	7.4 (244/3312)	Ref		Ref	
	Yes	8.6 (40/465)	1.18 (0.83, 1.68)	0.345	1.00 (0.62, 1.61)	0.990
Heart failure	No	7.4 (262/3529)	Ref		Ref	
	Yes	8.9 (22/248)	1.21 (0.77, 1.91)	0.404	1.45 (0.80, 2.62)	0.222

Significant values ($p < 0.05$ for multivariable) are indicated in bold

OR odds ratio, *CI* confidence interval, *Ref* Reference, *HIV* human immunodeficiency virus, *SOFA* Sequential Organ Failure Assessment, *CCI* Charlson Comorbidity Index, *ICU* intensive care unit, *GI* gastrointestinal, *CKD* chronic kidney disease, *COPD* chronic obstructive pulmonary disease, SBP systolic blood pressure

with in-hospital mortality, in addition to having a shorter length of stay, an admission diagnosis of malignancy or stroke, and being more acutely ill on presentation.

We posit that the increased in-hospital mortality for individuals with NCDs early in the pandemic may be driven by several factors. First, access to ambulatory/outpatient clinical services for NCDs was significantly reduced due to the societal lockdown, with the limited resources and health care providers turning their attention to pandemic response [14, 15]. The lack of access to care was exacerbated by disruptions in the healthcare supply chain and subsequent stockouts of essential medications, which are critical to the longitudinal nature of NCD care [19, 29]. Second, the societal lockdown starting in March 2020 had personal impact on Ugandans, leading to loss of income, difficulties in transportation, and food insecurity [30]. Food insecurity, in particular, has an important impact on individuals with NCDs, where diet is a central part to disease management [31]. Finally, many people avoided health facilities for fear of contracting COVID-19, a phenomenon exacerbated by inadequate supplies of personal protective equipment (PPE) and social media propagated conspiracies about COVID-19 [12]. Similar to our study, Bartolomeo and colleagues found an increase in relative mortality for Italian patients early in the pandemic, though this was especially true for patients with lower CCI, which was felt to represent a reduction in non-critical hospitalizations with only the sickest presenting to the hospital [32].

Taken together, while the increased mortality early in the pandemic does overlap with a COVID-19 wave in Uganda—occurring roughly between August 1, 2020, and January 31, 2021—these deaths were unlikely to be primarily driven by undiagnosed COVID-19 infection. The wave of COVID-19 cases between August 2020 and January 2021 was associated with relatively low mortality of 0.8% among confirmed COVID-19 patients in Uganda [33]. Additionally, our study overlaps with the wave of COVID-19 cases that occurred in Uganda between May 1, 2021, and September 30, 2021 [11]. While that wave was associated with a mortality of 3.4% among confirmed COVID-19 patients, we found that the in-hospital mortality rate for NCD patients was comparable to pre-pandemic rates [33].

There may be other possible explanations for our finding of increased in-hospital NCD mortality early in the pandemic. Firstly, since we excluded COVID-19 patients from our analysis, this may have represented a biased sample. Given that NCDs were widely known to be a risk factor for COVID-19-related mortality [34], we believe that NCD patients with COVID-19 would have been sicker than those without COVID-19 and thus have higher mortality, which means our results are potentially underestimating NCD mortality during these periods. Secondly, there may have been differing admission practices during the early pandemic period with only the sickest being admitted to the hospital, similar to other studies [32]. Only admitting the sickest patients would likely have meant a drop in total admissions during the early pandemic period and found that the number of admissions did not change significantly during the early pandemic, Finally, our study does not include population-level data, which would allow us to see if the in-hospital population was skewed, and if only the sickest patients were presenting to tertiary care during

the early pandemic period, or if very sick patients were dying before reaching our facility.

Few studies to date have assessed in-hospital mortality rates for non-COVID-19 patients in Uganda during the pandemic. Miller and colleagues found no changes in overall in-hospital mortality rates between the periods early in the COVID-19 pandemic and before the pandemic, though they did not focus on individuals with NCDs or evaluate trends in mortality as we do here [35]. Kazibwe and colleagues found significantly higher in-hospital mortality rates during the COVID-19 pandemic among individuals with HIV as compared with rates before the pandemic, though this study did not evaluate mortality beyond December 2020 [36]. Outside of Uganda, McIntosh and colleagues looked at all hospitalized patients in KwaZulu-Natal, South Africa and found a similar rise in mortality at roughly 2–3 months after the beginning of their first COVID-19 lockdown [37]. Cuschieri and colleagues found high rates of NCD mortality early in the COVID-19 pandemic in Cyprus, Iceland and Malta that well surpassed COVID-19 mortality rates on the islands [38]. Most importantly, Tu and colleagues found a reduction in admissions in China for cerebrovascular disease early in the pandemic but an increase in mortality for ischemic stroke, and Pourasghari and colleagues found a similar trend with patients lower admissions and increased hospital mortality for patients with myocardial infarction [39, 40].

This work highlights the broad range of NCD patients hospitalized in Uganda. We agree with calls from the Lancet NCDs and Injuries (NCDI) Poverty Commission to broaden the approach to NCDs beyond the diseases outlined by the World Health Organization (WHO) Package of Essential Noncommunicable Disease Interventions (PEN), which includes cardiovascular disease, diabetes, chronic respiratory diseases, and cancers [41–43]. Hospitals in sub-Saharan Africa must be prepared to care for a broad range of NCDs in addition to those described by WHO-PEN. Specifically, we must expand NCD training for generalists, increase the number of specialists, and ensure adequate access to medications [9].

The major strength of this study is that it is, to our knowledge, the first to evaluate trends of in-hospital mortality rates in NCD patients in Uganda during a portion of the early COVID-19 pandemic, comparing to mortality rates prior to the onset of the pandemic and as the pandemic waned. Additionally, we looked at NCDs beyond the traditional set as outlined by WHO PEN such as chronic liver disease, alcohol-related disease, and severe psychiatric illness and poisonings (most often suicide attempts).

A major limitation of this study was that it was at a single regional referral hospital, and likely missed many individuals who were unable to access care during these time periods and died in the community. Additionally, our dataset only included individuals admitted to the medical ward with a diagnosis of an NCD, limiting the scope of our analysis and omitting individuals who passed away in the emergency department and those without a history of NCD.

Future research should focus on understanding determinants of NCD morbidity and mortality for hospitalized patients, including medication and supplies stockouts, availability of diagnostic equipment, and provider staffing. In preparation for a growing burden of NCDs and to plan for future pandemics, both outpatient and inpatient services should be bolstered in Uganda and elsewhere for NCD patients who remain vulnerable to disruptions in care. We recommend ensuring access to critical NCD medications during pandemics, modeled on the systems rolled out to ensure patients had uninterrupted access to HIV medications during the COVID-19 pandemic [44]. Additionally, rolling out mobile and wearable technologies for patient self-monitoring could allow providers to better identify patients who require early interventions and prevent hospitalization. Such preparedness is critical given the ever-present threat of other infections (e.g., Ebola virus disease, Rift Valley fever virus) and the increasing likelihood of further pandemics with climate change [45, 46].

Conclusions

In summary, we found that NCD-related admissions without COVID-19 at a Ugandan regional referral hospital early in the COVID-19 pandemic were associated with high increased mortality. While our data cannot definitively explain the underlying cause of this increased mortality, individuals who were admitted to the hospital were sicker, possibly related to disruptions in outpatient NCD care. Future work must go into evaluating how best to ensuring uninterrupted outpatient and inpatient care for patients with NCDs during pandemics and future societal lockdowns.

Abbreviations

CCI	Charlson Comorbidity Index
CI	Confidence interval
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
COVID	Coronavirus disease
DALY	Disability-adjusted life year
GI	Gastrointestinal
HIV	Human immunodeficiency virus
ICU	Intensive care unit
MRRH	Mbarara Regional Referral Hospital
NCD	Non-communicable disease
NCDI	Non-communicable diseases and injuries
OR	Odds ratio
PEN	Package of Essential Noncommunicable Disease Interventions

SD Standard deviation
SOFA Sequential Organ Failure Assessment
SSA Sub-Saharan Africa
WHO World Health Organization

Acknowledgements
We would like to express our deep appreciation to all the health care providers and administration of Mbarara Regional Referral Hospital for their compassion, bravery, and tireless commitment to caring for patients throughout the COVID-19 pandemic. We are inspired by your work as we continue to fight for equitable care for all.

Authors' contributions
PKO Conceived and designed the analysis, performed the analysis, wrote the paper. EN, PSO conceived and designed the analysis, managed data collection, and edited the paper. NM and JS performed the analysis, reviewed and edited the paper. LT, RN, SM, DM, RO, and LA performed data collection and edited the paper. GK, JE, and SO conceived and designed the analysis, and reviewed and edited the paper. All authors read and approved the final manuscript.

Funding
This study was funded through the generosity of the Wyss Medical Foundation through the Massachusetts General Hospital's program entitled "First Mile: Powering the Academic Medical Center to Deliver Healthcare in the Community in Uganda."

Data availability
The datasets used and/or analyzed during the current study have been published in the Harvard Dataverse (https://doi.org/doi:10.7910/DVN/RM7ELU).

Declarations

Ethics approval and consent to participate
This study received approval from the Mbarara University of Science and Technology Research Ethics Committee (protocol No 28/10-20), the Uganda National Council for Science and Technology (HS1535ES), and the Mass General Brigham Institutional Review Board (2021P001772).) A waiver of informed consent was requested because this was a minimal risk retrospective chart review in which no patient interaction occurred, and patient identifiers were not collected. This research conformed to the principles of the Helsinki Declaration.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 19 July 2024 Accepted: 9 April 2025
Published online: 17 April 2025

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