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All-cause mortality of hospitalised patients with suspected COVID-19 in Sierra Leone: a prospective cohort study

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ABSTRACT

Objectives To study the mortality of patients with COVID-19 in Sierra Leone, to explore the factors associated with mortality during the COVID-19 pandemic and to highlight the complexities of treating patients with a novel epidemic disease in a fragile health system.

Study design A prospective single-centre cohort study. Data were extracted from paper medical records and transferred onto an electronic database. Specific indicators were compared between survivors and non-survivors, using descriptive statistics in Stata V.17.

Study setting The infectious diseases unit (IDU) at Connaught Hospital in Freetown, Sierra Leone

Participants Participants were all patients admitted to the IDU between March and July 2020.

Aims of study The primary outcome of the study was to examine the all-cause mortality of hospitalised patients with suspected COVID-19 in Sierra Leone and the secondary outcome measures were to examine factors associated with mortality in patients positive for COVID-19.

Results 261 participants were included in the study. Overall, 41.3% of those admitted to the IDU died, compared with prepandemic in-hospital mortality of 23.8%. Factors contributing to the higher mortality were COVID-19 infection (aOR 5.61, 95% CI 1.19 to 26.30, p=0.02) and hypertension (aOR 9.30, 95% CI 1.18 to 73.27, p=0.03)

Conclusions This study explores the multiple factors underpinning a doubling in facility mortality rate during the COVID-19 pandemic in Sierra Leone . It provides an insight into the realities of providing front-line healthcare during a pandemic in a fragile health system.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study reports robust observational data pertaining to mortality at facility level during the COVID-19 pandemic in Sierra Leone.
⇒ We report the likely contributing factors to the higher mortality rate in our cohort, many of them preventable and relevant to public health programmes in future.
⇒ Some data were missing on comorbidities and demographics as many patients were too unwell to provide us with this information.
⇒ Data on coinfections was limited by problems with testing availability due to lack of funding and interruptions in supply chain.
⇒ The results may be limited in their generalisability due to a small sample size.

INTRODUCTION

As the COVID-19 pandemic swept across China, Europe and North America in early 2020, overwhelming health systems in the wealthiest countries in the world, epidemiologists predicted the worst for countries in Sub-Saharan Africa. In Sierra Leone, the combination of a fragile health system and significant social deprivation[1] made public health interventions such as social distancing and home isolation almost impossible. Early modelling based on an estimated population number of 8 million predicted that without robust mitigation strategies such as physical distancing and shielding Sierra Leone could potentially see 2.3–3 million COVID-19 cases within 12 months.[2] The life expectancy at birth in Sierra Leone is 42 years,[1] with high rates of both non-communicable and communicable diseases. There is poor access to healthcare, with 72% of people reporting a serious problem in accessing healthcare for themselves when they are sick, most commonly due to lack of money.[3] In January 2020, investments in global health security frameworks following the 2014–2016 Ebola outbreak gave the country's experts a head start in the public health approach to COVID-19.[4] Key existing health facilities were advised to identify and prepare isolation beds to admit patients with suspected COVID-19 as they presented to hospital. This system was devised during the Ebola epidemic and had been a successful strategy to ensure separation of suspected cases from the existing health infrastructure to limit nosocomial

transmission, allow empirical treatments to be started for the common causes of fever in the outbreak setting while maintain patient flow in the main health facility.[5] COVID-19 treatment centres, like Ebola treatment centres, allowed for confirmed cases to be separated from the health infrastructures to maintain trust and functioning in the system, in addition to providing an opportunity for resources and best practice to be pooled in one location.

There is a wealth of research pertaining to COVID-19 across the world, but few studies are centred around the facility-level response in Sub-Saharan Africa. This observational study collected data on patients admitted to the infectious disease unit (IDU) at Connaught Hospital, the main tertiary referral centre in Freetown which was the epicentre of the Sierra Leone epidemic. At the time of writing, there have been 125 confirmed deaths from COVID-19 in Sierra Leone,[6] many of whom passed through Connaught Hospital IDU. The primary outcome of the study was to examine the all-cause mortality of patients with suspected COVID-19 who passed through the Connaught Hospital IDU, with a secondary outcome to examine factors associated with mortality in those patients who tested positive for COVID-19.

METHODS

This cohort study took place between March and July 2020 in the IDU of Connaught Hospital in Freetown. Connaught Hospital is a 280-bed tertiary referral centre, with a 10-bed respiratory isolation centre, the IDU. The IDU of Connaught Hospital was adapted to become the COVID-19 isolation centre during the pandemic. The adapted system of patient flow is depicted in figure 1.

Patients presenting to Connaught Hospital, ambulance referrals from other facilities and in-patient ward cases were triaged and screened using an adapted COVID-19 screening tool based on the national case definition, see online supplemental appendix 1, adapted from the WHO surveillance case definition.[7] Patients screened as suspected COVID-19 cases were transferred to the IDU for testing for COVID-19. When patients had a confirmed COVID-19 test result, they were either transferred to a treatment centre if positive or discharged to the ward or to their home if negative. Study participants were all patients admitted to the IDU during the first wave of the COVID-19 epidemic in Sierra Leone between 1 March 2020 and 31 July 2020.

Data were collected prospectively between May and July using an electronic database set up in the IDU, and retrospectively from March to April when data was collected from case files, with data collection done by trained staff. Data was collected on demographics; admission vital signs; medical history; length of illness; admission diagnosis; and results of COVID-19, HIV, malaria and tuberculosis (TB) diagnostic tests. Mortality data was collected from case files for those who had died in the IDU. For patients transferred to a treatment centre, mortality data was collected from the national COVID-19 mortality database, which recorded all confirmed deaths from COVID-19 across the country.

Definition of variables

Age was used as a binary variable in regression analysis. Occupation was categorised as 'formal' sector, 'informal' sector, 'retired/student' and 'unemployed'. Hypertension and diabetes were included in the analysis as comorbidities. Chronic renal failure, chronic heart failure and previous stroke were analysed together as 'other cardiovascular disease'. Other comorbidities were not included in the analysis as there was not sufficient numbers reported. Mortality was presented in total and disaggregated by sex. Length of illness was reported as time from symptom onset to hospital admission.

Diagnosis of infection

COVID-19 infection was diagnosed using 2019-nCoV Real-Time Reverse Transcription PCR on nasopharyngeal swabs taken by the laboratory team. If the test was inconclusive, it was repeated until a conclusive result was sought. If there was a high suspicion of COVID-19 and the test was negative, it was repeated at the discretion of the clinician. HIV testing was performed using the Alere Determine HIV rapid diagnostic test (RDT), and if reactive, confirmed using the Bioline HIV RDT. Malaria testing was performed using the CareStart Malaria HRP2 RDT. TB was tested using Xpert MTB/RIF on sputum.

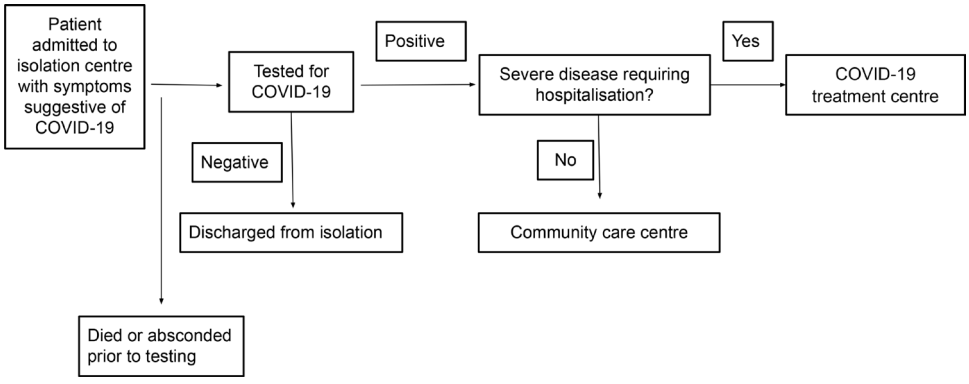


Figure 1 Patient flow during the COVID-19 pandemic in Sierra Leone.

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Outcomes

The primary aim was to examine the all-cause mortality of patients admitted to the IDU during the study period. The secondary aim was to examine the factors contributing to mortality in the patients who tested positive for the disease.

Statistical analysis

Data were analysed using Stata V.17. Data are described as n (%) or measure of central tendency and spread, depending on distribution. Factors associated with mortality in all patients was explored using binary logistic regression with forced entry. Variables included in the multivariable analysis were COVID-19 result, background of hypertension, diabetes, other cardiovascular disease and age. This was a priori decision based on previous research on the associations between these factors and mortality. Separate univariate analysis was done to examine the mortality in those who were COVID-19 positive to identify risk factors using χ^2 test for categorical variables and student's t-test for continuous variables. A complete case analysis was done.

Patient and public involvement

No patients were involved in the design of this study.

RESULTS

There were 261 patients admitted to the IDU from 18 March to 19 July 2020. Participants were mostly male (140/221, 63.3%) with a uniform age distribution across a range of 17–87 years (see table 1). The majority of participants were employed in the informal sector (51/123, 41.5%), followed by the formal sector (41/123, 33.3%), with the remaining either retired, studying or unemployed.

Of all of the patients admitted to the IDU, 29.8% of patients (78/261) reported at least one comorbidity. The most commonly reported condition was hypertension (46/78, 59.0%), followed by diabetes (18/78, 23.0%) and other cardiovascular disease (12/78, 15.4%). A prior history of HIV was reported in 10 (12.8%) participants; and an additional 27/74 (36.5%) of HIV RDTs performed in the IDU were positive. A malaria RDT was performed in 98 patients, of which 27 were positive (27.6%). History of TB was noted in 9/78 (11.5%) of participants, and sputum Xpert MTB/Rif for those tested for *Mycobacterium tuberculosis* yielded 7/13 (53.8%) positive results.

Out of 189 patients tested for COVID-19, 56% (106/189) were negative and 43.9% (83/189) were positive. Figure 2 shows the positivity rate of patients admitted over the course of the study period. The rest of the patients who were admitted to the IDU either died (61/261) or absconded (11/261) before being tested. Coinfections were common in patients with COVID-19. Of patients positive for COVID-19 who were tested for malaria, 14.7% (5/34) had a positive malaria RDT. Similarly, 34.8% (8/23) of patients tested for both HIV and

Table 1 Baseline demographics of the study population

	Overall total (n (%) or mean (SD))	Univariate analysis all-cause mortality (p value)
Age/years (N=206)		
	49.9 (18.02)	1.01 (0.06)
Sex (N=221)		
Female	81 (36.7)	1
Male	140 (63.3)	1.00 (0.99)
Occupation (N=123)		
Formal sector	41 (33.3)	1
Informal sector	51 (41.5)	0.86 (0.75)
Retired/student	22 (17.8)	0.41 (0.13)
Unemployed	9 (7.3)	0.08 (0.03)
Medical history (N=78)		
Hypertension	46 (59.0)	3.06 (0.03)
Diabetes	18 (23.0)	1.38 (0.57)
Other cardiovascular disease	12 (15.4)	0.80 (0.74)
HIV	10 (12.8)	0.46 (0.40)
TB	9 (11.5)	0.29 (0.15)
HIV RDT results performed in IDU (N=74)		
Negative	47 (63.5)	1
Positive*	27 (36.5)	0.69 (0.41)
Malaria RDT result (N=98)		
Negative	67 (68.3)	1
Positive*	27 (27.6)	0.69 (0.34)
TB sputum GenXpert result (N=13)		
Negative	3 (23.0)	1
Positive*	7 (53.8)	0.40 (0.69)
COVID-19 PCR results (N=189)		
Negative	106 (56.0)	1
Positive*	83 (43.9)	3.71 (0.001)
Mean admission vital signs (N=173)		
Respiratory rate (breaths per min)	27.3 (25.0–29.6)	1.01 (0.25)
Oxygen saturation (%)	88.8 (87.2–90.5)	0.95 (0.005)
Heart rate (beats per min)	104.9 (101.1–108.7)	1.01 (0.08)
Systolic blood pressure (mm Hg)	130.6 (126.6–134.7)	1.00 (0.80)
Temperature (°C)	37.2 (37.0–37.4)	1.13 (0.36)
Mortality		
Overall	108/261 (41.3)	–
Patients positive for COVID-19	35/83 (42.2)	–

Continued

Table 1 Continued

	Overall total (n (%) or mean (SD))	Univariate analysis all-cause mortality (p value)

*Three patients had an HIV RDT, four patients had a malaria RDT and three patients had a TB GenXpert performed but the result was not documented in the patient record. Overall, 72 patients were admitted to the IDU and either died or absconded before being tested .
IDU, infectious disease unit; RDT, rapid diagnostic test; TB, tuberculosis.

COVID-19 were positive for both infections. Of patients testing positive for TB on admission, 2/7 (28.6%) patients had COVID-19 coinfection.

Mean oxygen saturations on admission were 88.8% (SD 10.9) and mean respiratory rate was 27.3 (SD 14.7) breaths per min. Mean admission systolic blood pressure was 130 (SD 28.6) mm Hg, mean heart rate was 104 (SD 25.0) beats per min and temperature was 37.2°C (SD 1.15). Median length of illness prior to admission was 7 days, there was no statistically significant difference in length of illness in those who later tested positive for COVID-19. Mean length of stay in the IDU was 1.3 (SD 2.2) days.

Overall mortality, regardless of COVID-19 status, in the IDU was 41.3% (108/261), and of those that had a documented length of stay, 51.3% (38/74) of patients died within 24 hours of admission.

Univariable logistic regression analysis revealed a higher likelihood of all-cause mortality in the IDU if patients were COVID-19 positive (OR 3.71, 95% CI 1.73 to 7.90, p=0.001) or had hypertension (OR 3.06, 95% CI 1.12 to 8.37, p=0.03), see table 1. There were no associations between dying and sex or age, and the associations between dying and a history of diabetes or other cardiovascular disease were not statistically significant. Multivariable analysis to control for hypertension, diabetes, other cardiovascular disease and age strengthened the association between dying and being positive for COVID-19 (OR 5.61, p=0.02), see table 2.

Table 2 Multivariable logistic regression of factors associated with all-cause mortality

	aOR	95% CI	P value
COVID-19			
Negative	Ref		
Positive	5.61	1.19 to 26.30	0.02
Hypertension			
No	Ref		
Yes	9.30	1.18 to 73.27	0.03
Diabetes			
No	Ref		
Yes	2.95	0.55 to 15.63 3	0.20
Other cardiovascular disease			
No	Ref		
Yes	4.07	0.44 to 37.42	0.21
Age			
<50 years	Ref		
>50 years	0.64	0.09 to 4.53	0.66

Of those who tested positive for COVID-19, 39.7% died during admission (35/88 patients). Of those patients who died, 18 died in the IDU before they could be transferred and 17 patients died after transfer to the treatment centre.

Examining the factors associated with death in patients positive for COVID-19 revealed a higher mean age (mean=60.1, mean difference 17.1 years, SD=13.41,

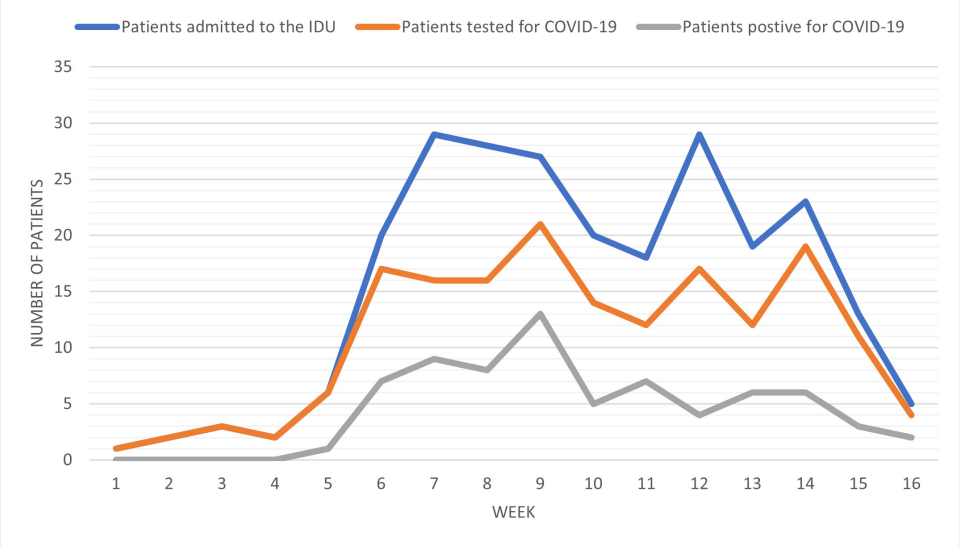


Figure 2 Percentage of patients positive for COVID-19 versus patients negative for COVID-19 over the study period. IDU, infectious disease unit.

p=0.0018) than COVID-19 negative patients, but there was no statistically significant association between dying of COVID-19 and sex (p=0.59), having hypertension (p=0.40), diabetes (p=1.0) or another cardiovascular disease (p=0.31).

DISCUSSION

The findings in this study reveal the high overall mortality of patients at Connaught Hospital IDU during the COVID-19 pandemic, regardless of the result of the COVID-19 test. The overall mortality of 41.3% is almost double than that of the previous audit data at the hospital, which showed an inpatient mortality of 23.8%, although slightly higher in patients with HIV.[8 9] In addition, data from the COVID-19 treatment centre, which treated the majority of patients positive for COVID-19 in Sierra Leone, had a lower mortality at 18.8%.[10] This higher mortality is likely due to several compounding factors. First, patients positive for COVID-19 had five times the odds of dying in multivariable analysis (aOR 5,61, p=0.02), so there is a clear association between COVID-19 infection and death in this cohort. Second, the combination of median length of illness prior to admission (7 days), the amount of people who died on the first day of admission (51.3%) and the degree of hypoxia at admission (mean oxygen saturations 88.8%) reveals much about how late people presented to health services during the COVID-19 epidemic in Sierra Leone. Outside of an epidemic setting, it is a common reality in Sierra Leone that people only attend health services if they have advanced illness both from a combination of being unable to meet the cost of services,[11] and the distrust in services that exist for a myriad of reasons.[12] This was made worse by the epidemic, with attendance data across the health service showing a reduction in healthcare attendance from March 2020,[13] a phenomenon also seen during the Ebola epidemic of 2014–2016, when admissions decreased and those patients that did present, did so with more severe illness.[5 14]

Third, oxygen was frequently unavailable at the IDU, which is the case in most hospitals in Sierra Leone and other similar settings.[15] Oxygen at the IDU is either delivered via an oxygen concentrator which needs a constant supply of electricity and can only deliver a maximum of 10 L oxygen per min. Oxygen from concentrator machines must have a minimum concentration of 82% to achieve the required concentration of inspired oxygen. The oxygen concentrators in the IDU were consistently found to have less than 60% purity on output by the maintenance team.[16] This means that even at the highest flow rate, the concentration of inspired oxygen for patients in the IDU was far less than they required, which is likely to have contributed to the higher mortality in this cohort. For those needing higher flow rates, oxygen is delivered via an oxygen cylinder. This requires almost hourly refills from a functioning oxygen factory which was often not possible, especially with multiple unwell patients.

Fourth, patient care for adults in the government system of Sierra Leone is commonly paid out of pocket by the patient and relatives, with an incidence of catastrophic healthcare expenditure, when health expenditure exceeds 10% of household total expenditure, of 18%.[16] It is beyond the scope of this paper to examine the direct effects of this method of health financing on acute patient outcomes, but this has been documented when looking at the barriers to accessing preventative medicine,[17] pertinent here given the high rates of hypertension and diabetes seen in this cohort of patients. Financing for COVID-19 care in Sierra Leone within Treatment and Community Care Centres was funded by National COVID-19 Emergency Response Centre (NACOVERC), but participants in this study admitted to the IDU did not receive financing and were required to self-fund all costs associated with admission and treatment out of pocket. This is further emphasised given the comparatively lower mortality rate of patients in the treatment centres of 18.8%, where drugs and consumables were funded by NACOVERC and oxygen delivery was not compromised to the same degree.

Patients positive for COVID-19 were more likely to die if they were older, a pattern that is reflected across the world.[18 19] The reasons behind this association of age and severe illness from COVID-19 are thought to be related to immunosenescence seen in older adults, the consequences of which leads to reduced ability to fight novel infections and a state of chronic inflammation.[20] There has been a particular focus on the reduced adaptive T-cell response of older adults as to why they are more at risk of severe disease when infected with SARS-CoV-2, but the key mechanism for this association continues to be investigated.[21] In addition, older adults have a higher prevalence of comorbidities such as hypertension and diabetes, key risk factors for severe COVID-19 disease.[22 23] This is reflected in this study with patients more likely to have hypertension if they were older.

Hypertension was the most common comorbidity, reported by 59% of patients, followed by diabetes (23%) and other cardiovascular disease (15.4%) This reflects the community prevalence of hypertension in Sierra Leone of more than 40%.[24] Hypertension was an independent predictor of death in this cohort of patients (aOR 9.30, 95% CI 1.18 to 73.27, p=0.03), which has significant implications for the non-communicable disease control programmes in Sierra Leone. There was a large disparity between reported HIV positive status and subsequent result of the HIV test performed in the IDU. Only 10 people self-reported HIV as a comorbidity on admission, with a further 27 patients testing HIV positive in the unit. These are either new diagnoses, reflecting the importance of HIV testing of all individuals presenting to care at health facilities[25] or they reflect reporter bias, of patients unwilling to report their status, due to stigma associated with the diagnosis.[26]

Coinfections were common in our cohort, with patients positive for COVID-19 commonly being diagnosed with

malaria, HIV and TB. Despite the best efforts of the clinical team, not all patients were tested for these infections. Universal HIV and malaria testing for suspected patients with COVID-19 was a key part of management protocols drawn up by the clinical team given the similar presentations of these infections. Indications for TB testing were in line with national guidelines. There were issues with testing due to a combination of logistical difficulties with COVID-19 testing and stockouts of malaria and HIV RDTs. It is difficult to infer the significance of these findings given the small sample size, but it does contribute to the evidence around the WHO clinical guidelines for COVID-19 and coinfections,[27] in addition to using the opportunity to strengthen supply chains around the consumables for HIV and malaria testing.

This study sits in contrast to the idea that Sierra Leone and other countries in Sub-Saharan Africa have not been affected by COVID-19. The community seroprevalence of COVID-19 in Sierra Leone has been found to be 2.6%,[28] with an enormous under-reporting of cases, and likely therefore, of deaths attributable to COVID-19.

LIMITATIONS

The limitations of this study are predictable of research undertaken in a fragile healthcare system. Information regarding the medical history and drug history was incomplete mostly because many patients present late to health services. In addition, patients pay out of pocket for all investigations and treatment at the hospital apart from malaria, HIV, TB and COVID-19 diagnostics, so there was no robust, consistent data on either additional investigations such as basic biochemistry and haematology or treatments, which are not always given on the basis of clinical need, but availability. Due to the short length of stay at the IDU, further investigations such as CD4 count of patients with HIV were not documented, these results typically take 2–5 days to become available, so we are unable to comment on COVID mortality with regard to HIV stage. Routine use of malaria and HIV RDTs was only introduced to the IDU during the COVID pandemic to ensure that common infections that present in the same way to COVID were not missed. This process was only embedded in late April and May, including training of staff, reporting and supply chain management, which is why not all participants were tested in this study. Another reason for missing data in the study was that the database for prospective electronic data entry was only set up in May. Efforts were made by the research team to enter the data for patients seen prior to May retrospectively; however, this was often not possible due to the limitations of the hospital records system.

In addition, due to the unavailability of a panel of PCR for the aetiology of acute respiratory infections, we could not determine other respiratory viral or bacterial coinfection, which may have been the cause of the acute respiratory illness. In Sierra Leone during the COVID-19 pandemic, people were not tested for COVID-19 after they had died so this study cannot comment on the 61 people who died before being tested in the IDU. Given the high positivity rate of 43.9% in the IDU, a large proportion of these patients are likely to have been positive for COVID-19. Finally, we are unable to comment on the severity of COVID-19 disease in this study for multiple reasons such as lack of access to interventions such as X-ray of the chest, ECG, arterial blood gases and patient monitoring.

CONCLUSION

In conclusion, this study provides an insight into the challenges of treating patients during an epidemic in an under-resourced setting. We found a mortality rate almost double than that of the mortality rate in the same hospital before the COVID-19 pandemic. It shows the contribution of COVID-19 to the higher mortality, in addition to the late presentation of patients and the lack of resources in the health system. Much of the focus since the start of the COVID-19 pandemic has been on the fewer deaths of COVID-19 in Sub-Saharan Africa compared with Western nations, but this paper shows the hidden burden that this extra strain has put on an already fragile system, the staff that work tirelessly within it, and the patients that rely on it.

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Contributors OF: Conceptualisation, data curation, formal analysis, investigation, methodology, software and writing—original draft, guarantor MB: Conceptualisation, investigation, data curation and project administration. JK: Investigation, data curation and project administration. EB: Conceptualisation, data curation, project administration and writing—review & editing. SS, GD, JR, DY and AL: Writing—review & editing. JD and SL: Writing—review & editing and supervision.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. Ethical approval was gained from the Sierra Leone Ethics and Scientific Review Committee in August 2020. This ethical review board do not provide reference numbers.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The anonymised dataset which supports the findings of this study are available uponon reasonable request from the corresponding author as cited in the publication. Access for further investigation and analysis will be granted to researchers following the signing of a data access agreement. Data was taken from routinely collected patient files, with no identifiable data in the analysis or publishing. All data are available upon request.

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