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## Investigation of possible preventable causes of COVID-19 deaths in the Kampala Metropolitan Area, Uganda, 2020–2021

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## ABSTRACT

**Background:** Identifying preventable causes of COVID-19 deaths is key to reducing mortality. We investigated possible preventable causes of COVID-19 deaths over a six-month period in Uganda.

**Methods:** A case-patient was a person testing reverse transcription polymerase chain reaction-positive for SARS-CoV-2 who died in Kampala Metropolitan Area hospitals from August 2020 to February 2021. We reviewed records and interviewed health workers and case-patient caretakers.

**Results:** We investigated 126 (65%) of 195 reported COVID-19 deaths during the investigation period; 89 (71%) were male, and the median age was 61 years. A total of 98 (78%) had underlying medical conditions. Most (118, 94%) had advanced disease at admission to the hospital where they died. A total of 44 (35%) did not receive a COVID-19 test at their first presentation to a health facility despite having consistent symptoms. A total of 95 (75%) needed intensive care unit admission, of whom 45 (47%) received it; 74 (59%) needed mechanical ventilation, of whom 47 (64%) received it.

**Conclusion:** Among hospitalized patients with COVID-19 who died in this investigation, early opportunities for diagnosis were frequently missed, and there was inadequate intensive care unit capacity. Emphasis is needed on COVID-19 as a differential diagnosis, early testing, and care-seeking at specialized facilities before the illness reaches a critical stage. Increased capacity for intensive care is needed.

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## Introduction

The coronavirus disease 2019 (COVID-19) pandemic began in Wuhan City, China in December 2019 (World Health Organization, 2020a) and quickly spread globally (World Health Organization, 2020c). In Africa, the first case was registered on February 14, 2020, in Egypt, and as of April 20, 2021, the continent had registered 3.2 million cases and more than 100,000 deaths (World Health Organization, 2020c). Uganda registered its first COVID-19 case on March 21, 2020. Although small numbers of cases occurred from March 2020 to August 2020, the first major wave of COVID-19 in Uganda occurred from August 2020 to De-

ember 2020, resulting in approximately 32,000 confirmed cases and 200 deaths. This was followed by a larger second wave from April 2021 to July 2021, comprising approximately 53,000 recorded cases and 2,400 registered deaths (Government of Uganda, 2020).

As the pandemic progressed in Uganda, public health efforts shifted away from detecting every case and toward reducing COVID-19-related morbidity and mortality. In Uganda, district surveillance focal persons were initially responsible for case investigations, including investigations of COVID-19 deaths. However, during the first wave, the caseload rapidly exceeded the capacity of district surveillance focal persons for investigation of individual events. Anecdotal reports from the public suggested that many patients who died from COVID-19 infection in hospitals were not tested until they died. This indicated that there were challenges with accessing care early, conducting early testing, or both, suggesting opportunities for interventions to reduce COVID-19 deaths.

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A comprehensive understanding of specific modifiable factors associated with COVID-19 deaths is essential to reducing case mortality. We investigated the characteristics and possible preventable causes of COVID-19 deaths in the Kampala Metropolitan Area (KMA) during the first wave to recommend interventions to reduce COVID-19 deaths in the country.

## Methods

### *Study design, investigation area, and population*

This was a descriptive cross-sectional study conducted from February 21, 2021, to March 20, 2021, in three of the four districts of the KMA (Kampala, Mukono, and Wakiso). The three districts where the study was conducted represented 30% of the COVID-19 deaths in Uganda reported at the time. The KMA is currently the second-fastest-growing urban area in Eastern Africa. It is an industrial, commercial, and educational center and is vital to Uganda's economic growth (Kasimbazi, 2018).

At the time of the investigation, all persons confirmed to have SARS-CoV-2 infection who had underlying medical conditions putting them at an increased risk of severe disease were encouraged to be hospitalized pre-emptively, even if they did not have symptoms (Fedrica et al., 2020a). The purpose of this was to ensure they could access medical care should their condition deteriorate.

### *Case definition*

At the time of the study, reverse transcription polymerase chain reaction (RT-PCR) was the only test being done to detect SARS-CoV-2 infections in Uganda. A case-patient was defined as a person with a PCR-positive nasopharyngeal or oropharyngeal swab for SARS-CoV-2 who died in a hospital in either Kampala, Wakiso, or Mukono districts from August 26, 2020, to February 7, 2021.

### *Sampling and data collection*

At the time of investigation, KMA only had three designated public COVID-19 treatment units, which were in government referral hospitals and treated patients from throughout Uganda. However, other private hospitals within KMA were also managing patients with COVID-19. Patients from all 33 hospitals in Kampala, Wakiso, and Mukono districts that were treating any patients with COVID-19 at the time, including government hospitals (n = 6), private for-profit hospitals (n = 19), and private not-for-profit hospitals (n = 8), were included in this study.

We designed and pretested an investigation tool in Open Data Kit (ODK), which we used to enter information about case-patients. This tool captured data for confirmed COVID-19 deaths at all the 33 hospitals in the three districts from August 26, 2020, to February 7, 2021. We only captured data for case-patients who had sufficient data in their medical records and from interviews to provide a broad picture of their clinical course. A team of investigators from the Uganda Ministry of Health and the Uganda National Institute of Public Health reviewed mortuary records from the 33 hospitals to identify case-patients. We cross-checked the names of the case-patients in the national online laboratory results dispatch system to confirm the positive SARS-CoV-2 test result. For case-patients for whom we confirmed a positive result, we retrieved clinical files in the hospitals in which they died and abstracted clinical data and phone numbers of the next-of-kin. We made phone calls to the next-of-kin to make an appointment for an in-person meeting. During the in-person meeting, we interviewed the next-of-kin to obtain information on case-patient demographics and reconstruct a timeline of events from illness onset to death. We also reviewed the Medical Certificate of Cause of

Death form to obtain information on the cause of death. Patients were eligible for inclusion if 'COVID-19' was listed as the primary or secondary cause of death on Part 1 of the form or if they died while being treated for COVID-19 symptoms and had a positive RT-PCR for SARS-CoV-2 after their death. We reviewed village health team (community health worker) registers, if available, for the villages of the case-patients to verify the data already collected. We also conducted interviews with the clinicians to understand their opinions on whether or not the death of the case-patient could have been prevented if something had been done differently. If affirmative, we asked about what could have been done differently. A preventable death was defined by the clinicians as a patient death that could have been avoided with more timely and/or effective health care interventions available in Uganda at the time.

### *Data analysis*

Data from ODK were downloaded into a Microsoft Excel format. Data were analyzed in Microsoft Excel. Both demographic and clinical characteristics were descriptively summarized. Age was presented as median and interquartile range (IQR), and the remaining categorical variables were expressed as frequencies and percentages.

### *Clinical spectrum of SARS-CoV-2 infection*

Illness severity at admission to the hospital where the case-patient died was classified according to medical record data and using definitions from the United States National Institutes of Health (National Institutes of Health, 2021). In brief, asymptomatic infection included individuals who tested positive for SARS-CoV-2 but had no symptoms consistent with COVID-19. Mild illness was defined as any of the signs and symptoms of COVID-19 (e.g., fever [ $\geq 39.4^\circ\text{C}$ ], cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste, and loss of smell) but no shortness of breath, dyspnea, or abnormal chest imaging. Moderate illness included evidence of lower respiratory disease (patient with pneumonia without features or signs of severe pneumonia) during clinical assessment or imaging and oxygen saturation ( $\text{SpO}_2$ )  $\geq 94\%$  on room air. Severe illness was  $\text{SpO}_2 < 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ )  $< 300$  mm Hg, respiratory frequency  $> 30$  breaths/min, or lung infiltrates in  $> 50\%$  of the lung. Critical illness included respiratory failure, septic shock, and/or multiple organ dysfunction.

## Results

The KMA had 195 (67%) of the 290 reported COVID-19 deaths in the country from August 26, 2020, to February 7, 2021. Among these, 126 (65%) had sufficient clinical data available to be eligible for inclusion. Of the 126 case-patients, 89 (71%) were male. Their median age was 61 years (IQR: 50–71); 78% were  $\geq 50$  years of age; 88% were Ugandan citizens, and 7% were Indian citizens.

### *Clinical characteristics of the COVID-19 deaths investigated in three districts of the KMA of Uganda, 2021*

Of the 126 deaths investigated, 63% were among case-patients at three hospitals with the highest patient loads. A total of 98 (78%) case-patients had underlying medical conditions; hypertension (54%) and diabetes (45%) were the most common. Most (90; 71%) case-patients had cough. A total of 98 (78%) case-patients sought care at a formal health facility at the onset of symptoms. Nearly all had severe (51%) or critical (43%) disease on admission to the hospital in which they died (Table 1). One case-patient with

diabetes was hospitalized after testing positive for SARS-CoV-2, despite an absence of symptoms at the time of his admission. However, he subsequently developed severe disease and died.

A total of 82 (65%) case-patients received a COVID-19 test the first time they interfaced with a health facility for their illness; of these, 91% tested positive. Among the 44 (35%) case-patients who did not receive a test at their first interface with a health facility, failure to suspect COVID-19 by the healthcare worker was the most common reason for not receiving testing (20; 45%), followed by a lack of a testing capacity at the facility (18; 41%) (Table 1). Among the 20 case-patients in whom COVID-19 was not suspected, 18 (90%) had symptoms that could have indicated COVID-19 infection (cough, difficulty breathing, chest pain, headache, runny nose, fever, and/or general weakness).

SARS-CoV-2 test results were available for 81% of case-patients on the same day (19%) or one day after (62%) their sample was collected. A total of 30 (24%) case-patients died within three days of first seeking care (Table 1).

A total of 95 (75%) case-patients needed intensive care unit (ICU) admission (defined as those who were oxygen-desaturated and having severe respiratory distress indicating a need for mechanical ventilation), of whom only 46 (48%) were able to access it. A total of 99 (79%) case-patients needed high-dependency care unit (HDU) (defined as those who were oxygen-desaturated but could use normal oxygen masks or continuous positive airway pressure [CPAP]) admission, and of these, 89 (90%) received it when it was needed. (Table 2). Only 46 (61%) of case-patients who needed mechanical ventilation were able to obtain it. Among those who did not receive it, 20 (27%) did not get it because of a lack of ventilators or ICU space at their facility (Table 2).

Among 62 (49%) case-patients with a Medical Certificate Cause of Death form, 50% had COVID-19 listed as primary (26%) or secondary (26%) cause of death (Table 3). Among 71 patients for whom clinicians felt that death could have been prevented, 36 (51%) of the deaths were considered to have been preventable if ICU space had been available; 23 (33%) were thought to have been preventable if the patient had sought care earlier (33%) (Table 3).

## Discussion

In our evaluation of COVID-19 hospital deaths in the KMA from August 2020 to February 2021, we found several modifiable factors present among COVID-19 deaths. These included missed opportunities for diagnosis and insufficient capacity for advanced patient care. Identifying such factors is critical to designing targeted interventions to reduce COVID-19 deaths. Our data highlight the need for increasing the advanced patient care capacity in the country and enhancing public awareness of the importance of prompt presentation for care if they become seriously ill with symptoms of COVID-19.

In this investigation, receiving hospital care late in the course of illness was frequent among fatal cases. Indeed, more than 80% of patients in this investigation had severe or critical illness by the time they were hospitalized, and one-quarter died within three days of seeking care. It is unclear whether this was related to late care-seeking by individuals or whether care was sought earlier and patients were turned away. However, ensuring early care-seeking is a well-described challenge in African settings, where patients frequently employ home remedies or traditional healers before seeking more advanced care, even when illness is serious (Wasswa, 2021; Mpimbaza et al., 2019; Kasujja et al., 2021). Beyond this, the cost of hospital care presents a challenge for many people living in low-resource settings, which can discourage early presentation (Peters et al., 2008). Widespread publicization of the high costs of hospitalization dissuaded at least some patients from seeking hospital care in Uganda (Wasswa, 2021; Athumani, 2021;

Agiresaasi, 2021; Muhumuza, 2021) until late in their course of illness.

Early detection of COVID-19 and effective, timely treatment are important to enable supportive care that can promote patient survival (Skríp et al., 2020; The Hindu, 2021; Cobre et al., 2020; World Health Organization, 2021). The emergency use authorization of the antiviral drugs Paxlovid and molnupiravir in late 2021 to treat COVID-19 has increased the importance of early presentation—both drugs need to be taken within 5 days of symptom onset—and future treatments are likely to make early detection even more relevant (Sara, 2021; United States Food and Drug Administration, 2021a; United States Food and Drug Administration, 2021b). However, many patients in our investigation were not tested at their first presentation for COVID-19. Although appropriate supportive treatment for patients in respiratory distress does not necessarily depend on a COVID-19 diagnosis, early during the pandemic in Uganda, lifesaving supportive equipment such as ventilators were largely shifted to COVID-19 treatment units (Ministry of Health, 2020; Fedrica et al., 2020b), for which admission was restricted to persons who had a positive COVID-19 test (Fedrica et al., 2020b). Compounding this issue, having sufficient test kits and distributing them to facilities presented challenges in Uganda (Padula, 2020; International Organization for Migration, 2020; Wetaya, 2020) and other African countries (Kobia and Gitaka, 2020; Voice of America, 2020). Among patients in our investigation who were not tested at their first presentation, 41% were not tested because of a lack of testing capacity at the facilities they presented. However, the primary reason for not testing patients at their first presentation to a health facility in our investigation was that COVID-19 was not suspected as a differential diagnosis, despite nearly all the patients having symptoms consistent with COVID-19 disease. Equipping lower-level health facilities with rapid diagnostic test kits and training clinicians to have a higher index of suspicion for COVID-19 could have facilitated earlier diagnosis and helped ensure patients who needed care were able to receive it.

The absence of or limited ICU space was faced by approximately half of the case-patients in this investigation. This is a common problem across low-income countries in Africa (Siaw-Frimpong et al., 2021; Barasa et al., 2020): estimates from a study on critical care capacity in 54 African countries in 2020 found an average of 3.1 ICU beds per 100,000 people, fewer than half the beds per 100,000 that exist in upper-middle-income countries (Craig et al., 2020). An assessment of the ICU bed capacity in Uganda just before the pandemic indicated that 12 out of 14 ICUs reviewed in public facilities were functional. However, among these 12 ICUs, only 55 beds were available, for a ratio of 1.3 ICU beds per million population (Atumanya et al., 2019). In contrast, the World Health Organization recommends that countries have a ratio of 1:3 ICU beds per 10,000 persons (Palamim and Marson, 2020). Although the presence of surge capacity is critical to an effective COVID-19 response (Aziz et al., 2020; Blumenberg et al., 2020; Ministry of Health, 2020), it is challenging to consider surge capacity when basic intensive care needs remain unmet. Although efforts on the part of the Uganda Ministry of Health expanded the ICU bed capacity to 97 available beds in the country as of September 2021 (PE, personal communication), this still only yields a ratio of approximately 2.2 beds per million population.

One-third of patients who needed mechanical ventilation were not able to access it, primarily because of a lack of ventilators or ICU space. This, too, is a common problem in sub-Saharan Africa (Ruth and Marks, 2020). A 2020 report showed that 41 African countries had fewer than 2,000 functional ventilators in total (World Health Organization, 2020b). The ventilator-to-population ratio in Africa was lowest in East Africa, at only 0.23 ventilators per 100,000 people (Craig et al., 2020). Even when ventila-

tors are available, oxygen demand can present challenges. A media report in June 2021 showed that the demand for oxygen by patients with COVID-19 had outpaced the manufacturing capacity in Uganda (Olukya, 2021). Although the Uganda Ministry of Health acquired 109 critical care ventilators in 2021 (Gradian Health Systems, 2021), and an increase in medical oxygen production and donations of oxygen gas cylinders to support the COVID-19 response (ReliefWeb, 2021; United Nations Children's Fund, 2021), there is still a shortage of trained staff to operate them. In 2019, 171 nurses were working in 12 ICUs, with only 13 that had been formally trained to work as critical care nurses (Atumanya et al., 2019). Recent advertising to hire intensive care specialists (Gradian Health Systems, 2021) might help address some of these shortages.

Our investigation faced a number of limitations. First, we did not have a control group with whom to compare the deaths presented in this paper. Thus, we cannot identify some exposures, such as late presentation, as risk factors for death. Second, we did not capture the patients' condition at first presentation to a health facility, nor did we capture if the first facility was the one in which they died. Thus, we cannot evaluate their care-seeking behaviors, if any, early in the course of their illness. Third, this investigation was retrospective and subject to both recall bias and/or perhaps social desirability bias (interest in saying the 'right thing') during the interviews. For example, very few patients reported going to a traditional healer, yet this is a common practice in many parts of Uganda. We tried to mitigate this issue by using a variety of data sources to triangulate information, but it is possible that there are some inaccuracies. Fourth, we conducted this investigation in only three districts of the country, all in the capital region, and thus the data are not representative of the entire country. However, it is worth noting that the challenges identified would only be expected to be greater in other areas of the country, where access to care is less, and transport and diagnostics are more difficult to obtain. Thus, it is likely that the recommendations that apply to the KMA may apply more strongly to other areas of the country. Fifth, not all patients had sufficient data to build a complete picture of their clinical course and death, which might result in bias if these patients were qualitatively different from those with data. Sixth, we asked clinicians' opinions on whether or not deaths were preventable; these were anecdotal and not based on any validated metrics. Finally, we were unable to capture community deaths, which are undoubtedly different from facility deaths. Thus, our data apply only to patients who were able to reach the hospital in this area.

## Conclusions

In conclusion, we identified late receipt of specialized care, missed opportunities for diagnosis, lack of ICU space, and lack of mechanical ventilation as possible contributing factors to COVID-19 patient deaths in KMA during the first wave of the pandemic. Our data suggest that there might be value in making the public aware of the importance of seeking care before patients reach a critical stage of COVID-19 disease to improve outcomes and reduce the impact of critical cases on the limited ICU resources. Clinicians across all health facility levels could be re-sensitized to consider COVID-19 as a differential diagnosis and test early when patients present with consistent symptoms. In addition, plans for surge capacity in ICUs and with hospital staff could facilitate improved outcomes during future waves of infection.

## Disclaimer

The findings and conclusions in this investigation are those of the author(s) and do not necessarily represent the official position

of the United States Centers for Disease Control and Prevention and the Uganda Ministry of Health.

## Conflict of interest

The authors have no competing interests to declare.

## Funding source

We did not have funding to conduct this study.

## Ethical considerations

The Uganda Ministry of Health gave the directive to conduct epidemiological investigations and response to COVID-19 disease in the country. We sought permission from the local council authorities of residences of the case-patients to undertake the investigation. We obtained verbal consent from the next-of-kin before conducting the interviews. The questionnaires were kept under lock and key to prevent the disclosure of personal information of the respondents to individuals who were not part of the investigation.

This activity was reviewed by the Centers for Disease Control and Prevention and was conducted in a manner consistent with applicable federal law and Centers for Disease Control and Prevention policy.§

§See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

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