Rates of refusal of clinical autopsies among HIV-positive decedents and an overview of autopsies in Uganda [version 2; peer review: 1 approved]

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Abstract
Background: Human immunodeficiency virus (HIV)-related mortality remains high in sub-Saharan Africa. Clinical autopsies can provide invaluable information to help ascertain the cause of death. We aimed to determine the rate and reasons for autopsy refusal amongst families of HIV-positive decedents in Uganda.

Methods: We consented the next-of-kin for post-mortem examinations among Ugandan decedents with HIV from 2017-2020 at Kiruddu National Referral Hospital. For those who refused autopsies, reasons were recorded.

Results: In this analysis, 165 decedents with HIV were included from three selected wards at Kiruddu National Referral Hospital. Autopsy was not performed in 45% of the deceased patients; the rate of autopsy refusal was 36%. The most common reasons for autopsy refusal were time constraints (30%), family satisfaction with clinical diagnosis (15%), fear of disfigurement of the remains (15%), and lack of perceived benefit (15%). By seeking consent from multiple family members and clearly explaining to them the purpose of performing the autopsy, we found a reduction in the rate of autopsy refusal among relatives of the deceased patients at this hospital compared to previous studies at the same site (36% vs. 60%).

Conclusions: We found lower rates of autopsy refusal compared to previous studies at the same site. This underscores the importance of clearly explaining the purpose of autopsies as they increase active sensitization about their relevance and dispel myths related to autopsies among the general population. Good, culturally sensitive,
and timely explanations to the family of the benefits of autopsy increase the rate of obtaining permission. Building capacity for performing autopsies by training more pathologists and increasing laboratory resources to decrease the turn-around-time for autopsy reports and extending these services to peripheral health facilities could improve autopsy acceptance rates.

**Keywords**
Autopsy, postmortem changes, autopsy refusal, mortality, HIV Seropositivity, Uganda, Africa South of the Sahara, Investigative Techniques

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**Amendments from Version 1**

Following these helpful comments from the reviewer, we have made a number of changes in v1 of the text. Nationally, the number of Anatomical Pathologists in the country is low and indeed those that are actively involved in autopsy work is low. The autopsy work in the Regional Referral and District Hospitals is handled by Medical Officers who are not Specialist Pathologists. The Anatomical Pathologists are at the National Referral Hospital and in the Medical School. The findings are indeed a reflection of what happens at the national referral hospital level. The study methodology could have overestimated the rate of autopsy observed. This has been added to the limitations. The fact that the hospital admits patients across the entire country and of whom were enrolled into the study, we assumed this gives a general representation of those from a greater distance. Consent is always obtained from the next-of-kin that are available on the wards after the death has occurred. Also, consent to the study and consent to autopsy are the same thing in this context. We have also added a brief description of the autopsy procedure outside the study settings, in routine practice. Analysis was not stratified by religion. This has been modified in the text. People tend to associate stigma more with the living than the dead. Next of kin were given verbal feedback after the autopsy was done. It provided closure for most of them especially those whose patients died after a few days of hospitalisation. There was an increased challenge during the pandemic time mainly because of the difficulties with getting transportation that made next of kin always to be in a hurry before curfew hours. Increasing public awareness on the importance of autopsies preferably through the media would be a solution.

Any further responses from the reviewers can be found at the end of the article.
of admission and death were collected by hospital records. Next of kin were given verbal feedback about the outcome of the autopsy done.

For those who refused to have an autopsy performed for their deceased relative, the reasons for refusing were recorded. This was done as a non-structured interview by one of the nurses (OCN) in a private room. It involved only one open ended question, i.e., “why wouldn’t you want an autopsy performed on your deceased relative?”. This took about 5–10 minutes, and their responses were written on the screening log without audio/video recording.

To reduce sampling bias, we used the three wards that accommodate more than 95% of all HIV patients in this hospital. The records staff doublechecked all entries by medical staff in the daily ward report book. We carried out the study at a national referral hospital which gets patients from all over the country and could be representative of the whole country.

Outside the study settings, in routine practice, the autopsy procedure is as follows:

- Upon a death occurring in the hospital ward, the treating physician/clinician requests for an autopsy (by filling in the autopsy request form). The request is based on several reasons that include lack of a clinical diagnosis, death within 24 hours of admission on the ward etc.
- The next-of-kin of the deceased are then approached for consenting after receiving an explanation for the need of an autopsy
- Upon signing the consent, the request and consent form are forwarded to the mortuary to be received by the pathology team
- The pathology team (Pathologist and mortuary technicians) prepare for and conduct the autopsy.

Ethical considerations
All caregivers/next-of-kin of the deceased patients provided written informed consent (the consent form can be found as Extended data). Ethical approval occurred from the Uganda National Council of Science and Technology (HS24ES), and Mulago Hospital Research and Ethics Committee (MHREC 1023).

Statistical analysis
Investigators had full access to the database population used to create the study population to extract the patients’ data. Data cleaning was mainly done on the responses for “reasons for autopsy refusal” by modifying responses that mean the same to look alike. Data were then analyzed using STATA version 14 (STATA, College Station, Texas). The rate of autopsy refusal and distribution of baseline demographic characteristics were reported as proportions. Frequencies and percentages were reported for each baseline characteristic when considered categorical, and medians (interquartile range) for continuous variables.

Results
Patients’ characteristics
This analysis included 165 deceased HIV-positive patients who died while on the emergency, pulmonary, and infectious disease wards at Kiriudu National Referral Hospital from February 2017 to August 2020. Of those deceased patients with available demographic data (n=119), 55% (65/119) were male with an overall median age of 37 years (n=118; IQR= 30 to 43), and 28% (43/152) were ART naïve (Table 1).6

The median length of hospitalization for all deceased patients was 6 days (n=118; IQR= 2 to 13). Of the 165 deceased HIV-positive patients, 55% (n=90) of their relatives consented to autopsy procedures; 45% (n=75) of autopsies were not performed for refusal of autopsy amongst other various reasons (Table 2). For those who had an autopsy performed, the days to an autopsy from time of death ranged from zero (0) to one day, with the majority (76.7%) performed on the same day as the patient death (Table 1).

Rate of autopsy refusal and reasons for not performing an autopsy
Of the 165 deceased HIV patients, 75 (45.4%) did not have an autopsy performed for various reasons (Table 2). The refusal of autopsy by family members was the most common reason for not performing autopsies (36%; 27/75), followed by the deceased person having been removed from the mortuary before next-of-kin was approached for informed consent (24/75) and the absence of a pathologist (15/75). For four of the deceased patients, two reasons were given for refusal for each. The most common reasons given for autopsy refusal were; time constraints and distant location of internment; family satisfaction with the clinical diagnosis; fear of body mutilation; and many

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N with data</th>
<th>N (%) or Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>119</td>
<td>65 (54.6%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>118</td>
<td>37 (30, 43)</td>
</tr>
<tr>
<td>Receiving HIV therapy</td>
<td>152</td>
<td>109 (71.7%)</td>
</tr>
<tr>
<td>Length of Hospitalization, days</td>
<td>118</td>
<td>6 (2, 13)</td>
</tr>
<tr>
<td>Autopsy performed</td>
<td>165</td>
<td>90 (54.6%)</td>
</tr>
<tr>
<td>Time to autopsy, days</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Performed same day of death</td>
<td>69 (76.7%)</td>
<td></td>
</tr>
<tr>
<td>Performed one day following death</td>
<td>21 (23.3%)</td>
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For those who refused an autopsy for their deceased relative, in this study, we found that the most common reasons were due to time constraints and distant location of interment, in addition to families’ satisfaction with the clinical diagnosis of HIV and HIV-related opportunistic infections, and fear of body mutilation. Failure of families to perceive any benefit of the autopsy could partly be seen as caregivers of the deceased expressing “care-fatigue,” especially when it was among relatives who had been ill for a long time. However, we posit that active sensitization about the relevance of autopsies in the general population, emphasizing the point that the clinical diagnosis may not necessarily be the cause of death, will increase the likelihood of consent for autopsies. Healthcare workers need to clearly explain the purpose of performing autopsies. In our setting, next of kin were given verbal feedback after the autopsy was done. We believe that this provided closure for most of them especially those whose patients died after a few days of hospitalisation. However, this cannot be confirmed since there was no questionnaire administered after the autopsy had been done, to assess the usefulness of the information given. Worth still, for future studies, we plan to incorporate feedback from the family members, and although, this was outside the scope of the current study. The concern of body mutilation during the autopsy with some parts of the deceased being retained by the pathologist was raised by several relatives. This reason was more frequent among Muslim families. The concern for body mutilation was also noted among healthcare workers, which may influence their attitude towards requesting autopsies when patients they are treating die of unknown causes. The issue of pathologists retaining body organs is a myth. People think that entire organs are retained yet only very tiny tissues from each organ are taken off and the rest of the organs are put back.

In Uganda today, verbal autopsies are more commonly used in peripheral health facilities based on clinical and/or confirmed laboratory diagnosis. However, verbal autopsies have limitations as they are not always reliable/accurate, may be incomplete, cannot be replicated, and are often problematic with diseases that have less specific symptoms, hence only a presumed or probable cause of death may be given. Despite these limitations, clinical autopsies are infrequently performed at regional and national referral hospitals in Uganda. The majority of autopsies are performed on request for either research purposes or forensic medicine. Yet, they would be useful in targeted patients’ populations given the uncertainty of infectious causes of death and unknown pathologies.

Similarly, the high cost of the autopsy procedure (approximately 162 USD), is out of reach by most families who have relatives admitted in public health facilities especially given the out-of-pocket expenses incurred for treatment of the decedent. This prohibitive cost contributes to the increased rates of decline for autopsies. Having the cost of the procedure subsidized as part of healthcare costs incurred by public health care facilities could help to solve this. Assurance should be given to families that no extra charges will be encountered.
to perform the treatment and autopsy understudy settings. Similarly, expanding the capacity of health facilities to perform autopsies in terms of having equipped morgues and more trained personnel to perform autopsies while extending these services to peripheral health centers could potentially improve autopsy acceptance rates. However, an unknown, but presumably significant, number of patients die in their communities at home without the relatives of the deceased seeking to have an autopsy or embalming services from health facilities. This practice has not only occasionally been the focal point of infectious disease epidemics, but this lack of documentation of deaths also underestimates the burden of disease in the country.

As observed in this study, there is a shortage of logistical support in terms of basic medical and laboratory supplies and personal protective gear to favor autopsy procedures for all hospitalized who die. The small number of trained pathologists in the country is a major hindrance to autopsies since the pathologists tend to be overstretched, especially when forensic autopsies are ongoing. In most cases, morgue attendants are quick to embalm the deceased shortly after death, either due to the absence of a healthcare worker to order an autopsy or due to pressure from the family of the deceased, who typically want to leave the hospital as soon as possible to arrange the funeral. This practice does not allow sufficient time for the doctors to discuss the reasons and obtain consent for autopsies. Finally, dilapidated morgues at most public health care facilities are a deterrent to encourage autopsies at these facilities.

Misconceptions about clinical autopsies in Uganda
A number of misconceptions surround autopsies in Uganda. According to our respondents or family members, most people believe that when autopsies are performed, all internal organs are removed and replaced with cotton wool. In some communities, autopsies are completely unacceptable culturally or are perceived as taboo. Some religions, including Islam, consider autopsies as an unacceptable practice for Muslims because they believe the dead have to return whole just as they were born. There is also a myth about the deceased coming back to torment the family members because of the procedures performed on the deceased relatives’ body.

Potential benefits of clinical autopsies
Autopsies can be beneficial in understanding the primary cause of death, which may be different from the clinical diagnosis. Establishing and understanding the primary cause of death, in turn, helps to improve the care of patients still living with the disease. Autopsies aid improvement in diagnosis, a better understanding of disease progression, and the development of more targeted therapies, which reduce mortality and save lives in the future. Of importance in forensic medicine, autopsies provide evidence that helps to apprehend criminals and/or by establishing the true cause of death, puts suspicions to rest. Autopsy reports are also important in enabling the next-of-kin to obtain official certification of death, which may be required as part of the administrative processes of the estate of the deceased. Autopsy reports are used as part of hospital audits to identify areas of improvement and the gaps that need to be bridged.

Challenges in consenting and performing autopsies in Uganda
It is often emotionally difficult for the nurse or doctor to talk to grieving family members, especially when a death has just occurred. Despite the lengthy consenting process involved in this study, we endeavored to provide bereavement counseling first to comfort the family before discussing the importance of performing an autopsy for their deceased relative. We learned early on that understanding family dynamics is important, given the communal setting in Uganda. In order for the consenting process to be successful, we sought consent from the first line caregivers but also ensured we identified the family decision-makers and involved them in these discussions for the autopsies.

Additional challenges we noted were the prolonged waiting time for families at the morgue to receive the decedent and system constraints. We found the wait time to be typically 4 hours, which may be inexplicably long, creating anxiety and consternation. Kiruddu/ Mulago National Referral Hospital has about 14 pathologists only, which means the few pathologists have a heavy workload, which contributes to delayed or missing final autopsy reports. Nationally, the number of Anatomical Pathologists in the country is low and indeed those that are actively involved in autopsy work is low. Autopsy work in the Regional Referral and District Hospitals is handled by Medical Officers (MOs) who are not Specialist Pathologists. The Anatomical Pathologists are at the National Referral Hospital and in the Medical School. Lastly, the shortage of instruments and personal protective equipment can expose staff to occupational health hazards and are additional challenges in conducting autopsies in Uganda.

Limitations to the study
The main limitation to the study is that it was conducted at only one National Referral Hospital among HIV infected patients only, but we believe the challenges discussed here apply to the general population in the context of obtaining autopsies in most resource limited settings. The fact that study staff checked inpatient registers for deaths, actively contacted next-of-kin, offered bereavement counseling, and communicated that no costs would be incurred, all could have positively impacted or overestimated the rate of autopsy acceptance observed. Some patients included had incomplete data sets.

Conclusion
Clinical autopsies remain relevant procedures to determine the cause of death. In the current study, we observed a lower autopsy refusal rate under normal hospital conditions among HIV-positive patients in Uganda compared to previously reported rates in the same setting. By seeking consent from more family members and clearly explaining to the families
the purpose of performing autopsies, we reduced the refusal rate for autopsies among relatives of deceased patients at this hospital. Healthcare workers need to clearly explain the purpose of performing autopsies as they increase active sensitization about the relevance of autopsies and dispel misconceptions related to autopsies among the general population. Building capacity for performing autopsies by training more pathologists and laboratory resources to decrease the turn-around-time for autopsy reports and extending these services to peripheral health facilities could improve autopsy acceptance rates in Uganda.

Data availability
Underlying data

References
   PubMed Abstract | Publisher Full Text | Free Full Text
   PubMed Abstract | Publisher Full Text
   Reference Source
   PubMed Abstract | Publisher Full Text | Free Full Text
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    http://www.doi.org/10.6084/m9.figshare.16929499.v1
    PubMed Abstract | Publisher Full Text | Free Full Text
    PubMed Abstract | Publisher Full Text | Free Full Text

Extended data

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

Acknowledgements
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Open Peer Review

Current Peer Review Status: 

Version 2

Reviewer Report 02 February 2022
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2 Division of Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, NC, USA
3 Department of Community Health, Faculty of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda

The authors have addressed my comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Malaria, Vector-borne diseases, Infectious diseases epidemiology, surveillance

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 16 November 2021
https://doi.org/10.21956/wellcomeopenres.19144.r47002

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? Ross M. Boyce
The submitted manuscript reports the rate of clinical autopsies performed among HIV-positive deceadents at the national referral hospital in Uganda, while also exploring reasons that autopsies were not performed, including both administrative/logistical issues and the stated rationale of next-of-kin. Understanding cause of death is an important, albeit somewhat neglected, topic both for routine disease surveillance and clinical/epidemiological research and the authors should be commended for nesting this work within the parent study. The manuscript is well organized and written. The results are straightforward and presented in a clear manner. The conclusions are generally appropriate to the results presented, although I believe the generalizability of the findings may be more limited than the authors suggest, as noted in my comments below.

**Major Comments:**

1. The study site, located in close proximity to the capital city and co-located with the most prestigious university/medical school, is the most capable and well-resourced public health facility in Uganda. While the authors state that MNRH has "only" 14 pathologists, I suspect that the majority of regional referral centers, district hospitals, and other such facilities that care for inpatients have much fewer, if any, trained pathologists. Thus, the findings are likely to be a best-case estimate of autopsy rates, especially in regard to the issue of overburdened clinical staff, which accounted for ~25% of autopsy non-performance.

2. Similarly, I suspect that study methodology in which study staff checked inpatient registers for deaths, actively contacted next-of-kin, offered bereavement counseling, and communicated that no costs would be incurred all positively impacted the rate of autopsy acceptance. This is a relatively unavoidable consequence of the study design (and appropriate to ethical requirements), but again, probably overestimates the "real world" (i.e., non-study) rate of autopsy. This should be mentioned in the limitations section.

3. "We carried out the study at a national referral hospital which gets patients from all over the country and could be representative of the whole country." Without data, this is largely speculation. It is well documented that distance/travel burden substantially impacts the ability to pursue higher-level care. In contrast to the statement, I would suspect that most participants were from the immediate environs with a substantial decrease as one moves further from MNRH (i.e., distance decay). Those who were from a greater distance were likely those with more resources available to make the trip and thus are likely to be different. If data is available on district of residence of participants, I would consider including to support (or refute) this assertion.

**Minor Comments:**

1. Methods
   - Unclear if consent in the sentence. "Those who were still in the hospital premises were approached to seek for informed consent" refers to consent for the study or consent for the
autopsy?
- Would be helpful if there was some description of how the process of autopsies is done in routine practice (i.e., outside of this study).

2. Discussion
- "This reason was notably greater among Muslim families." The stratified data (by religion) to support this conclusion is not presented.

Questions / Suggestions:
1. Any reason to think that issues relating to HIV stigma may have influenced family decision to pursue autopsy?

2. Would be valuable to get feedback on Next-of-Kin / Family experiences with autopsy when performed. In other words, did they find it useful or informative? Did it provide closure? This could be helpful in informing future interventions.

3. It appears that at least a portion of the study period took place during the COVID-19 pandemic. Was there any difference, statistically or anecdotally in the rates or reason for non-performance during the pandemic potentially as a result of fear or national lockdowns?

4. The Discussion section outlines many of the current challenges in achieving a high rate of autopsies, but would benefit from further discussion of potential ways/interventions to improve the rate in routine practice.

5. Are non-physician professionals (i.e., clinical officers) who might be able to be trained to perform clinical autopsies?

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

**Competing Interests:** No competing interests were disclosed.
Reviewer Expertise: Malaria, Vector-borne diseases, Infectious diseases epidemiology, surveillance

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Jan 2022

Olivie Carolyne Namuju, 1. Infectious Diseases Institute, College of Health Sciences, Makerere University, Kampala, Uganda

Following these helpful comments from the reviewer, we made a number of tracked changes in v1 of the text. Nationally, the number of Anatomical Pathologists in the country is low and indeed those that are actively involved in autopsy work is low. Yes, the autopsy work in the Regional Referral and District Hospitals is handled by Medical Officers (MOs) who are not Specialist Pathologists. The Anatomical Pathologists are at the National Referral Hospital and in the Medical School. The findings are indeed a reflection of what happens at the national referral hospital level. Yes, the study methodology could have overestimated the rate of autopsy observed. This has been added to the limitations. The fact that the hospital admits patients across the entire country and of whom were enrolled into the study, we assumed this gives a general representation of those from a greater distance. Consent is always obtained from the next-of-kin that are available on the wards after the death has occurred. Also, consent to the study and consent to autopsy are the same thing in this context. We have also added a brief description of the autopsy procedure outside the study settings, in routine practice. Analysis was not stratified by religion. This has been modified in the text. People tend to associate stigma more with the living than the dead. Next of kin were given verbal feedback after the autopsy was done. It provided closure for most of them especially those whose patients died after a few days of hospitalisation. Yes, there was an increased challenge during the pandemic time mainly because of the difficulties with getting transportation that made next of kin always to be in a hurry before curfews hours. Increasing public awareness on the importance of autopsies preferably through the media would be a solution. Currently in Uganda, autopsies are conducted by Medical Officers and Pathologists. No other cadre is permitted to do otherwise.

Competing Interests: None