COVID-19 Testing among Deceased Persons Undergoing Verbal Autopsy — University Teaching Hospital, Zambia, April 2020—August 2021

Priscilla Kapombe

24 May 2023
21 bodies brought in Dead due to COVID-19 in the last 24 hours

By Chief Editor - August 2021

UTH MORGUE FULL

By Kasakha Muchimba

The University Teaching Hospitals - UTH - Main Mortuary is full to capacity.

And management says in addition to deaths which occur at the hospital the facility has also been receiving an average of 10 brought-in-dead - BID - every day since the third wave of Covid 10 started about 2 weeks ago.

Hospital Coordinator of Modernization Elizabeth Chiinde has since advised that only 3 relatives to deceased persons should visit the mortuary in order to manage crowds.

Meanwhile the Lusaka City Council issued over 600 burial permits last week.

Council Director for Public Health Christopher Mwanya says the authority is now faced with challenges in monitoring funeral homes due to limited resources.

Zambia has recorded a total of twenty-three COVID-19 related deaths in the last 24hrs. Out of the 23 deaths, 21 were brought in dead (BIDs) and two were facility deaths.
Introduction

• Zambia experienced a COVID-19 epidemic, with >340,000 confirmed cases and >4,000 deaths through April 2023

• The number of deaths is likely an underestimate because:
  – Testing limitations, especially early in the pandemic
  – A large proportion (30-50%) of people die in the community in Zambia
  – Limited medical services during waves, especially the delta wave (i.e., Jun/Jul 2021)

• Assessing the toll of COVID-19 on the country might inform public health and clinical actions for COVID-19 and future potential pandemic threats in Zambia
Methods – Study Setting

• Cross-sectional study of deceased persons at University Teaching Hospital (UTH) in Lusaka
  – UTH is a tertiary care center / referral hospital for entire country
• In Zambia, VAs are done for deceased persons who died in the community or within 48hrs of admission *
  – (VA mortality surveillance done in 25 districts in Zambia, including Lusaka)
  – An MCCD form is completed by the attending clinician on in-patient deaths that occur ≥48hrs of admission
• UTH Mortuary accepts community deaths for most (~90%) of Lusaka District
  – A burial permit is required for funerals within Lusaka District
  – Proof of a verbal autopsy (VA) or MCCD form is required to obtain a burial permit
Methods – Data Collection

• A WHO questionnaire is administered by trained surveillance officers
  – InterVA5 software analyzes WHO VA questionnaire responses to output a probable underlying cause of death (COD)

• UTH mortuary did COVID-19 testing on deceased person
  – PCR and RDT tests
  – When supplies were available

![WHO VA questionnaire](image-url)
Methods – Data Analysis

• Analyzed deceased person with both a VA and COVID test results
  – Underlying COD by COVID test result status (positive vs. negative)
  – Other VA questions (i.e., symptoms, comorbidities) by COVID test result status
  – Factors associated with testing COVID-19 positive estimated using logistic regression

• Data in this analysis cover April 2020 to August 2021
  – VA questions on antemortem COVID diagnosis/testing added to questionnaire in October 2020
Sample Size

- 12,919 deceased persons BID during April 2020 to August 2021
- 5,555 (43.0%) had both a VA and COVID-19 test
- 422 (4.6%) were COVID-19 positive

12,919 BIDs to UTH from Apr 2020 to Aug 2021

- 10,247 (79.3%) with a VA
  - 9,145 (70.8%) tested for COVID-19
  - 3,590 (27.8%) with no VA
- 2,672 (20.7%) not tested for COVID-19
  - 1,102 (8.5%) no VA or COVID-19 test

5,555 (43.0%) had VA and COVID test
## COVID-19 Positivity by VA Status

<table>
<thead>
<tr>
<th>All deceased person tested, n (%) (N = 9,147)</th>
<th>Had a VA done, n (%) (N = 5,555)</th>
<th>Did not have a VA done, n (%) (N = 3,592)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tested COVID-19 positive</td>
<td>422 (4.6)</td>
<td>278 (5.0)</td>
<td>144 (4.0)</td>
</tr>
</tbody>
</table>

VA: Verbal autopsy
VA and COVID Test Coverage by Month

Sample size of deceased persons with VA and COVID test by month at UTH, Apr 2020 to Aug 2021

- Apr-20: 2% VA done, 28% Both VA & COVID-19 test done
- May-20: 44% VA done, 5% Both VA & COVID-19 test done
- Jun-20: 54% VA done, 5% Both VA & COVID-19 test done
- Jul-20: 5% VA done, 42% Both VA & COVID-19 test done
- Aug-20: 45% VA done, 45% Both VA & COVID-19 test done
- Sep-20: 38% VA done, 22% Both VA & COVID-19 test done
- Oct-20: 62% VA done, 64% Both VA & COVID-19 test done
- Nov-20: 49% VA done, 49% Both VA & COVID-19 test done
- Dec-20: 46% VA done, 46% Both VA & COVID-19 test done
- Jan-21: 50% VA done, 50% Both VA & COVID-19 test done
- Feb-21: 58% VA done, 58% Both VA & COVID-19 test done
- Mar-21: 56% VA done, 56% Both VA & COVID-19 test done
- Apr-21: 47% VA done, 47% Both VA & COVID-19 test done
- May-21: 50% VA done, 50% Both VA & COVID-19 test done
- Jun-21: 44% VA done, 44% Both VA & COVID-19 test done
- Jul-21: 56% VA done, 56% Both VA & COVID-19 test done
- Aug-21: 44% VA done, 44% Both VA & COVID-19 test done

No. deaths at UTH morgue
### Patient Characteristics and Circumstances of Death

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall, n (%)</th>
<th>Positive, n (%)</th>
<th>Negative, n (%)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 5,555</td>
<td>N = 278</td>
<td>N = 5,277</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3,282 (59.1)</td>
<td>163 (58.6)</td>
<td>3,119 (59.1)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Female</td>
<td>2,273 (40.9)</td>
<td>115 (41.4)</td>
<td>2,158 (40.9)</td>
<td>1.0 (0.8-1.3)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-17</td>
<td>765 (13.8)</td>
<td>13 (4.7)</td>
<td>752 (14.3)</td>
<td>Ref.</td>
</tr>
<tr>
<td>18-49</td>
<td>2,374 (42.7)</td>
<td>87 (31.3)</td>
<td>2,287 (43.3)</td>
<td>2.2 (1.2-4.0)</td>
</tr>
<tr>
<td>≥50</td>
<td>2,416 (43.5)</td>
<td>178 (64.0)</td>
<td>2,238 (42.4)</td>
<td>4.6 (2.6-8.1)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>1,184 (21.3)</td>
<td>67 (24.1)</td>
<td>1,117 (21.2)</td>
<td>1.2 (0.9-1.5)</td>
</tr>
<tr>
<td>Place of death (n miss = 9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>4,421 (79.6)</td>
<td>222 (79.9)</td>
<td>4,199 (79.6)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Health facility</td>
<td>1,123 (20.2)</td>
<td>55 (19.8)</td>
<td>1,068 (20.2)</td>
<td>1.0 (0.7-1.3)</td>
</tr>
<tr>
<td>Died during a COVID wave period*</td>
<td>3,511 (63.2)</td>
<td>250 (89.9)</td>
<td>3,261 (61.8)</td>
<td>5.5 (3.7-8.2)</td>
</tr>
<tr>
<td>Died suddenly†</td>
<td>1,451 (26.1)</td>
<td>61 (21.9)</td>
<td>1,390 (26.3)</td>
<td>0.8 (0.6-1.1)</td>
</tr>
<tr>
<td>Received care before death‡</td>
<td>3,724 (67.0)</td>
<td>185 (66.5)</td>
<td>3,539 (67.1)</td>
<td>1.0 (0.8-1.3)</td>
</tr>
<tr>
<td>Tested for COVID-19 antemortem¶</td>
<td>1,854 (33.4)</td>
<td>97 (34.9)</td>
<td>1,757 (33.3)</td>
<td>3.7 (2.5-5.4)</td>
</tr>
</tbody>
</table>

* Wave period defined as Jun 30 to Sep 21, 2020 (wildtype/wave 1), Jan 3-Mar 19, 2021 (beta/wave 2), and May 28-Aug 22, 2021 (delta/wave 3)
† A sudden death was defined as dying within 24 hours of being in regular/good health
‡ Indicates person received care for the condition that led to death
¶ Questions about antemortem COVID-19 testing not added to VA until October 2020 (observations in logistic regression were 4,074)
Causes of Death by COVID-19 Status*

<table>
<thead>
<tr>
<th>Rank</th>
<th>Probable cause of death</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acute cardiac disease</td>
<td>51</td>
<td>18.3</td>
</tr>
<tr>
<td>2</td>
<td>Respiratory tract infections/pneumonia</td>
<td>46</td>
<td>16.5</td>
</tr>
<tr>
<td>3</td>
<td>Other/unspecified cardiac disease</td>
<td>36</td>
<td>12.9</td>
</tr>
<tr>
<td>4</td>
<td>Stroke</td>
<td>20</td>
<td>7.2</td>
</tr>
<tr>
<td>5</td>
<td>HIV/AIDS related death</td>
<td>17</td>
<td>6.1</td>
</tr>
<tr>
<td>6</td>
<td>Pulmonary tuberculosis</td>
<td>16</td>
<td>5.8</td>
</tr>
<tr>
<td>7</td>
<td>Diabetes mellitus</td>
<td>14</td>
<td>5.0</td>
</tr>
<tr>
<td>8</td>
<td>Diarrheal diseases</td>
<td>11</td>
<td>4.0</td>
</tr>
<tr>
<td>9</td>
<td>Digestive neoplasms</td>
<td>8</td>
<td>2.9</td>
</tr>
<tr>
<td>10</td>
<td>Indeterminate</td>
<td>7</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* Underlying COD determined by verbal autopsy using WHO 2016 tool. This COD is considered probable (i.e., it was not an official COD)
# Symptoms Prior to Death

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Positive, n (%)</th>
<th>Negative, n (%)</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 278</td>
<td>n = 5,277</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>111 (39.9)</td>
<td>1,791 (33.9)</td>
<td>1.3 (1.0-1.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cough</td>
<td>125 (45.0)</td>
<td>1,783 (33.8)</td>
<td>1.6 (1.3-2.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>142 (51.1)</td>
<td>2,171 (41.1)</td>
<td>1.5 (1.2-1.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>72 (25.9)</td>
<td>1,123 (21.3)</td>
<td>1.3 (1.0-1.7)</td>
<td>0.07</td>
</tr>
<tr>
<td>Chest pain</td>
<td>88 (31.7)</td>
<td>1,353 (25.6)</td>
<td>1.3 (1.0-1.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Headache</td>
<td>90 (32.4)</td>
<td>1,524 (28.9)</td>
<td>1.2 (0.9-1.5)</td>
<td>0.29</td>
</tr>
<tr>
<td>Classic covid symptoms*</td>
<td>201 (72.3)</td>
<td>3247 (61.5)</td>
<td>1.6 (1.3-2.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Asymptomatic†</td>
<td>44 (15.8)</td>
<td>1,135 (21.5)</td>
<td>0.7 (0.5-1.0)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* Defined as fever, cough, or shortness of breath
† Defined as an absence of any of the following: fever, cough, shortness or breath, tachypnea, chest pain, headache, diarrhea, vomiting, abdominal pain, rash, or mental confusion
Antemortem COVID-19 Diagnosis/Testing

- In total, 1,850 (42.9%) deceased persons were reportedly tested for COVID prior to death (i.e., antemortem) from Oct 2020 to Aug 2021.
- 201 (10.9%) were reportedly COVID-19 positive.
  - Most (90.5%) who reported testing positive were diagnosed with COVID-19 by an HCW.
- Analysis restricted to period that VA asked about COVID-19 diagnosis and testing history, which was Oct 2020-Aug 2021.

```
4,317 deceased persons with VA during Oct-20 to Aug-21

1,850 (42.9%) reported COVID test antemortem

201 (10.9%) reported COVID positive
1,553 (83.9%) reported COVID negative

182 (90.5%) diagnosed with COVID by an HCW
19 (9.5%) not diagnosed with COVID by an HCW

348 (22.4%) diagnosed with COVID by an HCW
1,200 (77.3%) not diagnosed by an HCW
5 (0.3%) NA

2,356 not tested
111 missing data
96 (5.2%) no result
```

Analysis restricted to period that VA asked about COVID-19 diagnosis and testing history, which was Oct 2020-Aug 2021.
Antemortem and Postmortem COVID Results

- 97 (73.5%) of deceased persons who tested positive at UTH had been tested for COVID prior to death
  - Of these, 64 (66.0%) were reportedly COVID positive
- Of 201 who reported testing positive, 64 (31.8%) tested COVID positive postmortem
  - Odds of testing COVID positive postmortem if reporting COVID test positive antemortem were 22.2 (95% CI: 14.0-35.1)

Analysis restricted to October 2020 to August 2021

* One person with antemortem test but no result tested COVID positive postmortem (not shown)
Diagnostic Accuracy of COVID-19 History prior to Death

- Antemortem COVID diagnosis by a HCW and positive COVID test results had low sensitivity but moderate specificity for testing COVID positive after death
- Negative predictive value was high of antemortem COVID diagnosis and test results

<table>
<thead>
<tr>
<th></th>
<th>COVID test postmortem</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)</td>
</tr>
<tr>
<td><strong>COVID diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>antemortem (+)</td>
<td>66</td>
</tr>
<tr>
<td>antemortem (-)</td>
<td>66</td>
</tr>
<tr>
<td>Se: 0.50</td>
<td><strong>PPV: 0.11</strong></td>
</tr>
<tr>
<td>Sp: 0.87</td>
<td><strong>NPV: 0.98</strong></td>
</tr>
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<td><strong>COVID test</strong></td>
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<td>64</td>
</tr>
<tr>
<td>antemortem (-)</td>
<td>32</td>
</tr>
<tr>
<td>Se: 0.67</td>
<td><strong>PPV: 0.32</strong></td>
</tr>
<tr>
<td>Sp: 0.92</td>
<td><strong>NPV: 0.98</strong></td>
</tr>
</tbody>
</table>

Analysis restricted to October 2020 to August 2021
Limitations

• Findings reflect experience from a large tertiary referral hospital in a capital city. Generalizability of findings in other parts of Zambia is not known.

• Not all deceased persons at UTH were tested because of inconsistent supply of testing kits/reagents.

• Unable to distinguish between PCR and RDT tests (data not collected).

• Timing of antemortem COVID-19 test results was not collected.

• Timing of postmortem COVID-19 testing and COVID-19 assay test properties could affect findings:
  - Deceased persons with COVID-19 might no longer be shedding virus by the time of postmortem testing.
  - RDTs can result in false negatives. PCR tests can result in false positive (from cross-contamination).

• InterVA5-coded COD is considered probable.
Discussion (1)

- A notable portion of deceased persons from the community or recently admitted tested COVID-19 positive during the wild-type and delta waves in Zambia
  - However, few tested COVID-19 positive during the beta wave
- Only a minority persons testing COVID-19 positive at deaths were coded as respiratory tract infections
  - Cardiac disease and stroke CODs might reflect sequelae of the hypercoagulable state described with severe COVID-19
- Most persons testing COVID-19 positive postmortem reportedly displayed classic symptoms and were tested before dying
  - This could indicate a strained medical system during COVID-19 waves in Zambia
Discussion (2)

- Overall findings generally align with another concurrent COVID-19 postmortem study at UTH
  - This study demonstrated much lower percent positivity of deceased persons and greater antemortem diagnosis and COVID-19 testing coverage
  - Many more persons tested in this study (5,555 vs. 1,118)
  - Potential reasons for differences include different testing approaches, unmeasured bias in either study’s recruitment, the period of testing cover a larger non wave period (summer) hence proportion of positivity is lower.

Sources: Mwananyanda, BMJ 2021; Gill, BMJ Open 2022
Recommendations

- Enhancing mortality surveillance during outbreaks can provide useful information to inform public health and clinical care
  - However, relying on respiratory COD from VA as surrogate for COVID-19 deaths might underestimate true burden. This points to the value of also measuring all-cause mortality

- Improved availability of antivirals, anticoagulants, and other therapeutics might avert mortality during future waves in Zambia

- Low sensitivity of antemortem COVID-19 history points to value of postmortem surveillance
Way-Forward

• In an effort to enhance and ensure a coordinated mortality surveillance system that enables timely collection, processing, analysis and dissemination of quality data; following lessons learnt from Covid-19:
  - Stakeholder buy in (reviving of a Technical Committee focusing on MS - MSSC).
  - Political will/support – following launch of the African Continental Framework in Zambia.
Steps Taken

- Mortality Surveillance Subcommittee has held monthly meetings from the launch.
- Undertook a comprehensive stakeholder mapping workshop with support from the Africa CDC – Regional Coordinating Committee.
- Conducting national MS assessment.
- Initiated phase 1 of drafting the national strategic action plan (process guided by the framework and supported by A-CDC).
- Planning for implementation of Sample Registration System are underway.
Study Collaborators

- Zambia Ministry of Health
  - Mweene Cheelo
  - Lloyd B. Mulenga
  - Patrick Lungu

- University Teaching Hospital Mortuary/Ministry of Home Affairs (National Forensic Authority)
  - Adam Mucheleng’anga

- Zambia National Public Health Institute
  - Stephen L. Chanda
  - Amos Hamukale

- U.S. Centers for Disease Control and Prevention
  - Jonas Z. Hines
  - Kashala Kamalonga
  - Leigh Tally
  - Andrew F. Auld