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Post-mortem examination of Hospital Inpatient COVID-19 Deaths in Lusaka, Zambia - A Descriptive Whole-body Autopsy Series



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ABSTRACT

Background: Since information on the pathology of COVID-19 from sub-Saharan Africa (SSA) remains scarce, the objective of our study was to define the gross pathology and histological features of COVID-19. We report data from 29 whole-body autopsies of COVID-19 deaths occurring in hospitals in Lusaka, Zambia - the first large autopsy case series from Africa.

Methods: We performed a descriptive post-mortem examination study of inpatient COVID-19 related deaths at two hospitals in Lusaka, Zambia. Whole-body autopsies were conducted according to Standard Operating Procedures. Gross and histopathological examinations of all organs were performed. Patient demographics, history, co-morbidities, autopsy gross and microscopic findings, and cause(s) of death were recorded and analyzed using STATA version 14. Variables were grouped and presented as frequencies and percentages.

Findings: Autopsies were performed on 29 decedents (mean age = 44 ± 15.8 years; age range = 19–82; 17/29 [58.8%] males). 22/29 [75.9%] cases were <55 years of age. A spectrum of pathological manifestations of COVID-19 were seen in all organs. The commonest causes of death were pulmonary thromboembolism (13/29, 45%), Diffuse Alveolar Damage (9/29, 31%), and COVID-19 pneumonia (7/29, 25%). 22/29 (76%) had co-morbidities. Common co-morbidities included HIV (8/29, 28%), Hypertension (6/29, 20%), Tuberculosis (3/29, 10%), Diabetes (3/29, 10%).

Conclusions: A spectrum of gross anatomical and histopathological findings are seen in COVID-19 deaths in hospitalized decedents. These appear broadly similar to those reported from China, Europe and USA. Differences include a younger age group, and co-morbidities of HIV and TB co-infection which require further investigation.

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Introduction

The SARS-CoV-2 pandemic has caused 171,292,827 confirmed COVID-19 cases with 3,687,589 deaths globally as of June 4th, 2021. Of these 3,530,845 cases occurred in sub-Saharan Africa (SSA) with 131,630 deaths (WHO Coronavirus dashboard, 2021; Africa CDC - Coronavirus Disease 2019 (COVID-19), 2021). Zambia reported its first COVID-19 case in March 2020 and has since recorded 96, 563

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cases with 1,284 deaths as of June 4th, 202 (World Health Organisation, 2021). Eighteen months after the first COVID-19 cases were reported from Wuhan, China, several major knowledge gaps on COVID-19 pathology and pathogenesis remain, particularly in SSA. The case-fatality ratio (CFR) for COVID-19 in Africa appears lower than the Case Fatality Rate in western countries, indicating that COVID-19 may manifest less severe disease and that the pathogenesis of COVID-19 in SSA may be different (Lawal, 2021; Bamgboye et al., 2020).

An area of continuing neglect and missed opportunities for COVID-19 research in SSA is that of accurately defining the pathological features of COVID-19 and ascertaining the underlying cause(s) of death from COVID-19 in hospitals (Bamgboye et al., 2020; Mawalla, 2020; Mucheleng'anga and Himwaze, 2020). Whilst several reports of whole body autopsy case series and organ specific pathology have been published from China, Europe and USA (Maiese et al., 2020), there is little information on post-mortem examination and the pathology of COVID-19 in SSA. There remains scanty information on the actual causes of death and pathogenesis of COVID-19 from the African continent. There are only two individual case reports of whole body autopsies and lung biopsy studies of four South African ICU patients obtained after death (Mulale et al., 2021; Khaba et al., 2020; Bruce-Brand et al., 2020). Several reports have emphasized the need for rekindling and revamping autopsy and post-mortem studies in SSA (Mawalla, 2020; Mucheleng'anga and Himwaze, 2020; Maiese et al., 2020; Mulale et al., 2021; Khaba et al., 2020; Bruce-Brand et al., 2020; Mudenda et al., 2020), to determine the underlying pathology and causes of COVID-19 deaths occurring in hospital inpatients.

Whole-body autopsies in general, and on confirmed or suspected SARS-CoV-2 cases in Africa have not been forthcoming due to scarcity of pathologists, inadequate infrastructure, and difficulties in obtaining consent for autopsies (Mawalla, 2020; Mucheleng'anga and Himwaze, 2020; Khaba et al., 2020; Rampatige and Gilks, 2015). In addition, performing autopsies in environments where infectious pathogens such as SARS-CoV-2 are suspected or confirmed, requires optimal biosafety facilities (World Health Organization, 2020; Baj et al., 2021; Liang et al., 2020), which are unavailable in most African countries.

The objective of our case series study was to present the histopathological findings following whole-body autopsies in COVID-19 inpatients. We present post-mortem examination data from 29 whole-body autopsies of COVID-19 deaths occurring in hospitals, in Lusaka, Zambia - the first large autopsy case series study from Africa.

Methods

Study design and sites

We conducted a retrospective descriptive study of reports of 29 whole body autopsies we had performed of COVID-19 inpatient deaths whose proximate cause of death was SARS-CoV-2 infection (positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR)). The hospital deaths occurred between March 2020 and March 2021 in the COVID-19 isolation wards at the University Teaching Hospital (UTH) and Levy Mwanawasa University Teaching Hospital (LMUTH), Lusaka, Zambia. Selection for autopsy was based according to request by physician

Ethics permission

Informed consent from the next-of-kin was obtained to conduct the autopsy and publish the findings. The Office of State Forensic Pathology (OSFP) granted permission to access postmortem data.

Pre-autopsy procedures

All staff involved underwent safety training procedures. Clinical case notes were reviewed prior to autopsy. The two autopsy pathologists had rehearsed on how they were to work together, classify and define the autopsy findings. Placement and handling of equipment was also planned. The manner in which the pathologists' assistant would operate was also discussed and practiced.

The mortuary and autopsy rooms used to perform the autopsy are had a working refrigeration system and good lighting and water reticulation system, but have no negative pressure ventilation. The bodies were well preserved as the refrigeration was in working condition. The bodies were placed in the mortuary two to three hours after death. The timing of autopsy was between 24 to 72 hours after death. The body was washed using chlorine before autopsy.

Autopsy procedures

Whole body autopsies were performed in accordance with the Practice Manual for Medicolegal Death Investigations. The practice manual for medicolegal death investigation is used in Zambia as a local guideline for conducting forensic postmortem examinations. It covers processes to follow for autopsies on bodies infected with category three and four infectious organisms including SARS-CoV-2. In all cases, we followed universal precautions using personal protective equipment (PPE) (hair caps, eye protection, goggles), long sleeved, non-waterproof gown, covered by a water-proof apron. Double pair of standard disposable surgical latex gloves were used. Cut resistant gloves were also used. We used guidance in place with regards to dressing and undressing of PPE when dealing with infected bodies as in the practice manual for medicolegal death investigations.

Tissues sampled and histological examination

Representative samples were obtained from the various organs (Brain, Lungs, Heart, Liver, Spleen, Kidneys) and other tissues as required and submitted in standard tissue cassettes and fixed in 10% neutral buffered formalin for 72 hours. The samples were processed, embedded in paraffin, sectioned, mounted onto glass slides, and stained using hematoxylin and eosin (H&E) staining according to the Standard Operating Procedure Manual at the UTH histopathology Laboratory. All slides were examined together by the two forensic and anatomical pathologists.

The cause of death was formulated within the context of the history, clinical findings, circumstances of death, autopsy findings, and ancillary studies.

Data collection and analyses

Data on the decedents' demographics, history, circumstances, autopsy findings, and opinion of the cause of death was entered in excel and analyzed using STATA version 14. The variables were grouped and presented as frequencies and percentages.

Results

Decedent demographics

Demographics of the autopsied cases are given in Table 1. Autopsies were performed on 29 decedents (mean age = 44 ± 15.8years; age range = 19–82; 17/29 [58.8%] males).

Table 1
Demographic characteristics of COVID-19 hospital decedents autopsied.

Characteristic/Variable	Hospital Decedents autopsied
Gender	N (%)
Male	17 (58.8)
Female	12 (41.4)
Total No. decedents autopsied	29
Mean Age (years)	44
Age range	19–82
Age group	
15–25	2 (6.9)
26–35	5 (17.2)
36–45	9 (31.0)
46–55	6 (20.7)
56–65	4 (13.8)
66–75	2 (6.9)
76–85	1 (3.5)

Table 2
Symptoms and Comorbidities of 29 decedents autopsied.

SYMPTOM(S) AT ADMISSION	Number (%)
Difficulty breathing	24(82.8)
Cough	9(31.0)
Fever	11(37.9)
Headache	6(20.7)
General Body Weakness	4(13.8)
Vomiting	2(6.9)
Diarrhea	2(6.9)
Oral Thrush	1(100)
Abdominal Pain	1(3.4)
CO-MORBIDITIES AT ADMISSION	
HIV positive	8(27.6)
Hypertension	6(20.7)
Tuberculosis	3(10.3)
Diabetes	3(10.3)
Pregnancy	2(6.9)
Cerebral Vascular Accident	1(3.4)
Malaria	1(3.4)
Leprosy	1(3.4)
Atherosclerotic heart disease	1(3.4)
Paraquat toxicity	1(3.4)
Sickle Cell Anaemia	1(3.4)

Symptoms and Co-morbidities

The symptoms and comorbidities of the 29 decedents are given in **Table 2**. Common symptoms observed were; difficulty breathing (n = 24/29, 83%), cough (n = 9/29, 31%), fever (n = 11/29, 38%), headache (n = 6/29, 21%), general body weakness (n = 4/29, 14%).

Overall, 22/29 (76%) decedents had comorbidities. Co-morbidities were present in 22/29 (76%) of decedents. Common comorbidities included HIV (8/29, 27%), Hypertension (6/29, 21%) Tuberculosis (3/29, 10%), Diabetes (3/29, 10%).

Autopsy findings

The main gross pathology and microscopic autopsy findings, and cause(s) of death, are given in **Table 3**.

The commonest causes of death were pulmonary thromboembolism (13/29, 45%), Diffuse Alveolar Damage (DAD) (9/29, 31%), and COVID-19 pneumonia (7/29, 25%).

Gross pathology and Microscopic Findings

A selection of images representative gross and microscopic autopsy findings are given. **Figure 1** (**Figures 1A to G**) show gross pathology findings.

Table 3
Main autopsy findings and causes of death.

Autopsy findings	Number (%)
Diffuse Alveolar Damage	12/29 (41.4)
Emboli	10/29 (34.5)
<i>Saddle Emboli</i>	6/29 (20.7)
<i>Shower Emboli</i>	4/29 (13.8)
Pneumonia	9/29 (31)
Granular kidneys	5/29 (17.2)
Deep Venous Thrombosis	3/29 (10.3)
Disseminated Thrombi	4/29 (13.8)
Tuberculosis	1/29 (3.4)
Anaemia	1/29 (3.4)
Kaposi Sarcoma	1/29 (3.4)
Colorectal adenocarcinoma	1/29 (3.4)
Main Autopsy Causes of Death	
Pulmonary Thromboembolism	13/29 (44.8)
Diffuse Alveolar Damage	9/29 (31.0)
Pneumonia	7/29 (24.2)

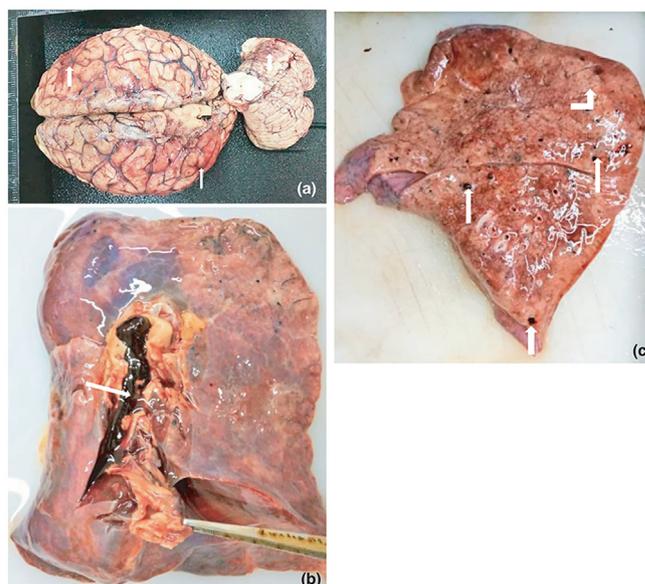


Figure 1. A: Brain: Gross appearance showing hyperaemia (white arrow heads). B: Lung: Pulmonary thrombus in the pulmonary artery (white arrow head). C: Lung: Shower thrombo-emboli and grey hepatisation (white arrow head and bent white arrow up). D: Leg: Deep venous thrombosis (white arrow head). E: Liver: Thromboemboli in the liver in a case with disseminated thrombosis (white arrow head). F: Kidney: Granular surfaces of the kidneys in a case with hypertension. G: Kidney: Infarction due to disseminated thrombosis (white arrow heads).

Figure 2 (**Figures 2A-F**) shows microscopic histopathological findings.

Overall individual decedent characteristics and autopsy findings

Table 4 depicts demographic, clinical and autopsy characteristics of each of the 29 decedents that were autopsied.

Discussion

To our knowledge, this is the first large COVID-19 whole-body autopsy series of hospital inpatient deaths to be reported from sub-Saharan Africa (SSA) to date. Autopsy studies and data on the pathology of COVID-19 from SSA is scanty and has been restricted only to examination of tissue samples obtained through minimally invasive post-mortem examination of 4 cases in South Africa

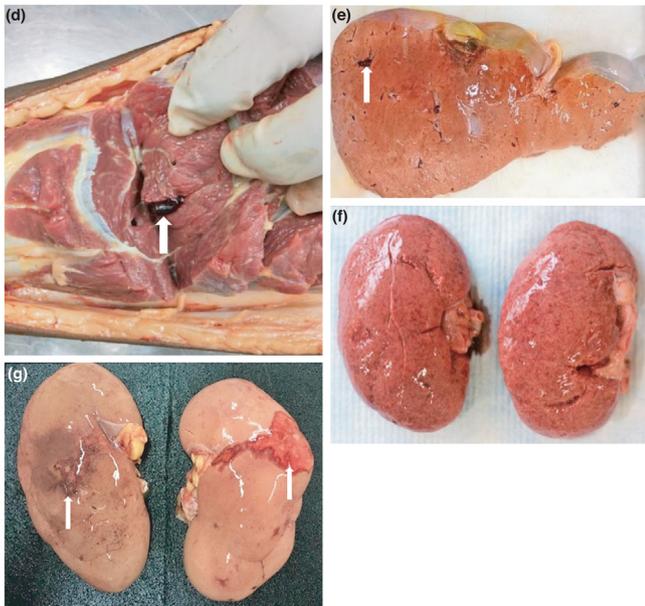


Figure 1. (Continued)

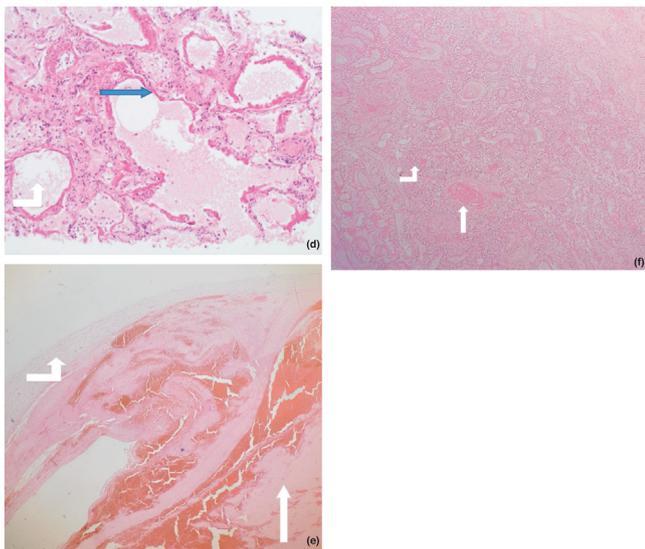


Figure 2. (Continued)

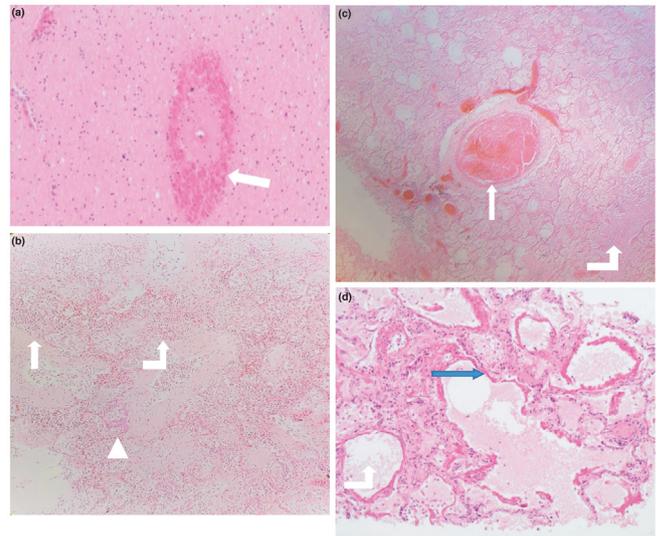


Figure 2. A: Brain: Micrograph (X 40) of the brain parenchyma showing hemorrhage (white arrow head), around a vessel. B: Micrograph (X 20) of lung showing acute (white arrow head) and organising pneumonia (bent white arrow up), and squamous metaplasia (triangle). C: Micrograph (X 20) of lung showing a thrombus (white arrow head) and organising pneumonia (bent white arrow up). D: Micrograph (X 40) of lung tissue showing diffuse alveolar damage within the lung. The hyaline membranes (blue arrow head) are observed to line the alveolar walls. The alveolar space is indicated by the bent white arrow up. E: Micrograph (X 40) of a vessel (bent white arrow up) showing a thrombus (white arrow head). F: Micrograph (X 20) of an infarcted kidney showing disseminated thrombus (white arrow head) and neutrophils in the parenchyma in a case (bent white arrow up).

(Bruce-Brand et al., 2020) and two autopsy reports, one of a COVID-19 and HIV co-infected person (Khaba et al., 2020) and another of an infant co-infected with SARS-CoV-2 and *Mycobacterium tuberculosis* (Mulale et al., 2021). Our study provides data from 29 autopsies of hospital COVID-19 deaths. Our descriptions of symptoms ante-mortem, comorbidities, the extent of disease, the cause(s) of death, fill an important knowledge gap on COVID-19 pathology in Africa.

There were more males than females in our autopsied cases. Published reports suggest that males may be more susceptible to SARS-CoV-2 infection due to their higher plasma Acetylcholinesterase Enzyme 2 (ACE2) levels, less effective antiviral immune defenses than women (Gadi et al., 2020). Understanding COVID-19 the gender differences in Africa will require larger cohort studies and include biopsychosocial and immunological investigations (Griffith et al., 2020).

The age of our study decedents ranged from 19–82 years, with a mean age of 44. Notably, 22/29 (76.0%) were below the age of 55 years. This is at variance with reported autopsy studies from Europe, China and North America, where the deaths were commonly observed in those above 65 years old (Edler et al., 2020; Falasca et al., 2020; Bryce et al., 2021; Bian and The COVID-19 Pathology Team, 2020). The comparatively younger age may be attributed to Zambia’s age structure, where people above the age of 55 are less than 6% of the entire population (Index Mundi, 2021). It could also be due to HIV being more prevalent in people less than 55 years (Himwaze et al., 2020). HIV may also play a role since it is associated with a higher risk of mortality from COVID-19 (Ssentongo et al., 2021).

As reported from autopsy studies from outside Africa (Edler et al., 2020; Falasca et al., 2020; Bryce et al., 2021; Bian and The COVID-19 Pathology Team, 2020), difficulty in breathing, cough, fever, and headache were the most common symptoms. This may reflect admission criteria, which selected patients with moderate and severe respiratory symptoms (COVID CONTINENT HUB, 2021; Grant et al., 2020) and assessment of temperatures during admission (Bian and The COVID-19 Pathology Team, 2020).

HIV infection and hypertension co-morbidities were common among our study group and these comorbidities are important compared to the observations made in other autopsy studies from outside Africa (Maiese et al., 2020; Edler et al., 2020; Falasca et al., 2020; Bryce et al., 2021; Bian and The COVID-19 Pathology Team, 2020).

The range of macroscopic and microscopic pathological features of COVID-19 in hospital deaths in Lusaka, Zambia, greatly resemble those seen in autopsy case series from China, Europe, and USA (Maiese et al., 2020; Edler et al., 2020; Falasca et al., 2020;

Table 4
Summary: demographic, clinical and autopsy characteristics of each individual decedent autopsied.

Case #	Sex/ Age	Symptoms	Duration of illness	Comorbidities	Gross pathology and microscopic findings	Cause(s) of death
1	M/ 38	Cough, Oral thrush, Diarrhea, Fever, Difficulty in breathing	7 days	Leprosy Pneumonia	Heavy lungs (>1000 g each), consolidation of lungs and neutrophils in alveolar spaces and DAD	Pulmonary thromboembolism due to COVID-19
2	M/ 37	Cough Difficulty in breathing	6 days	HIV	Consolidation of lungs and neutrophils in alveolar spaces	Pneumonia due to COVID-19
3	M/ 40	Difficulty in breathing Headache, Fever	14 days	None	Heavy lungs (>1000 g each), and DAD	Diffuse Alveolar Damage due to COVID-19
4	M/ 29	Difficulty in breathing	5 days	Disseminated Kaposi Sarcoma HIV/AIDS	Heavy lungs (>1000 g each), Kaposi sarcoma lesions in the esophagus, stomach, bowel, lungs, skin and DAD	Diffuse Alveolar Damage due to COVID-19
5	F/ 40	General body weakness Vomiting, Fever	7 days	HIV Malaria	Consolidation of lungs and neutrophils in alveolar spaces	Pneumonia due to COVID-19
6	M/ 62	Cough Difficulty in breathing, Fever	4 days	Diabetes, Hypertension	Heavy lungs (>1000 g each), shower thromboemboli, thromboemboli in the heart, granular kidneys, and DAD	Pulmonary thromboembolism due to COVID-19
7	F/ 47	Cough Difficulty in breathing, Fever	5 days	HIV	Consolidation of lungs and organising pneumonia	Pneumonia due to COVID-19
8	M/ 55	Cough, Fever	120 days	HIV Disseminated Tuberculosis	Heavy lungs (>1000 g each) and DAD	Diffuse Alveolar Damage due to COVID-19
9	33/ F	Difficulty in breathing, cough, Pregnant on claxane	5 days	None	Heavy lungs (>1000 g each), shower thromboemboli, iliac artery thromboembolic, thromboemboli in the heart, and DAD	Pulmonary thromboembolism due to COVID-19
10	38/ M	Cough Difficulty in breathing, Fever	14 days	Colorectal adenocarcinoma HIV	Heavy lungs (>1000 g each), colorectal adenocarcinoma, and DAD	Diffuse Alveolar Damage due to COVID-19
11	37/ F	Cough Difficulty in breathing Diarrhea and on claxane	5 days	Hypertension	Heavy lungs (>1000 g each), shower thromboemboli, iliac artery thromboembolic, thromboemboli in the heart, and DAD	Pulmonary thromboembolism due to COVID-19
12	48/ F	Difficulty in breathing, headache	8 days	Hypertensive heart disease HIV	Consolidation of lungs, granular kidneys, large heart (700 g) and neutrophils in alveolar spaces, glomerular sclerosis	Pneumonia due to COVID-19
13	M/ 62	Difficulty in breathing	3 days	Hypertension, Diabetes	Consolidation of lungs, granular kidneys and neutrophils in alveolar spaces	Pneumonia due to COVID-19
14	32/ M	General body pains, vomiting	14 days	Diabetes	Heavy lungs (>1000 g each) and DAD	Diffuse Alveolar Damage due to COVID-19
15	27/ F	Difficulty in breathing in pregnancy	3 days	Sickle cell anemia	Heavy lungs (>1000 g each), and DAD. No sickle cells identified	Diffuse Alveolar Damage due to COVID-19
16	42/ F	Difficulty in breathing Palpitations	7 days	Pulmonary tuberculosis	Consolidation of lungs, and neutrophils in alveolar spaces	Pneumonia due to COVID-19
17	47/ F	Difficulty in breathing	5 days	None	Saddle emboli, heavy lungs (>1000 g each), deep venous thrombosis, and DAD	Pulmonary thromboembolism due to Deep Venous Thrombosis due to COVID-19
18	65/ M	Difficulty in breathing	None	Cerebral Vascular Accident	Saddle emboli.	Pulmonary thromboembolism due to COVID-19
19	58/ M	Difficulty in breathing, Headache, Fever on claxane	5 days	Hypertension Obese	Heavy lungs (>1000 g each), shower emboli, deep venous thrombosis, myocarditis, kidney and brain infarcts and DAD	Pulmonary thromboembolism due to Deep Venous Thrombosis due to COVID-19
20	19/ F	Difficulty in breathing and Fever	3 days	Paraquat toxicity treated for 14 days	Heavy hemorrhagic lungs (>1000 g each), and DAD	Diffuse Alveolar Damage due to COVID-19
21	82/ M	Difficulty in breathing	1 day	Diabetes, Atherosclerotic coronary artery heart disease	Heavy lungs (>1000 g each) and DAD	Diffuse Alveolar Damage due to COVID-19
22	66/ M	Difficulty in breathing	14 days	Hypertension	Heavy lungs (>1000 g each), granular kidneys, and DAD	Diffuse Alveolar Damage due to COVID-19
23	70/ F	Cough Difficulty in breathing on claxane. Death on operation table	6 days	Hypertension	Heavy lungs (>1000 g each), deep venous thrombosis, thrombosed mesenteric vessels, saddle emboli, and DAD	Pulmonary thromboembolism due to COVID-19
24	33/ M	Difficulty in Breathing, Fever	6 days	HIV	Saddle emboli, heavy lungs (>1000 g each), consolidated lungs, and neutrophils in alveolar spaces and DAD	Pulmonary thromboembolism due to COVID-19
25	36/ M	Difficulty in in breathing, Abdominal pains	14 days	Abdominal TB	Multiple abdominal caseating nodules, saddle thromboembolism	Pulmonary thromboembolism due to COVID-19
26	20/ F	Headache, general body weakness	3 days	None	Heavy lungs (>1000 g each), shower emboli, and DAD	Pulmonary thromboembolism due to COVID-19
27	43/ M	Difficulty in in breathing	1 day	None	Disseminated thrombi in lungs, liver, iliac vessels	Pulmonary thromboembolism due to COVID-19
28	50/ M	General body weakness, headache	1 day	None	Heavy lungs (>1000 g each), bilateral shower emboli, and DAD	Pulmonary thromboembolism due to COVID-19
29	47/ F	Difficulty in in breathing, fever, headache	6 days	None	Shower emboli, heavy lungs (>1000 g each), organising pneumonia and DAD	Pulmonary thromboembolism due to COVID-19

Abbreviations: DAD = Diffuse Alveolar Damage.

Bryce et al., 2021; Bian and The COVID-19 Pathology Team, 2020). Diffuse Alveolar Damage (DAD), pulmonary thromboembolism, and pneumonia were the most prevalent autopsy findings, respectively.

Pulmonary thromboembolism due to SARS-CoV-2 was the most common cause of death in our series. It is now known that thrombosis in decedents with SARS-CoV-2 infection is part of the microangiopathic changes observed in COVID-19 (Maiese et al., 2020). We observed that four patients on anticoagulant therapy (enoxaparin) had died of pulmonary thromboembolism with disseminated thrombosis. Further studies are required to establish the reason why coagulopathy occurs despite anticoagulant preventive therapy. Thromboembolic disease is not uncommon in Zambia at autopsy, however the occurrence of deep vein thrombosis, pulmonary embolism and microthrombi in smaller pulmonary vessels should alert the physician to the possibility of COVID-19 and perform a SARS-CoV-PCR test to confirm or rule out COVID-19.

Nonetheless, It is important to emphasize that deep vein thrombosis and pulmonary embolism, and microthrombi in the small pulmonary vessels should alert clinicians that they may be pathognomonic signs of COVID-19, especially in SSA.

DAD due to SARS-CoV-2 was the second most common cause of death. SARS-CoV-2 enters the epithelial lining cells of the respiratory tract using the ACE2 enzyme as a viral receptor leading to DAD and eventually death (Mohanty et al., 2020). Pneumonia due to COVID-19 was the third most common cause of death. Patients admitted to the hospital were empirically treated with ceftriaxone and azithromycin (COVID-19 rapid guideline, 2020) to cover the possibility of bacterial pneumonia. Pneumonia due to SARS-CoV-2 was a common finding and thus empiric use of antibiotics may not be appropriate in these cases and needs further study and discussion.

Autopsies provide the most accurate data about cause of death, but remain operationally difficult and expensive. The World Health Organisation (WHO) recommended that autopsy rooms must be adequately ventilated (World Health Organization, 2020). Maximal infection prevention should be provided using full-body suits with air-purifying respirators (Baj et al., 2021; Liang et al., 2020). Autopsies were conducted in a mortuary with inadequate ventilation, and 2 cases were conducted in a well-ventilated mortuary. Although there is no evidence of transmission of SARS-CoV-2 from decedents, we washed the bodies with chlorine and used standard personal protective equipment during the autopsy (World Health Organization, 2020; Baj et al., 2021; Liang et al., 2020). The autopsy team members were tested for COVID-19 every two months (or when they became symptomatic) by reverse transcriptase-polymerase chain reaction (RT-PCR) on nasopharyngeal swabs. None of our pathologists or the assistants have tested positive for SARS-CoV-2 indicating that optimal infection control practice reduces risk of acquiring SARS-CoV-2 during autopsies.

There are several limitations to our study which are inherent to all autopsy studies, including selection bias and the relatively small numbers. However, our study illustrates that autopsies during the COVID-19 era are possible to conduct on SARS-CoV-2 infected subjects in Zambia. There is a need to revive clinical and research autopsies throughout sub-Saharan African countries (Mawalla, 2020; Mucheleng'anga and Himwaze, 2020; Bruce-Brand et al., 2020; Mudenda et al., 2020; Rampatige and Gilks, 2015; Barth et al., 2020; Yi et al., 2020) to add to the provisional information provided by our study. Further autopsies with accurate data are required to conjure a more comprehensive picture of the pathogenesis and impact of COVID-19 in SSA.

Our autopsy study serves as a pivotal starting point for conversations around future autopsy studies in SSA and

worldwide, to further understand factors which influence expression of clinical spectrum of disease and the impact on other co-morbidities such as HIV, tuberculosis, malaria, hypertension, and diabetes. The COVID-19 pandemic serves as a reminder to authorities responsible for health care and policy formulation to invest more into autopsy pathology services (Yi et al., 2020). Furthermore, with new SARS-CoV-2 variants in circulation and decedents dying after re-infection, sequencing data will need to be aligned to autopsy studies to better understand the full scope of COVID-19 in Zambia and the rest of Africa. Further investments are required to improve the accuracy of diagnosis, recording and reporting of all causes of death and to ascertain the generic validity of our findings, An international COVID-19 postmortem platform is required for gathering uniform autopsy and postmortem data, and for enabling comparisons between countries.

Conflicts of interest

All authors declare no conflict of interest.

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References

- Africa CDC - Coronavirus Disease 2019 (COVID-19). Latest updates on the COVID-19 crisis from Africa CDC. <https://africacdc.org/COVID-19/> -accessed June 4th, 2021.
- Baj J, Ciesielka M, Buszewicz G, Maciejewski R, Budzyńska B, Listos P, Teresiński G, et al. COVID-19 in the autopsy room—requirements, safety, recommendations and pathological findings. *Forensic Sci Med Pathol* 2021;17:101–13.
- Bangboye EL, Omiye JA, Afolaranmi OJ, et al. COVID-19 Pandemic: Is Africa Different?. *J Natl Med Assoc* 2020; S0027-9684(20)30345-X.pmid:33153755.
- Barth RF, Xu X, Buja LM. A Call to Action: The Need for Autopsies to Determine the Full Extent of Organ Involvement Associated With COVID-19. *Chest* 2020;158 (July (1)):43–4.
- Bian Xiu-Wu, The COVID-19 Pathology Team. Autopsy of COVID-19 patients in China. *National Science Review* 2020;7(9)1414–8, doi:<http://dx.doi.org/10.1093/nsr/nwaa123> -Accessed on 10th April, 2021.
- Bruce-Brand C, Allwood BW, Koegelenberg CFN, Lalla U, Louw E, Diacon AH, et al. Postmortem lung biopsies from four patients with COVID-19 at a tertiary hospital in Cape Town, South Africa. *S Afr Med J* 2020;110(October (12))1195–200, doi:<http://dx.doi.org/10.7196/SAMJ.2020.v110i12.15290> PMID: 33403965.
- Bryce C, Grimes Z, Pujadas E, et al. Pathophysiology of SARS-CoV-2: the Mount Sinai COVID-19 autopsy experience. *Mod Pathol* 2021;(April)1–12, doi:<http://dx.doi.org/10.1038/s41379-021-00793-y> Epub ahead of print. PMID: 33795830.
- COVID CONTINENT HUB, Interim Clinical Guidance for Management of Patients with Coronavirus Disease 2019 (COVID-19). <https://www.c19hub.io/interim-clinical-guidance-for-management-of-patients-with-coronavirus-disease-2019-COVID-19/>. -Accessed on 24/03/2021.
- COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital. London: National Institute for Health and Care Excellence (UK); 2020 (NICE Guideline, No. 173.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK566162/> -Accessed April 10th, 2021.
- Edler C, Schröder AS, Aepfelbacher M, et al. Dying with SARS-CoV-2 infection—an autopsy study of the first consecutive 80 cases in Hamburg, Germany. *Int J Legal Med* 2020;134(July (4)):1275–84.
- Falasca L, Nardacci R, Colombo D, et al. Postmortem Findings in Italian Patients With COVID-19: A Descriptive Full Autopsy Study of Cases With and Without Comorbidities. *J Infect Dis* 2020;222(11):1807–15.
- Gadi N, Wu SC, Spihlan AP, et al. What's Sex Got to Do With COVID-19? Gender-Based Differences in the Host Immune Response to Coronaviruses. *Frontiers in Immunology* 2020;11:2147, doi:<http://dx.doi.org/10.3389/fimmu.2020.02147>.
- Grant MC, Geoghegan L, Arbyn M, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One* 2020;15(6) e0234765, doi:<http://dx.doi.org/10.1371/journal.pone.0234765> PMID: 32574165; PMCID: PMC7310678.
- Griffith DM, Sharma G, Holliday CS, et al. Men and COVID-19: A Biopsychosocial Approach to Understanding Sex Differences in Mortality and Recommendations for Practice and Policy Interventions. 2020. https://www.cdc.gov/pcd/issues/2020/20_0247.htm.
- Himwaze C, Mucheleng'anga L, Siyumbwa S, et al. Prevalence of Human Immunodeficiency Virus, Hepatitis B, and Hepatitis C Viral Infections among Forensic Autopsy Cases at the University Teaching Hospital in Lusaka, Zambia. *Forensic Science International: Reports* 2020;2:100133, doi:<http://dx.doi.org/10.1016/j.fsr.2020.100133>. <https://www.sciencedirect.com/science/article/pii/S2665910720300827>.
- Index Mundi. Zambia Age structure, <https://www.indexmundi.com/zambia/age-structure.html>. Accessed on 14/03/2021.
- Khaba MC, Ngale TC, Madala N. COVID-19 in an HIV-infected patient. Lessons learned from an autopsy case. *Int J Infect Dis* 2020;101:243–6.
- Lawal Y. Africa's low COVID-19 mortality rate: A paradox?. *Int J Infect Dis* 2021;102:118–22.
- Liang T, Cai H, Chen Y, et al. Handbook of COVID-19 prevention and treatment: The First Affiliated Hospital, Zhejiang University School of Medicine, compiled according to clinical experience. 2020. <https://books.google.pl/books?id=p8dzzQEACAAJ>.
- Maiese A, Manetti AC, La Russa R, et al. Autopsy findings in COVID-19-related deaths: a literature review. *Forensic Sci Med Pathol* 2020;(October)1–18, doi: <http://dx.doi.org/10.1007/s12024-020-00310-8> Epub ahead of print. PMID: 33026628; PMCID: PMC7538370.
- Mawalla WF. The contribution of autopsy in COVID-19 pandemic: Missed opportunity in Sub-Saharan Africa. *Forensic Science International: Reports* 2020;2:100136. . ISSN 2665-9107 <https://www.sciencedirect.com/science/article/pii/S2665910720300852>.
- Mohanty SK, Satapathy A, Naidu MM, et al. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and coronavirus disease 19 (COVID-19) - anatomic pathology perspective on current knowledge. *Diagn Pathol* 2020;15(August (1)):103, doi:<http://dx.doi.org/10.1186/s13000-020-01017-8>.
- Mucheleng'anga L, Himwaze C. The role of forensic pathology in the COVID-19 pandemic in Zambia. *Forensic Science International: Reports* 2020;2:100147, doi:<http://dx.doi.org/10.1016/j.fsr.2020.100147>. . ISSN 2665-9107 <https://www.sciencedirect.com/science/article/pii/S2665910720300979>.
- Mudenda V, Malyangu E, Sayed S, et al. Addressing the shortage of pathologists in Africa: Creation of a MMed Programme in Pathology in Zambia. *Afr J Lab Med* 2020;9(1):974, doi:<http://dx.doi.org/10.4102/ajlm.v9i1.974>.
- Mulale UK, Kashamba T, Stryko J, Kyokunda LT. Fatal SARS-CoV-2 and Mycobacterium tuberculosis coinfection in an infant: insights from Botswana. *BMJ Case Rep* 2021;14(April (4))e239701, doi:<http://dx.doi.org/10.1136/bcr-2020-239701> PMID: 33883111.
- Rampatige R, Gilks CF. Autopsies and better data on causes of death in Africa. *Lancet Infect Dis* 2015;15(May (5))492–4, doi:[http://dx.doi.org/10.1016/S1473-3099\(15\)70096-4](http://dx.doi.org/10.1016/S1473-3099(15)70096-4) Epub 2015 Mar 10. PMID: 25765218.
- Ssentongo P, Heilbrunn ES, Ssentongo AE, et al. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. *Sci Rep* 2021;11(1):6283, doi:<http://dx.doi.org/10.1038/s41598-021-85359-3>.
- WHO Coronavirus dashboard 2021. <https://covid19.who.int/> -accessed June 4th, 2021.
- World Health Organisation, Zambia, <https://www.who.int/countries/zmb/> -accessed June 4th, 2021.
- World Health Organization. Infection prevention and control for the safe management of a dead body in the context of COVID-19. 2020. https://apps.who.int/iris/bitstream/handle/10665/331538/WHO-COVID-19-IPC_DBMgmt-2020.1-eng.pdf.
- Yi ES, Cecchini MJ, Bois MC. Pathologists in pursuit of the COVID-19 culprit. *Lancet Infect Dis* 2020;20(October (10))1102–3, doi:[http://dx.doi.org/10.1016/S1473-3099\(20\)30449-7](http://dx.doi.org/10.1016/S1473-3099(20)30449-7) Epub 2020 Jun 8. PMID: 32526191; PMCID: PMC7279719.