RESEARCH ARTICLE

Pathognomonic Factors Associated with COVID-19 Mortality in 100 Postmortem Completed Full Body Autopsies

Begum RA[1], Chowdhury MIB[2], Sharmin N[3]

Abstract :

Background: Because of essential epidemiologic and preventive actions, autopsies on COVID-19 dead patients have several constraints. One area of ongoing neglect and missed possibilities for COVID-19 research is correctly characterizing the pathological characteristics of COVID-19 and determining the underlying cause(s) of COVID-19 death in hospitals. **Objective:** The goal of this study was to identify the pathognomonic parameters linked with COVID-19 mortality in 100 postmortem completed body autopsies. **Materials and Methods:** An observational descriptive analysis of reports from 100 COVID-19 inpatient fatalities whose proximate cause of death was SARS-CoV-2 infection (positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction) (RT-PCR). The hospital fatalities happened in the COVID-19 isolation wards of the different government medical college hospital in Bangladesh between March 2020 and March 2021. The autopsy was chosen based on the physician's request. **Results:** Diffuse alveolar damage was detected in (45%), while emboli were identified in 36%. pneumonia was 29%, granular kidneys were 18%, disseminated thrombi was 12%, and deep venous thrombosis was 8%. The primary gross pathology and microscopic autopsy findings, as well as the cause(s) of death were pulmonary thromboembolism (46.0%), diffuse alveolar damage (DAD) (33.0%), and COVID-19 pneumonia (21.0%). **Conclusion:** COVID-19 fatalities in hospitalized decedents exhibit a wide range of gross anatomical and histological abnormalities. The primary gross pathology and microscopic autopsy findings, as well as the cause(s) of death Pulmonary thromboembolism, Diffuse Alveolar Damage (DAD), and COVID-19 pneumonia were the leading reasons of mortality.

Keywords: Pathognomonic factors, COVID-19, postmortem, autopsies.

SMAMC Journal, 2024; 10(1):43-49

Introduction:

Autopsies on COVID-19 deceased patients have many limitations due to necessary epidemiologic and preventative measures. The ongoing pandemic has caused a significant strain on healthcare systems and is being extensively studied around the world. Clinical data does not always correlate with post-mortem findings.[1] An area of continuing neglect and missed opportunities for COVID-19 research that of accurately defining the pathological features of COVID-19 and ascertaining the underlying cause(s) of death from COVID-19 in hospitals.[2,3] Whilst several reports of whole body autopsy case series and organ specific pathology have been published from China, Europe and USA[4], there is little information on postmortem examination and the pathology of COVID-19 in sub-Saharan

1. Dr. Rowsan Ara Begum, Associate Professor and Head, Department of Forensic Medicine and Toxicology, Shaheed Monsur Ali Medical College, Dhaka, Bangladesh. **(Corresponding Author) E-mail:** rowsonarawmch@gmail.com, **Phone:** 01727826562
2. Dr. Md Iqbal Bahar Chowdhury, Associate Professor, Department of Forensic Medicine and Toxicology, Shaheed Monsur Ali Medical College, Dhaka, Bangladesh
3. Dr. Nazia Sharmin, Assistant Professor, Department of Forensic Medicine and Toxicology, Shaheed Monsur Ali Medical College, Dhaka.

Africa (SSA). There remains scanty information on the actual causes of death and pathogenesis of COVID-19 from the African continent[5]. Autopsy findings are crucial to gaining a better understanding of how this infection affects the human body, similar to how these findings are important to understanding other infectious diseases.[6,7,8]. Histopathological evidence of damage to the surface layers of airway epithelial cells and massive lung involvement with diffuse alveolar damage (DAD) and microvascular thrombi have been reported.[9,10] The pathological characteristics of COVID-19 pulmonary changes have been previously addressed, yet most studies present a small number of cases.[11,12] Several reports of pathological characteristics of extrapulmonary manifestations have also been reported.[13,14] The goal of our study was to assess the pathological features of COVID-19-related deaths during autopsy.

Materials and Methods :

We conducted an observational descriptive study of reports of 100 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 different government medical college hospital in Bangladesh. Selection for autopsy was based according to request by physician.

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 different government hospital in Bangladesh 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 was 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. Data on the decedents' demographics, history, circumstances, autopsy findings, and opinion of the cause of death was entered and analyzed using SPSS version 23. The variables were grouped and presented as frequencies and percentages.

Results:

Out of 100 patients, majority 28(38.0%) patients belonged to age group 51-60 years. Mean age was found 52.5±12.0 years. Male patients was found in 61(61.0%) and female was 39(39.0%) (Table-1). Regarding symptoms at admission, majority 91(91.0%) patients had fever, 79(79.0%) had difficulty breathing, 67(67.0%) had cough, 21(21.0%) had headache, 15(15.0%) had taste loss, 11(11.0%) had smell loss, 13(13.0%) had general body weakness, 8(8.0%) had vomiting, 7(7.0%) had diarrhea and 3(3.0%) had abdominal pain (Table-2). Regarding co-morbidities at admission, it was observed that 5(5.0%) had HIV positive, 21(21.0%) had hypertension, 7(7.0%) had tuberculosis, 17(17.0%) had diabetes, 2(2.0%) had pregnancy, 3(3.0%) had cerebral vascular disease, 2(2.0%) had malaria, 1(1.0%) had atherosclerotic heart disease, 1(1.0%) had paraquat toxicity and 1(1.0%) had anaemia (Table-3). Diffuse Alveolar Damage was found in 45(45.0%), emboli was 36(36.0%). Pneumonia was 29(29.0%), Granular kidneys 18(18.0%), Disseminated Thrombi 12(12.0%), Deep Venous Thrombosis 8(8.0%). The main gross pathology and microscopic autopsy findings, and cause(s) of death. The commonest causes of death were pulmonary thromboembolism (46.0%), Diffuse Alveolar Damage (DAD) (33.0%) and COVID-19 pneumonia (21.0%) (Table-4).

Table 1: Demographic characteristics of the study patients (n=100)

Parameters	Frequency	Percentage
Age group (years)		
≤30	1	1.0
31-40	5	5.0
41-50	27	27.0
51-60	38	38.0
61-70	21	21.0
>70	8	8.0
Mean±SD	52.5±12.0	
Sex		
Male	61	61.0
Female	39	39.0

Table 2: Distribution of the study patients by symptoms (n=100)

Symptoms at admission	Frequency	Percentage
Fever	91	91.0
Difficultly breathing	79	79.0
Cough	67	67.0
Headache	21	21.0
Taste loss	15	15.0
Smell loss	11	11.0
General body weakness	13	13.0
Vomiting	8	8.0
Diarrhoea	7	7.0
Abdominal pain	3	3.0

Table 3: Distribution of the study patients by co-morbidities (n=100)

Co-morbidities at admission	Frequency	Percentage
HIV positive	5	5.0
Hypertension	21	21.0
Tuberculosis	7	7.0
Diabetes	17	17.0
Pregnancy	2	2.0
Cerebral Vascular disease	3	3.0
Malaria	2	2.0
Atherosclerotic heart disease	1	1.0
Paraquat toxicity	1	1.0
Anaemia	1	1.0

Table 4: Distribution of the study patients by main autopsy findings and causes of death (n=100)

Autopsy findings	Frequency	Percentage
Diffuse Alveolar Damage	45	45.0
Emboli	36	36.0
Saddle Emboli	22	22.0
Shower Emboli	14	14.0
Pneumonia	29	29.0
Granular kidneys	18	18.0
Deep Venous Thrombosis	8	8.0
Disseminated Thrombi	12	12.0
Tuberculosis	3	3.0
Anaemia	3	3.0
Kaposi Sarcoma	2	2.0
Colorectal adenocarcinoma	1	1.0
Main Autopsy Causes of Death		
Pulmonary Thromboembolism	46	46.0
Diffuse Alveolar Damage	33	33.0
Pneumonia	21	21.0

Discussion :

In this study we observed that majority 28(38.0%) patients belonged to age group 51-60 years. Mean age was found 52.5±12.0 years. Male patients was found in 61(61.0%) and female was 39(39.0%). Himwaze et al.[15] reported mean age = 44±15.8years; age range = 19-82 years. Male was 58.8% and female was 41.4%. 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.[16-19] 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.[20] It could also due to HIV being more prevalent in people less than 55 years.[21] HIV may also play a role since it is considered a risk factor for acquiring SARS-CoV-2 infection and is associated with a higher risk of mortality from COVID-19.[22] Mikhaleva et al.[1] observed total of 100 autopsies were performed (53 females, 47 males). The mean age of the deceased patients was 70.8 years (range: 45–95 years).

Regarding symptoms at admission, majority 91 (91.0%) patients had fever, 79 (79.0%) had difficulty breathing, 67 (67.0%) had cough, 21 (21.0%) had headache, 15 (15.0%) had taste loss, 11 (11.0%) had smell loss, 13 (13.0%) had general body weakness, 8 (8.0%) had vomiting, 7 (7.0%) had diarrhea and 3 (3.0%) had abdominal pain. Himwaze et al.[15] reported 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%). As reported from autopsy studies from outside Africa[16-19], 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[23-24] and assessment of temperatures during admission.[19]

Regarding co-morbidities at admission, it was observed that 5 (5.0%) had HIV positive, 21(21.0%) had hypertension, 7 (7.0%) had tuberculosis, 17 (17.0%) had diabetes, 2 (2.0%) had pregnancy, 3 (3.0%) had cerebral vascular disease, 2(2.0%) had malaria, 1(1.0%) had atherosclerotic heart disease, 1 (1.0%) had paraquat toxicity and 1(1.0%) had anaemia. Himwaze et al.[15] reported overall, 22/29 (76%) decedents had comorbidities. Co-morbidities were present in 22/29 (76%) of decedents. Common comorbities included HIV (8/29, 27%), Hypertension (6/29, 21%) Tuberculosis (3/29, 10%), Diabetes (3/29, 10%). HIV infection and hypertension co-morbidities were common among in their study group and these comorbidities are important compared to the observations made in other autopsy studies from outside Africa.[16-19] Mikhaleva et al.[1] reported hypertensions was the most common comorbidity. 48% of patients had more than one comorbidity.Eight patients presented with malignancies: lung, breast, colon cancers, B-cell and T-cell lymphoma, cutaneous plasmacytoma (one case each), and chronic lymphocytic leukemia (two patients). Alcohol related hepatic micronodular cirrhosis was observed in three patients, one of which was diagnosed with the hepatocellular carcinoma. Hepatic steatosis without cirrhosis was noted once. Two deceased patients were diagnosed with COPD and bronchial asthma, one patient had a congenital polycystic kidney disease, and another one suffered from systemic amyloidosis with cardiac involvement.

In this study observed that Diffuse Alveolar Damage was found in 45 (45.0%), emboli was 36(36.0%). Pneumonia was 29 (29.0%), Granular kidneys 18(18.0%), Disseminated Thrombi 12 (12.0%), Deep Venous Thrombosis 8(8.0%). The main gross pathology and microscopic autopsy findings, and cause(s) of death. The commonest causes of death were pulmonary thromboembolism (46.0%), Diffuse Alveolar Damage (DAD) (33.0%) and COVID-19 pneumonia (21.0%). Himwaze et al.[15] reported the main gross pathology and microscopic autopsy findings, and cause(s) of death. 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%). 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. 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 their series. It is now known that thrombosis in decedents with SARS-CoV-2 infection is part of the microangiopathic changes observed in COVID-19.[4] They 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 of 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. 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.[25] Maximal infection prevention should be provided using full-body suits with air-purifying respirators.[26,27] 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, they washed the bodies with chlorine and used standard personal protective equipment during the autopsy.[25-27] 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. Mikhaleva et al.[1] reported the exudative and productive phases of diffuse alveolar damage (mixed DAD phase) with signs of local interalveolar edema, hyaline membranes, desquamated alveolar epithelium combined with fibrin, alveolar fibroblastic component, alveolar and bronchial squamous cell metaplasia were found in 36 autopsy cases. In 31 cases, microscopic findings of bronchopneumonia and in 3 cases viral-bacterial-mycotic pneumonia were identified, and it was proven by microbiological evaluation. In 1 case only a bacterial aspiration bronchopneumonia with no DAD criteria was identified, despite positive PCR testing.

Conclusion:

COVID-19 fatalities in hospitalized decedents exhibit a wide range of gross anatomical and histological abnormalities. Diffuse Alveolar Damage was seen, as well as emboli. Pneumonia, Granular Kidneys, Disseminated Thrombi, and Deep Venous Thrombosis are all possible diagnoses. The primary gross pathology and microscopic autopsy findings, as well as the cause(s) of death Pulmonary thromboembolism, Diffuse Alveolar Damage (DAD), and COVID-19 pneumonia were the leading reasons of mortality.

References:

1. Mikhaleva LM, Cherniaev AL, Samsonova MV, Zayratyants OV, Kakturskiy LV, Vasyukova OA, Birukov AE, Kontorshchikov AS, Sorokina AV, Sinelnikov MY. Pathological features in 100 deceased patients with COVID-19 in correlation with clinical and laboratory data. Pathology and Oncology Research. 2021; 27.
2. Bamgboye EL, Omiye JA, Afolaranmi OJ, Davids MR, Tannor EK, Wadee S, Niang A, Were A, Naicker S. COVID-19 Pandemic: Is Africa Different?. J Natl Med Assoc 2020; S0027-9684(20)30345-X.
3. 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.
4. Maiese A, Manetti AC, La Russa R, Di Paolo M, Turillazzi E, Frati P, Fineschi V. Autopsy findings in COVID-19-related deaths: a literature review. Forensic Science, Medicine and Pathology. 2021;17(2):279-96.

5. Mulale UK, Kashamba T, Strysko J, Kyokunda LT. Fatal SARS-CoV-2 and Mycobacterium tuberculosis coinfection in an infant: insights from Botswana. BMJ Case Rep 2021; e239701.
6. Franks TJ, Chong PY, Chui P, Galvin JR, Lourens RM, Reid AH, Selbs E, Mcevoy CP, Hayden CD, Fukuoka J, Taubenberger JK. Lung pathology of severe acute respiratory syndrome (SARS): a study of 8 autopsy cases from Singapore. Human pathology. 2003;34(8):743-8.
7. Sheng ZM, Chertow DS, Ambroggio X, McCall S, Przygodzki RM, Cunningham RE, Maximova OA, Kash JC, Morens DM, Taubenberger JK. Autopsy series of 68 cases dying before and during the 1918 influenza pandemic peak. Proceedings of the National Academy of Sciences. 2011;108(39):16416-21.
8. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet respiratory medicine. 2020;8(4):420-2.
9. Zhang H, Zhou P, Wei Y, Yue H, Wang Y, Hu M, Zhang S, Cao T, Yang C, Li M, Guo G. Histopathologic changes and SARS-CoV-2 immunostaining in the lung of a patient with COVID-19. Annals of internal medicine. 2020;172(9):629-32.
10. Calabrese F, Fortarezza F, Fortarezza F, Hofman P, Kern I, Panizo A, and Lunardi F. Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNECH). Virchows archive, 2020: 1–7.
11. Batah SS and Fabro AT. Pulmonary pathology of ARDS in COVID-19: A pathological review for clinicians. Respir Med. 2020:106239.
12. Barton L. M, Duval E. J, Stroberg E, Ghosh S, and Mukhopadhyay S. COVID-19 Autopsies, Oklahoma, USA. Am J Clin Pathol. 2020;153(6):725–33.
13. Hanley B, Lucas S. B, Youd E, Swift B, and Osborn M. Autopsy in suspected COVID-19 cases. J Clin Pathol. 2020; 73:239–42.
14. Mauad T, Hajjar L. A, Callegari G. D, da Silva L. F. F, Schout D, Galas F. R. B. G, et al. Lung pathology in fatal novel human influenza A (H1N1) infection. Am J Respir Crit Care Med. 2010; 181(1):72–9.
15. Himwaze CM, Telendiy V, Maate F, Mupeta S, Chitalu C, Chanda D, Julius P, Mumba C, Marimo C, Hamukale A, Mulenga L. Post-mortem examination of hospital inpatient COVID-19 deaths in Lusaka, Zambia-a descriptive whole-body autopsy series. International Journal of Infectious Diseases. 2021; 108:363-9.
16. Edler C, Schröder AS, Aepfelbacher M, Fitzek A, Heinemann A, Heinrich F, Klein A, Langenwalder F, Lütgehetmann M, Meißner K, Püschel K. Dying with SARS-CoV-2 infection—an autopsy study of the first consecutive 80 cases in Hamburg, Germany. International journal of legal medicine. 2020;134(4):1275-84.
17. Falasca L, Nardacci R, Colombo D, Lalle E, Di Caro A, Nicastri E, Antinori A, Petrosillo N, Marchioni L, Biava G, D'Offizi G. Postmortem findings in Italian patients with COVID-19: a descriptive full autopsy study of cases with and without comorbidities. The Journal of infectious diseases. 2020; 222(11):1807-15.
18. Bryce C, Grimes Z, Pujadas E, Ahuja S, Beasley MB, Albrecht R, Hernandez T, Stock A, Zhao Z, AlRasheed MR, Chen J. Pathophysiology of SARS-CoV-2: the Mount Sinai COVID-19 autopsy experience. Modern Pathology. 2021; 34(8):1456-67.
19. Bian Xiu-Wu, The COVID-19 Pathology Team. Autopsy of COVID-19 patients in China. National Science Review 2020;7(9)1414–8.
20. Index Mundi, Zambia Age structure, https://www.-indexmundi.com/zambia/age_structure. html. Accessed on 14/03/2021.
21. Himwaze C, Mucheleng'anga L, Siyumbwa S. 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

22. Ssentongo P, Heilbrunn ES, Ssentongo AE, Advani S, Chinchilli VM, Nunez JJ, Du P. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. Scientific reports. 2021;11(1):1-2.
23. COVID CONTINENT HUB, Interim Clinical Guidance for Management of Patients with Coronavirus Disease 2019 (COVID-19). https://www.c19hub.io/interimclinical-guidance-for-management-of-patients-with-coronavirus-disease-2019-COVID-19/. -Accessed on 24/03/2021.
24. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, Wade RG. 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.
25. 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-lPC_DBMgmt-2020.1-eng.pdf.
26. Baj J, Ciesielka M, Buszewicz G, Maciejewski R, Budzynska B, Listos P, Teresinski G, et al. COVID-19 in the autopsy room–requirements, safety, recommendations and pathological findings. Forensic Sci Med Pathol 2021;17:101–13
27. Liang T, Cai H, Chen Y. Handbook of COVID-19 prevention and treatment: The First Affiliated Hospital, Zhejiang University School of Medicine, complied according to clinical experience. 2020. https://books.google.pl/books? id=p8dzzQEACAAJ.