



## Case Report

# Lassa fever coinfection with COVID-19 among health care workers: Report of two cases

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## ABSTRACT

Lassa fever (LF) coinfection with hepatitis B and HIV has been reported among hospitalized patients in Southwest Nigeria and HIV patients coinfecting with COVID-19 have been described among hospitalized patients in North Central Nigeria, no study has reported cases of coinfection of Lassa disease and COVID-19 among health care workers (HCWs) worldwide. A case report of two HCWs who were infected with both LF virus and SARS-CoV-2 virus at same time and were successfully managed without any sequelae. Both cases presented with typical signs of LF with COVID-19 suspected, they were promptly diagnosed with positive outcomes after treatment. While case 1 became negative for LF virus and SARS-CoV-2 after 6 and 30 days, respectively, case 2 became negative for both viruses after 14 and 32 days, respectively. The diagnosis of LF-COVID-19 coinfection in HCWs is a frightening dimension to the health risks faced by HCWs, therefore, HCWs now more than ever before want to know what comes next and how safe is the practice of medicine.

**Keywords:** Lassa fever, COVID-19, Health care workers, Federal Medical Centre Owo, Ribavirin

## INTRODUCTION

Lassa fever (LF) is a viral hemorrhagic disease caused by the Lassa virus – a single-stranded RNA virus of *Arenaviridae* family. It is a febrile infectious disease and was first described in Nigeria in 1969.<sup>[1]</sup> The primary mode of transmission is through exposure to the excreta, urine, or saliva of infected multimammate rodents. However, secondary human-to-human transmission has been reported and can occur through direct contact with the blood or bodily fluids of infected patients and thus a risk for health care workers (HCWs) involved in caring for LF patients.<sup>[1]</sup> For several years, LF has been known to cause severe infections and deaths of HCWs who are involved in treating and managing infected patients.<sup>[2]</sup> This has been attributed to inadequate adherence to infection prevention and control practices including lack of use, non-adherence, or partial use of personal protective equipment during provision of care to infected patients.<sup>[3]</sup> Most nosocomial transmissions are usually due to poor pathogen containment such as non or poor application of barrier nursing, ineffective sterilization, needle pricks, and direct contact with infected blood and blood products during clinical procedures.<sup>[3,4]</sup> The 2020 LF situation report Epi week 51 from the Nigeria Centre for Disease Control (NCDC) reported that 4.1% (48) of the total confirmed (1175) cases in Nigeria were HCWs from 13 states.<sup>[5]</sup>

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The coronavirus disease (COVID-19) is a potentially severe acute respiratory infection caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>[6]</sup> According to the World Health Organization-China joint mission on coronavirus, the virus was first isolated on December 30, 2019, from a patient with pneumonia of unknown etiology.<sup>[7]</sup> COVID-19 is the third coronavirus that is said to be highly pathogenic in humans after the SARS and Middle East respiratory syndrome coronaviruses that have emerged in the past 20 years.<sup>[8]</sup> The first case of COVID-19 in Nigeria was confirmed on the February 27, 2020, and as at April 21, 2021, the NCDC had 164,488 cases with 2061 deaths.<sup>[9]</sup> The virus has an incubation period that ranges from 1 to 14 days. Transmission occurs through close contact with respiratory droplets produced when an infected individual exhales, sneezes, talks, coughs, or aerosols generated during medical procedures or more rarely, through contact with fomites.<sup>[10,11]</sup> SARS-CoV-2 seropositivity in asymptomatic frontline health workers in Ibadan, Nigeria, has been reported to be 45%, despite having no symptoms and providing routine services to patients presenting with a myriad of clinical conditions.<sup>[12]</sup>

In the past 3–5 years, Ondo State in the Southwest part of Nigeria has consistently recorded high morbidity and mortality from LF. Since March 2020, COVID-19 and LF infections are occurring concurrently in Ondo State as the state records the highest burden of LF cases in Nigeria and the eleventh highest for COVID-19.<sup>[5,9]</sup> The Infection Control and Research Centre (ICRC) of the Federal Medical Centre Owo is the main tertiary institution managing both viral infections in the state. Therefore, HCWs in this institution experience high-risk exposures to both infections. Although reports of HIV patients coinfecting with COVID-19 have been described among hospitalized patients in North Central Nigeria<sup>[13]</sup> and LF cases coinfecting with hepatitis B and HIV among hospitalized patients in Southwest Nigeria,<sup>[14]</sup> no study has reported cases of coinfection of Lassa virus and SARS-CoV-2. This study presents a description of two cases of LF-COVID-19 coinfection admitted at the Federal Medical Centre Owo and aims to provide an understanding of the clinical course and outcomes of HCWs affected by these viruses concurrently. The diagnosis of the cases was done using the Quantitative PCR machine, Model Rotor-Gene Q, S/N RO516117, Qiagen Hilden, Germany, manufactured in Malaysia.

## CASE 1

A.A. was a 40-year medical doctor that presented to the hospital with complaints of headache, joint pains, and fever which had lasted for 3 days. Headache was generalized and throbbing. There was no associated history of photophobia, neck stiffness, or neck pains. Joint pain was generalized. Fever was acute in onset, high grade (38.9°C) with associated history of chills and rigor. No history of cough, sore throat or difficulty with breathing. No history of vomiting, diarrhea anosmia or ageusia. No history of hematuria or bleeding from any parts of his body. He had no known underlying comorbidity (hypertension, diabetes, or asthma). A.A works at the LF treatment center and the wife, a medical doctor was managed as a confirmed case of COVID-19, 3 weeks before presentation. Medical and social history was not contributory. Physical examination was not remarkable. An impression of LF disease to keep in view COVID-19 was made. Blood and nasal, as well as throat samples, were taken for LF and COVID-19 screening, respectively, with results coming out positive for both LF and COVID-19 infections.

LF CT values – G: 35.9; L: 38.82

COVID-19 CT values – N-gene 17.20; ORF gene 18.55

He was admitted into the infection control ward of ICRC following the outcome of the result and was commenced on parenteral ribavirin (National regimen),<sup>[15]</sup> broad-spectrum antibiotics (ceftriaxone), intravenous fluid, Tab. Vitamin D 25 µg daily, Vitamin C 1 g daily, Tab. zinc 100 mg bd, and multivitamin TABLETS. Patient's condition remained stable all through the period of admission.

Baseline investigations done (RBS; urinalysis; FBC; E/U/Cr; and LFT) were essentially normal:

### FBC

E/U/Cr and LFT

RBS: 101 mg/dl

Urinalysis: Normal

His blood sample was taken for repeat LF PCR analysis 6 days after admission and result was negative. He was discharged home to continue self-isolation and home management for COVID-19. He was negative for COVID-19 after 30 days.

WBC	RBC	HB	HCT	MCV	MCH	MCHC	PLT	LYM	MON	NEUT	RDW	PDW
5.0×10 <sup>3</sup> /UL	5.02×10 <sup>3</sup> /UL	15.2 g/dl	42.2%	84.2 fl	30.2 pg	36.0 g/dl	166×10 <sup>3</sup> /UL	29.8%	10.3%	59.9%	38.9 fl	15.1fl

Na	K	HCO <sub>3</sub>	CL	Ca	Urea	Cre	ALP	ALT	AST	TBIL	ALB	TB
(mmole/l)	(mmole/l)	(mmole/l)	(mmole/l)	(mmole/l)	(mmole/l)	(µmole/l)	(IU/L)	(IU/L)	(IU/L)	(µmole/l)	(g/l)	(g/dl)
137	4.1	27	108	2.6	4.0	95	32	18	21	23.8	34	66

## CASE 2

O.A; a 32-year-old female nurse presented to the hospital with complaints of fever and generalized body weakness of 6 days duration, vomiting of four episodes, and passage of watery stool of three episodes. Despite completion of antimalarial treatment and ongoing parenteral antibiotics, there was no appreciable improvement in her condition. Her physical examination revealed, temperature of 36.6°C, respiratory rate of 24 Cpm, pulse rate: 68 bpm, blood pressure of 116/65 mmHg, and peripheral capillary oxygen saturation (SPO<sub>2</sub>): 98%. She was conscious and alert.

A diagnosis of malaria fever and septicemic illness (gastrointestinal focus) to rule out LF was made and was admitted into the general ward.

Blood sample for Lassa PCR investigation was done and result was positive with a cycle threshold of G: 29.67; L: 29.49.

She was transferred to the infection control ward of ICRC and commenced parenteral ribavirin (National regimen),<sup>[15]</sup> in addition to antibiotics (ceftriaxone and metronidazole), antiemetic (promethazine), and anti-diarrhea (loperamide).

### Baseline investigation results

RBS: 94 mg/dl

Urinalysis: Glucose: +, Blood: ++, Protein: Negative, SG: 6.0, pH: 1.0. Other parameters on urinalysis were normal.

FBC

E/U/Cr

MP (RDT): Negative

Serology (RVS; anti-HCV; HBsAg; VDRL): Non-reactive

She was subsequently noticed to be having intermittent cough that was non-productive, not associated with sore throat, chest pains, or difficulty with breathing. A suspicion of COVID-19 was made and sample collected for analysis. COVID-19 result was positive with cycle threshold (Ct) of N: 35.5; ORF: 36.01) and she was placed on Tab. zinc 100 mg bd, Vitamin C 1 g daily, Vitamin D 25 µg daily, and multivitamin tablets. She made progressive improvements in her condition and was discharged home after completion of 10 days regimen of intravenous ribavirin. She was discharged home to continue self-isolation and home management for COVID-19. She was negative for LF after 32 days and COVID-19 after 14 days.

## DISCUSSION

Occupationally acquired LF and COVID-19 have become serious public health challenges in Nigeria. During the 2018 epidemic of LF, high morbidity and mortality were recorded among HCWs with case fatality rates as high as 31.6%.<sup>[16]</sup> The COVID-19 pandemic has recently entered a new phase with many West African countries recording their highest figures of new infections and COVID-19-related deaths. As in the case of LF, HCWs have suffered disproportionately with an estimated global average health worker infection rate of 15% (WHO, 2020) and 20–30% in Nigeria based on street estimates.

The diagnosis of LF-COVID-19 coinfection in HCWs is, therefore, a frightening dimension to the health risks faced by HCWs. Such diagnosis is not only psychologically traumatic to the patients but also a management conundrum to the physician. Aside this, it is important to bear in mind the possibility of increase severity of disease in those who may be dually infected with the two viruses. Although it does not appear to confer a particularly worse outcome in our two cases, we must bear in mind that they are relatively of younger age group without significant comorbid conditions. This may not have been the case if these factors were different. It is also very difficult based on symptoms or signs alone to suspect both conditions as we see in the index case who had no respiratory symptoms and the fever could have been due to other infective agents. However, in view of the endemicity of LF and the current COVID-19 pandemic, a high index of suspicion is needed to ensure prompt investigation using standard PCR for diagnosis. Studies have demonstrated an inverse relationship between PCR Ct and viremia and clinical outcome. This implies that the higher the Ct values, the lower the viremia and severity of clinical features for both SARS-CoV-2 and Lassa virus. The limits of diagnosis are based on the primer and virus strain used.<sup>[17,18]</sup> In this study, both patients who had been placed on ribavirin for 6 and 10 days, respectively, recovered without any sequelae. Although the Ct values for Lassa were relatively high for the first case, the Ct value for COVID-19 in contrast to the second case was low but did not reflect the severity of symptoms as the patient had no respiratory symptoms and recovered with no sequelae. The use of ribavirin in the treatment of both cases and successful outcome may serve as a reason for the entry of ribavirin in the clinical trial for the treatment of COVID-19.<sup>[19,20]</sup>

WBC	RBC	HB	HCT	MCV	MCH	MCHC	PLT	LYM	MON	NEUT	RDW	PDW
2.1×10 <sup>3</sup> /UL	4.7×10 <sup>6</sup> /UL	12.5 g/dl	35%	47.9 fl	26.5 pg	35.5 g/dl	204×10 <sup>3</sup> /UL	33.2%	5.3%	61.5%	36.9 fl	10.3 fl

Na (mmole/l)	K (mmole/l)	HCO <sub>3</sub> (mmole/l)	CL (mmole/l)	Ca (mmole/l)	Urea (mmole/l)	Cre (µmole/l)
133	3.8	26	105	2.4	3.2	62

HCWs now more than ever before want to know what comes next: Will they be safe? What has changed or will change in their organization in response to the crisis? What can they expect from the future? As the number of HCW infections and deaths rises around the world, it is becoming increasingly important to understand the driving forces behind occupational acquisition of COVID-19. Although there are varied factors influencing the risk for occupational acquisition of both LF and SARS-CoV-2 infections, depending on which part of the globe the health worker is practicing, and many schools of thought as to how best to protect HCWs, one thing that is clearly incontrovertible however is the fact that implementing adequate health and safety measures and providing multiple layers of protection in the work environment is no longer negotiable. The health sector must deliberately create and promote a supportive work environment for all her employees if the business continuity of health services is to be sustained at these challenging times.

“Health workers have always been, unfortunately, the mine’s canary in epidemic response, particularly in areas that don’t have strong surveillance systems.”

- Michael J. Ryan, Chief Executive Director of the WHO Health Emergencies Program

Every effective health and safety program aimed at protecting HCWs in the COVID-19 era must rely on an integrated approach based on several layers and with the full participation of workers and their employees. The Legge’s aphorism still holds true:

“*Unless and until the employer has done everything and everything means a good deal – the work man can do next to nothing to protect himself, although he is naturally willing enough to protect himself; although he is naturally willing enough to do his share*” (Sir Thomas Morrison Legge [1863–1932], *first aphorism*).

In the face of progressively increasing morbidity and mortality among HCWs due to occupational acquisition of LF and SARS-CoV-2, a disregard to the health and safety of HCWs will result in a critical mass of these workers staying away from work due to ill health (or death) and a looming disaster for a health system that is already very fragile from years of neglect and poor financing.

## CONCLUSION

The diagnosis of LF-COVID-19 coinfection in HCWs is a frightening dimension to the health risks faced by HCWs. Therefore, HCWs now more than ever before want to know what comes next and how safe is the practice of medicine in the face of increasing epidemics.

## Ethical consideration

Ethical clearance/approval was obtained from the Institutional Health Research Ethical Committee of the Federal Medical Centre, Owo, with reference number FMC/OW/380/VOL.CVII/106. Informed consent was obtained from the two HCWs involved and documented.

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## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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## Conflicts of interest

There are no conflicts of interest.

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