

SHORT REPORT

Lassa fever in pregnancy: Report of two maternal deaths in a tertiary center in the middle-belt region of Nigeria

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Abstract

Lassa fever is endemic in West Africa, with an estimated 300,000 to 500,000 infections occurring annually and approximately 5,000 deaths. Two Lassa fever cases in pregnancy with maternal and fetal complications were presented. The age range was 20 to 30 years and the range of parity was 1 to 3. The duration of symptoms was 13 to 14 days. Clinical presentation and complications common to the two cases were fever, abnormal bleeding, cough/sore throat, anaemia, IUFD/Stillbirth, and maternal deaths. Others are vomiting, restlessness/confusion, hypotension and thrombocytopenia. Major challenges encountered are late presentation, delay in confirming diagnosis and instituting definitive treatment, limited facility, and the impact of traditional and religious factors in safe burial for Lassa fever cases. In resource-constrained settings; diagnosis, treatment and surveillance for Lassa fever may be challenging. Early clinical suspicion and appropriate case management are critical for good reproductive outcome. (*Afr J Reprod Health* 2022; 26[2]: 137-143).

Keywords: Lassa fever, haemorrhagic fever, infection prevention, pregnancy outcome

Résumé

La fièvre de Lassa est endémique en Afrique de l'Ouest, avec environ 300 000 à 500 000 infections par an et environ 5 000 décès. Deux cas de fièvre de Lassa au cours d'une grossesse avec complications maternelles et fœtales ont été présentés. La tranche d'âge était de 20 à 30 ans en moyenne et la tranche de parité était de 1 à 3. La durée des symptômes était de 13 à 14 jours. La présentation clinique et les complications communes aux deux cas étaient la fièvre, les saignements anormaux, la toux/le mal de gorge, l'anémie, le DIU/la mortinaissance et les décès maternels. D'autres sont les vomissements, l'agitation/la confusion, l'hypotension et la thrombocytopénie. Les principaux défis rencontrés sont la présentation tardive, le retard dans la confirmation du diagnostic et l'instauration du traitement définitif, les installations limitées et l'impact des facteurs traditionnels et religieux sur l'inhumation en toute sécurité des cas de fièvre de Lassa. Dans des environnements à ressources limitées ; le diagnostic, le traitement et la surveillance de la fièvre de Lassa peuvent être difficiles. Une suspicion clinique précoce et une prise en charge appropriée des cas sont essentielles pour un bon résultat reproductif. (*Afr J Reprod Health* 2022; 26[2]: 137-143).

Mots-clés: Fièvre de Lassa, fièvre hémorragique, prévention des infections, issue de la grossesse

Introduction

Lassa fever, a form of viral haemorrhagic fever caused by the Lassa virus, is endemic in West Africa¹. The virus was first identified in 1969 when two missionary nurses died from complications of the disease in the town of Lassa in Nigeria^{2,3}. Lassa virus is spread by a rodent called *Mastomys natalensis*, common in West and East Africa. An

estimated 300,000 to 500,000 infections occur annually, with approximately 5,000 deaths²⁻⁴.

Viral transmission can occur through contact with the infected rodent, consumption of food products contaminated by urine or droppings of the infected rodent, aerosol, or airborne transmission via tiny particles in the air contaminated with infected excretions, and by human-to-human transmission when a person is

exposed to body fluids, excretions, and tissue of another infected person³.

Lassa fever in pregnancy is associated with high maternal and foetal morbidity and mortality due to high viral concentrations in the maternal blood, placenta, and fetal tissue^{1, 5, 6}. Good maternal outcome has been previously documented^{5, 7}. In a prospective study of maternal and fetal outcomes in acute Lassa fever infection during pregnancy, 71% of cases were complicated by spontaneous abortion, and the overall fetal and neonatal death rates were 87% and 75%, respectively⁶. The overall maternal death rate was 21% compared to 13% in non-pregnant women; the death rate was higher (30%) in the third trimester of pregnancy⁶. A recent systematic review and meta-analysis of Lassa fever in pregnancy found a threefold increased risk of maternal death than non-pregnant women⁸.

In Lassa fever management, a high index of clinical suspicion is essential for early detection, especially in pregnancy, where symptoms can mimic pregnancy complications. The most widely used confirmatory test is the Reverse transcription-polymerase chain reaction (RT-PCR)⁸⁻¹⁰. Ancillary investigations are carried out as part of supportive care and for monitoring of response to care. The drug of choice for the treatment of Lassa fever is IV Ribavirin, even though there is currently no conclusive evidence to support the efficacy of Ribavirin in managing pregnant women with Lassa fever⁸⁻¹⁰.

The situation in Kogi State and Nigeria in the first quarter of 2020

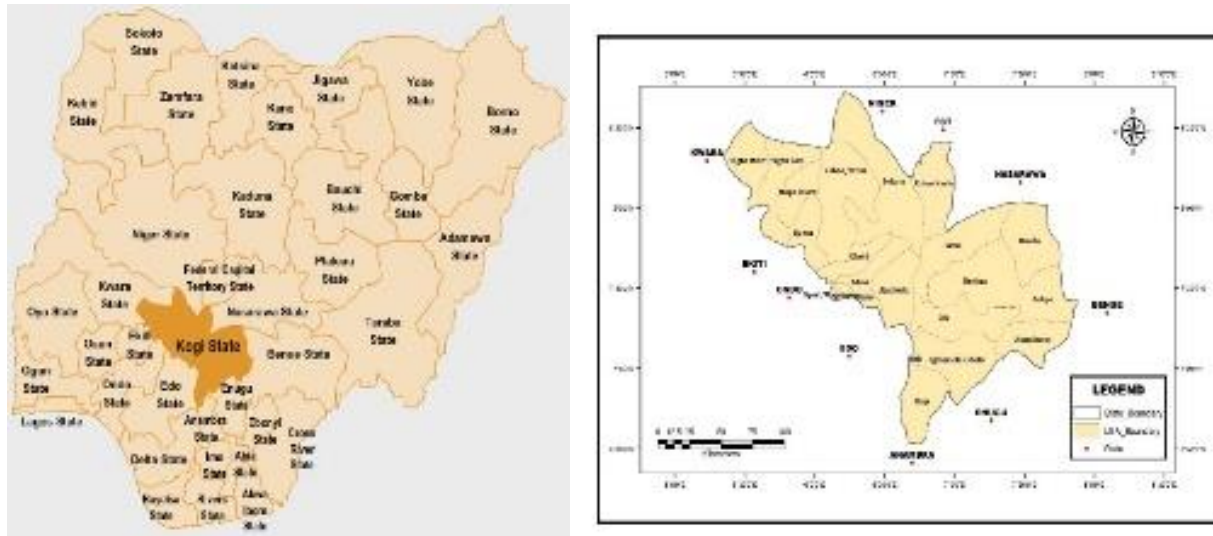
In the first quarter of 2020 (1st January to 29th March), the Lassa fever outbreak statistics for Nigeria revealed total deaths/confirmed cases of (185/951) while in Kogi State it was (11/28), given a case fatality rate (CFR) of 19.5% and 39.3% respectively (Figures 1, 2 & 3)¹¹. Idah LGA had the highest number of cases (10) followed by Okene LGA (6). This is probably because of the population density and the farming activities of these two LGA's which increases the risk of encountering the rodent *Mastomys natalensis* and their excreta in the houses thereby increasing Lassa fever cases. We reviewed two fatal cases of Lassa fever infection in pregnancy that occurred in our facility within the same period.

Description of cases

This is a short report of two confirmed Lassa fever virus cases managed at the Maternity Unit of the Department of Obstetrics and Gynaecology: Federal Medical Centre Lokoja, a tertiary center in the Middle-belt region of Nigeria. The case files were obtained from the electronic hospital record, reviewed, and analysed using simple numbers, and percentages. There is a temporary isolation unit for highly infectious diseases like Lassa fever, Ebola, and COVID-19 virus. The patients were managed according to the NCDC National Guidelines for Lassa fever case management. Reverse transcriptase-polymerase chain reaction (RT-PCR) test for Lassa fever virus was performed at the national reference laboratory Gaduwa, Abuja.

Case 1

A 30-year-old trader Gravida 4 Para 3+0, 3 alive at 32 weeks and 5 days gestation, was referred from a general hospital with demographic variables and clinical presentation shown in Table 1. She received antimalaria, intravenous antibiotics, and analgesics without any improvement before referral to our centre. An assessment of severe malaria in pregnancy was made to rule out pneumonia in pregnancy. Multidisciplinary management was instituted with the physicians and haematologist when abnormal bleeding from punctured sites prompted suspicion of Lassa fever. There was no vaginal bleeding. She was admitted into the isolation ward, samples were taken for baseline investigations and RT-PCR. She had supportive treatment with fluid therapy, parenteral antibiotics, and fresh whole blood transfusion. She also had parenteral Dexamethasone 12mg 12hours apart for fetal lung maturity and regular monitoring of maternal and fetal condition was instituted with strict adherence to infection prevention practices. There was no worsening of the bleeding episode before she was referred. However, she was transferred to the national reference centre at Kogi State Specialist Hospital (KSSH) immediately RT-PCR result became positive, from where she was referred to Irrua Specialist Teaching Hospital (ISTH) due to logistic reasons at KSSH. The details of subsequent management at ISTH were not known. However, she received IV Ribavirin at ISTH but died within 24 hours.



Source: Gamers 2019, Geospatial Analysis Mapping Environmental Research Solutions Database 2019, www.gamers.com.ng. (Permission granted Tuesday 21st April 2020).
Coordinates: 7°30'N 6°42'E

Figure 1: Location Kogi State in Nigeria and its 21 Local Government Areas (LGA's)

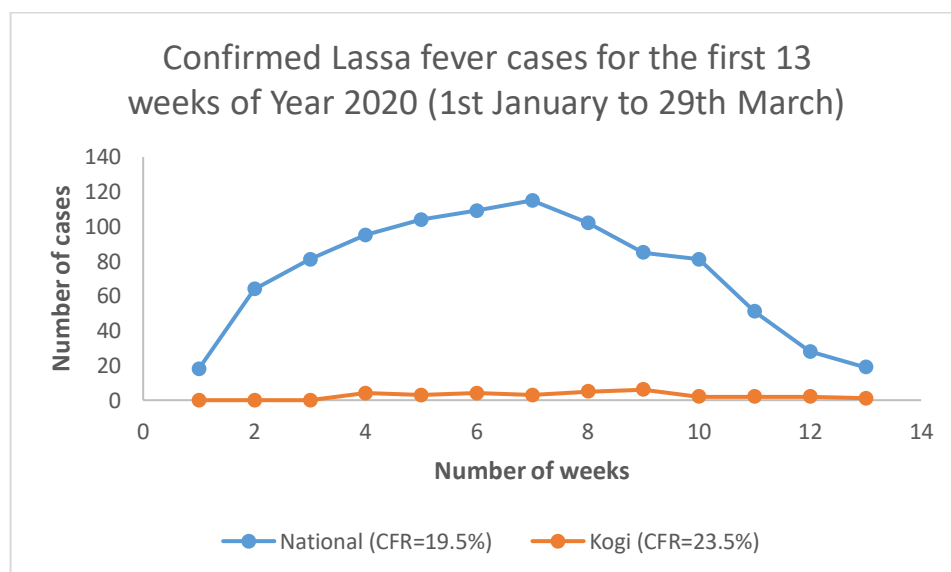


Figure 2: Confirmed Lassa fever cases in Nigeria and Kogi State for the first quarter of the year 2020

Case 2

A 20-year-old primiparous woman was referred from a general hospital with demographic variables, clinical presentation, and complications shown in Tables 1 and 2. Lassa fever was suspected due to haematemesis episodes, but there was a primary delay in seeking care. She presented at our emergency with primary PPH due to retained placenta following delivery of a macerated female

stillborn baby at home. She had supportive treatment with blood transfusion, oxygen and fluid therapy, parenteral antibiotics, and respiratory, cardiovascular, and renal monitoring. Manual removal of placenta was done. Intravenous oxytocin 10mg and oxytocin infusion was administered along with rectal misoprostol 1,000microgram and uterine massage to control vaginal bleeding. Intravenous tranexamic acid 1.0gm stat and repeated after 12hours, two doses of

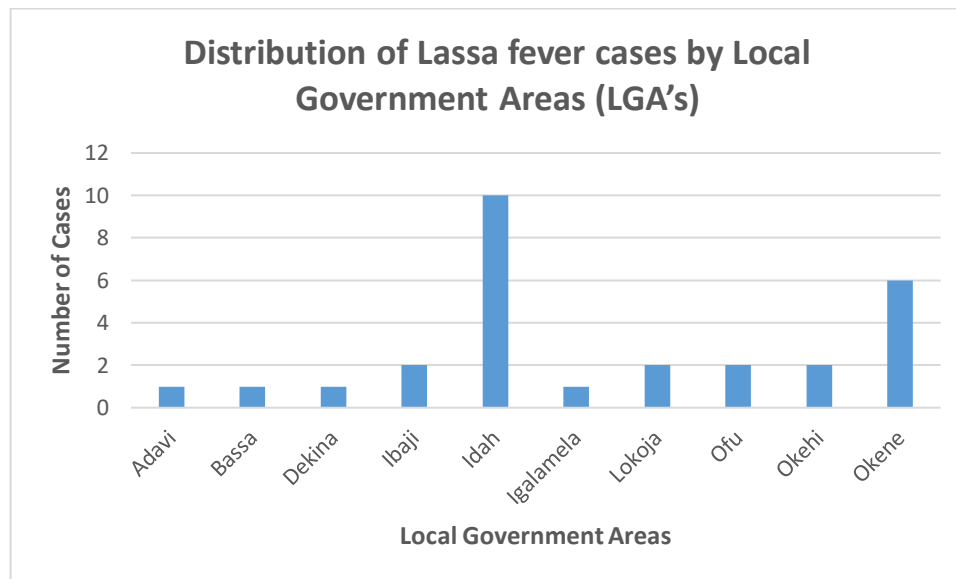


Figure 3: Distribution of Lassa fever cases by Local Government Areas (LGA's)

Table 1: Patients' demographics, clinical presentation and complications

DEMOGRAPHY AND CLINICAL PRESENTATION	Patient 1	Patient 2
Age (Years)	30	20
Parity	3 ⁺ 0	1 ⁺ 0
Onset of symptoms to presentation (days)	14	13
Fever	Yes	Yes
Vaginal bleeding	No	Yes
Bleeding from punctured sites	Yes	Yes
Vomiting	No	Yes
Haematemesis	No	Yes
Cough/Sore throat	Yes	Yes
Restlessness/confusion	No	Yes
Breast pain/tenderness	Yes	No
Hypotension	No	Yes
Fetal death/stillbirth	Yes	Yes
Maternal death	Yes	Yes

IV Etamsylate (Dicynone) 500mg 8hourly was also administered. The bleeding subsided thereafter and eventually stopped after more fresh whole blood was transfused while performing uterine massage. Fluid therapy was monitored with urine output. However, she died from the disease's complications before IV Ribavirin could be administered. The result of RT-PCR test for Lassa fever virus subsequently turned out positive. After sorting out traditional and religious issues, safe burial was arranged by the epidemiologists according to the national guidelines for Lassa fever case management by NCDC.

Discussion

Unfortunately, pregnant women are more at risk of dying with Lassa fever than non-pregnant women^{6,8-10}. The high maternal and fetal mortality associated with pregnancy is seen in the two cases presented^{1,5,6,9}. They received supportive treatment before the availability of the confirmatory test results which took an average of 48hours to obtain in both cases. Although there was strict adherence to IPC measures, prophylactic Ribavirin tablets was used by exposed healthcare workers including doctors and nurses^{6,9,12}. The first patient was transferred immediately the result of RT-PCR was obtained to the national reference center at KSSH from where she was referred to ISTH where she died with the baby in-utero. The second patient was managed at our center after the expulsion of a stillborn baby at home complicated by PPH. Despite adequate management of the PPH she still succumbed to the complications of the Lassa fever. The fatality observed in this study reflects the higher CFR in Kogi state compared to the national CFR (39.3% vs. 19.5%). This finding may be due to the various challenges encountered in the diagnosis and treatment of Lassa fever in Kogi state and calls for action by government agencies and relevant stakeholders^{10,13}. In this case report, the mean duration of symptoms before presentation was 13.5 days, so the two cases presented late after the onset of the disease's symptoms with resultant

Table 2: Patients' laboratory findings

LABORATORY FINDINGS	Patient 1	Patient 2	Reference range
Packed cell volume (PCV)	28%	24%	30 – 45%
Clotting profile			
PT	13s	15s	12 – 14s
INR	1.0	1.1	1 – 1.1s
PTTK	37s	42s	32 – 38s
Liver function test			
Alanine aminotransferase (ALT)	52	68	0 – 35iu/l
Aspartate aminotransferase (AST)	58	72	0 – 35iu/l
Bilirubin (Total)	35	52	3 – 20umol/l
Conjugated	8	12	<5% of Total Bilirubin
Unconjugated	27	40	
Platelet count	82,000	65,000	100 – 400 cells/ul
RT-PCR	Positive	Positive	

delay in commencement of both the supportive treatment and IV Ribavirin, which may have contributed to the poor outcome. Evidence has shown that outcome is more favorable if treatment (IV Ribavirin) is commenced within six days of onset of symptoms^{9, 12}. The mean duration of symptoms before the commencement of treatment was lower in Ibadan, and the outcome was better¹³. Similarly, in a study in Ebonyi state, Nigeria, there was a shorter mean duration of symptoms, with prompt diagnosis and commencement of IV Ribavirin, which may have been responsible for the good outcome⁷. This conclusion is still debatable because of the concerns about the efficacy of Ribavirin in the treatment of Lassa fever¹⁰.

The challenges encountered in managing these cases are delay in presentation, community ignorance about the disease's signs and symptoms, and poverty. Financial constraints at the family level with low socioeconomic status may also have contributed to the delay in presentation. Other challenges are delay in the confirmation of diagnosis and commencement of supportive care and IV Ribavirin to treat the Lassa fever. Diagnostic facilities for Lassa fever are restricted to few NCDC reference laboratories across the country, and there is currently none in Kogi state. With the advent of COVID-19 pandemic, RT-PCR facilities are being distributed to states reporting COVID-19 except for Kogi State. Blood samples for the RT-PCR test for these two patients were sent to the national reference laboratory Gaduwa, Abuja 200km away⁹. This factor: coupled with other logistic issues regarding treatment at KSSH, necessitated transfer to ISTH, thereby adding to the delay in instituting the appropriate management. Furthermore, poverty and out-of-pocket payment for healthcare are

significant contributors to treatment delays in low-resource settings¹⁵.

Lassa fever is highly infectious, and the national guideline has provided a strict modality for the deceased's body's disposal. However, our cultural and religious burial practices as rites to the dead may pose challenges to achieving this, and it could be a potential source of disease spread in the community. Although in the two cases presented, the bodies were disposed of as provided by the national guideline⁹, it may not always be the practice. There may be a need to create awareness about this to improve acceptance.

Conclusion

The diagnosis of Lassa fever in pregnancy is often delayed due to late presentation to the health facility and the non-availability of diagnostic facilities at the hospitals of first presentation. Thus, Lassa fever is associated with poor maternal and fetal outcomes, especially when treatment commencement is long. Community education and enlightenment about Lassa fever, provision of diagnostic tools and treatment with IV Ribavirin should be prioritized by government and her agencies. Further research is needed to unravel the grey areas concerning the efficacy of IV Ribavirin in the treatment of Lassa fever in pregnancy.

Conflict of interest

No conflict of interest to declare.

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Ethical consideration

Ethical approval was obtained from Ethical Review Committee of the Federal Medical Center, Lokoja, Kogi state, Nigeria.

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Author's contribution

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Final approval of the version submitted: AA Adewole, O Amode, EH Gbejegbe, AN Adamu, AO Musa, OJ Nnorom, A Ojotule, AA Ladan, A Adesanya, AA Ojiah, OC Onwufor, GM Olarinoye, OD Kassim.

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