A Family Cluster of Lassa fever Cases in the UK

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EMORY
UNIVERSITY

Project ECHO®

Mother’s background

Female, 38 years

PMH:

- Gestational diabetes mellitus
- Depression

SH:

- Mali-born
- Lives with husband and 4 children
- Last travel to Mali 2019

Mother's timeline

10th Jan 2022 (D1) – onset of symptoms, whilst 34/40 weeks pregnant

23rd Jan (D14) – attends Urgent Care Centre at her local hospital

24th Jan (D15) – admission to local hospital in labour (EDD 13/2/22)

- Vaginal delivery
- Fever during labour

26th – 31st Jan (D21)

- Fever, fluctuating GCS 13-15, polyuria, thrombocytopenia (nadir platelet count 24), hepatitis (peak ALT 1082)
- CT and MRI head imaging normal; CSF studies: WCC 8 RBC 4 protein 0.19 glucose 2.2
- Serum sample sent to national reference laboratory with no clinical details

1st Feb (D22) – transfer to regional neuro-intensive care unit

Mother's timeline continued

2nd – 3rd Feb (D24) – Regional Neurological Intensive Care Unit

- Fluctuating GCS 9-13 with confusion, agitation, anuria (CVVHF), hyponatraemia (nadir Na^+ 125)

4th – 8th Feb (D29)

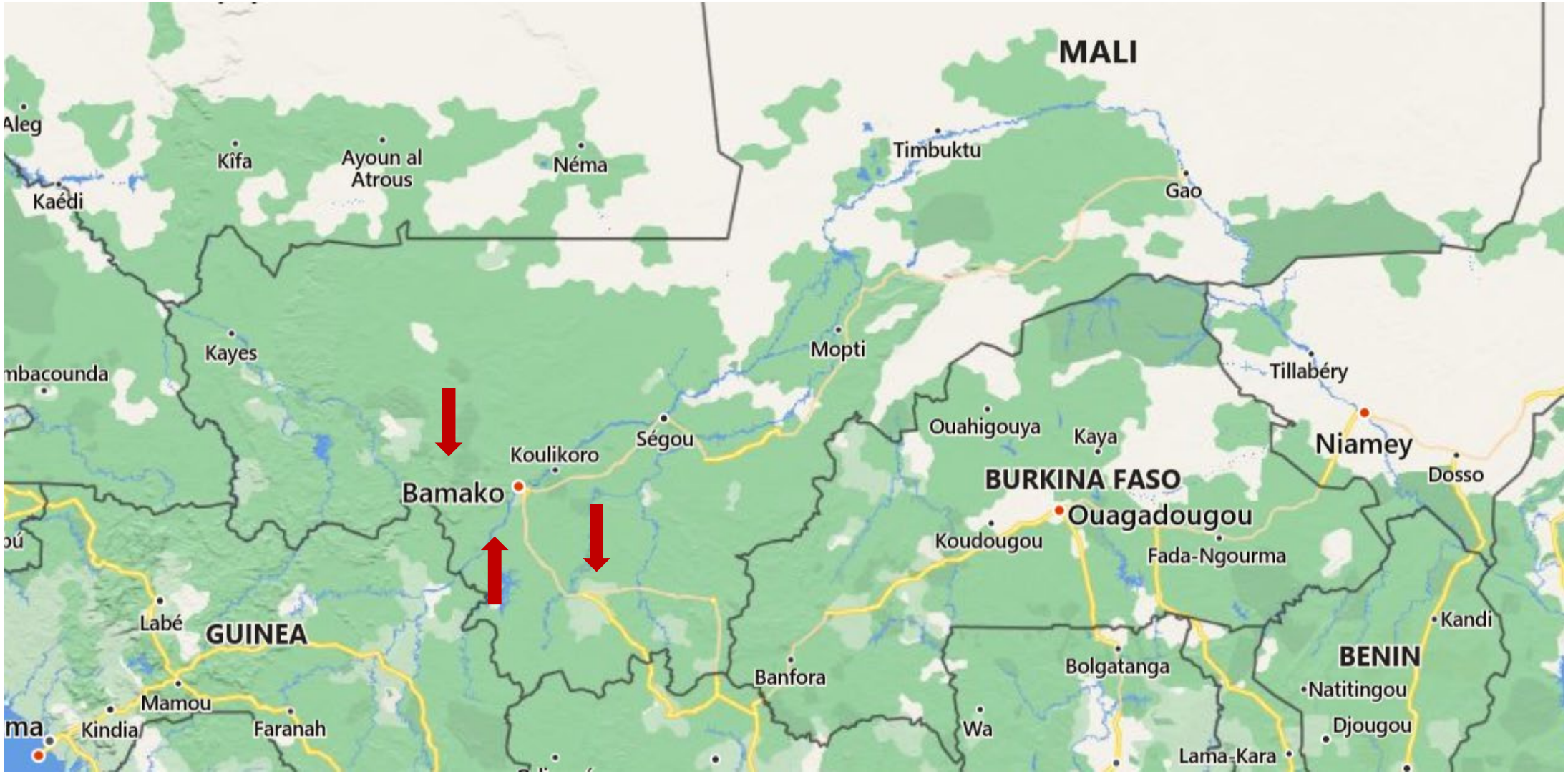
Managed as thrombotic thrombocytopenic purpura (TTP; ADAMTS13 level <10%): plasmapheresis, caplacizumab (anti-vWF), methylprednisolone

Baby’s timeline

- 25/01/22 – born well at 36 weeks
- 05/02/22 (D11) – baby becomes septic – fever, hepatitis, bloody diarrhoea
- 07/02/22 (D13) – sepsis screens negative; discussed with regional Paediatric Infectious Diseases service and national reference lab
- Mother’s illness discussed
- Father’s travel history and recent illness revealed

Father's timeline (retrospective review, 7th Feb)

- Mali 3rd – 27th Dec 2021
- Travelled around Manden region, Southern Mali, & visited Bamako
- Rural areas; no contact with animals or unwell persons; no funerals
- Saw traditional healer in Djoliba for neuropathy right hand; ingestion of herbal teas and medication rubbed into incisions in arm
- Symptoms onset in UK, 29/12: fatigue, lethargy, myalgia, loose stool, fever
- Admitted to local hospital 3rd to 6th Jan – empirical antibiotics for presumed bacterial infection, no diagnosis, got better and discharged. Full recovery.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Banfora
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Faranah
Wa
Djougou
Lama-Kara

Diagnostics

- Decision to test father's stored (untested) serum and mother's serum for viral haemorrhagic fevers using PCR assays at reference laboratory
- 08th Feb, 22:00h: mother and father's serum & plasma positive for Lassa fever virus
  - UK High Consequence Infectious Diseases Network activated
- 9th Feb: Baby tests positive for Lassa fever virus; dies in situ at local NICU (with enhanced infection prevention and control measures in place)
- 9th Feb: mother transferred to Royal Free High Level Isolation Unit (HLIU)

One of two Trexler patient isolators in the Royal Free HLIU

Mother's progress

9th Feb (D26) – Transfer to HLIU

- Overnight preparation of unit & simulation of admission prior to arrival
- Patient intubated locally for critical care transfer to Royal Free
- Remained mechanically ventilated and received CVVHF for acute renal failure

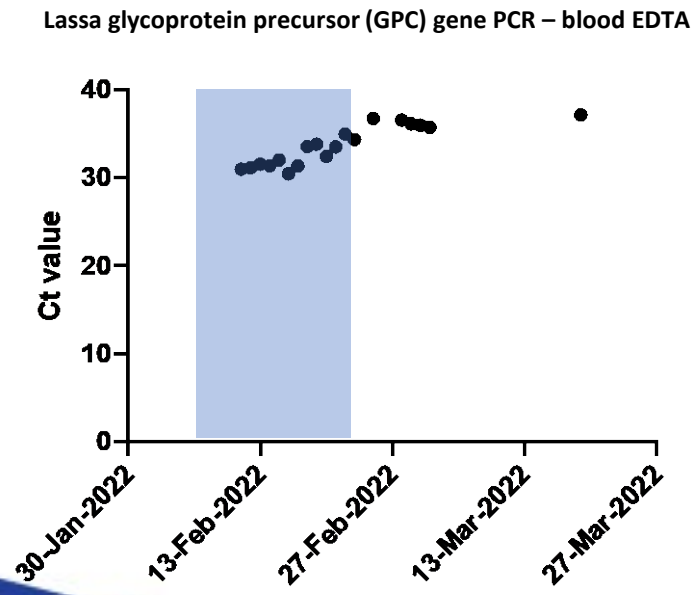
10th Feb (D27) – 24th Feb (D41) – HLIU

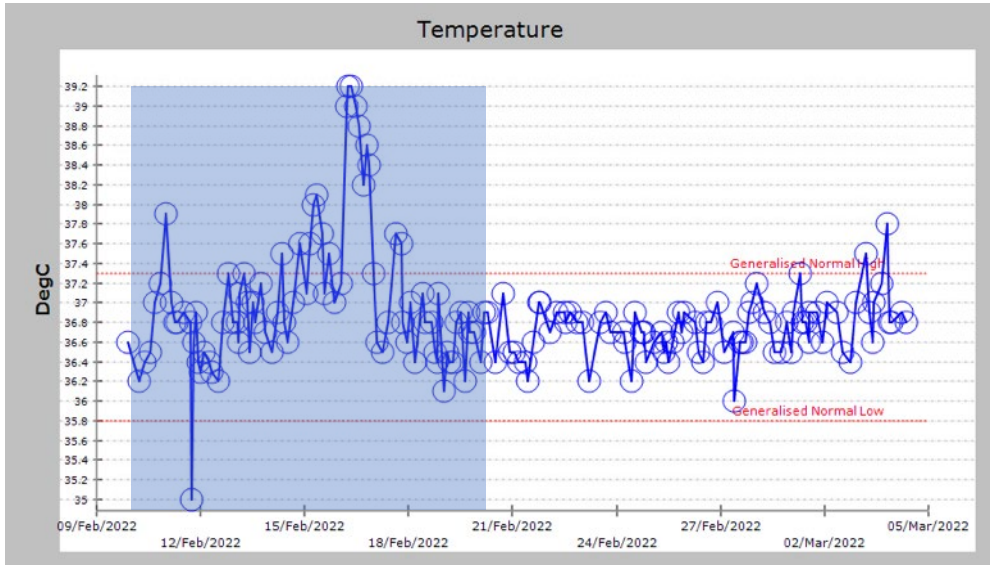
- Started favipiravir via NG tube on D27
- CVVHF no longer required by D30; polyuria in recovery phase
- Vasopressor support no longer required by D30
- Defervesced D32
- Extubated on D33; received antibiotics for presumed ventilator-associated pneumonia

Antiviral therapy

Favipiravir

- Initiated on day 27 of illness/day 17 admission
- 10.02.22- 20.02.22
- Loading dose 2400mg
- 1200mg BD via NGT (6x200mg tablets crushed and mixed with 50ml water)





Favipiravir

Antiviral therapy

Why favipiravir?

Efficacy against Lassa virus infection

- *In vitro* and non-human primate models

Phase 3 studies of use in COVID, Ebola & Influenza

Local experience of favipiravir as PEP

Why not ribavirin?

Uncertain efficacy (ALT 54 at HLIU admission)

Adverse effects

Limited availability

PLOS NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Ribavirin for treating Lassa fever: A systematic review of pre-clinical studies and implications for human dosing

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OPEN ACCESS

Citation: Salam AP, Duvignaud A, Jaspard M, Malvy D, Carroll M, Tarning J, et al. (2022) Ribavirin for treating Lassa fever: A systematic review of pre-clinical studies and implications for human dosing. PLoS Negl Trop Dis 16(3): e0010289. https://doi.org/10.1371/journal.pntd.0010289

Editor: Andrea Marzi, National Institute of Allergy and Infectious Diseases Division of Intramural Research, UNITED STATES

Received: November 11, 2021

Accepted: February 28, 2022

Published: March 30, 2022

Abstract

Ribavirin is currently the standard of care for treating Lassa fever. However, the human clinical trial data supporting its use suffer from several serious flaws that render the results and conclusions unreliable. We performed a systematic review of available pre-clinical data and human pharmacokinetic data on ribavirin in Lassa. In in-vitro studies, the EC50 of ribavirin ranged from 0.6 μg/ml to 21.72 μg/ml and the EC90 ranged from 1.5 μg/ml to 29 μg/ml. The mean EC50 was 7 μg/ml and the mean EC90 was 15 μg/ml. Human PK data in patients with Lassa fever was sparse and did not allow for estimation of concentration profiles or pharmacokinetic parameters. Pharmacokinetic modelling based on healthy human data suggests that the concentration profiles of current ribavirin regimes only exceed the mean EC50 for less than 20% of the time and the mean EC90 for less than 10% of the time, raising the possibility that the current ribavirin regimens in clinical use are unlikely to reliably achieve serum concentrations required to inhibit Lassa virus replication. The results of this review highlight serious issues with the evidence, which, by today standards, would be unlikely to support the transition of ribavirin from pre-clinical studies to human clinical trials. Additional pre-clinical studies are needed before embarking on expensive and challenging clinical trials of ribavirin in Lassa fever.

Mother’s outcome

- Stepped down to ID ward isolation room on 24th Feb (D41)
- Still weakly positive for Lassa RNA in urine; risk management
- Renal, haematological and liver dysfunction were resolving
- Discharged from Royal Free 4th March (D49; 39 days in hospital)
- Appropriate grief reaction; depression; fatigue
- No hearing loss

BBC ‘Hospital’ documentary episode, 15 April 2022

Key Takeaways

- Lassa fever is the most common ‘imported’ African viral hemorrhagic fever seen in the UK & Europe; also imported into the USA
- It is a rare infection, mild in most, can be severe/fatal, and can be transmitted between humans
- No proven treatments or vaccines currently
- Good supportive care saves lives – sometimes it has to be ICU-level care
- Mostly seen in recently returned travelers; first household transmission in UK
- Take a good travel history and be aware of country-based ID risks
- Expand the exposure history-taking in those with undiagnosed illnesses