LASSA FEVER IN PAEDIATRIC PATIENTS: IGBINEDION UNIVERSITY TEACHING HOSPITAL, (OKADA, OVIDIA NORTH EAST, EDO STATE) EXPERIENCE.

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ABSTRACT

Lassa fever is endemic in Nigeria, with outbreaks reported in several Local Government Areas in Edo State over the last few years; but little is known about lassa fever in children living in Ovia North East Local Government Area. We present case reports of Lassa fever in two paediatric patients presenting at Igbinedion University Teaching Hospital (IUTH), Okada (located in Ovia North East LGA), between June 2017 and March 2018. We highlight the absence of the distinct clinical stages of the disease in a 3 year old, but its presence in an 11 year old; however, high fever (up to 40.5°C) was a constant feature in both cases reported. Both patients died, due to late effective referral to Irrua specialist Teaching Hospital, Irrua (Lassa fever Centre). This was mainly as a result of inability to afford transportation cost and hospital bills in addition to late diagnosis. Thus, we emphasize the need for free/affordable transportation for such cases to encourage early referral and treatment. Also, a high index of suspicion of Lassa fever is advised in managing all paediatric cases with high fever (>39°C) presenting to IUTH, Okada.

Keywords: Igbinedion University Teaching Hospital, Lassa Fever, Ovia North East LGA, Paediatrics

INTRODUCTION

Lassa Fever is the only Viral Haemorrhagic Fever with a possible cure.1,2 It is caused by Lassa fever virus, which is transmitted to man by Mastomys Natalensis, a multimammate rat (Primary host).1,2 The natural habitat of the rat is bushes surrounding the home; however, due to activities of man, such as bush burning, they invade houses. The Lassa virus is transmitted to humans via ingestion of food (especially locally made ‘garri’) contaminated with rodent urine or faeces or contact with contaminated household items. Person-to-person infections and laboratory transmission can also occur, particularly in hospitals with lack of/poor practice of adequate infection prevention and control measures.2

Lassa fever occurs in all age groups and both sexes. Persons at greatest risk are those living in rural areas where Mastomys are usually found, especially in communities with poor sanitation or crowded living conditions.2 Lassa fever is endemic in Nigeria; since the identification of the Lassa fever virus in 1969, several outbreaks of the disease have been reported.3 The most recent outbreaks of Lassa fever in Nigeria started December 2016, with up to 179 confirmed cases in 2017 and 317 confirmed cases between January and March 2018.4 These outbreaks occurred in several states in Nigeria including several LGAs in Edo State. In Edo state, cases have

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Table I: Clinical stages of Lassa Fever

<table>
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<tr>
<th>STAGE</th>
<th>SYMPTOMS</th>
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<tr>
<td>1 (days 1-3)</td>
<td>General weakness, malaise, high fever &gt;39°C, constant with peaks of 40-41°C</td>
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<tr>
<td>2 (days 4-7)</td>
<td>Sore throat (with white exudative patches) very common; headache; back, chest, side, or abdominal pain; conjunctivitis; nausea and vomiting; diarrhea; productive cough; proteinuria; low blood pressure (systolic &lt;100mmHg); anaemia</td>
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<tr>
<td>3 (after 7 days)</td>
<td>Facial edema; convulsions; mucosal bleeding (mouth, nose, eyes); internal bleeding; confusion or disorientation.</td>
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<tr>
<td>4 (after 14 days)</td>
<td>Coma and death</td>
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been reported in 13 LGA concentrated in Edo North and Edo Central. To the best of our knowledge, prior to these cases reported in this publication, no confirmed paediatric case of Lassa fever has been reported in Edo South, including Ovia North East LGA.

Following infection with the virus, only about 20% of persons develop symptoms, with the remaining 80% demonstrating serological evidence of infection. After 3(6)-21 days following exposure, illness begins abruptly; there are three (3) clinical stages: Table I shows these stages and their features. In children, fever is a constant feature, while haemorrhage, acute renal failure, convulsion and coma are indicators of poor outcome. In severe cases, death usually occurs within two weeks following onset of symptoms.

Due to the varied and non-specific symptoms of Lassa fever, clinical diagnosis is often difficult, especially early in the course of the disease, when it can easily be mistaken for malaria, tonsillopharyngitis or gastroenteritis. Thus, Lassa fever is usually a late consideration when managing children with fever in malaria endemic regions, such as Nigeria, where Lassa fever is also endemic.

In resource-limited areas, diagnostic confirmation is difficult, requiring sophisticated laboratory facilities, which are few in Nigeria. Due to these challenges in diagnosis, in 2005, the World Health Organization (WHO) developed a case definition of Lassa fever (Table II), based on clinical symptoms, to assist with the diagnosis. However, some authors have observed some problems with its use, especially for children, and this may delay the suspicion and diagnosis of Lassa fever cases.

As shown in Table II, None of the major and minor features is specific for Lassa fever. Also, waiting for 48-72 hours for non-response to effective anti-malarial and broad spectrum antibiotics, further delays diagnosis and thus treatment with Ribavarin, which is more effective if administered within a few days after onset of clinical illness.

**CASE REPORTS**

The cases presented in this report, were seen at IUTH, Okada, between June 2017 and February 2018. Between this period, there were nine (9) suspected cases of Lassa fever: 5 males and 4 females; all aged between 2-11 years. Only 4 (44%) of the suspected cases were effectively referred; 2 (50%) were confirmed cases of Lassa fever. These confirmed cases are presented here.

**CASE ONE**
A.L was an 11 year old orphan girl, who was rushed into the children emergency room (CHER) with complaints of fever and abdominal pain of 3 days duration. The Fever was high grade, worse at night, intermittent, associated with chills and rigors. Abdominal pain was described as burning, located in the epigastrium; pain was relieved by magnesium trisilicate suspension, with no known aggravating factor (including meals). At onset of symptoms, she presented at Utese Primary Health Care Centre, where magnesium trisilicate, oral medications (names unknown), intravenous drugs and fluids were administered for 36 hours. However, symptoms persisted, thus, she presented at CHER, IUTH. She was on family diet which included a staple meal of soaked “garri”. No similar symptoms in siblings; no history of recent demise of members of household. She lived with her aunty in a one bedroom apartment; and household foodstuffs are usually stored uncovered.

Significant findings on examination included: an ill-looking, pyrexic (Temp: 39.5 °C) girl in painful distress; with marked tenderness in epigastric region and right renal angle tenderness. Differential diagnosis included: Pyelonephritis; Peptic Ulcer Disease; and severe malaria.

Full Blood Count (FBC) was essentially normal: Packed Cell Volume (PCV): 35%, White Blood Cell

### TABLE II: Adapted WHO Case Definition of Lassa Fever at GRC (Gondama Referral Hospital), Sierra Leone

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>FEATURES</th>
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| MAJOR CRITERIA | Abnormal bleeding  
Swollen neck or face  
Conjunctivitis or sub-conjunctival haemorrhage  
Spontaneous abortion  
Unexplained tinnitus or altered hearing during a febrile illness  
Persistent low systolic blood pressure  
Known exposure to a suspect, probable or confirmed patient with Lassa fever or participated in funeral practices in the last 21 days  
Readmitted within three weeks of inpatient care for illness with fever  
Markedly elevated aspartate aminotransferase (AST)/alanine aminotransferase (ALT)  
Positive coagulation test |
| MINOR CRITERIA | Headache  
Sore throat  
Persistent vomiting  
Diffuse abdominal pain/tenderness  
Retro-sternal pain  
Diarrhoea  
Generalized myalgia and arthralgia  
Profuse weakness  
Proteinuria  
WBC count <4000 |

One or Two major and at least two minor criteria found in a patient with fever >38°C not responding to effective anti-malarial and broad spectrum antibiotics within 48 h if artemisinin is used or 72 h if quinine is used, with no obvious localizing signs of infection. This patient must either be living in, or have travelled to, an endemic zone in the past 6–21 days.
(WBC) Count: 8.2 x 10^9/L, Differential WBC: unavailable, Platelet: 167 x 10^9/L, blood film for Malaria Parasite showed: +; Human Immunodeficiency Virus screening test was negative; Random Blood Sugar (RBS) was within normal range: 73mg/dl; Electrolyte/Urea/Creatinine, Genotype and Blood culture were not done due to financial constraint.

She was commenced on: Intravenous (IV) Artesunate 2.4 mg/kg at 0, 12, and 24hrs; Tabs Magnesium trisilicate; IV Ceftriaxone at 100mg/kg/day in 2 divided doses; Genticin at 3mg/kg/day in 2 divided doses. Paracetamol (PCM) was administered at 10mg/kg start dose, then if temperature rose above 39°C; Intravenous fluids with 4.3% Dextrose in 0.18 Saline was commenced at 100% maintenance.

Due to financial constraint, medications were purchased and commenced 20 hours post admission. At 36 hours (5th day of illness), patient had new onset cough and sore throat; she began passage of loose stools about 3 episodes within 12 hours. Patient was still febrile with temperature range: 37.5°C - 39.5°C.

At 60-hour review (6th day of illness), she still had cough; sore throat; and loose stools about 5 episodes in 24 hours. Temperature ranged from 37.2 to 40.2 °C. She had tachycardia and tachypnea; she had commenced oral Artemisinin Combination Therapy (ACT).

At 4th day on admission (7th day of illness), fever persisted, up to 40.5°C. She developed neck stiffness, positive brudzinsky and generalised abdominal tenderness with guarding. Differential diagnosis at this time included: Meningitis, Sepsis, Viral Haemorrhagic Fever - Lassa fever. Patient was prepared for referral to ISTH. Meanwhile, Cerebrospinal fluid (CSF) analysis result showed: Glucose: 68.4mg/dl (40% of RBS) and Protein 0.5g/dL (both suggestive of meningitis). Urine (sample collected at admission) culture yielded growth of *Escherichia coli*, with multi-drug resistance (including Ceftriaxone, Genticin and ofloxacin). Ceftriaxone was substituted with Chloramphenicol at 100mg/kg/day.

Due to financial constraint, transfer of patient to ISTH was delayed till 5th day (Money had to be contributed by IUTH Hospital staff for transport and care); Crude clotting time was delayed (22 minutes) at this time. She arrived ISTH in the company of a Nurse and care was given to the patient; Polymerase chain reaction (PCR) for Lassa fever was positive after 24 hours at ISTH. She developed haemoptysis and haematochezia on the first day on admission (8th day of illness) at ISTH. Patient died 2 days after admission (10th day of illness) in ISTH.

**CASE TWO**

F.P was a 3 year old female, who resided with parents (father and step-mother) at Uhen (Ovia North East LGA). She was rushed into the children emergency room (CHER) with complaints of: Fever for six days; Passage of dark-coloured stool for two days; vomiting of blood and bleeding from nostril for one day. The fever was high grade, continuous with rigors. No history of a prior episode of unprovoked bleeding, no haematuria, no bleeding from other part of the body, no yellowness of the eyes, no similar illness in other siblings.

She lived with her father and step-mother, who is a 40 year old “garri” trader (who usually air dries the garri on the floor (outside the house) before selling it) in a one bedroom apartment; household foodstuffs are usually stored uncovered.

On examination, she was prostrated, febrile (Temperature of 38.3 °C), and mildly pale. Her nostrils were clogged with dried blood; no signs of
trauma. She was tachypnoemic with tachycardia. Differential diagnosis included: Severe sepsis with Disseminated Intravascular Coagulopathy (DIC), severe malaria with DIC, Viral Hemorrhagic disease- Lassa fever.

Blood was urgently grouped and cross-matched for transfusion. FBC result: PCV: 28%, WBC: 4.6 x 109/L, Neutrophils, Eosinophils, Basophils: 67%, Lymphocytes: 28%, Monocyte: 5%, Platelet: 71 x 109/L; Erythrocyte Sedimentation Rate: 75; blood film for malaria parasite: +; Blood group: O Rh D positive; Bleeding Time: > 20 minutes; Clotting Time: >8 minutes; RBS: 73mg/dl; E/U/Cr, and Genotype were not done due to financial constraint.

Patient was Isolated and available standard precautions (in the absence of effective barrier nursing) was observed. IV Ceftriazone 100mg/kg/day, IV Vitamin K 10mg, PCM at 15mg/kg, IVF at 100 % maintenance, IV Artesunate at 2.4mg/kg at 0, 12, and 24hrs were commenced.

Within the first 14 hours post admission, she had a repeat episode of haematemesis and epistaxis. Fever continued with a temperature range of: 37.8 to 39.0 °C. She continued receiving IV antibiotics, IV antimalaria, and had blood transfused.

AT 20th hour review, patient had a total of 2 episodes of epistaxis and haematemesis; high grade fever persisted; she was markedly pale. A diagnosis of Lassa fever was made. She was prepared for transfer to ISTH for confirmatory diagnosis and treatment for Lassa fever; meanwhile, a second aliquot of compatible fresh whole blood was transfused. She was effectively referred after several hours, due to delay in sourcing for funds for medical transportation. She arrived at ISTH in the company of a Paediatric Medical Officer. PCR for Lassa fever was positive at ISTH. Patient died 9 days after care in ISTH, Irrua.

**DISCUSSION**

Lassa fever has become a major febrile illness in West Africa, including Nigeria, where Malaria is also endemic. The early features of Lassa fever are varied and non-specific and similar to the clinical features of common febrile illnesses, such as malaria. Thus, clinical diagnosis of Lassa fever is often missed at the early stage, as seen in this case series. Other factors contributing to late diagnosis include general lack of awareness amongst medical practitioners, and the inability to carry out sophisticated confirmatory laboratory diagnosis in many centres in the country. As at the time of this report, only one of such is available in Edo State; it is located at Irrua specialist centre, Edo State.

There are four clinical stages of LF. In this case series; we emphasize the absence of these distinct stages in the three year old patient, and the presence of all four distinct stages of the disease in the twelve year old patient. While mucosal bleeding and internal bleeding occurred as expected (after the first week of the illness) in the twelve year old patient; bleeding occurred much earlier (at the fourth day of the illness) in the three year old child. This may be due to a faster progression of illness in younger children compared to older ones due to lower immunity in younger children. In addition, the absence of other common features of LF (sore throat, headache, abdominal pain and chest pain) in the younger child, may be due to the fact that a young child is less likely to notice or effectively communicate the presence of these symptoms compared to an older child. However, this explanation cannot account for the absence of cough, which is also a common feature of LF.
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Thus, it can be inferred that though the features of LF are varied, the clinical staging may vary for different age groups; being less distinct in younger children, than in older children.

A major factor contributing to the poor outcome (death) in both cases is delay in effective referral, due to inability to afford cost of medical transportation to ISTH, Irrua and other hospital bills (such as: admission fees and cost of managing intercurrent illnesses at ISTH). Most patients presenting to IUTH, Okada are indigent, thus payment of medical bills is a major challenge, causing further delay in early diagnosis and prompt commencement of treatment with Ribavarin, which is only available at no cost at ISTH. Early treatment with Ribavarin is paramount in ensuring a favourable outcome, and increasing the likelihood of survival of these patients.

CONCLUSION

Lassa fever is currently a common febrile illness in children, living in Nigeria, including Ovia North East LGA. It is the only Viral Haemorrhagic Fever that can be treated with Ribavarin, if diagnosed early and treatment commenced as promptly as possible. Increased awareness and heightened index of suspicion are needed for the early diagnosis and prompt treatment of this potentially fatal disease.

RECOMMENDATION

Advocacy for Lassa fever Prevention and control in communities should be heightened, so as to increase awareness, encourage good hygiene and practices that discourage the spread of this disease in the community.

There is an urgent need for the Ministry of Health to ensure affordable Rapid Diagnostic Test (RDT) kits are readily available in all LGA in Edo State, especially those that have had an outbreak of LF.

The LF control and prevention programme should include funding of other medical expenses of all patients who have LF. Such funds will cover medical transportation fee, admission fee, feeding fee, and others.

REFERENCES


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