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Lassa Fever: Patients Profile and Treatment Outcomes at Benue State University Teaching Hospital Makurdi, North-Central Nigeria

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Abstract

Lassa fever is a viral haemorrhagic fever found mostly in West Africa where it is endemic but generates periodic outbreaks in the dry seasons. The virus is spread by the rat species named mastomys natalensis. While the illness is minor in most cases, the mortality is significant in hospitalized patients. Few completely equipped treatment centers existed in Nigeria previous to current increase in frequency requiring demand for new treatment centers without the full complement of essential capabilities. **Aim:** To analyze the profile and treatment outcome in patients hospitalized in one of such new resource-constrained centers at the Benue State University Teaching Hospital Makurdi, Nigeria. **Methodology:** This was a retrospective, descriptive hospital-based research encompassing January 2020 to March 2023. Medical records of those admitted to the isolation center were reviewed. The relevant data was coded and analyzed using IBM SPSS version 23. **Results:** One hundred and ten (110) individuals were hospitalized for probable or suspected Lassa fever throughout the research period. A total of 35 confirmed patients satisfied the inclusion criteria and were included as the study subjects. There were 23 (65.7%) men and 12 (34.3%) females. Their mean age was 35.36 ± 12.21 years (range 15 - 61 years). The treatment outcome showed that 24 (75%) survived and were discharged, 5 (15.6%) were referred out of the facility for dialysis and 3 died, providing a mortality of 8.6%. The causes of mortality in study patients were acute kidney injury and encephalopathy. **Conclusion:** Lassa fever is endemic in Benue state with all types of individuals afflicted. The outcome of treatment was good despite resource difficulties. Lassa fever can be successfully managed even in resource-challenged situations typically encountered in developing countries.

Keywords

Lassa Fever, Treatment Outcome, Benue State, Nigeria

1. Introduction

Lassa fever is a viral Haemorrhagic fever carried by rats. It has been recognized since the 1950s, but the virus was not identified until 1969, when two missionary nurses died from it in the town of Lassa in Nigeria [1] [2]. Lassa Fever is prevalent in West Africa, with 300,000 to 500,000 cases and 5000 fatalities occurring yearly in Nigeria, Sierra Leone, Guinea, and Liberia. Epidemics emerging from human-to-human transmission have likewise been demonstrated in healthcare institutions in West Africa. It is a zoonotic illness caused by a single-stranded RiboNucleic Acid (RNA) virus, the Lassa Virus (LASV) that causes systemic primary viral infection [1] [3]. The animal reservoir or host of the Lassa virus is Mastomys Natalensis a rodent of the genus Mastomys, widely known as the "multimammate rat." The rats infected with Lassa virus do not become ill, but they can shed the virus in their urine and faeces. Other rodents have also been proven to spread the virus [4] [5]. The Lassa fever virus is spread by contact with excretions or secretions (including feces and urine) of infected rats accessing food items and water within human households and other locations with human activities such as when the rats are killed and processed for consumption. The information available demonstrates that human-to-human transmission occurs by contact with the bodily fluids, secretions, excretions, blood of the infected individual, and sexual transmission [6]. There is no epidemiological data indicating airborne transfer between people [7] [8]. Between 70% - 80% of Lassa virus infections remain asymptomatic, moderate, or self-limiting and in most cases may pass undetected although mortality is significant in hospitalized patients [9] [10] [11]. The incubation period of the illness is 3 - 21 days. The clinical manifestation of the disease is nonspecific and includes fever, fatigue, haemorrhaging, gastrointestinal symptoms (vomiting, diarrhoea, and stomachache), respiratory symptoms (cough, chest pain, and dyspnoea), and neurologic symptoms (disorientation, seizures, and unconsciousness) [7] [9]. These symptoms are difficult to separate from other illnesses and other viral haemorrhagic fevers. Mortality is high in hospitalized patients especially with late presentation being at an average of 15% - 20% [8] [9] [12].

In Nigeria, there has been a significant seasonal spike in the previous few years with Ondo, Edo, Ebonyi and Bauchi states of the country having the greatest number of cases [13] [14]. Several additional states that were not previously afflicted have observed increased incidence of the virus [7] [15]. In Nigeria, the disease had previously been managed in designated treatment facilities in Edo, Ebonyi and Ondo states until recently. These centers are well-equipped with diagnostic, therapeutic and dialysis services. The rising frequency and expansion

to neighbouring states have forced the development of new treatment centers without the full complement of services. One such center was established by the Benue State government at its university teaching hospital in Makurdi North Central Nigeria in response to Lassa fever, Covid-19 and other infectious diseases.

Aims of the study: This retrospective descriptive study aimed to establish the profile and outcome of treatment of Lassa fever patients at the Benue State University Teaching Hospital Makurdi North-Central Nigeria who were managed under these resource-limited and challenging conditions.

2. Materials and Methods

Study design: This was a retrospective, descriptive hospital-based study that covered the period of January 2020 to March 2023.

Study Site: The study was conducted in the Infectious Diseases Isolation and Treatment facility of Benue State University Teaching Hospital Makurdi, North Central Nigeria which is the only one in the state. This institution is a state-owned university teaching hospital that provides tertiary health care mostly for residents of the state and sections of bordering states of Nassarawa, Taraba and Cross River.

Ethical Consideration: Ethical permission was requested and granted from the Health Research Ethical Committee of the Benue State University Teaching Hospital, Makurdi for the conduct of the study. Strict confidentiality was maintained in the management of patient's medical records that were utilized for data extraction.

Methodology: Staff of the medical records department of the hospital identified and retrieved case folders of all patients admitted as suspected or confirmed cases of Lassa fever throughout the research period using the admission register at the Isolation and Treatment center. Relevant information from these case files was retrieved by the researchers and entered into a standardized proforma. These included the demographic data *i.e.*, Gender, Age, Local government of residence and occupation, clinical information including all symptoms and signs, laboratory investigation results mainly the RT-PCR for Lassa virus, liver function test, urinalysis for the presence of haematuria or proteinuria, the time taken for confirmation of diagnosis and initiation of Ribavirin, duration of hospital stay, complications, treatment and outcome of treatment. Data such as age were categorized into ranges. The variables were assigned numerical values and coded for statistical analysis using the Excel spreadsheet.

Inclusion criteria:

1) Patients hospitalized for suspected Lassa fever that were proven RT-PCR positive for Lassa virus.

2) Patients who were hospitalized as already confirmed Lassa fever (RT-PCR positive for Lassa virus).

Exclusion criteria:

1) Patients who were hospitalized for suspected Lassa fever but showed nega-

tive RT-PCR for Lassa virus.

2) Patients whose RT-PCR findings for Lassa virus were not accessible in their records.

Statistical analysis: The data was analyzed using the statistical package for social sciences (SPSS) software (version 23); SPSS, Chicago, IL, USA). Descriptive statistics was used to determine the range and mean for quantitative variables as well as frequencies and percentages. Results were provided in tables and charts. Chi-square and Fisher's exact tests were employed to examine for statistical significance between categorical variables. A p-value of < 0.05 was deemed as statistically significant.

3. Results

Socio-demographic characteristics: A total of 35 Lassa virus RT-PCR positive patients representing (31.8%) of 110 patients hospitalized during the study period satisfied the inclusion criteria and were enrolled as the study participants. There were 23 (65.7%) men and 12 (34.3%) females. The mean age was 35.36 ± 12.21 years (range 15 - 61 years). The confirmed cases came from 14 of the 23 local government areas of the Benue state with 15 (42.9%) from Makurdi, 4 (11.4%) from Ogbadibo, 3 (8.6%) each from Obi and Otukpo being those with the highest number of cases. The most impacted occupational categories were farmers 10 (28.6%) public servants, 7 (20.2%) traders/businesses, 6 (17.1%) and health care workers 5 (14.3%) as indicated in Table 1.

Clinical presentation and Laboratory features. The symptoms at presentation in descending order of frequency were: Fever (defined as temperature of 38˚C) 35 (100%), headache 23 (65.7%), malaise 21 (60.0%), abnormal bleeding 19 (54.3%), myalgia 19 (54.3%), abdominal pain 15 (42.9%) retrosternal chest pain and cough 14 (40%) each, diarrhea 12 (34.3%), vomiting (20%) and sore throat 4 (11.4%) as shown Figure 1. The commonest signs were fever 35 (100%), bleeding 20 (57.1%) pallor 14 (40%), CNS involvement 9 (25.7%), Lung consolidation 7 (19.4%), jaundice 4 (11.1%), body swelling and hepatomegaly 3 (8.3%) each and pleural effusion in 1 (2.8%) of the study subjects (patients) as shown in Figure 2. Laboratory indices showed impaired liver function in 15 of 18 in whom it was carried out. The RT-PCR for Lassa fever virus was positive in 35 (100%) whereas 25 (71.4%) had haematuria and 23 (65.7%) had both haematuria and proteinuria on urinalysis as shown in Table 2.

Identified possible risk factors were recent travel out of the area of domicile 4 (11.4%), contact with rats 4 (11.4%) and contact with a probable, suspected or diagnosed Lassa fever 4 (11.4%) as shown in Table 3. The mean duration of symptoms (illness) to presentation to the treatment center was 10.02 ± 4.85 days (Range = 3 - 21), time from admission to confirmation of diagnosis by RT-PCR (for those whose diagnosis were not confirmed prior to admission) was 5.57 ± 2.66 days (Range = 1 - 13) and from admission to initiation of intravenous Ribavirin was 2.77 ± 2.66 days (Range = 1 - 14) as shown in Table 4.

Table 1. Socio-demographic characteristics.

Variables	Frequency	Percent
Gender		
Male	23	65.7
Female	12	34.3
Total	35	100
Age Group (years)		
15 - 20	5	14.3
21 - 25	5	14.3
26 - 30	4	11.4
31 - 35	4	11.4
36 - 40	7	20.0
>40	10	28.6
Mean Age(years) = 35.36 ± 12.21 (Range = 15 - 61)		
Cases per Local Govt. Area		
Ado	1	2.9
Buruku	1	2.9
Gboko	2	5.7
Guma	2	5.7
Gwer	1	2.9
Katsina Ala	1	2.9
Konshisha	1	2.9
Makurdi	15	42.9
Obi	3	8.6
Ogbadibo	4	11.4
Otukpo	3	8.6
Ushongo	1	2.9
Occupation		
Trading/Bussiness	6	17.1
Civil Servant	7	20.2
Farmer	10	28.6
Housewife	4	11.4
Healthcare worker	5	14.3
Student	3	8.6

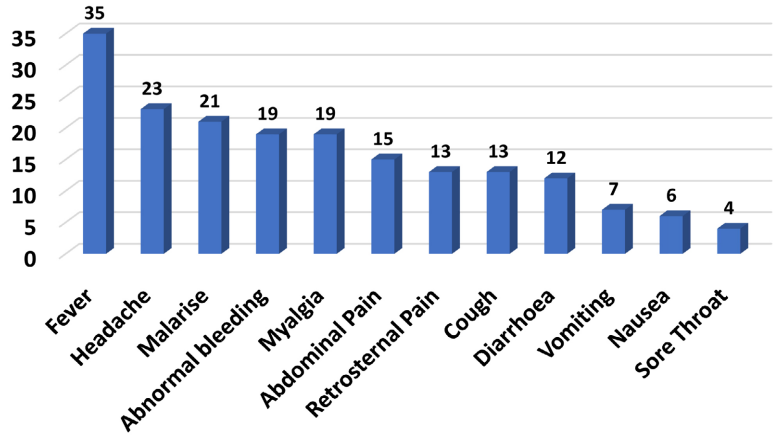

Figure 1. Bar chart showing symptoms.

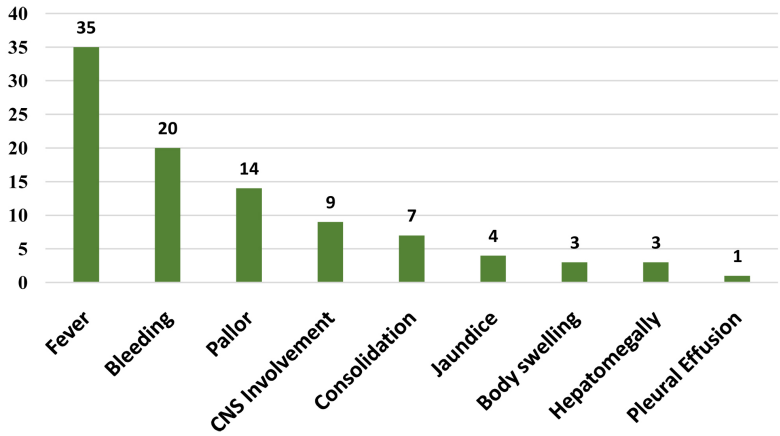

Figure 2. Bar chart showing signs.

Table 2. Laboratory indices.

Variable	Frequency	Percent
Liver Function Test (n = 18)		
Normal	3	16.7
Deranged	15	83.3
RT-PCR for Lassa Virus		
Positive	35	100.0
Negative	0	0.0
Haematuria		
Yes	25	71.4
No	10	28.6
Proteinuria		
Yes	23	65.7
No	12	34.3
Proteinuria and Haematuria		
Yes	23	65.7
No	12	34.3

Table 3. Risk factors, complications, treatment outcome, reason for referral and cause of death.

Variable	Frequency	Percent
Risk factors for infection		
Recent travel out of domicile		
Yes	4	11.4
No	31	88.6
Handled or consumed rats		
Yes	4	11.4
No	31	88.6
Contact with a suspected case		
Yes	4	11.4
No	31	88.6
Complications		
Acute kidney injury	14	40.0
Neurological involvement	9	25.7
DIC	1	2.9
Treatment outcome		
Recovered and discharged	27	77.1
Referred	5	14.3
Died	3	8.6
Reason for referral (n = 5)		
Acute kidney injury	5	100.0
Cause of death (n = 3)		
Acute kidney injury	1	33.3
Acute kidney injury and encephalopathy	2	66.7

Table 4. Time variables in days.

Variable	Mean	Range
Onset of symptoms to presentation in treatment center	Mean = 10.02 ± 4.85	Range = 3 - 21
From admission to the confirmation of diagnosis	Mean = 5.57 ± 2.66	Range = 1 - 13
From Admission to the first dose of Ribavirin	Mean = 2.77 ± 2.66	Range = 1 - 14

Treatment: All study participants (patients) were treated with Ribavirin (which is the recommended drug for treatment) following the Irrua regimen. This regimen comprised a loading dose of 100 mg/kg (max 7 g) in 2 divided

Table 5. Association between socio-demographic characteristics and treatment outcome.

Variables	Outcome			Chi-square χ^2	p-value
	Cured N (%) (n = 27)	Referred N (%) (n = 5)	Died N (%) (n = 3)		
Age Group (in years)				Fisher's exact = 7.51	0.698
15 - 20	4 (80.0)	0 (0.0)	1 (20.0)		
21 - 25	5 (100.0)	0 (0.0)	0 (0.0)		
26 - 30	4 (100.0)	0 (0.0)	0 (0.0)		
31 - 35	2 (50.0)	1 (25.0)	1 (25.0)		
36 - 40	5 (71.4)	2 (28.6)	1 (10.0)		
>40	7 (70.0)	2 (20.0)	1 (10.0)		
Gender				Fisher's exact = 4.59	0.091
Male	15 (65.2)	5 (21.7)	3 (13.0)		
Female	12 (100.0)	0 (0.0)	0 (0.0)		
Occupation				Fisher's exact = 10.49	0.212
Trading	5 (83.3)	1 (16.7)	0 (0.0)		
Civil Servant	5 (71.4)	1 (14.3)	1 (14.3)		
Farming	8 (80.0)	0 (0.0)	0 (0.0)		
Housewife	4 (100.0)	0 (0.0)	0 (0.0)		
Healthcare worker	2 (40.0)	3 (0.0)	0 (0.0)		
Student					

doses given as 2/3rd stat and 1/3rd given 8hrs later. Ribavirin was continued on days 2 - 7 as 25 mg/kg single daily dose and on days 8 - 10 as 12.5 mg /kg single daily dose [16]. The treatment started before RT-PCR results for very ill suspected cases whereas less ill patients were commenced on treatment after positive RT-PCR results. They additionally received supportive care with intravenous fluids, antibiotics, analgesics. Oxygen and blood transfusion were given if indicated by the patient's clinical condition and laboratory results. The outcome of treatment showed that 24 (75%) survived and were discharged based on clinical improvement, 5 (15.6%) were referred out of the facility for dialysis and 3 (8.6%) died. The causes of mortality in these study subjects were acute kidney injury and neurological involvement. **Table 3**. There was a significant correlation between exposure to a probable or suspected Lassa fever patient (P = 0.000), acute kidney injury (P = 0.007) and treatment outcome. The demographic variables and other complications did not demonstrate any link with the outcome of treatment as shown in **Table 5** and **Table 6**.

Table 6. Association between complications, risk factors and treatment outcome.

Variables	Outcome			Chi-square χ^2	p-value
	Cured N (%) (n = 27)	Referred N (%) (n = 5)	Died N (%) (n = 3)		
AKI				Fisher's exact = 14.13	0.000
Yes	6 (42.9)	5 (35.7)	3 (21.4)		
No	21 (100.0)	0 (0.0)	0 (0.0)		
DIC				Fisher's exact = 1.53	1.000
Yes	1 (100.0)	0 (0.0)	0 (0.0)		
No	26 (75.8)	5 (15.2)	3 (9.1)		
Deafness				Fisher's exact = 1.50	1.000
Yes	1 (100.0)	0 (0.0)	0 (0.0)		
No	24 (75.0)	5 (15.6)	3 (9.4)		
Travel				Fisher's exact = 3.86	0.117
Yes	2 (50.0)	2 (50.0)	0 (0.0)		
No	25 (80.6)	3 (9.7)	3 (9.7)		
Handled or consumed rat				Fisher's exact = 3.05	0.218
Yes	2 (50.0)	1 (25.0)	1 (25.0)		
No	25 (80.6)	4 (12.9)	2 (6.5)		
History of contact with suspected of Lassa fever				Fisher's exact = 8.99	0.007
Yes	1 (25.0)	3 (75.0)	0 (0.0)		
No	26 (83.9)	2 (6.5)	3 (9.7)		

AKI = Acute kidney injury, DIC = disseminated intravascular coagulation.

4. Discussion

Approximately a third of the patients who were admitted to the treatment center were proven positive showing a significant prevalence of the illness in Benue state Nigeria. The mean age of the study individuals in this study was 35.36 ± 12.21 years with a broad range and more men were afflicted than females. It has been proven that Lassa fever affects all age groups and sexes as well as occupational categories [17] [18]. However, it is more prevalent in people whose surroundings or activities place them at risk of interaction with Mastomys Natalensis the multimammate rat which is the host of the virus or sick persons. As shown in earlier research these include farmers who are rural inhabitants and

who kill rats for food. Most of our metropolitan centers have inadequate environmental sanitation with various hips of trash on which the host agent feeds and then finds itself to houses where they can urinate or defecate on unprotected foodstuff [3] [14] [17]. The prevalent habit of drying foodstuff by the roadside where it is easily contaminated by rodents is another cause of illness of the general population. The health personnel in this investigation were all in active practice and would possibly have attended to patients afflicted with undiagnosed Lassa fever without effective infection prevention and control methods [8]. The distribution of the patients (study subjects) demonstrates that the condition is common in practically all sections of the state and asks for a high index of suspicion on the part of health workers in the state so that early diagnosis and treatment may be begun.

Clinical features: The most prevalent symptoms were fever, headache and malaise, haemorrhage, retrosternal chest discomfort, cough, stomach, diarrhea and vomiting as described in earlier research [8] [14] [18]. Fever, and abnormal bleeding from orifices (haematuria, vaginal, nose and conjunctival bleeds were the usual locations) were prevalent indications. Others included pallor suggesting varied degrees of anaemia, central nervous system involvement in the form of seizures and altered consciousness as well as lung consolidation. The clinical characteristics are not different from those of other viral haemorrhagic fevers and infections such as malaria or enteric fever [6] [12] [19]. This explains the delay in presenting to the treatment facility since practically all patients took treatment for malaria or typhoid for many days previous to presentation at the treatment center. It is widely proven that early diagnosis and treatment enhance the chances of survival [20].

Travel outside the region of habitation, and handling of rats was discovered in some of the study subjects. Though it is not feasible to confirm the source of infection, these are proven risk factors and may have been responsible for their infection [21]. Health professionals are at risk owing to both occupational dangers and exposure in their home environment. The host rats shed the virus in their urine and droppings therefore contaminating food and fomites. Direct contact with these materials, whether handling filthy things, eating contaminated food, or exposure of open injuries or sores, can lead to illness. Some environmental conditions that contribute to exacerbating the incidence of Lassa fever include weak environmental hygiene laws, poor housing, and regional planning, indiscriminate disposal of wastes, poor food handling, and storage, absence of a law against eating Mastomys natalensis, deforestation, and poor agricultural practices as well as climate change [3] [14] [17].

The urinalysis demonstrated the presence of both haematuria and proteinuria in a large number patients indicating a high frequency of renal involvement in the condition. In resource-deprived situations a combination of proteinuria and haematuria might act as a substitute for urea and electrolytes tests which need more advanced equipment. There should be early suspicion of Lassa fever in fe-

brile individuals presenting with this combination in the absence of other potential explanations. Acute renal damage has been demonstrated to be a primary cause of death in Lassa fever infection [21]. A substantial percentage of our study subjects in whom it was possible to test had liver enzymes indicating hepatic involvement in the condition. As a result of the out-of-pocket payment system, most patients could not afford adequate follow-up investigations. The delay in confirmation of diagnosis reported in this study was due to the logistics required in transferring samples to the nearest molecular laboratory which is a distance of more than 300 kilometers away. This also explains the difficulty of carrying out follow-up studies including a pre-discharge RT-PCR as indicated [15].

Treatment outcomes: Out of the 35 study subjects 27 (77.1%) survived and were discharged based on clinical improvement while 5 (14.3%) were sent to the centers with dialysis services. The mortality was 3 (8.6%) which is within the typical mortality rate for hospitalized patients handled in better-equipped, standard institutions [7] [12] [22] [23]. It was lower than that seen in other research findings from better-equipped centers [14] [18] [20]. This outcome might be explained by the fact that our patients who needed advanced care like dialysis were sent early for proper therapy thereby lowering the mortality that would have happened in the facility.

Conclusion: The study has found that there is a significant frequency of Lassa fever in Benue state affecting all categories of persons. Also, Lassa fever was effectively handled in our center with good clinical outcomes despite inadequate resources. Acute kidney injury and neurological sequelae were the causes of death in our study subjects.

Recommendations

Health personnel in resource-restricted environments but with adequate knowledge may treat Lassa fever in their facilities.

Patients with life-threatening complications should be recognized and referred early for advanced therapy to prevent death from the condition.

Limitations of the Study

Our limitation was the inability to conduct full investigations on the patients. This and missing results hampered the sample size in this study.

Conflicts of Interest

No conflict of interest was disclosed by any of the authors.

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