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The Impact and Morphology of Anaemia among Lassa Fever Patients Treated in a Dedicated Treatment Center in South West Nigeria

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Abstract

Background: The haematological indices in Lassa fever infection is not documented in the literature. The clinical relevance of anaemia on the disease course is also largely unknown.

Aim: In this study, we aim to determine the impact and morphologic types of anaemia in patients with Lassa fever infection using the red cell indices and to also determine the impact of anaemia on clinical course of the infection.

Method: Retrospective observational analytic study of data of confirmed Lassa fever cases managed in the Infection Control and Research Centre of federal Medical Centre Owo Nigeria from November 2018 to June 2019.

Results: A total of one hundred and eighty seven (187) confirmed cases were treated at the Infection Control Centre during this period of which we were able to obtain one hundred relevant data for our study (100). The age range was 1-90 years with a mean age range of 33.95 ± 18.80 , with 54% male and 46% female. A total of 69% (31 males, 38 females) had anaemia, while 31% had no anaemia, 47% had microcytic hypochromic anaemia, 22% had normocytic normochromic anaemia, 19% had bleeding diathesis, 16% had acute kidney injury, 12% had haemodialysis, 29% with severe anaemia were transfused, 80% had haematinics. The median duration of illness in days was 21 vs. 16.5 for those with or without anaemia respectively. The median duration in days for ribavirin use was 11 vs. 10 days for those with or without anaemia respectively. Four (4) people each died in both group, the low mortality may have been influenced by the readily availability of blood transfusion services, the other four from the non- anaemic group died from other complications not related to anaemia. All of the patients with anaemia were placed on haematinics as against 31% without anaemia. At discharge, 18(22.5%) patients with anaemia still remained positive with a positive Lassa PCR result after completion of 10days I.V ribavirin while 6(30%) had a negative Lassa PCR result.

Conclusion: This study has shown the significant impact of anaemia among Lassa fever patients, classified the morphology of anaemia in these categories of patients and reduced mortality outcome following a readily available blood transfusion service and relevant personnel. The study thus, emphasizes the role of a functional blood transfusion service and clinical haematologist in the management of Lassa fever patients. The recognition of these findings will help in management of Lassa fever patients with timely intervention where necessary.

Keywords: Anaemia; Clinical Haematologist; Fmc Owo; Hypochromic; Microcytic; Normochromic; Lassa Fever

Introduction

Lassa fever is an acute viral haemorrhagic fever caused by the Lassa fever virus [1,2]. It is a single-stranded RNA virus belonging to the arenaviridae [3]. The Lassa fever virus is an arena virus of public health importance with the reservoir host been the multimammate rat [4,5]. The virus is transmitted through contact with blood, urine, or excreta of infected rats or the body fluid of infected humans [5]. Lassa fever is endemic in West African countries such as Nigeria, Ghana, Benin, Mali, Sierra Leone, and Guinea. It is responsible for yearly epidemics with 300,000-500,000 cases per year and an estimated 5,000 deaths in West Africa [2]. It was first identified in Lassa town, Borno State, Nigeria in 1969 [6]. The mortality of Lassa fever is 10-20% but can be as high as 65% in hospital outbreaks [4,7,8]. Sporadic cases of Lassa fever are seen all year round with regular outbreaks in endemic areas [4]. These outbreaks have devastating health and socioeconomic implications [4]. The disease is transmitted to humans through contact with foods or household items contaminated with the rodent's urine or faeces. Person to person infection as well as laboratory transmission can also occur particularly in hospitals lacking adequate infection prevention and control measures [5,9]. The clinical spectrum of LF disease ranges from asymptomatic to fulminant multisystemic affection with a case fatality rate of 24 % from a retrospective review at Irrua Specialist Teaching Hospital, Edo, State, Nigeria [10]. The incubation period is six to twenty-one days however the virus is shed in urine for three to nine weeks and in semen for three months [3]. Anaemia is a condition in which haemoglobin concentration and/or Red Blood Cell (RBC) numbers are lower than normal and insufficient to meet the individual's physiologic needs [11]. It is defined as a reduction in haemoglobin concentration in peripheral blood below the reference range for the age and gender of the individual [12]. It affects roughly a third of the world's population and is associated with increased morbidity and mortality in women and children, poor birth outcomes, and decreased work productivity [11]. Its pathogenesis ranges from reduced or ineffective erythropoiesis, increased red cell loss or reduced RBC life span and dilutional anaemia due to plasma volume expansion [12-15]. Viral infections can cause direct and indirect damage to hematopoietic stem cells (HSPCs) and surrounding tissues, numerous viral infections have been associated with bone marrow failure or hyperproliferative syndrome. Examples of such viruses are Parvovirus B19, CMV, EBV, HIV. Acute viral infections usually cause transient aplasia which is partly related to the effect of cytokines such as type 1 interferon and the depletion of HSPCs and stromal cells [16,17].

It has also been reported in certain viral haemorrhagic fevers such as Ebola and Dengue though the exact mechanism is poorly

understood, it is postulated that the above stated could play a role alongside the disseminated intravascular coagulopathy which is due to the massive systemic inflammatory response leading to diffuse dilatation of small vessels and increased permeability of their endothelial linings. Most haemorrhagic viruses are hepatotropic hence causing direct complications such as acute kidney injury which may arise from Lassa fever can result in anaemia. In a study to evaluate the intradialytic complications of Lassa fever patients with AKI, anaemia was found in 65.1% of the study population [18]. In another study done among hospitalized patients with Ebola virus, there was no report of anaemia on the first visit or hospitalization day however, anaemia was observed between the 17th and 20th day of illness. It was difficult to postulate the exact mechanism in these cases and further studies were suggested [19]. Anaemia can also result from the treatment of these viral infections. Drugs implicated are pegylated interferon and ribavirin. Pegylated interferon causes medullary suppression however it is not used in the treatment of Lassa fever [20]. Ribavirin which is the drug of choice in the management of Lassa fever is known to cause haemolytic anaemia. It is an antiviral nucleoside analogue and causes severe anaemia in about 10% of treated patients for chronic hepatitis C [21].

It exerts its toxicity through inhibition of intracellular energy metabolism and oxidative membrane damage leading to accelerated extravascular haemolysis by the reticuloendothelial system. Recent studies suggest that erythrocyte oxidative defence mechanisms may play an important role in ribavirin induced anaemia. Clinical risk factors for severe ribavirin induced anaemia are impaired renal function, advanced age, high dose per body weight, and female gender [21]. The reduction in haemoglobin levels appears to correlate with the degree of haemolysis and inversely with the erythropoietic ability of the bone marrow [22]. Few studies have documented evidence of anaemia among Lassa fever patients; the impact, clinical course and morphology of anaemia among Lassa fever patients have not been widely reported. This study is anchored on determining the impact, clinical course, morphologic types of anaemia among patients with Lassa fever infection using the red cell indices.

Materials and Methods

Study Site: The study was conducted in the Infection Control and Research Center (ICRC) of Federal Medical Center, Owo, Ondo State Nigeria. It was a retrospective study that targets those individuals that were tested positive for lassa virus using PCR.

Data source: Case records of patients admitted in the ICRC of Federal Medical Center Owo, were retrieved and analysed using SPSS version 21. Frequencies and proportions were generated and presented using tables and figures where necessary. Bivariate analysis was carried out using Pearson correlation test, Chi-square test and Fisher exact test for comparison of proportions for

categorical variables and independent student t-test for comparison of means for continuous variables where necessary. The level of statistical significance was defined by $p < 0.05$.

Equipment: Automated Haematology analyzer pocH-100i, S/N G5669, Sysmex Corporation, 03/2018 made in Japan, Quantitative PCR machine, Model Rotor-Gene Q, S/N RO516117, Qiagen Hilden, Germany, manufactured in Malaysia. Extraction centrifuge, Eppendorf AG, S/N 5418FL724392, Designed and engineered in Germany, assembled in USA Glove box, PLAS LABS, Model 815-PGB/EXP, S/N 14618, Manufactured in 5/11/18 at Lansing, MI 48906. Other equipment includes, consumables, vacutainer sample collection tubes.

Study design: The medical case record files of 187 cases of confirmed Lassa fever managed at Infection Control Center of Federal Medical Center Owo, over a period of eight (8) months, November 2018 to June 2019 was assessed, only 100 case records were relevant to the study of which 54 (54%) and 46 (46%) were male and female respectively.

Inclusion Criteria

- All confirmed LF infected patients that were managed at the Infection Control Unit of the hospital provided they signed their informed consent to participate in this study.
- All confirmed LF infected patients who had their Full Blood Count done (FBC).

Exclusion Criteria

- Those confirmed LF infected patients who did not sign their informed consent were deemed ineligible and were therefore excluded from this study.
- Those confirmed LF infected patients with incomplete data or no evidence of FBC were excluded.
- Suspected LF cases that turned-out to be negative to the Lassa Polymerase Chain Reaction (PCR) test.

Ethical Consideration and Informed Consent

Ethical clearance/approval was obtained from the Institutional Health Research Ethical Committee before commencing this study. In addition, a duly signed written informed consent was obtained from each of the patients whose medical case record files were used while the medical case record files for those who did not sign their informed consent were excluded from this study.

Participants' confidentiality was respected and maintained by ensuring that no unauthorized person had access to the information on the data information sheets, that no information can be traced to the subjects (as coding system was used for the data information sheets instead of writing the patients' names on them) and no unauthorized use of information was made.

Results

A total of one hundred and eighty seven (187) confirmed cases were treated at the Infection Control and Research Centre during this period of which we were able to obtain one hundred relevant data for our study (100). The age range was 1-90 years with a mean age range of 33.95 ± 18.80 , with 54% male and 46% female. A total of 69% had anaemia (31males and 38females), while 31% had no anaemia, 47% had microcytic hypochromic anaemia, 22% had normocytic normochromic anaemia, 19% had bleeding diathesis, 16% had acute kidney injury, 12% had haemodialysis, 29% (42% of anaemic patients) with severe anaemia were transfused, and all patients had haematinics. The median duration of illness in days was 21vs.16.5 for those with or without anaemia respectively. The median duration in days for ribavirin use was 11 vs. 10 days for those with or without anaemia respectively. Four (4) people each died from both group, among the anaemic population, the low mortality may have been influenced by the readily availability of blood transfusion services, the other four from the non-anaemic group died from other complications not related to anaemia (Tables 1 and 2). At discharge, 18(22.5%) patients with anaemia still remained positive with a positive Lassa PCR result after completion of 10days I.V ribavirin while 6(30%) had a negative Lassa PCR result (Figures 1-4).

Characteristic	Frequency (N=100)
Age, mean \pm SD, years	33.8 ± 18.9
Age, range, years	1-90
Male, n	54
Female, n	46
Hepatitis B co-infection, n	5
HIV co-infection, n	1
*Anaemia, n	
M=31	69
F=38	
^Microcytic hypochromic, n	47
^Normocytic normochromic, n	22
Bleeding, n	19
Blood transfusion, n	29
Acute Kidney Injury, n	16
Haemodialysis, n	12
Encephalopathy, n	8
Hypertension, n	6
Diabetes, n	1

*Anaemia is defined according to WHO criteria: <13 g/dL in males and <12 g/dL in females

^ The morphologic system divides anaemias into (1) microcytic (MCV < 80), hypochromic (MCH < 27); (2) macrocytic (MCV > 100), normochromic (MCH 30-34); and (3) normocytic (MCV 80-100).

Table 1: Demographic and Clinical Characteristics of Lassa fever Infected Patients.

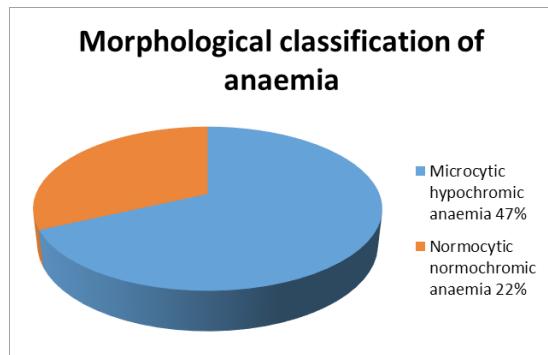


Figure 1: The Morphology of Anaemia among Lassa fever Patients.

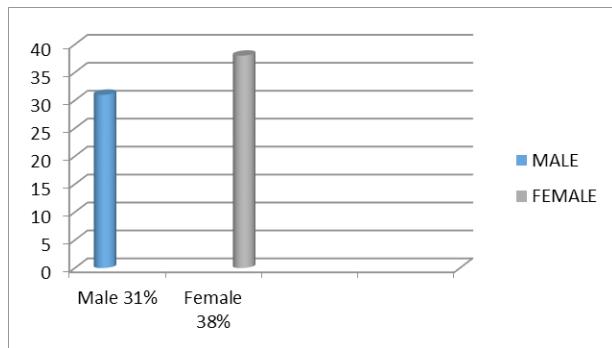


Figure 2: Gender Distribution of Anaemia.

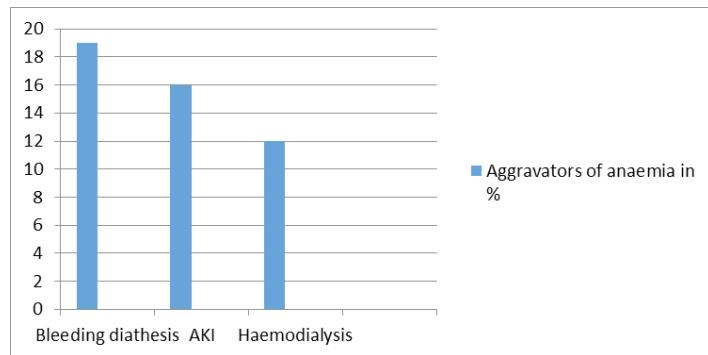


Figure 3: Aggravators of Anaemia among Lassa fever Patients.

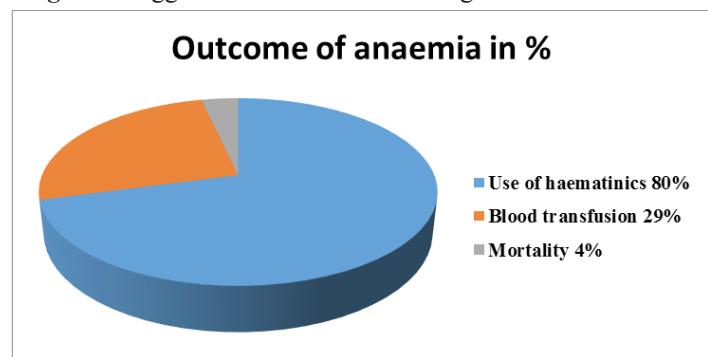


Figure 4: Shows the Outcome of Anaemia among Lassa fever Patients.

Discussion

Anaemia is a condition in which haemoglobin concentration and/or Red Blood Cell (RBC) numbers are lower than normal and insufficient to meet the individual's physiologic needs [11]. Viruses such as such Parvovirus B19, CMV, EBV and HIV have been reported to cause anaemia [16]. Lassa fever patients with anaemia are classified to be in stage 2 of McCarthy clinical staging [23]. However, not much emphasis has been placed on the burden and morphology of anaemia among Lassa fever patients, a knowledge gap that has now been bridged by the findings in this research article. The prevalence of anaemia was found to be 69%, 29% of these patients were transfused with at least two units of packed red cells to as high as twenty one (21) units in severe cases, while 80% of patients received haematinics. Microcytic hypochromic anaemia was seen in 47% of these patients as against 22% of patients with normocytic normochromic anaemia. The following conditions were observed to worsen anaemia in these patients, bleeding diathesis (Haematuria, bleeding from IV sites, cutaneous bleeds), AKI and haemodialysis in this order, 19%, 16% and 12% respectively. The incidence of death was 6% (4/69) among the population with anaemia, the low incidence of death is largely attributed to a readily available, functional blood transfusion system, use of haematinics and services of a clinical haematologist.

Variable	Day 1 Mean±SD	Day 5 Mean±SD	Day 10 Mean±SD
RBC,	4.25±0.71	4.00±0.76	3.76±0.91
Haemoglobin,	11.50±2.11	10.63±1.97	9.79±2.25
Haematocrit,	33.06±5.68	30.56±5.83	28.33±5.86
MCV,	76.82±10.39	76.42±9.17	76.36±9.46
MCH,	27.84±5.76	27.09±2.90	26.76±2.83
MCHC,	35.00±3.05	35.07±2.91	34.65±2.79
RDW,	41.39±7.90	NA	NA
WBC	8.34±7.61	9.40±11.05	7.30±4.07
Neutrophils	4.79±4.99	4.87±4.11	NA
Lymphocytes	5.87±23.76	2.85±2.69	2.33±1.25
Monocytes	1.21±1.87	NA	NA
Platelet count	244.49±160.31	275.97±147.92	
PDW	15.01±0.72	NA	NA

Table 2: Haematological Parameters of Lassa fever Infected Patients.

Conclusion

This study has shown the significant impact of anaemia among Lassa fever patients, classified the morphology of anaemia in these categories of patients and reduced mortality outcome following a readily available blood transfusion service and relevant personnel. The study has emphasized the role of a functional blood transfusion service and clinical haematologist in the management of Lassa fever patients. The recognition of these findings will help in monitoring and evaluation of Lassa patients with timely intervention where necessary.

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Conflict of Interest

There is no conflict of interest.

Contributions

All authors contributed equally in data collection, writing and result analysis.

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God almighty, the father of all knowledge.

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