



Contribution and Characterization of Lassa fever in Severe Acute Kidney Injury (AKI) in Endemic Areas of Southern Nigeria: A Retrospective Observational Study

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Abstract

Background : Amongst the diverse etiologies of severe acute kidney injury (AKI), Lassa fever (LF) occupies a prominent position in endemic areas of West Africa. However, there is a paucity of studies that compare the characteristics of LF and non-LF-associated cases.

Objectives : To determine the contribution of LF to severe AKI in an endemic area, and compare the illness characteristics and factors associated with mortality in LF versus non-LF-associated AKI.

Methods : We reviewed the records of patients admitted with severe AKI from 1st January 2019 to 30th September 2022 at Irrua Specialist Teaching Hospital (ISTH), and retrieved data on patients' demography, clinical presentation, treatment, and outcome. We compared the frequencies of categorical data and means of continuous data between patients with LF and those without LF using chi-square test, t-test, and Mann-Whitney U test as appropriate, with the level of statistical significance set at $p < 0.05$.

Results : Fifty-four (41.5%) of 130 patients with severe AKI had LF. LF was associated with a significantly lower mean age ($p = 0.013$), platelet count ($p = 0.010$), and mean levels of indices of renal dysfunction ($p = 0.02 - <0.001$) but there was no significant difference in mortality rates (LF 27.8%; non-LF 39.5%; $p = 0.1674$). The overall mortality was associated with need for inotropes, requirement for supplemental oxygen, and hemodialysis, and length of admission while the association of mortality with the latter and need for supplemental oxygen was only significant among patients without LF.

Conclusions : LF is a major cause of severe AKI in endemic areas, but it is not associated with any differential risk of mortality perhaps because the associated renal dysfunction is not as severe as in non-LF AKI.

Keywords: Severe acute kidney injury; Hemodialysis; Lassa fever; Mortality; Non-LF-AKI.

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INTRODUCTION

Lassa fever (LF) is an acute viral haemorrhagic disease caused by the Lassa virus, a member of the arenavirus family of viruses. The virus is transmitted through contact with blood, urine or excreta of infected Mastomys rats, and through contact with the blood and body fluids of infected humans. It is endemic in West African countries, and Nigeria is one of the most affected [1,2]. About 100,000 to 300,000 cases of LF occur annually with about 5,000 deaths [3,4].

Acute kidney injury (AKI) is a significant public health problem in Sub-Saharan Africa (SSA), with incidence rates ranging from 5.7% to 50% [5-7], and with mortality of up to 58% in a cohort study [5]. One of the contributors to the high mortality rates is the dearth of hemodialysis services [5]. Acute kidney injury (AKI) is a frequent complication of LF



and prevalence rates as high as 28.5% among hospitalized patients with LF have been reported [6], while its presence increases the risk of death in LF by as much as 60% [6].

Despite its prevalence and significance however, and the prevalence and significance of AKI in the general population, epidemiological data on the contribution of LF to the general burden of AKI in SSA is hard to come by. This dearth constitutes an important constraint in the formulation of guidelines for the management of AKI. It could also be a constraint in the formulation of policies for the diagnosis, treatment, and prevention of AKI in endemic countries, which might be one of the reasons why effort has been slow in the provision of facilities for hemodialysis of infected patients in endemic areas. While the management of AKI is mainly supportive with intravenous fluids, antibiotics, blood product transfusion, and use of inotropes, hemodialysis is not infrequently indicated when conservative management fails.

We have been fortunate at Irrua Specialist Teaching Hospital (ISTH) to have facilities for the diagnosis and management of LF including facilities for hemodialysis of LF-infected and non-infected persons since 2010. Thus, we have had the opportunity to build up a pool of experience in the management of both sets of patients, which should enable us to contribute to knowledge of the proportion of AKI associated with LF and on the differences in presentation as well as outcomes. We believe that this provides important insights that can improve our understanding and treatment of AKI in endemic areas.

MATERIALS AND METHODS

We carried out this study at the Institute of Viral and Emergent Pathogens Control and Research (IVEPCR) (formerly Institute of Lassa Fever Research and Control, ILFR&C), ISTH, in the South-South geopolitical zone of Nigeria. The Institute is a dedicated Lassa fever diagnosis and treatment facility with an isolation ward, molecular laboratory and dialysis unit which receives referrals from all over Nigeria [8].

We reviewed the records of all patients >18 years in age with severe AKI between 1st January 2019 and 30th September 2022 and retrieved information on their demography (age, sex, and residential address), clinical and laboratory data at the time of presentation, co-morbid medical conditions, number of days of illness before the first session of hemodialysis, number of hemodialysis sessions, duration of hospital stay and outcomes, died versus survived. The diagnosis of AKI was made using Kidney Disease Improving Global Outcomes [KDIGO] criteria [9]: increased serum creatinine by at least 0.3 mg/dl [26.5/mmol/l], within 48 hours or by 1.5 times baseline value known or presumed to have occurred within the prior 7 days or urine output <0.5 ml/kg/h for 6 hours. Severe AKI was as defined by Acute Kidney Injury Network (AKIN) as AKI stage 3 [9].

We managed the patients conservatively but had to dialyze them whenever conservative management failed as evidenced by worsening clinical state or azotemia, or the development of any feature consistent with uremia. We carried out hemodialysis using Fresenius 4008S (Fresenius Medical Care Australia Pty Ltd., Northpoint, North Sydney), and Gambro AK 98 (Gambro Lundia AB, Magistratsvagen, LuN, Sweden) hemodialysis machines. Intermittent hemodialysis sessions were continued until AKI resolved or the patient died. The diagnosis of LF in our patients was confirmed using reverse transcriptase polymerase chain reaction (RT-PCR) test (one-step RT-PCR kit reagents, number 210210 or 210212; RealStar®, Altona, Hamburg, Germany) as described previously [10]. The treatment of patients with LF in our center has also been described previously [6,8].

DATA ANALYSIS

We carried out statistical analyses using SPSS version 23.0 (IBM, Chicago, IL, USA). We explored for the significance of differences between groups (LF- versus non-LF-AKI) using chi-square test for categorical

variables and independent sample t-test or Mann-Whitney U test for continuous variables depending on the nature of the distribution. Furthermore, we analysed for the interdependence of variables found to have significant associations with mortality on bivariate analysis using multiple logistic regression. The variables entered included age, duration of admission for more than one-week, and need for inotropes, supplemental oxygen, and renal replacement therapy. The level of statistical significance was set at $p < 0.05$ in all the analyses.

ETHICAL CONSIDERATIONS

Ethical clearance for the study was obtained from the Health Research Ethics Committee (HREC) of ISTH (approval letter ISTH/HREC/20222610/428). Confidentiality of Data was assured using questionnaires with codes assigned in retrieving information and removing all personal identifiers from the questionnaires.

RESULTS

Our study included 130 patients with severe AKI. 54 (41.5%) had LF-AKI and 76 (58.5%) had non-LF etiologies including sepsis ($n = 33$, 25.4%), acute glomerulonephritis ($n = 12$, 9.2%), obstetric complications ($n = 9$, 6.9%), malignant hypertension ($n = 6$, 4.6%), cardio-renal syndrome ($n = 5$, 3.8%), hepatorenal syndrome ($n = 4$, 3.1%), surgical complications ($n = 4$, 3.1%), and COVID-19 ($n = 3$, 2.3%).

Overall, 52 (40.0%) of the 130 patients with severe AKI had medical comorbidities including systemic hypertension ($n = 29$, 22.3%), chronic kidney disease, CKD ($n = 12$, 9.2%) and diabetes mellitus ($n = 11$, 8.5%). Patients with non-LF AKI had a significantly higher prevalence of systemic hypertension (26/76, 34.2% versus 3/54, 5.6%; $p = 0.001$) and diabetes mellitus (11/76, 14.5% versus 0/54, $p = 0.03$), than those with LF-AKI.

The overall age range of our patients was 18 - 78 years; 87 (66.9%) of the patients were 18 - 44 years old, 28 (21.5%) 45 - 64 years and 16 (12.3%) >65 years old. The proportion of patients with LF-AKI decreased significantly with age (42/87, 48.3% versus 11/28, 39.3% versus 1/16, 6.2%, respectively; $p = 0.010$). The mean age of our patients was 40.9 ± 14.9 years but those with LF-AKI had a significantly lower mean age (37.3 ± 11.3 years versus 43.5 ± 16.6 years; $p = 0.013$) compared to those with non-LF-AKI.

Most ($n = 115$, 88.5%) of our patients were from Edo State and 15 (11.5%) from other states (Ondo State 4, Delta State 4, Lagos State 3, Imo State 2, Benue State 1, and Anambra State 1). The cohort included 94 males (72.3%) and 36 females (27.7%) but there was no significant association between gender and AKI etiology (37/94 M, 39.4% versus 17/36 F, 47.2%; $p = 0.416$) had LF-AKI. About two-thirds of the patients (66.2%) were married.

The mean of vital signs, blood counts, serum electrolytes, urea and creatinine, and random blood glucose of the patients on admission are shown in Table 1 in relation to the etiology of AKI (LF versus non-LF) and the corresponding differences in frequencies and proportions (%) of those with abnormalities in Table 2. LF-AKI was associated with a significantly younger mean age ($p = 0.013$), lower mean platelet counts ($p = 0.01$), and lower mean serum bicarbonate ($p = 0.011$), potassium ($p = 0.02$), urea ($p < 0.001$) and creatinine ($p < 0.001$) levels. The other differences were not significant (Table 1). LF-AKI was also associated with a significant higher proportion with fever ($p = 0.005$) and hypokalemia ($p = 0.001$) and non-LF-AKI with hyperkalemia ($p = 0.007$) (Table 2). The other differences were not significant (Table 2).

TREATMENT AND FACTORS ASSOCIATED WITH HOSPITAL OUTCOMES IN LF- VERSUS NON-LF-AKI

One hundred and eighteen patients (90.8%) had hemodialysis while 12 (9.2%) were managed conservatively. The overall mean duration ($\pm$ standard deviation) of illness before the first session of hemodialysis was



Table 1: Mean admission vital signs, blood counts, serum electrolytes, urea, creatinine, and random blood glucose levels in LF- versus non-LF-AKI

Variables	Reference range	Mean $\pm$ standard deviation in patients with		p
		LF-AKI (N = 54)	Non-LF-AKI (N = 76)	
Temperature ($^{\circ}$ C)	36.6 – 37.2	37.50 $\pm$ 1.29	37.1 $\pm$ 1.1	0.06
Respiratory rate/min	12 – 18	24.15 $\pm$ 3.6	24.6 $\pm$ 3.9	0.519
Pulse rate/min	60 – 100	90.83 $\pm$ 16.26	93.1 $\pm$ 15.6	0.432
Average DBP (mmHg)	60 – 89	80.22 $\pm$ 8.79	80.3 $\pm$ 15.3	0.970
Average SBP (mmHg)	90 – 129	127.67 $\pm$ 15.28	130.8 $\pm$ 26.6	0.395
PCV (%)	38.5 – 48.6*	28.03 $\pm$ 9.04	29.9 $\pm$ 7.9	0.234
Platelet count ($\times 10^3/\mu$ L)	150 – 450	190 $\pm$ 84.68	237.3 $\pm$ 121.9	0.010
Sodium (mmol/L)	135 – 145	136.02 $\pm$ 5.60	135.1 $\pm$ 6.7	0.386
Bicarbonate (mmol/L)	22 – 29	13.2 $\pm$ 5.1	15.3 $\pm$ 4.2	0.011
Potassium (mmol/L)	3.5 – 5.0	4.4 $\pm$ 0.9	4.9 $\pm$ 0.9	0.020
Urea mg/dL	17 – 43	157.7 $\pm$ 62.1	206.6 $\pm$ 81.1	<0.001
Creatinine mg/dL	0.6 – 1.2	7.0 $\pm$ 3.0	10.5 $\pm$ 5.6	<0.001
RBG (mg/dL)	70 – 140	114.4 $\pm$ 41.0	130.3 $\pm$ 55.8	0.630
WBC ($\times 10^3/\mu$ L)	4.5 – 11	12.6 $\pm$ 7.9	13.2 $\pm$ 7.9	0.649

Abbreviations: PCV = packed cell volume, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, WBC = White blood cell, RBG = Random blood glucose.

*35.5 - 44.9% in non-pregnant females.

Table 2: Proportion of patients with LF- versus non-LF-AKI who had clinical and laboratory abnormalities on admission.

	Definition of abnormality	No. (%) of patients with		OR (95% CI)	<i>P</i>
Variables		LF-AKI (N = 54)	Non-LF-AKI (N = 76)		
Clinical abnormalities					
Fever	Temp. >37.2°C	22 (40.7)	14 (18.4)	3.04 (1.38, 6.74)	0.005
Tachycardia	PR >100/min	18 (33.3%)	29 (38.2%)	0.81 (0.39, 1.68)	0.573
Syst. hypotension	SBP <90mmHg	NIL	1 (1.3)	UD	0.397
Syst. hypertension	SBP ≥130mmHg	12 (12.2)	16 (21.1)	0.99 (0.43, 2.29)	0.984
Diast. hypotension	DBP <60mmHg	NIL	2 (2.6%)	UD	0.278
Diast. hypertension	DBP ≥80mmHg	5 (9.3)	10 (13.2)	0.67 (0.22, 2.10)	0.278
Laboratory abnormalities					
Anemia	PCV <35.5%	33 (61.1)	43 (57.3)	1.21 (0.59, 2.45)	0.605
Leukopenia	WBC <4.5 x 10 ³ /μL	3 (5.6)	2 (2.6)	2.18 (0.35, 13.49)	0.393
Leukocytosis	WBC >11 x 10 ³ /μL	25 (46.3)	38 (50.0)	0.86 (0.43, 1.73)	0.677
Thrombocytopenia	Platelets <150 x 10 ³ /μL	6 (11.1)	15 (19.7)	0.51 (0.18, 1.41)	0.188
Hypokalemia	Serum K ⁺ <3.5mmol/L	10 (18.5)	1 (1.3)	17.05 (2.11, 137.7)	0.001
Hyperkalemia	Serum K ⁺ >5.0mmol/L	10 (18.5)	31 (40.8)	0.33 (0.14, 0.75)	0.007
Hyponatremia	Serum Na ⁺ <135mmol/L	16 (29.2)	34 (85.0)	0.52 (0.25, 1.09)	0.081
Hypernatremia	Serum Na ⁺ >145mmol/L	1 (1.9)	4 (5.3)	0.34 (0.04, 3.13)	0.319
Metabolic acidosis	Serum HCO ₃ ⁻ <22mmol/L	50 (92.6)	69 (90.8)	1.27 (0.35, 4.57)	0.716
Hypoglycemia	RBG <70mg/dL	9 (16.7)	7 (9.2)	1.97 (0.68, 5.67)	0.203
Hyperglycemia	RBG >180mg/dL	20 (37.0)	34 (44.7)	0.73 (0.36, 1.48)	0.380

Abbreviations: LF = Lassa fever, AKI = acute kidney injury, OR (95% CI) = Odds Ratio (95% Confidence Interval), Temp = temperature, PR = pulse rate, Syst = systolic, Diast = diastolic, SBP = systolic blood pressure, DBP = diastolic blood pressure, PCV = packed cell volume, WBC = white blood cell count, RBG = random blood glucose, UD = undefined.



6.7 ± 2.9 days, and the mean number of hemodialysis sessions was 3.7 ± 2.3, while the mean duration of admission was 3.0 ± 1.4 weeks. The differences in proportions of those in need of supportive care therapies among LF and non-LF patients are shown in Table 3 as is the difference in duration of illness before the first session of hemodialysis. The only significant difference was the higher need for inotropic support among patients with LF (p = 0.031).

Overall, 45/130 (34.6%) patients died. Mortality rate was higher in non-LF-AKI, but the difference did not attain our set level of statistical significance (30/76, 39.5% versus 15/54, 27.8% in LF; Odds Ratio (95% Confidence Interval) = 1.70 (0.80, 3.60), p = 0.167). We show the results of bivariate analysis of the association between presenting clinical features and outcome in LF- and non-LF-AKI in Tables 4A and B. The presence of dyspnea at presentation in the overall cohort of patients with AKI (p <0.001), patients with non-LF AKI (p <0.001) and LF- versus non-LF-AKI (p <0.001) was associated with a significantly higher risk of death Tables 4A and B. The other relationships were not significant.

We performed multivariate logistic regression analysis to ascertain the interaction between the effects of age, requirements for inotropes, hemodialysis and supplemental oxygen, duration of admission, and putative cause of AKI (LF versus non-LF) and outcome (death versus survival). The duration of admission, and requirements for inotropes, oxygen supplementation, and hemodialysis were significantly associated with overall mortality (Table 5), while the duration of hospital admission and requirement for oxygen therapy were significantly associated with death in non-LF-AKI (Table 5). None of the factors was significantly associated with death among patients with LF-AKI (Table 5).

DISCUSSION

We had earlier described the prevalence of AKI among our patients with LF, 28.5% in adults and 40% in children [6, 8,11]. We had also described the response of our patients with LF to hemodialysis [11], as well as shared our experience of the impact of dedicated treatment centers on the outcome of LF [8]. Our focus in the present study was to

Table 3: Differences in supportive care needs and pre-dialysis duration of illness between LF and non-LF patients with severe AKI.

Variables	Etiology of AKI		OR 95% CI	P
	LF (N = 54)	Non-LF		
	No. (%)	(N = 76) No. (%)		
No. (%) given dopamine infusion	47 (87.0)	54 (71.1)	2.73 (1.07, 6.97)	0.031
No. (%) hemodialyzed	51 (94.4)	67 (88.2)	3.28 (0.59, 8.86)	0.222
No. (%) given supplemental oxygen	35 (64.8)	47 (61.8)	1.14 (0.55, 2.35)	0.729
Mean ± SD no. of days of illness before 1 st hemodialysis	6.5 ± 2.8	6.7 ± 2.9	Not applicable	0.717

Abbreviations: LF = Lassa fever; AKI = acute kidney injury; OR (95% CI) = Odds Ratio (95% Confidence Interval)

Table 4A: Association between presenting symptoms and mortality in LF- and non-LF AKI

Presenting symptoms	LF-AKI (n = 54)			Non-LF-AKI (n = 76)		
	No. died/N with symptom (%)	*OR (95% CI) of death	p	No. died/N with symptom (%)	*OR (95% CI) of death	p
Fever	14/51 (27)	0.76 (0.06, 9.02)	0.825	19/53 (36)	0.61 (0.23, 1.64)	0.326
Headache	8/30 (27)	0.68 (0.27, 2.92)	0.838	8/28 (29)	0.47 (0.17, 1.20)	0.138
Confusion	4/13 (31)	1.21 (0.31, 4.75)	>0.999	5/17 (29)	0.57 (0.18, 1.81)	0.335
Hiccups	3/9 (33)	1.37 (0.30, 6.38)	0.966	5/17 (22)	0.57 (0.18, 1.81)	0.335
Cough	2/10 (20)	0.51 (0.10, 2.71)	0.699	6/12 (50)	1.67 (0.48, 5.78)	0.616
Hemoptysis	2/7 (29)	1.05 (0.18, 6.08)	>0.999	8/16 (50)	1.73 (0.57, 5.78)	0.332
Chest pain	3/12 (25)	0.83 (0.19, 3.62)	>0.999	7/16 (44)	1.25 (0.41, 3.82)	0.694
Dyspnea	4/12 (33)	1.41 (0.35, 5.62)	0.879	27/47 (57)	11.7 (3.10, 44.13)	<0.001
Vomiting	10/32 (31)	1.54 (0.44, 5.37)	0.492	8/28 (29)	0.92 (0.35, 2.40)	0.867
Diarrhea	7/17 (41)	2.54 (0.13, 8.80)	0.247	3/10 (30)	0.62 (0.15, 2.61)	0.771
Dehydration	4/14 (29)	1.05 (0.23, 4.07)	>0.999	21/1 (52)	2.08 (0.75, 5.78)	0.155
Abdominal pain	6/23 (26)	0.86 (0.26, 2.90)	0.811	11/34 (32)	0.58 (0.23, 1.48)	0.254
Jaundice	2/14 (14)	0.42 (0.08, 2.16)	0.494	4/10 (40)	1.03 (0.26, 3.99)	>0.999
GI bleeding	3/9 (33)	1.37 (0.30, 6.38)	0.966	8/14 (57)	2.42 (0.74, 7.88)	0.134
Oliguria	4/16 (25)	0.82 (0.22, 3.10)	>0.999	9/28 (32)	0.61 (0.23, 1.62)	0.318

Abbreviations: LF-AKI = Lassa fever AKI, AKI = acute kidney injury, OR (95% CI) = Odds Ratio (95% Confidence Interval), GI = gastrointestinal tract

*Mortality associated with presence vs absence of symptom



Table 4B: Association between presenting symptoms and mortality in all patients with AKI and in patients with LF- versus non-LF-AKI

Presenting symptoms	All cases (n = 130)			Mortality in LF patients with symptom	Mortality in non-LF patients with symptom	**OR (95% CI) of death in LF versus non-LF AKI	p
	No. died/N with symptom (%)	*OR (95% CI) of death	p				
Fever	33/104 (32)	0.54 (0.23, 1.3)	0.167	14/51 (27)	19/53 (36)	8.10 (0.93, 70.3)	0.063
Headache	16/58 (28)	0.56 (0.27, 1.19)	0.131	10/32 (31)	8/28 (29)	3.14 (0.86, 11.5)	0.078
Confusion	9/30 (30)	0.76 (0.32, 1.84)	0.545	4/13 (31)	5/17 (29)	1.82 (0.41, 8.10)	0.677
Hiccups	8/26 (31)	0.80 (0.32, 2.03)	0.645	3/9 (33)	5/17 (29)	1.25 (0.25, 6.12)	>0.999
Cough	8/22 (36)	1.10 (0.42, 2.85)	0.850	2/10 (20)	6/12 (50)	0.61 (0.11, 3.49)	0.916
Hemoptysis	10/23 (43)	1.58 (0.63, 3.96)	0.325	2/7 (29)	8/16 (50)	0.42 (0.08, 2.30)	0.539
Chest pain	10/28 (26)	1.06 (0.44, 2.55)	0.890	3/12 (25)	7/16 (44)	0.82 (0.18, 3.76)	>0.999
Dyspnea	31/59 (52)	4.51 (2.07, 9.80)	<0.001	4/12 (33)	27/47 (57)	0.04 (0.01, 0.211)	<0.001
Vomiting	29/81 (36)	1.15 (0.54, 2.43)	0.714	10/32 (31)	19/49 (39)	1.16 (0.31, 4.27)	0.826
Diarrhea	10/27 (37)	1.14 (0.47, 2.76)	0.766	7/17 (41)	3/10 (30)	7.87 (1.64, 37.69)	0.018
Dehydration	15/35 (43)	1.62 (0.73, 3.61)	0.231	4/14 (26)	11/21 (52)	0.63 (0.16, 2.46)	0.502
Abdominal pain	17/57 (30)	0.68 (0.33, 1.43)	0.312	6/23 (26)	11/34 (32)	1.15 (0.32, 4.11)	0.828
Jaundice	6/24 (25)	0.57 (0.21, 1.56)	0.274	2/14 (14)	4/10 (40)	1.00 (0.16, 6.19)	>0.999
GI bleeding	11/23 (48)	1.97 (0.79, 4.91)	0.142	3/9 (33)	8/14 (57)	0.69 (0.15, 3.09)	0.920
Oliguria	13/44 (29)	0.71 (0.32, 1.55)	0.385	4/16 (25)	9/28 (32)	0.85 (0.21, 3.39)	>0.999

Abbreviations: LF-AKI = Lassa fever AKI, AKI = acute kidney injury, OR (95% CI) = Odds Ratio (95% Confidence Interval), GI = gastrointestinal tract

*Mortality associated with presence vs absence of symptom

**Mortality in LF- vs non-LF-AKI associated with presence of symptom

Table 5: Unadjusted Odds Ratios (95% Confidence Intervals) of death associated with clinical presentation and treatment of Lassa and non-Lassa AKI in multiple regression analysis.

Variable	OD (95% CI), p		
	All patients (n = 130)	LF-AKI (n = 54)	Non-LF-AKI (n = 76)
Age in years	1.03 (1.00, 1.06), 0.105	0.85 (0.70, 1.04), 0.105	1.03 (1.00, 1.07), 0.072
Duration of admission, weeks	3.54 (1.05-11.92), 0.042	0.75 (0.05, 11.92), 0.836	8.28 (1.25, 54.81), 0.028
Inotropic support	0.20 (0.07, 0.59), 0.004	0.00 (0.00, 0.00), 0.998	0.53 (0.14, 1.97), 0.341
Supplementary oxygen	3.81 (1.20, 12.05), 0.023	2.29 (0.29, 18.35), 0.436	7.43 (1.55, 35.53), 0.012
Hemodialysis	0.22 (0.05, 0.93), 0.039	0.07 (0.00, 1.12), 0.060	0.28 (0.05, 1.59), 0.275
Lassa fever as etiology	0.85 (0.33, 2.18), 0.729	Not applicable	Not applicable



compare the characteristics of illness on presentation, and the hospital course and outcome of patients with LF- and non-LF-AKI.

The male preponderance among our patients is as in previous reports [6,11]. Although Ibrahim et al., had reported a nearly equal gender distribution [12], it is generally accepted that the risk of AKI is higher in males independent of other risk factors [13]. This has been explained as due to the protective effect of the female sex chromosome in the presence of ischemia-reperfusion injury [14-16]. The healthcare assess bias in favor of males in developing countries may be an additional factor in the male preponderance [17].

LF was a prominent cause of severe AKI in this study, although previous studies have reported sepsis, volume depletion and nephrotoxins as the main causes [17-20]. The prominent role of LF among our patients could be because Isth has a dedicated facility for the treatment of LF [11]. LF is itself an etiologic agent of sepsis and our findings could therefore simply be reflective of the etiology of AKI in LF endemic areas/countries. Without bias to these considerations, we saw an opportunity to contribute to data on the similarities and differences between LF- and non-LF AKIs in this report.

The pattern of vital signs could be predictive of the risk of renal damage in some infections such as malaria [21]. While to the best of our knowledge, there is paucity of studies on presenting vital signs in patients with AKI, our findings could be in keeping with this observation [21]. The pattern could be related to the accompanying derangement in electrolyte levels, anemia, and anxiety among the patients. It is understandable that more patients with LF had fever on admission compared to those without LF because the latter group of patients included non-infective causes of AKI. The mean serum sodium, potassium, bicarbonate, urea, and creatinine levels among our patients are consistent with the usual findings in AKI [21-26]. The preponderance of hypokalemia in the LF subgroup could be explained by the observed higher incidence of diarrhea among them.

Thrombocytopenia on presentation has been associated with AKI among elderly patients [24]. The mean platelet counts were however within normal among our patients, many of whom were not elderly, although the mean count was expectedly lower among those with LF [27]. The white blood cell counts among our patients are in keeping with those in earlier reports on patients with AKI, and both leukopenia and leukocytosis have been associated with increased mortality among patients with AKI [28-30].

Ours is probably the first report on the differences between LF- and non-LF-AKI in adults. While the degree of acidosis was higher among patients with LF-AKI, the general trend was that of milder derangements in serum potassium, urea, and creatinine levels among them. Although the benefit is yet to be confirmed in patients with LF [31], other reports suggest that the institution of hemodialysis at lower serum urea and creatinine thresholds could enhance the chances of survival in critically ill patients with AKI [32-34]. The milder degree of azotemia in patients with LF AKI at presentation in this index study is however not explained by our set lower threshold for institution of hemodialysis but might theoretically be due to a lower rate of production of urea by the liver and creatinine by the muscles in LF [31]. More studies are required in this regard.

We observed that a longer duration of admission, and the need for inotropes, supplemental oxygen, and hemodialysis, all four of which are indices of a more severe disease with multiorgan dysfunction, predicted mortality in patients with AKI generally but not when subcategorized based on etiology into LF- versus non-LF-AKI. Abebe et al. [35], demonstrated that the severity and persistence of AKI are associated with increased mortality. At the same time, shorter periods of admission have also been associated with increased risk of death owing to issues of late referral, admissions in severe stages of AKI and presence of complications,

factors that may also be operative among long-staying patients [35,36]. There is therefore no real contradiction between our results and those of earlier studies [35, 36]. The apparent contradiction might be explained by the fact that improved supportive care could prolong the lives of critically ill patients.

Interestingly, there was no significant difference between the outcomes of LF- and non-LF-AKI. This may reflect the beneficial effect of early commencement of hemodialysis in those with LF as discussed earlier (vide supra). The impact of AKI on the outcome of LF has been described in earlier studies, [6,8,31,37], but to our knowledge, no previous study has described the impact of LF on the outcome of AKI. While the presence of two (longer duration of admission and need for supplemental oxygen) of the four factors noted in the preceding paragraph were associated with an increased risk of mortality among patients with non-LF-AKI, none of the factors had a significant association with mortality among those with LF. Dyspnea and diarrhea were the only presenting symptoms that had a significant association with mortality in non-LF-AKI while none of the presenting symptoms was associated with mortality in LF-AKI.

CONCLUSION

We conclude that LF is a prominent cause of AKI in endemic areas, but while there are important differences between LF and non-LF-AKI in the clinical and laboratory features on presentation as well as in the hospital course, there is no significant difference between them in mortality rates. This could be due to the use of lower thresholds of azotemia for initiation of hemodialysis in the former.

LIMITATION

Our study has a few limitations at least. Among them is the inclusion of only patients with severe AKI, which might mean that the observations made may be unapplicable to patients with mild to moderate AKI. A second potential limitation is the heterogenous etiological nature of the group of patients with non-LF AKI. Etiology is an important determinant of the presentation and outcome of AKI [12,17,19], and grouping patients with varied etiologies into one group could introduce some bias into the analysis and conclusions by artificially reducing or exaggerating the impact of different etiologic agents on presentation and outcome through the 'averaging' due to such grouping. For example, sepsis-associated AKI is known to carry a poorer outcome than other etiologies [37,38].

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