Am. J. Trop. Med. Hyg., 92(1), 2015, pp. 172–177
doi:10.4269/ajtmh.14-0418

Factors Associated with Mortality in Febrile Patients in a Government Referral Hospital in the Kenema District of Sierra Leone

Prerana J. Roth, Donald S. Grant, Amara S. Ngegbai, John Schieffelin, R. Scott McClelland, and Olamide D. Jarrett*

Department of Medicine, University of Illinois at Chicago School of Medicine, Chicago, Illinois; Kenema Government Hospital, Kenema, Sierra Leone; College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leone; Department of Medicine, Tulane University, New Orleans, Louisiana; Department of Medicine, University of Washington, Seattle, Washington

Abstract. There is a paucity of data on the etiologies and outcomes of febrile illness in rural Sierra Leone, especially in the Lassa-endemic district of Kenema. We conducted a retrospective study of patients with subjective or documented fever (T ≥ 38.0°C) who were admitted to a rural tertiary care hospital in Kenema between November 1, 2011 and October 31, 2012. Of 854 patients admitted during the study period, 429 (50.2%) patients had fever on admission. The most common diagnoses were malaria (27.3%), pneumonia (5.1%), and Lassa fever (4.9%). However, 53.4% of febrile patients had no diagnosis at discharge. The in-hospital mortality rate was 18.9% and associated with documented temperature ≥ 38.0°C (adjusted odds ratio [AOR] = 2.89, $P = 0.001$) and lack of diagnosis at discharge (AOR = 2.04, $P = 0.03$). Failure to diagnose the majority of febrile adults and its association with increased mortality highlight the need for improved diagnostic capacity to improve patient outcomes.

INTRODUCTION

Fever is one of the most common reasons that people seek healthcare in low-income countries.[1] In countries with limited healthcare resources, awareness of the local epidemiology of fever-causing pathogens is crucial to developing cost-effective healthcare, in which diagnostics, treatments, and public health programs are tailored to the most prevalent etiologies of infection. In addition to understanding the local epidemiology of febrile illness, it is also important to identify factors associated with increased mortality in febrile patients to identify modifiable risk factors, which through appropriate intervention, can prevent avoidable deaths.

In Sierra Leone, there have been few studies investigating the epidemiology of specific fever-causing pathogens, such as Lassa fever and malaria.[2–6] The Kenema District of Sierra Leone is a Lassa-endemic region, although it is currently unknown what the burden of Lassa fever is in relation to other febrile illnesses in the region. In addition, there are no studies to date that broadly examine the etiologies and outcomes of febrile illness in patients seeking healthcare in Sierra Leone. The primary objectives of this study were to describe the clinical presentations, diagnoses, outcomes, and factors associated with increased mortality in febrile adult patients presenting to a government referral hospital in a Lassa-endemic region in rural Sierra Leone.

MATERIALS AND METHODS

Study site. This study was conducted at a government referral hospital in Eastern Province of Sierra Leone, which serves a primarily rural population of approximately 1,187,532 according to the 2004 census.[7] This hospital is the site of the only dedicated Lassa ward in Sierra Leone. Although patients from other regions in Sierra Leone may be admitted to the Lassa ward for suspected Lassa fever, most of the patients admitted reside in the Kenema District. Some basic laboratory tests, such as serum chemistries, complete blood counts, malaria smears, and liver function tests, are available at the hospital. These tests are provided gratis for those patients admitted to the Lassa ward. However, for those admitted to the medical male and female wards, the performance of these laboratory tests is dependent on the patient's ability to pay for such testing. Microbiological testing, including blood and urine culture, is rarely performed because of a lack of a stable power source for bacterial incubation.

Study design and data collection. We conducted a retrospective chart review of patients admitted to the medical adult wards (male and female) and the Lassa ward of the hospital between November 1, 2011 and October 31, 2012 who met the following criteria: (1) age ≥ 18 years old and (2) reported subjective fever on admission or had a documented temperature ≥ 38°C within 24 hours of admission. We included patients with subjective fever, because vitals were often taken one time per day, and patients may have defervesced before the temperature was recorded. Data abstracted from medical charts included patient demographics, clinical symptoms on presentation, serum chemistries, hemoglobin, white blood cell (WBC) counts, malarial blood smears, any culture or gram stain data, radiographic tests, discharge diagnoses, antimicrobial treatments given, duration of hospitalization, and in-hospital mortality. Of note, the hospital laboratory calculated the malaria parasite density using a standard WBC counts of 8.0×10^9/L. Data for patients admitted to the Lassa ward were obtained from an existing Lassa fever database maintained by the Tulane University Lassa Fever Project in partnership with the Sierra Leone Ministry of Health. This study was approved by the Sierra Leone Ethics Committee and the Institutional Review Boards of the University of Illinois at Chicago and Tulane University.

Data analysis. Baseline characteristics and treatment outcomes of febrile patients were explored using medians and interquartile ranges (IQRs) for continuous variables and frequencies and percentages for categorical variables. Factors associated with mortality were initially explored by univariate logistic regression, and variables found to be significant to $P < 0.1$ were further explored in a multivariate logistic regression model. Analyses were completed with SPSS, version 22 (SPSS, Inc.). The significance level was set at $P < 0.05$.

*Address correspondence to Olamide D. Jarrett, 808 South Wood Street, Room 888, Mail Code 735, Chicago, IL 60612. E-mail: ojarrett@uic.edu

RESULTS

During the study period, 854 patients were admitted to the general adult wards ($N = 821$) and Lassa ward ($N = 33$) of the referral hospital. Of these patients, 429 (50.2%) patients had either a subjective or documented fever recorded within the first 24 hours of admission: 296 (69%) patients had subjective fever only, 92 (21.4%) patients had both subjective and documented fevers, 19 (4.4%) patients did not complain of fever but were febrile on admission, and the remaining 22 patients had missing data for either the presence of subjective fever or documented body temperature. Of note, all patients evaluated from the Lassa ward were febrile with documented ($N = 22$) or subjective fever ($N = 11$).

The demographics, initial vital signs, baseline laboratory data, and outcomes of febrile patients are presented in Table 1. The median age was 40 years old, and 62.9% were male. Occupation was recorded for 268 patients, with farming (15.4%) and housewife (11.2%) being the most commonly reported. A higher percentage of febrile patients (54.3%) were admitted during the rainy season (May 1 through October 30) than during the dry season (November 1 to April 30; admitted = 45.5%). The median pulse and blood pressure measurements were within normal ranges, but the median respiratory rate was slightly elevated at 22 (IQR = 22–24). Only 73% of patients had any laboratory data available, with less than 50% of patients having WBC measurements. For those with available data, median WBC and creatinine were within normal range, but the median hemoglobin was slightly low at 9.6 g/dL. Of note, of 26 patients who received human immunodeficiency virus (HIV) testing, 15 patients were found to be HIV-positive. However, HIV testing is not routine and usually only performed when there is a high *a priori* suspicion that the patient is infected with HIV. The in-hospital mortality of febrile patients was 18.9%, which was significantly higher than the in-hospital mortality of afebrile patients admitted during the study period (13.3%; $P = 0.03$, χ^2 test). The median length of hospitalization before death in febrile patients was 3 days (IQR = 2–7) compared with a median of 6 days (IQR = 4–10) for febrile patients who survived.

Over one-half (53.4%) of febrile patients did not have a diagnosis for their febrile illness before hospital discharge. For those patients with a diagnosis, malaria was the most common (occurring in 27.3% of febrile patients) followed by pneumonia (5.1%) and Lassa fever (4.9%). Although only 27.3% of patients were diagnosed with malaria, 73.6% of febrile patients received antimalarial treatment during hospitalization. Almost all febrile patients (97.1%) received antibiotic therapy during their hospitalization, regardless of diagnosis.

We further examined the symptoms, vital signs, laboratory values, and outcomes that were associated with the most common diagnoses (malaria, Lassa fever, and pneumonia) and an unknown diagnosis (Table 2). On observation of the descriptive data, there was significant overlap in the clinical presentation of febrile patients across diagnoses, with headache, abdominal pain, vomiting, and dizziness present in all groups. In fact, the five most prevalent symptoms were the same among those patients diagnosed with malaria and those with an unknown diagnosis. As expected, patients diagnosed with pneumonia had more dyspnea and cough. Vital signs and laboratory values were also similar across groups, except for the malaria parasite density, which was predictably higher in those diagnosed with malaria. However, the levels of parasitemia were low overall in this malaria-endemic region, with a median parasite density of 235 parasites/μL (IQR = 120,380) in those diagnosed with malaria.

We then analyzed factors potentially associated with in-hospital mortality in febrile patients (Table 3). On univariate regression, febrile patients with a documented admittance temperature ≥ 38°C had an increased likelihood of mortality (odds ratio [OR] = 2.67, $P < 0.001$). We also found that baseline systolic blood pressure < 90 mmHg (OR = 4.26, 95% confidence interval [95% CI] = 2.01–9.07, $P < 0.001$), having a discharge diagnosis of Lassa fever (OR = 2.82, 95% CI = 1.13–7.06, $P = 0.03$) and having an unknown diagnosis (OR = 1.98, 95% CI = 1.19–3.28, $P = 0.01$) were associated with a

TABLE 1

Characteristics of febrile patients admitted to a referral government hospital in rural Sierra Leone ($N = 429$)

	n	Median [IQR] or *n* (%)
Demographics		
Age (years)	412	40 [29–60]
Female	429	159 (37.1)
Occupation	429	
Unknown		161 (37.5)
Farmer		66 (15.4)
Housewife		48 (11.2)
Trader		32 (7.5)
Student		34 (7.9)
Teacher		22 (5.1)
Other		66 (15.4)
Admission profile		
Season of admission*	429	
Dry		196 (45.7)
Rainy		233 (54.3)
Admission ward	429	
General adult		396 (92.3)
Lassa fever		33 (7.7)
Documented temperature ≥ 38°C	394	125 (29.1)
Vitals		
Temperature (°C)	394	37.0 [36.4–38.1]
Pulse (beats/minute)	402	84 [76–96]
Systolic blood pressure (mmHg)	395	120 [100–140]
Diastolic blood pressure (mmHg)	393	80 [60–80]
Respiratory per minute	344	22 [22–24]
Laboratory data		
WBC ($\times 10^3$ cells/μL)	173	6.9 [5.0–10.8]
Hemoglobin (g/dL)	315	9.6 [8.0–11.2]
Creatinine (μM/L)	163	122 [89–124]
HIV antibody test positive	26	15 (57.7)
Diagnoses and treatment outcomes		
Discharge diagnosis†	429	
Unknown		229 (53.4)
Malaria		117 (27.3)
Pneumonia		22 (5.1)
Lassa		21 (4.9)
Typhoid fever		14 (3.3)
Gastroenteritis		14 (3.3)
Other‡		28 (6.5)
Treatment received		
Antibiotics	409	397 (97.1)
Antimalarials	402	296 (73.6)
Length of hospital stay (days)	422	6 [4–10]
In-hospital mortality	429	81 (18.9)

Percentages listed represent valid percentages and thus, may poorly reflect true sample prevalence in the setting of > 5% missing data.

*Dry season is November 1 to April 30, and rainy season is May 1 to October 31.

†Twenty-one individuals who received dual diagnoses had each diagnosis counted separately.

‡Other diagnoses included four cases of tuberculosis, four cases of urinary tract infections, two cases of acute Hepatitis B, three cases of sinusitis, two cases of *Schistosoma* infections, two cases of appendicitis, two cases of skin/soft tissue infections, and one case each of deep vein thrombosis, HIV, pharyngitis, pelvic inflammatory disease, hookworm, lung abscess, meningitis, strongyloidiasis, surgical site infection, and Hepatitis B cirrhosis.

TABLE 2
Characteristics of the most common diagnoses (at least 4% prevalence)

	Malaria (N = 113)		Lassa fever (N = 21)		Pneumonia (N = 18)		Unknown (N = 229)	
	n	Median [IQR] or n (%)	n	Median [IQR] or n (%)	n	Median [IQR] or n (%)	n	Median [IQR] or n (%)
Demographics								
Age (years)	108	45 [28–60]	21	26 [20–31]	18	51 [38–66]	221	42 [30–60]
Female	113	46 (40.7)	21	16 (76.2)	18	6 (33.3)	229	73 (31.9)
Admission profile								
Season of admission	113		20		18		229	
Dry		49 (43.4)		10 (47.6)		9 (50)		109 (47.6)
Rainy		64 (56.6)		10 (47.6)		9 (50)		120 (52.4)
Symptoms								
Headache	113	55 (48.7)	21	21 (100)	18	8 (44.4)	226	86 (38.1)
Cough	113	36 (32.1)	21	14 (66.7)	18	16 (88.9)	226	88 (38.9)
Dyspnea	111	26 (23.4)	5	0	18	10 (55.6)	218	56 (25.7)
Abdominal pain	112	46 (41.1)	15	12 (80)	18	3 (16.7)	219	85 (34.7)
Vomiting	113	35 (31.0)	21	16 (76.2)	18	1 (5.6)	225	78 (33.7)
Dizziness	112	37 (33)	21	18 (85.7)	17	5 (29.4)	224	84 (37.5)
Anorexia	111	34 (30.6)	0		18	8 (44.4)	215	68 (31.6)
Weight loss	110	12 (10.9)	0		15	9 (60.0)	209	30 (14.4)
Vitals								
Temperature ≥ 38°C	109	31 (28.4)	16	15 (93.8)	16	5 (31.3)	207	58 (28.0)
Temperature (°C)	109	37.0 [36.4–38.0]	16	39.0 [38.4–39.0]	16	36.9 [36.1–38.3]	207	37.0 [36.3–38.0]
Pulse (beats/minute)	110	82 [74–91]	16	98 [90–104]	18	86 [65–106]	211	84 [76–96]
Systolic blood pressure (mmHg)	106	120 [110–150]	16	100 [83–110]	17	120 [100–137]	213	120 [100–140]
Diastolic blood pressure (mmHg)	106	80 [70–90]	16	60 [43–69]	17	80 [70–80]	211	80 [60–80]
Respirations per minute	88	22 [20–24]	15	24 [22–32]	11	20 [20–28]	190	22 [22–24]
Laboratory data								
WBC ($\times 10^3$ cells/μL)	53	7.5 [4.4–11.7]	1	*	10	5.5 [4.0–8.7]	90	6.7 [5.0–9.8]
Hemoglobin (g/dL)	105	9.9 [8.2–11.2]	5	12 [8.9–15.4]	12	9.3 [8.9–10.8]	156	9.3 [7.8–11.5]
Creatinine (μM/L)	51	121 [89–123]	13	82 [48–201]	3	123 [121–NR]	83	123 [90–124]
Malaria parasite density (parasites/μL)	105	180 [120–350]	0	–	11	120 [0–160]	140	0 [0–120]
Treatment outcomes								
Treatment received								
Antibiotics	113	112 (99.1)	13	11 (84.6)	18	18 (100)	217	209 (96.3)
Antimalarials	113	110 (97.3)	14	11 (78.6)	18	9 (50)	211	135 (64)
Length of hospital stay (days)	112	7 [4–9]	20	11 [5–14]	18	9.5 [7–12]	225	6 [3–9]
In-hospital mortality	113	16 (14.2)	21	8 (38.1)	18	1 (5.6)	229	54 (23.6)

Data were not available for all variables. NR = not reported because unable to determine 75th percentile with a sample size of three.
*One patient with Lassa fever had a WBC measurement (6.5×10^{-3} cell/μL).

TABLE 3
Factors associated with in-hospital mortality among all patients with documented or reported fever (N = 429)

	n	Unadjusted OR (95% CI)	P value	AOR* (95% CI)	P value
Age (years)	412	1.00 (0.98–1.01)	0.61		
Male	429	1.51 (0.89–2.54)	0.13		
Dry season	429	1.23 (0.77–1.96)	0.39		
Headache	426	0.81 (0.49–1.33)	0.41		
Cough	425	1.11 (0.67–1.82)	0.69		
Dyspnea	400	1.10 (0.62–1.95)	0.74		
Abdominal pain	412	1.59 (0.97–2.61)	0.07	1.55 (0.83–2.88)	0.17
Vomiting	425	1.56 (0.95–2.57)	0.08	1.08 (0.57–2.05)	0.81
Dizziness	422	1.42 (0.87–2.34)	0.16		
Anorexia	392	1.37 (0.80–2.35)	0.26		
Weight loss	379	1.08 (0.53–2.20)	0.84		
Temperature ≥ 38°C	394	2.67 (1.56–4.57)	< 0.001	2.89 (1.58–5.26)	0.001
Pulse (beats/minute)	402	1.01 (0.99–1.02)	0.28		
Systolic blood pressure < 90 mmHg	395	4.26 (2.01–9.07)	< 0.001	2.35 (0.94–5.89)	0.07
Diastolic blood pressure < 60 mmHg	393	1.59 (0.65–3.92)	0.31		
Respirations per minute	344	1.00 (0.99–1.02)	0.71		
WBC count ($\times 10^3$ cells/μL)	173	1.00 (1.00–1.00)	0.66		
Hemoglobin (g/dL)	315	0.80 (0.71–0.90)	< 0.001		
Creatinine (μM/L)	163	1.00 (1.00–1.01)	0.10		
Malaria parasite density (parasites/μL)	292	1.00 (1.00–1.00)	0.94		
Unknown diagnosis	429	1.98 (1.19–3.28)	0.01	2.04 (1.09–3.80)	0.03
Malaria	429	0.66 (0.37–1.18)	0.16		
Lassa fever	429	2.82 (1.13–7.06)	0.03	2.26 (0.47–10.81)	0.31
Pneumonia	429	0.42 (0.10–1.81)	0.24		
Length of hospitalization (days)	422	0.85 (0.79–0.91)	< 0.001	0.89 (0.82–0.96)	0.002

*Adjusted model sample size equals 357 and includes the following covariates: abdominal pain, vomiting, febrile, systolic BP < 90 mmHg, unknown diagnosis, and length of hospitalization.

higher likelihood of mortality. In contrast, higher baseline hemoglobin (OR = 0.81, 95% CI = 0.71–0.90, $P < 0.001$) and increasing length of hospital stay (OR = 0.85, 95% CI = 0.79–0.91, $P < 0.001$) were associated with a decreased likelihood of mortality.

In the initial adjusted analysis, we excluded baseline hemoglobin because of the significant amount of missing data, resulting in reduced sample size and predictive power of the adjusted model. Of the remaining variables found to be significant in the univariate regression, only documented fever (adjusted OR [AOR] = 2.89, $P = 0.001$), unknown diagnosis at discharge (AOR = 2.04, $P = 0.03$), and length of hospitalization (AOR = 0.89, $P = 0.002$) were significantly associated with mortality. Because baseline hemoglobin was strongly associated with mortality in the univariate regression, we explored its association with in-hospital mortality using the subset of data for which hemoglobin results were available (Table 4). We found that baseline hemoglobin remained strongly associated with in-hospital mortality in the adjusted analysis (AOR = 0.81, $P = 0.003$). The significantly reduced sample size in this model resulted in reduced power to detect associations between the other variables of interest and mortality compared with the untruncated model used in Table 3. Thus, univariate and multivariate associations for the remainder of the variables were ignored in this truncated model.

To assess whether the patients admitted to the Lassa ward were the major drivers of the associations seen with mortality, we repeated the above univariate and multivariate analyses excluding those admitted to the Lassa ward. In doing so, on univariate analysis, male gender became significantly associated with hospital mortality (OR = 1.86, 95% confidence interval [95% CI] = 1.03–3.35, $P = 0.04$). However, the significant univariate associations noted above remained unchanged for the following variables: admittance temperature ≥ 38°C, systolic BP < 90 mmHg, hemoglobin, having an unknown diagnosis at discharge, and length of hospital stay (data not shown). None of the patients admitted to the general ward were diagnosed with Lassa fever, and therefore, the association between Lassa fever and mortality could not be evaluated. On adjusted analyses, there were no changes in the significant associations noted above for temperature ≥ 38°C, hemoglobin, unknown diagnosis at discharge, and length of hospital stay (data not shown). However, when only evaluating those admitted to the general ward, systolic BP < 90 mmHg remained significant in the adjusted model (AOR = 3.08, 95% CI = 1.17–8.10, $P = 0.02$).

DISCUSSION

This study shows that fever is a very common complaint in patients presenting to a referral hospital in rural Sierra Leone, because 50.2% of the patients admitted during the study period had subjective or documented fever within 24 hours of admission. The most common diagnoses made were malaria, pneumonia, and Lassa fever. However, over one-half of the febrile patients in our study were undiagnosed by the time of discharge. The mortality rate among febrile patients was almost one in five. Documented fever on admission and lack of diagnosis at discharge were associated with higher likelihood of mortality. We also determined that baseline hemoglobin and length of hospitalization were associated with mortality among febrile patients.

Having an unknown discharge diagnosis is not uncommon in low-income countries because of the lack of diagnostic testing. Most diagnoses are based on clinical symptoms alone in these resource-limited settings. However, clinical diagnoses are often inaccurate, because symptoms of different diseases can overlap.[1] We observed this finding in our study, where we noted that those diagnosed with malaria, Lassa fever, or an unknown diagnosis had nearly identical clinical presentations on admission.

TABLE 4

Factors associated with in-hospital mortality among patients with documented or reported fever and available hemoglobin results ($N = 315$)

	n	Unadjusted OR (95% CI)	*P* value	AOR* (95% CI)	*P* value
Age (years)	306	1.00 (0.98–1.01)	0.76		
Male	315	1.24 (0.67–2.32)	0.50		
Dry season	315	0.95 (0.53–1.70)	0.86		
Headache	315	0.71 (0.39–1.29)	0.26		
Cough	314	1.23 (0.69–2.21)	0.48		
Dyspnea	303	1.07 (0.55–2.07)	0.84		
Abdominal pain	307	1.98 (1.10–3.57)	0.02	1.51 (0.74–3.08)	0.26
Vomiting	315	1.65 (0.90–3.03)	0.11	1.13 (0.53–2.42)	0.76
Dizziness	312	1.69 (0.94–3.03)	0.08	1.54 (0.77–3.07)	0.22
Anorexia	303	1.48 (0.81–2.73)	0.20		
Weight loss	291	1.60 (0.75–3.42)	0.22		
Temperature ≥ 38°C	298	2.84 (1.54–5.24)	0.001	2.62 (1.31–5.24)	0.01
Pulse (beats/minute)	305	1.01 (1.00–1.03)	0.17		
Systolic blood pressure < 90 mmHg	298	5.42 (2.21–13.29)	< 0.001	3.22 (1.08–9.58)	0.04
Diastolic blood pressure < 60 mmHg	297	2.40 (0.86–6.73)	0.09		
Respirations per minute	267	1.00 (0.98–1.02)	0.97		
WBC count ($\times 10^3$ cells/μL)	171	1.00 (1.00–1.00)	0.66		
Hemoglobin (g/dL)	315	0.80 (0.71–0.90)	< 0.001	0.81 (0.71–0.93)	0.003
Creatinine (μM/L)	150	1.01 (1.00–1.03)	0.05		
Malaria parasite density (parasites/μL)	284	1.00 (1.00–1.00)	0.86		
Unknown diagnosis	315	1.59 (0.88–2.85)	0.12	1.53 (0.78–3.01)	0.22
Malaria	315	0.81 (0.43–1.50)	0.50		
Lassa fever	315	19.85 (2.17–181.18)	0.01		
Pneumonia	315	0.70 (0.15–3.20)	0.65		
Length of hospitalization (days)	315	0.91 (0.84–0.97)	0.01	0.90 (0.83–0.98)	0.01

*Adjusted model sample size equals 269 and includes the following covariates: abdominal pain, vomiting, dizziness, febrile, systolic BP < 90 mmHg, hemoglobin, unknown diagnosis, and length of hospitalization.

The association between having an unknown diagnosis and increased likelihood of mortality may be because of various factors. One issue may be that undiagnosed patients are infected with pathogens that are not covered by the empiric antibiotic regimen. Even if the patient with an unknown diagnosis does receive appropriate empiric antibiotic therapy, the primary disease may result in complications that require additional treatment of which the healthcare team would be unaware without knowledge of the primary process. For example, perforation as a result of diverticulitis or recurrent septic emboli caused by endocarditis may not be fully treated without surgical intervention. The inverse relationship seen between length of hospital stay and mortality may represent survival bias, because the median length of hospitalization was 6 days for febrile patients who survived and only 3 days for febrile patients who died.

Of note, for those who received a diagnosis at discharge, malaria was the most common diagnosis provided. However, there may have been an overdiagnosis of malaria given the low parasite densities used to make the diagnosis in this malaria-endemic region. Previous studies have shown that malaria is often overdiagnosed in low-income countries for multiple reasons, such as reflexive treatment by medical staff and lack of trust in the quality of diagnostic testing.[8–11] Because of improved vector control and decreasing prevalence of malaria, there is evidence that supports decreasing the threshold levels of parasitemia from 2,500 to 500 parasites/μL for diagnosis to decrease false-negative results.[11] However, even with this decreased threshold, only 4.4% (19 of 429) of the patients in our study would meet criteria for a diagnosis of malaria. Thus, there may be other causes of fever that are left untreated because of a misdiagnosis of malaria, a phenomenon that has been shown in other studies.[12]

The high prevalence of unknown diagnoses in those admitted with fever to a referral government hospital in rural Sierra Leone and the high mortality of these patients highlight the need for additional research to determine the most prevalent etiologies of fever in this region. One important area of study would be to investigate bacterial etiologies of fever, because they may account for at least 25% of febrile illness in resource-poor countries.[13] Failure to identify serious bacterial infections could explain the excess mortality seen in our patients lacking a discharge diagnosis. Improved understanding of the local epidemiology of febrile illness would allow for the creation of more accurate diagnostic and treatment algorithms, with the expected outcome of reduced morbidity and mortality in this population. For example, a study conducted in rural Senegal found that borrelia and rickettsial species were present in 9.5% and 6.8% of patients, respectively, which led Sokhna and others[14] to conclude that empiric doxycycline should be considered in febrile patients.

The hospital evaluated in this study was unique, because it is the only hospital in Sierra Leone with a dedicated Lassa ward. However, even after excluding those admitted to the Lassa ward, we found that lack of diagnosis by discharge was still significantly associated with mortality. Hence, these findings may be generalized to other government referral hospitals in Sierra Leone, which receive similar support and staffing through the Sierra Leone Ministry of Health. The primary limitations of this study are its retrospective design and the limited data available in the medical charts used for data abstraction. The availability of free laboratory testing for those admitted to the Lassa ward had the potential to skew the laboratory findings presented in our study. However, given the small number of patients admitted to the Lassa ward ($N = 33$) and the significant amount of missing laboratory data in these patients, we believe that there is a low likelihood that these data skewed our results. Another limitation is that we used only medical records of the referral hospital and did not include any outpatient clinics. To obtain the most accurate data regarding etiologies of febrile illness in rural Sierra Leone, a future study should be conducted that includes outpatient clinics, because a substantial burden of illness does not present to a major referral medical center.[15,16] It will also be important to include children in these future studies, because febrile illness is a significant cause of morbidity and mortality in this population.[17]

In conclusion, we found that most febrile patients at a healthcare facility in rural Sierra Leone remained undiagnosed or possibly misdiagnosed as malaria. Lack of diagnosis was associated with higher mortality. Additional study with improved diagnostic testing for other etiologies of febrile illness, such as bacteremia, leptospirosis, dengue fever, etc., needs to be completed. Often, there is a push in low-income countries to obtain more resources for treatment. However, without a correct diagnosis, the risk of incorrect and potentially harmful treatment is unacceptably high. With accurate local surveillance data, health policy could be targeted toward interventions that optimize the use of healthcare resources to improve patient outcomes.

Received July 4, 2014. Accepted for publication September 16, 2014.

Published online November 17, 2014.

Authors' addresses: Prerana J. Roth and Olamide D. Jarrett, Department of Medicine, University of Illinois at Chicago School of Medicine, Chicago, IL, E-mails: preranaroth@gmail.com and ojarrett@uic.edu. Donald S. Grant, Kenema Government Hospital, Kenema, Sierra Leone, and College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leone, E-mail: donkumfel@yahoo.co.uk. Amara S. Ngegbai, College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leone, E-mail: drnas88@gmail.com. John Schieffelin, Department of Medicine, Tulane University, New Orleans, LA, E-mail: jschieff@tulane.edu. R. Scott McClelland, Department of Medicine, University of Washington, Seattle, WA, E-mail: mcclell@uw.edu.

REFERENCES

1. Crump JA, Gove S, Parry CM, 2011. Management of adolescents and adults with febrile illness in resource limited areas. *BMJ 343:* d4847.
2. Ansumana R, Jacobsen KH, Gbakima AA, Hodges MH, Lamin JM, Leski TA, Malanoski AP, Lin B, Bockarie MJ, Stenger DA, 2013. Presumptive self-diagnosis of malaria and other febrile illnesses in Sierra Leone. *Pan Afr Med J 15:* 34.
3. Branco LM, Grove JN, Boisen ML, Shaffer JG, Goba A, Fullah M, Momoh M, Grant DS, Garry RF, 2011. Emerging trends in Lassa fever: redefining the role of immunoglobulin M and inflammation in diagnosing acute infection. *Virol J 8:* 478.
4. Gakuruh T, 2009. *Sierra Leone*. Available at: http://www.who.int/countries/sle/en/. Accessed November 14, 2013.
5. Nnedu ON, Rimel B, Terry C, Jalloh-Vos H, Baryon B, Bausch DG, 2010. Syndromic diagnosis of malaria in rural Sierra Leone and proposed additions to the national integrated management of childhood illness guidelines for fever. *Am J Trop Med Hyg 82:* 525–528.
6. UNAIDS, 2012. *Sierra Leone*. Available at: http://www.unaids.org/en/regionscountries/countries/sierraleone/. Accessed November 14, 2013.

7. Leone SS, 2004. *Population Census*. Available at: http://www.statistics.sl/publications.htm. Accessed December 7, 2013.
8. Chandler CI, Jones C, Boniface G, Juma K, Reyburn H, Whitty CJ, 2008. Guidelines and mindlines: why do clinical staff overdiagnose malaria in Tanzania? A qualitative study. *Malar J 7:* 53.
9. Leslie T, Mikhail A, Mayan I, Anwar M, Bakhtash S, Nader M, Chandler C, Whitty CJ, Rowland M, 2012. Overdiagnosis and mistreatment of malaria among febrile patients at primary healthcare level in Afghanistan: observational study. *BMJ 345:* e4389.
10. Reyburn H, Mbatia R, Drakeley C, Carneiro I, Mwakasungula E, Mwerinde O, Saganda K, Shao J, Kitua A, Olomi R, Greenwood BM, Whitty CJ, 2004. Overdiagnosis of malaria in patients with severe febrile illness in Tanzania: a prospective study. *BMJ 329:* 1212.
11. Roucher C, Rogier C, Dieye-Ba F, Sokhna C, Tall A, Trape JF, 2012. Changing malaria epidemiology and diagnostic criteria for *Plasmodium falciparum* clinical malaria. *PLoS ONE 7:* e46188.
12. Nadjm B, Mtove G, Amos B, Walker NF, Diefendal H, Reyburn H, Whitty CJ, 2012. Severe febrile illness in adult hospital admissions in Tanzania: a prospective study in an area of high malaria transmission. *Trans R Soc Trop Med Hyg 106:* 688–695.
13. Reddy EA, Shaw AV, Crump JA, 2010. Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis. *Lancet Infect Dis 10:* 417–432.
14. Sokhna C, Mediannikov O, Fenollar F, Bassene H, Diatta G, Tall A, Trape JF, Drancourt M, Raoult D, 2013. Point-of-care laboratory of pathogen diagnosis in rural Senegal. *PLoS Negl Trop Dis 7:* e1999.
15. Ansumana R, Jacobsen KH, Gbakima AA, Hodges MH, Lamin JM, Leski TA, Malanoski AP, Lin B, Bockarie MJ, Stenger DA, 2013. Presumptive self-diagnosis of malaria and other febrile illnesses in Sierra Leone. *Pan Afr Med J 15:* 34.
16. Thomson A, Khogali M, de Smet M, Reid T, Mukhtar A, Peterson S, von Schreeb J, 2011. Low referral completion of rapid diagnostic test-negative patients in community-based treatment of malaria in Sierra Leone. *Malar J 10:* 94.
17. World Health Organization, 2014. *World Health Statistics 2014*. Geneva: World Health Organization, 72–89.