

Clinical Profile and Factors Associated with Mortality in Louse-Borne Relapsing Fever: A Cross-Sectional Study from a Referral Hospital in Addis Ababa, Ethiopia

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Abstract

Background

Louse-borne relapsing fever (LBRF) remains a severe public health threat in Ethiopia, driven by socioeconomic instability and vulnerability. Recent epidemiological data from Addis Ababa are scarce, highlighting the need for evidence to guide clinical management and public health policy. This study aimed to evaluate the clinical profile, complications, and predictors of mortality among patients with LBRF.

Methods

We conducted a retrospective cross-sectional study of patients aged ≥ 15 years diagnosed with LBRF at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, between August 2019 and August 2024. Descriptive statistics were used to summarise the cohort. Univariable logistic regression identified candidate predictors ($p < 0.20$). Because only 22 deaths occurred, backward elimination was performed using Firth's penalised logistic regression throughout, with BIC used as the primary criterion for model selection. Three sensitivity models were compared. Statistical significance was set at $p < 0.05$.

Results

Of 360 patients evaluated (median age 21.0 years, IQR 18–26; 97.8% male; 26.9% homeless), admissions increased substantially from 2021 onward, peaking in the first quarter of 2024. The most common symptoms at presentation were vomiting (30.8%), nausea (29.4%), and cough (28.1%). Notable laboratory findings included near-universal thrombocytopenia (92.8%), with 70.3% classified as severe or very severe; elevated AST in 70.6% and anaemia in 36.8%. Common complications included Jarisch–Herxheimer reaction (47.8%), sepsis (31.0%), and shock (17.8%). In-hospital mortality was 6.1% (95% CI 3.9–9.1%). In the primary Firth penalised logistic regression model, independent predictors of mortality were CNS symptoms (aOR 26.60, 95% CI 6.66–106.30, $p < 0.001$), chest crepitations (aOR 6.01, 95% CI 1.41–25.67, $p = 0.016$), septic shock (aOR 4.70, 95% CI 1.19–18.52, $p = 0.027$), and abdominal pain (aOR 4.00, 95% CI 1.02–15.68, $p = 0.047$). These findings were robust across three sensitivity models.

Conclusions

The rising burden of louse-borne relapsing fever and its severe complications pose an escalating urban public health challenge among vulnerable populations in Addis Ababa. Four bedside predictors, namely CNS symptoms, chest crepitations, septic shock, and abdominal pain, can guide triage and early escalation in resource-limited settings. High clinical suspicion, enhanced surveillance, and integration of control into poverty-reduction and housing strategies are needed to improve outcomes and mitigate worsening trends.

Introduction

Louse-borne relapsing fever (LBRF) is a febrile illness caused by *Borrelia recurrentis*, a large, motile spirochaete measuring 12–22 µm in length and 0.2–0.6 µm in thickness, characterized by tapering ends, an average wavelength of 1.8 µm, an amplitude of 0.8 µm, and 8–10 periplasmic flagella [1]. In contrast to other *Borrelia* species, the transmission of *B. recurrentis* is primarily mediated by a singular vector, the human body louse (*Pediculus humanus corporis*), though the head louse (*Pediculus humanus capitis*) has been identified as a potential vector [2]. Infection occurs when a louse is crushed during scratching, allowing the spirochaete to enter through abraded skin, a process further facilitated by the louse's feces [3]. Historically, LBRF is tightly linked to conditions of social upheaval including war, famine, forced migration, and extreme poverty [2].

LBRF is characterized by an acute febrile illness and a subsequent series of relapses, typically following an average incubation period of 7 days [2]. The clinical spectrum varies widely, encompassing manifestations from mild symptoms to life-threatening complications [4]. Early indicators include headache, dizziness, and generalized myalgia (particularly in the lower back and joints), accompanied by anorexia, nausea, vomiting, and diarrhea [2]. Severe cases can progress to critical conditions such as coma, shock, hyperpyrexia, myocarditis with acute pulmonary edema, Acute Respiratory Distress Syndrome (ARDS), hepatic failure, and hemostatic failure due to thrombocytopenia, liver damage, and Disseminated Intravascular Coagulation (DIC), resulting in intracranial, gastrointestinal, pulmonary, or peri-partum hemorrhages [5–8]. Moreover, co-infections with dysentery, salmonellosis, typhoid fever, typhus, tuberculosis, bacterial pneumonia, visceral leishmaniasis, and malaria frequently exacerbate the clinical course and increase mortality rates [5, 9].

While mortality rates among untreated patients have ranged from 30% to 70%, modern antibiotic therapy in Ethiopia has reduced these rates to between 2% and 13% [2]. However, factors influencing mortality in these patients remain insufficiently explored, particularly in the Ethiopian context, where LBRF remains endemic, with approximately 10,000 annual cases predominantly affecting homeless individuals living in crowded and unsanitary conditions, especially during the rainy season [10]. Ethiopia is the only nation where LBRF persists as an endemic disease, although occasional cases are reported in neighboring countries such as Eritrea, Sudan, and Somalia [11–13]. It ranks among the top ten causes of hospital admissions, contributing substantially to morbidity and mortality [14, 15].

Current socio-economic challenges, including global inflation and internal displacement due to civil unrest, are anticipated to exacerbate the prevalence of LBRF within urban centers like Addis Ababa, where overcrowding and inadequate housing further heighten population vulnerability [16–20]. While extensive research has described the general clinical features of LBRF in Ethiopia, contemporary data on the magnitude and drivers of mortality are scarce, with most available evidence being over a decade old [5, 8, 21–25]. This study addresses this gap by reviewing patient records at Zewditu Memorial Hospital (ZMH) in Addis Ababa to evaluate the current burden of mortality and its associated risk factors. Given its location near high-risk urban populations, such as homeless people, ZMH provides a critical context for investigating LBRF in an area where recent data is lacking. By identifying the factors that drive mortality, this study aims to inform clinical practice, public health policy, and serve as a contemporary reference for future research across Ethiopia.

Methods

Study design and setting

This study employed a hospital-based cross-sectional design conducted at ZMH, a referral hospital located in Addis Ababa, Ethiopia. The hospital offers comprehensive services, including inpatient wards, outpatient departments, emergency services, and intensive care units. ZMH is nationally recognized for its expertise in the diagnosis and treatment of LBRF, largely due to the significant population of homeless individuals residing in the surrounding urban area. This study was conducted over a five-year period, from August 2019 to August 2024.

Ethical Considerations

Ethical clearance was obtained from the SPHMMC (St. Paul's Hospital Millennium Medical College) Ethical Review Committee. An official letter from SPHMMC was submitted to the Addis Ababa City Administration Health Bureau Institutional Review Board, and subsequent permission was obtained from the ZMH administration. Given the retrospective nature of the study utilizing secondary medical records, a waiver of informed consent was granted. Participant details, such as names or phone numbers, were not included in the data extracted from patient files; instead, patients' card numbers were used for identification and tracking within the data abstraction tools, and strict confidentiality protocols were maintained throughout data handling to protect patient privacy.

Operational Definitions

Clinical Complications

For the purposes of this study, clinical complications including ARDS, myocarditis, Jarisch–Herxheimer Reaction (JHR), sepsis, shock, hepatic dysfunction, and nosocomial infections were defined based on the explicit clinical diagnoses documented by the treating physicians in the patient's medical records. These diagnoses were made during the course of routine clinical care at ZMH, where clinicians follow National Standard Treatment Guidelines (STG) [26] and institutional management protocols for LBRF and its complications.

Meningismus

Defined as the documented presence of nuchal rigidity, Kernig's sign, or Brudzinski's sign on physical examination.

Altered mental status

Defined as any documented acute change in consciousness, orientation, or behavior compared to the patient's baseline (e.g., confusion, stupor, or coma).

Confirmed LBRF

A diagnosis confirmed via blood film (microscopy) using thin and thick blood smears prepared with Giemsa or Wright's staining to visualize the spirochetes.

Study Population and Sample Size Determination

The source population comprised all adult patients diagnosed with LBRF and admitted to ZMH during the specified study period.

Eligibility Criteria

Inclusion Criteria

Patients were included in the study if they met the following criteria

- Age $\geq$ 15 years.
- Laboratory-confirmed diagnosis of LBRF via microscopic visualization of *Borrelia* spirochetes on peripheral blood smears.
- Complete medical records detailing the clinical course and final hospital outcome.

Exclusion Criteria

Patients were excluded if the medical records were incomplete regarding exposure variables or the final clinical outcome (discharged vs. died).

Sampling and Sample Size

The sample size was initially calculated to estimate the mortality rate using the single population proportion formula, with a 95% confidence level ($Z = 1.96$), a 5% margin of error ($d = 0.05$), and a 13% expected mortality rate based on previous literature ($p = 0.13$)[25], requiring a minimum of 174 participants. After adding a 10% contingency for potential data incompleteness, the target sample size was 192. To maximize statistical power for multivariable modeling, a total census approach was adopted, encompassing all 360 eligible patient records identified over the five-year study period.

Data Collection and Quality Assurance

The data abstraction tool was prepared after a thorough literature review of research done in similar areas[25]. The tool was maintained in English, the standard language for medical records in Ethiopia. Clinical complications were recorded based on documented diagnoses made by treating physicians at the time of care. To ensure data integrity, the tool was pretested on 5% of the sample size at SPHMMC, with subsequent refinements made based on the pretest. Data were collected electronically by two medical

doctors with prior experience in digital data extraction, following a half-day orientation. The process was supervised daily by the principal investigator.

Data Entry and Analysis

Data were exported to Stata version 14 for analysis. Continuous variables were summarized as medians with interquartile ranges (skewed data) or means with standard deviations (normally distributed data); categorical variables were expressed as proportions. The prevalence of in-hospital mortality was reported with a 95% confidence interval. Baseline characteristics were compared between survivors and non-survivors using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. All tests were two-sided, and a p-value < 0.05 was considered statistically significant for descriptive comparisons.

The proportion of missing values was quantified for all variables (Supplementary Table e1). Laboratory parameters had substantial missing values (AST: 54.7%; ALT: 56.9%; creatinine: 55.8%), and housing status was missing in 58.3% of patients. To assess whether missingness was systematic, patients with and without complete laboratory data were compared with respect to age, sex, and in-hospital mortality (Supplementary Table e2). Patients with missing WBC and platelet data had significantly higher mortality than those with complete data (18.4% vs. 4.2%, $p < 0.001$ for WBC; 14.8% vs. 4.6%, $p = 0.004$ for PLT), indicating that missingness was not random with respect to the outcome. Age and sex did not differ significantly between groups. Because of this non-random pattern, laboratory parameters were not included as predictors in the primary multivariable model, and this limitation is acknowledged in the Discussion.

Housing status was the only socioeconomic variable available in the dataset and was classified as homeless ($n = 97$, 26.9%), non-homeless ($n = 53$, 14.7%), or unknown/not documented ($n = 210$, 58.3%). To examine the relationship between housing and clinical outcomes, three analyses were performed. First, baseline characteristics and in-hospital mortality were compared between homeless and non-homeless patients using the Mann–Whitney U test, chi-square test, or Fisher's exact test as appropriate. Second, patients with known versus unknown housing status were compared to assess whether missingness of housing status was systematic with respect to demographic and clinical characteristics. Third, because the number of deaths among patients with known housing status was small ($n = 10$), housing status was not included in the primary multivariable model; instead, a sensitivity analysis was performed on the subset of patients with known housing status to assess whether the four core predictors remained associated with mortality after adjusting for homelessness. This analysis was underpowered and is reported as exploratory only.

Univariable logistic regression identified candidate predictors ($p < 0.20$ for inclusion). Because only 22 deaths occurred, backward elimination was performed using Firth's penalized logistic regression throughout, with BIC used as the primary criterion for model selection given the small number of events. The BIC-optimal model retained four predictors: abdominal pain, chest crepitation, septic shock, and CNS symptoms. Three sensitivity models were compared: a full standard logistic model (13 predictors), a

parsimonious standard logistic model (4 predictors), and a Firth penalized model retaining age alongside the four core predictors. Model fit was assessed using the Hosmer–Lemeshow test. Multicollinearity was assessed using the variance inflation factor (mean VIF 1.52 for the primary model). The events-per-variable ratio was calculated for each model (primary model: 5.5; age-containing model: 3.1; full model: 1.7). Model discrimination was evaluated using the area under the receiver operating characteristic curve (AUC) where applicable. The study is reported in accordance with STROBE guidelines.

Results

A total of 360 patients diagnosed with louse-borne relapsing fever were included in this analysis. In-hospital mortality was 6.1% (95% CI 3.9–9.1%), corresponding to 22 non-survivors and 338 survivors (Table 1). The overall median age was 21.0 years (IQR 18.0–26.0), and non-survivors were significantly older than survivors (median 25.0 years [IQR 21.0–30.0] vs. 21.0 years [IQR 18.0–26.0], $p = 0.015$). The majority of patients were male (97.8%), and 46.7% were aged 15–20 years. Housing status was documented in 150 patients (41.7%); of these, 97 (64.7%) were homeless and 53 (35.3%) were non-homeless. The remaining 210 patients (58.3%) had undocumented housing status. Admissions were approximately equal between the dry (52.5%) and wet (47.5%) seasons. The distribution of diagnoses differed significantly across years ($p = 0.019$), with the highest proportions recorded in 2023 and 2024 (29.3% each). The median duration of symptoms before hospital presentation was 96.0 hours (IQR 72.0–120.0) and did not differ significantly between survivors and non-survivors ($p = 0.785$).

Table 1: Baseline Demographic and Epidemiological Characteristics at Zewditu Memorial Hospital, Ethiopia from 2019-2024 G.C

Characteristics	Survivors (n = 338)	Non-survivors (n = 22)	Total (N = 360)	p-value
Age, years, median [IQR]	21.0 [18.0–26.0]	25.0 [21.0–30.0]	21.0 [18.0–26.0]	0.015
Sex, n (%)				0.446
Female	7 (2.1)	1 (4.6)	8 (2.2)	
Male	331 (97.9)	21 (95.5)	352 (97.8)	
Age group, years, n (%)				0.089
15–20	163 (48.2)	5 (22.7)	168 (46.7)	
21–25	91 (26.9)	7 (31.8)	98 (27.2)	
26–72	84 (24.9)	10 (45.5)	94 (26.1)	
Housing status, n (%)				—
Non-homeless	51 (15.1)	2 (9.1)	53 (14.7)	
Homeless	89 (26.3)	8 (36.4)	97 (26.9)	
Unknown/not documented	198 (58.6)	12 (54.5)	210 (58.3)	
Season of admission, n (%)				0.809
Dry season	178 (52.7)	11 (50.0)	189 (52.5)	
Wet season	160 (47.3)	11 (50.0)	171 (47.5)	
Year of diagnosis, n (%)				0.019
2019	12 (3.6)	0 (0.0)	12 (3.3)	
2020	15 (4.4)	3 (14.3)	18 (5.0)	
2021	46 (13.6)	7 (33.3)	53 (14.8)	
2022	61 (18.0)	5 (23.8)	66 (18.4)	
2023	102 (30.2)	3 (14.3)	105 (29.3)	
2024	102 (30.2)	3 (14.3)	105 (29.3)	
Duration of symptoms, hours, median [IQR]	96.0 [72.0–120.0]	72.0 [72.0–168.0]	96.0 [72.0–120.0]	0.785

Abbreviations: CI, confidence interval; IQR, interquartile range; LBRF, louse-borne relapsing fever.

Notes: Data are presented as median [IQR] for continuous variables and n (%) for categorical variables. Continuous variables were compared using the Mann–Whitney U test; categorical variables were

compared using the chi-square test unless otherwise specified. Denominators reflect the number of available cases for each variable.

- ☒ Fisher's exact test used because of small expected cell counts.
- ☒ p-value not computed because "unknown" is a missing-data category, not a clinical group. Comparison of homeless vs. non-homeless patients is reported in Supplementary Table e3.
- ☒ Chi-square test may be unreliable due to small expected cell counts; interpret with caution.

In-hospital mortality: 6.1% (95% CI 4.0–9.1%).

Clinical presentations and physical examination findings at admission are summarized in Table 2. The most commonly reported symptoms were vomiting (30.8%), nausea (29.4%), and cough (28.1%). Chest crepitations were documented in 18.6% of patients, shortness of breath in 14.2%, abdominal pain in 12.8%, and jaundice in 11.9%. Less common findings included epistaxis (8.9%), GCS < 15 (5.0%), altered mental status (4.7%), hepatomegaly (3.1%), decreased urine output (3.1%), splenomegaly (2.8%), S3 gallop (1.7%), neck stiffness (1.7%), and bleeding at other sites (1.4%). No patient had a focal neurological deficit. When compared by outcome, several symptoms were significantly more frequent among non-survivors. Abdominal pain was present in 36.4% of non-survivors versus 11.2% of survivors ($p = 0.001$). Signs of severe systemic involvement were substantially more prevalent among non-survivors: jaundice (50.0% vs. 9.5%, $p < 0.001$), shortness of breath (68.2% vs. 10.7%, $p < 0.001$), altered mental status (50.0% vs. 1.8%, $p < 0.001$), chest crepitations (86.4% vs. 14.2%, $p < 0.001$), S3 gallop (9.1% vs. 1.2%, $p = 0.005$), and GCS < 15 (54.5% vs. 1.8%, $p < 0.001$). In contrast, nausea ($p = 0.801$), vomiting ($p = 0.918$), cough ($p = 0.166$), neck stiffness ($p = 0.276$), hepatomegaly ($p = 0.090$), splenomegaly ($p = 0.063$), decreased urine output ($p = 0.675$), epistaxis ($p = 0.131$), and bleeding at other sites ($p = 0.192$) did not differ significantly between survivors and non-survivors (Table 2).

Table 2: Clinical symptoms and physical examination findings at Zewditu Memorial Hospital, Ethiopia from 2019-2024 G.C

Characteristics	Survivors (n = 338)	Non-Survivors (n = 22)	Total (N = 360)	p-value
Nausea				
No	239 (70.7)	15 (68.2)	254 (70.6)	0.801
Yes	99 (29.3)	7 (31.8)	106 (29.4)	
Vomiting				0.918
No	234 (69.2)	15 (68.2)	249 (69.2)	
Yes	104 (30.8)	7 (31.8)	111 (30.8)	
Jaundice				< 0.001
No	306 (90.5)	11 (50.0)	317 (88.1)	
Yes	32 (9.5)	11 (50.0)	43 (11.9)	
Abdominal pain				0.001
No	300 (88.8)	14 (63.6)	314 (87.2)	
Yes	38 (11.2)	8 (36.4)	46 (12.8)	
Diarrhea				0.058
No	265 (78.4)	21 (95.5)	286 (79.4)	
Yes	73 (21.6)	1 (4.5)	74 (20.6)	
Cough				0.166
No	246 (72.8)	13 (59.1)	259 (71.9)	
Yes	92 (27.2)	9 (40.9)	101 (28.1)	
Shortness of breath				< 0.001
No	302 (89.3)	7 (31.8)	309 (85.8)	
Yes	36 (10.7)	15 (68.2)	51 (14.2)	
Neck stiffness				0.276
No	333 (98.5)	21 (95.5)	354 (98.3)	
Yes	5 (1.5)	1 (4.5)	6 (1.7)	
Epistaxis				0.131
No	306 (90.5)	22 (100.0)	328 (91.1)	
Yes	32 (9.5)	0 (0.0)	32 (8.9)	
Bleeding at other sites				0.192
No	334 (98.8)	21 (95.5)	355 (98.6)	

Yes	4 (1.2)	1 (4.5)	5 (1.4)	
Decreased urine output				0.675
No	328 (97.0)	21 (95.5)	349 (96.9)	
Yes	10 (3.0)	1 (4.5)	11 (3.1)	
Altered Mental Status				< 0.001
No	332 (98.2)	11 (50.0)	343 (95.3)	
Yes	6 (1.8)	11 (50.0)	17 (4.7)	
Hepatomegaly				0.090
No	329 (97.3)	20 (90.9)	349 (96.9)	
Yes	9 (2.7)	2 (9.1)	11 (3.1)	
Splenomegaly				0.063
No	330 (97.6)	20 (90.9)	350 (97.2)	
Yes	8 (2.4)	2 (9.1)	10 (2.8)	
Chest crepitation				< 0.001
No	290 (85.8)	3 (13.6)	293 (81.4)	
Yes	48 (14.2)	19 (86.4)	67 (18.6)	
S3 gallop				0.005
No	334 (98.8)	20 (90.9)	354 (98.3)	
Yes	4 (1.2)	2 (9.1)	6 (1.7)	
GCS < 15				< 0.001
No	332 (98.2)	10 (45.5)	342 (95.0)	
Yes	6 (1.8)	12 (54.5)	18 (5.0)	

Abbreviations: GCS, Glasgow Coma Scale.

Note: Data are presented as n (%) for categorical variables. p-values were derived using Chi-square tests (or Fisher's exact tests where cell counts were small).

Analysis of quarterly admissions revealed substantial temporal variation between 2019 and 2024 (Figure 1). Admission counts remained low (≤ 11 cases per quarter) from the third quarter of 2019 through the second quarter of 2021, followed by a marked resurgence beginning in the third quarter of 2021 ($n = 19$). The highest number of admissions was recorded in the first quarter of 2024 ($n = 55$), followed by the third quarter of 2023 ($n = 37$). A subsequent decline was observed in the second and third quarters of 2024 ($n = 32$ and $n = 18$, respectively).

Laboratory analysis revealed a high prevalence of haematological abnormalities (Table 3). Thrombocytopenia was nearly universal (92.8%; 284/306), with 70.3% (215/306) classified as severe (<50,000/ μ L) and 25.5% (78/306) as very severe (<20,000/ μ L). Leukocyte counts were predominantly normal (47.6%; 148/311), with the remainder distributed between leukopenia (23.8%; 74/311) and leukocytosis (28.6%; 89/311). Anaemia was present in 36.8% (116/315) of patients, but severe anaemia (<8 g/dL) was rare (0.6%; 95% CI 0.2–2.5%). Hepatic transaminases diverged markedly: AST was elevated in 70.6% (115/163) of patients, with 9.8% (16/163) exceeding five times the upper limit of normal, whereas ALT was elevated in only 21.3% (33/155). Renal impairment was also common, with 33.5% (54/161) of patients meeting the criteria for acute kidney injury (creatinine >1.3 mg/dL).

Because laboratory parameters had substantial missingness (AST: 54.7%; ALT: 56.9%; creatinine: 55.3%; WBC: 13.6%; Hb: 12.5%; platelets: 15.0%; Supplementary Table e1), patients with and without complete laboratory data were compared with respect to age, sex, and in-hospital mortality (Supplementary Table e2). Patients with missing WBC data had significantly higher mortality than those with complete data (18.4% vs. 4.2%, $p < 0.001$), as did patients with missing platelet data (14.8% vs. 4.6%, $p = 0.004$). Age and sex did not differ significantly between patients with and without complete laboratory data ($p > 0.19$ for all comparisons). This non-random pattern of missingness, in which patients who died were more likely to have missing laboratory results, indicated that the missing data were not missing at random with respect to the outcome.

Table 3. Laboratory characteristics of patients with louse-borne relapsing fever at Zewditu Memorial Hospital, Ethiopia, 2019–2024.

Laboratory parameter	Category	n (%)	95% CI
WBC (per μL) (n = 311)	Leukopenia (<5,000)	74 (23.8)	19.3–28.9
	Normal (5,000–10,000)	148 (47.6)	42.1–53.2
	Mild leukocytosis (10,001–14,999)	57 (18.3)	14.3–23.1
	Moderate leukocytosis (15,000–20,000)	22 (7.1)	4.6–10.5
	Severe leukocytosis (>20,000)	10 (3.2)	1.6–5.8
Hb (g/dL) (n = 315)	Normal (12–18)	199 (63.2)	57.7–68.4
	Mild anemia (10–11.9)	88 (27.9)	23.2–33.2
	Moderate anemia (8–9.9)	26 (8.3)	5.7–11.9
	Severe anemia (<8)	2 (0.6)	0.2–2.5
Platelets (per μL) (n = 306)	Normal	22 (7.2)	4.8–10.7
	Mild thrombocytopenia (100,000–149,000)	14 (4.6)	2.7–7.6
	Moderate thrombocytopenia (50,000–99,000)	55 (18.0)	14.0–22.7
	Severe thrombocytopenia (20,000–49,999)	137 (44.8)	39.3–50.4
	Very severe thrombocytopenia (<20,000)	78 (25.5)	20.9–30.7
AST (IU) (n = 163)	Normal (15–37)	48 (29.4)	22.9–37.0
	$\leq 3\times$ ULN (64–189)	70 (42.9)	35.5–50.7
	$3-5\times$ ULN (190–314)	29 (17.8)	12.6–24.5
	$>5\times$ ULN (≥ 315)	16 (9.8)	6.1–15.5
ALT (IU) (n = 155)	Normal (14–63)	122 (78.7)	71.5–84.5
	$\leq 3\times$ ULN (64–189)	28 (18.1)	12.7–25.0
	$3-5\times$ ULN (190–314)	4 (2.6)	1.0–6.7
	$>5\times$ ULN (≥ 315)	1 (0.6)	0.1–4.5

Creatinine (mg/dL) (n = 161)	Normal (≤ 1.2)	107 (66.5)	58.7– 73.4
	AKI (>1.3)	54 (33.5)	26.6– 41.3

Abbreviations: AKI, acute kidney injury; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; Hb, haemoglobin; IU, international units; ULN, upper limit of normal; WBC, white blood cell.

Notes: Data are presented as n (%). Percentages are calculated using the number of patients with available data for each parameter as the denominator: WBC (n = 311), Hb (n = 315), platelets (n = 306), AST (n = 163), ALT (n = 155), creatinine (n = 161). Missing values resulted from unperformed laboratory tests during routine clinical care. Reference ranges were provided by the hospital laboratory. AKI was defined as serum creatinine >1.3 mg/dL.

Treatment-Related Factors

Nearly half of the study population (47.8%; 172/360) developed a JHR following treatment initiation, including 54.5% (12/22) of those with fatal outcomes; however, this association was not statistically significant ($p = 0.512$). Treatment regimens varied: 78 patients (21.7%) received oral tetracycline or doxycycline monotherapy, while parenteral monotherapy with ceftriaxone or penicillin was administered to 39 (10.8%) and 69 (19.2%) patients, respectively. Combination therapies involving oral agents plus parenteral penicillin (18.6%; 67/360) or ceftriaxone (24.7%; 89/360) were also common. Regarding supportive treatments, 13 patients (3.6%) received fresh frozen plasma, 54 (15.0%) received platelet transfusions, and 7 (1.9%) received whole blood transfusions; none of these differed significantly between survivors and non-survivors ($p > 0.15$ for all comparisons). The median duration of hospital stay was 2.0 days (IQR 2.0–4.0) overall and was significantly shorter among non-survivors (1.0 day [IQR 1.0–2.0] vs. 3.0 days [IQR 2.0–5.0], $p < 0.001$), reflecting the acute nature of fatal cases: 81.8% (18/22) of deaths occurred within two days of admission (Table 4).

Table 4. Treatment-related factors among patients with louse-borne relapsing fever at Zewditu Memorial Hospital, Ethiopia, 2019–2024.

Treatment characteristic	Category	Survivors (n = 338)	Non-survivors (n = 22)	Total (N = 360)	p-value
Jarisch–Herxheimer reaction, n (%)	No	178 (52.7)	10 (45.5)	188 (52.2)	0.512
	Yes	160 (47.3)	12 (54.5)	172 (47.8)	
Antibiotic regimen, n (%)	Oral tetracycline/doxycycline	77 (22.8)	1 (4.5)	78 (21.7)	<0.001*
	Parenteral ceftriaxone	33 (9.8)	6 (27.3)	39 (10.8)	
	Parenteral penicillin	60 (17.8)	9 (40.9)	69 (19.2)	
	Oral + parenteral penicillin	66 (19.5)	1 (4.5)	67 (18.6)	
	Oral + parenteral ceftriaxone	88 (26.0)	1 (4.5)	89 (24.7)	
	Other	14 (4.1)	4 (18.2)	18 (5.0)	
Fresh frozen plasma transfusion, n (%)	No	327 (96.7)	20 (90.9)	347 (96.4)	0.155
	Yes	11 (3.3)	2 (9.1)	13 (3.6)	
Platelet transfusion, n (%)	No	289 (85.5)	17 (77.3)	306 (85.0)	0.295
	Yes	49 (14.5)	5 (22.7)	54 (15.0)	
Whole blood transfusion, n (%)	No	332 (98.2)	21 (95.5)	353 (98.1)	0.362
	Yes	6 (1.8)	1 (4.5)	7 (1.9)	
Duration of hospital stay, n (%)	Up to 2 days	168 (49.9)	18 (81.8)	186 (51.8)	0.033
	3–4 days	83 (24.6)	2 (9.1)	85 (23.7)	
	5–10 days	66 (19.6)	1 (4.5)	67 (18.7)	
	More than 10 days	20 (5.9)	1 (4.5)	21 (5.8)	
Duration of hospital stay, median [IQR]	—	3.0 [2.0–5.0]	1.0 [1.0–2.0]	2.0 [2.0–4.0]	<0.001

Abbreviations: IQR, interquartile range; JHR, Jarisch–Herxheimer reaction.

Notes: Data are presented as n (%) for categorical variables and median [IQR] for continuous variables. Denominators reflect available cases (N = 360 for all variables except duration of hospital stay, where n = 359). P-values were derived using the chi-square test or Fisher's exact test for categorical variables and the Mann–Whitney U test for continuous variables. ☒ The association between antibiotic regimen and mortality is confounded by indication: patients with severe disease were more likely to receive parenteral therapy. This p-value should not be interpreted as evidence of a causal effect of antibiotic choice on mortality.

Burden of Jarisch-Herxheimer Reaction and Antibiotic Treatment

During their hospital stay, 172 of 360 patients (47.8%) developed a JHR. JHR occurred in 43.6% (34/78) of patients who received doxycycline, 49.3% (34/69) of those who received penicillin, and 51.3% (20/39) of those who received ceftriaxone. Among combination regimens, JHR occurred in 59.7% (40/67) of patients who received penicillin plus doxycycline and 39.3% (35/89) of those who received ceftriaxone plus doxycycline. (Table 5).

Table 5. Jarisch–Herxheimer reaction by antibiotic exposure among patients with louse-borne relapsing fever at Zewditu Memorial Hospital, Ethiopia, 2019–2024 (N = 360).

Antibiotic regimen	JHR, n (%)	No JHR, n (%)	Total, n (%)
Doxycycline only	34 (43.6)	44 (56.4)	78 (21.7)
Penicillin only	34 (49.3)	35 (50.7)	69 (19.2)
Ceftriaxone only	20 (51.3)	19 (48.7)	39 (10.8)
Penicillin + doxycycline	40 (59.7)	27 (40.3)	67 (18.6)
Ceftriaxone + doxycycline	35 (39.3)	54 (60.7)	89 (24.7)
Other antibiotics☒	9 (50.0)	9 (50.0)	18 (5.0)
Total	172 (47.8)	188 (52.2)	360 (100.0)

Abbreviations: JHR, Jarisch–Herxheimer reaction.

Notes: Data are presented as n (%).

☒ Other antibiotics include cefepime, ceftazidime, and meropenem.

Clinical parameters indicating severity among patients admitted with Relapsing fever

Clinical complications were common in this cohort (Figure 2). Jarisch–Herxheimer reaction was the most frequent event, occurring in 47.8% (172/360) of patients. Sepsis was documented in 31.0% (112/360) and shock in 17.8% (64/360). ARDS was identified in 13.3% (48/360), hepatic dysfunction (jaundice) in 11.9%

(43/360), and nosocomial infection in 10.0% (36/360). Neurological involvement was uncommon, with coma in 3.3% (12/360) and meningismus in 1.7% (6/360). Myocarditis occurred in 2.2% (8/360) of patients. The overall in-hospital mortality rate was 6.1% (22/360).

Factors Associated with Mortality among Patients Admitted for Relapsing Fever

In the primary Firth penalised logistic regression model (Table 6), four variables were independently associated with in-hospital mortality. CNS symptoms (altered mentation or GCS < 15) conferred the strongest association (adjusted odds ratio [aOR] = 26.60, 95% CI 6.66–106.30, $p < 0.001$), followed by chest crepitations (aOR = 6.01, 95% CI 1.41–25.67, $p = 0.016$), septic shock (aOR = 4.70, 95% CI 1.19–18.52, $p = 0.027$), and abdominal pain (aOR = 4.00, 95% CI 1.02–15.68, $p = 0.047$). The model demonstrated acceptable goodness-of-fit (Hosmer–Lemeshow $p = 0.063$), an events-per-variable ratio of 5.5, and a penalised log-likelihood of -36.20 (AIC = 82.39; BIC = 101.82) (Table 6).

Table 6. Factors independently associated with in-hospital mortality: Firth's penalized logistic regression (primary model, N = 360, 22 deaths).

Predictor	Adjusted OR	95% CI	p-value
Abdominal pain	4.00	1.02 – 15.68	0.047
Chest crepitation	6.01	1.41 – 25.67	0.016
Septic shock	4.70	1.19 – 18.52	0.027
CNS symptoms	26.60	6.66 – 106.30	<0.001

Abbreviations: CI, confidence interval; CNS, central nervous system; OR, odds ratio.

Notes: Firth's penalised logistic regression. Penalised log-likelihood = -36.20; AIC = 82.39; BIC = 101.82; events per variable = 5.5. Hosmer–Lemeshow goodness-of-fit $p = 0.063$, computed on the corresponding standard maximum likelihood logistic model. ☐ CNS symptoms defined as altered mentation or Glasgow Coma Scale score < 15.

To assess the robustness of the primary model, three complementary modelling strategies were compared (Table 7). Model A was a full standard logistic regression including all 13 candidate terms, which produced the highest AIC (91.23) and BIC (145.63) and the lowest events-per-variable ratio (1.7), consistent with overfitting. Model B was a parsimonious standard logistic regression restricted to the four BIC-optimal predictors, which had the best balance of fit and parsimony by BIC (107.15) and an acceptable goodness-of-fit ($p = 0.063$) but did not adjust for age. Model C was a Firth penalised logistic regression including age plus the four core predictors, which had the lowest AIC (78.05) but failed the goodness-of-fit test ($p = 0.007$) and had a lower EPV (3.1). Across all three models, CNS symptoms, chest crepitations, and abdominal pain remained significantly associated with mortality. Septic shock was significant in Models B and C ($p = 0.024$ and $p = 0.022$, respectively) and showed a consistent direction of effect in Model A ($p = 0.076$). Age was significantly associated with mortality in Model A (26–72 years: AOR 8.53, $p = 0.028$) but

not in Model C (AOR 4.88, $p = 0.054$), and the age-containing model failed goodness-of-fit. These findings suggest that the core clinical predictors are robust across model specifications, while the effect of age is not.

Table 7: Sensitivity analysis of factors associated with in-hospital mortality using three complementary modelling strategies (N = 360, 22 deaths).

Predictor	Model A: Full standard logistic (13 terms)	Model A p-value	Model B: Parsimonious standard logistic (4 predictors)§	Model B p-value	Model C: Firth penalised logistic (age quartile + 4 core predictors)	Model C p-value
Age group						
15–20 years	1.00 (Reference)	—	—	—	1.00 (Reference)	—
21–25 years	4.81 (0.63–36.68)	0.130	—	—	5.15 (0.94–28.28)	0.059
26–72 years	8.53 (1.27–57.41)	0.028	—	—	4.88 (0.97–24.55)	0.054
Jaundice	4.00 (0.81–19.86)	0.090	—	—	—	—
Abdominal pain	11.05 (1.43–85.18)	0.021	4.19 (1.01–17.39)	0.049	6.23 (1.25–31.08)	0.026
Shortness of breath	1.10 (0.16–7.37)	0.921	—	—	—	—
Hepatomegaly	0.50 (0.02–14.01)	0.685	—	—	—	—
Splenomegaly	0.55 (0.01–20.62)	0.748	—	—	—	—
Chest crepitations	11.16 (1.07–116.92)	0.044	6.91 (1.48–32.39)	0.014	5.88 (1.30–26.52)	0.021
S3 gallop	2.35 (0.19–28.73)	0.504	—	—	—	—
Septic shock	5.14 (0.84–31.27)	0.076	5.24 (1.24–22.16)	0.024	5.23 (1.26–21.67)	0.022
Cough	0.53 (0.10–2.64)	0.434	—	—	—	—
Diarrhoea	0.09 (0.01–1.05)	0.054	—	—	—	—
CNS symptoms	18.51 (3.16–108.23)	<0.001	33.07 (7.63–143.31)	<0.001	26.09 (6.04–112.64)	<0.001
Model fit statistics						
Penalised log-likelihood	—	—	—	—	–31.03	
AIC	91.23	—	87.72	—	78.05	

BIC	145.63	—	107.15	—	109.14
GOF p-value	0.731	—	0.063	—	0.007
EPV	1.7	—	5.5	—	3.1

Abbreviations: AIC, Akaike information criterion; AOR, adjusted odds ratio; BIC, Bayesian information criterion; CI, confidence interval; CNS, central nervous system; EPV, events per variable; GOF, goodness-of-fit.

Notes: Values are presented as adjusted odds ratio (95% confidence interval) with p-values. Bold indicates $p < 0.05$. Model A: standard maximum likelihood logistic regression including all 13 candidate terms (age quartile [2 terms] + 11 other variables). Model B: standard maximum likelihood logistic regression including the four BIC-optimal predictors identified through backward elimination. Model B is the standard logistic counterpart to the primary Firth model presented in Table 7. Model C: Firth's penalised logistic regression including age quartile plus the four core predictors, to address low events-per-variable and potential small-sample bias. ^a Model B does not include age; thus no reference category applies. ^b Model C did not meet goodness-of-fit criteria ($p = 0.007$), indicating inadequate fit; results should be interpreted with caution. GOF p-values for Firth models were computed on the corresponding standard maximum likelihood logistic version of each model.

Poverty-related factors.

Among the 150 patients with documented housing status (41.7% of the cohort), 97 (64.7%) were homeless and 53 (35.3%) were non-homeless. Baseline characteristics of homeless and non-homeless patients are compared in Supplementary Table e3. Homeless patients were significantly younger than non-homeless patients (median 19 years [IQR 17–24] vs. 23 years [IQR 20–30], $p = 0.0002$). Other demographic and clinical characteristics, including sex, jaundice, abdominal pain, chest crepitations, septic shock, and CNS symptoms, did not differ significantly between groups ($p > 0.05$ for all comparisons; Supplementary Table e3). In-hospital mortality was higher among homeless patients (8.2% [8/97] vs. 3.8% [2/53]), but this difference was not statistically significant ($p = 0.495$); the number of deaths in this subgroup was small ($n = 10$; 8 among homeless patients and 2 among non-homeless patients). Patients with known and unknown housing status did not differ significantly with respect to age, sex, in-hospital mortality, or clinical characteristics (Supplementary Table e4), suggesting that missingness of housing status was largely non-systematic.

In a sensitivity analysis restricted to patients with known housing status, homelessness was not independently associated with mortality after adjustment for the four core predictors (abdominal pain, chest crepitations, septic shock, and CNS symptoms) (aOR = 0.78, 95% CI 0.11–5.48, $p = 0.800$; Supplementary Table e5). CNS symptoms remained the only significant predictor in this subset (aOR = 14.86, 95% CI 2.23–98.86, $p = 0.005$), consistent with the primary analysis. This analysis was underpowered (10 deaths) and is reported as exploratory only.

Discussion

Our study reveals a substantial trend in relapsing fever admissions, with a progressive increase observed from 2019 to 2024. Notably, the epidemiological trajectory shifted from a low-incidence period (median approximately 3 cases per quarter) to a sharp epidemic surge beginning in late 2021, culminating in a peak of 55 admissions in the first quarter of 2024. The progressive increase in cases can be attributed, in part, to ongoing civil unrest and regional conflicts, as well as currency devaluation affecting Ethiopia's international purchasing power, which may have exacerbated socioeconomic conditions conducive to disease transmission [16–20]. This observation is consistent with historical evidence suggesting that LBRF has had a substantial impact, especially following political crises, socioeconomic disasters, and wars [14, 27]. The temporal synchronisation of this surge with regional instability suggests that LBRF serves as a sensitive biological indicator of social vulnerability in urban Ethiopia.

Our study identifies a bimodal temporal pattern in LBRF admissions, with the highest peak occurring during the first quarter of 2024 (January–March), coinciding with the dry season. This phenomenon is likely driven by the high-altitude climate of the Ethiopian highlands; even during the dry season, low nighttime temperatures compel individuals to seek warmth through communal huddling and the use of shared blankets. This behavioural adaptation creates a stable microclimate for *Pediculus humanus*, facilitating transmission, a pattern also documented in high-altitude regions of Peru [28, 29]. The second-highest peak in admissions occurred during the third quarter of 2023 (July–September), aligning with Ethiopia's primary rainy season. This finding is consistent with the estimated 10,000 cases occurring annually in the Ethiopian highlands during wet periods [9]. The rainy season peak observed in our study, particularly among Addis Ababa's homeless population, is attributed to increased indoor crowding as individuals seek shelter from the rains [9, 28].

Interestingly, while our study captures peaks in both dry and wet seasons, earlier reports from Jimma Hospital and Felegehiwot Referral Hospital predominantly found higher prevalence during dry seasons [13, 22]. This geographical discrepancy suggests that while crowding is the common denominator, the drivers vary by location: in urban Addis Ababa, transmission is intensified by rain-driven sheltering, whereas in Jimma and Bahir Dar, it may be driven by the large-scale influx of migrant labourers during the coffee and agricultural harvest cycles [30]. These findings underscore the profound influence of environmental factors and human migration on LBRF dynamics, warranting localised public health strategies.

Our study found a median age of 21 years (IQR 18–26), with approximately half of participants aged 15–20 years (46.7%) and a strong male predominance (97.8%). This demographic profile is likely driven by the migration of young men to the capital in search of labour; these individuals often reside in overcrowded, communal environments where louse infestation is endemic [9, 28]. This male preponderance aligns with prior findings from the Arsi Region and Jimma Hospital, suggesting a consistent demographic pattern across different regions of Ethiopia [22, 23]. Furthermore, 26.9% of the cohort was homeless, corroborating estimates that LBRF predominantly affects those in crowded and unhygienic conditions [9]. The concentration of cases within this economically active yet socially marginalised population highlights a key at-risk group for targeted intervention and active case-finding.

The clinical presentation in our study showed considerable regional variability compared to previous literature. Bleeding manifestations and jaundice were notably less frequent; epistaxis (8.9%) and jaundice (11.9%) were lower than rates reported in Sudan (40% and 50%) and various Ethiopian studies (up to 30.2% and 33%), respectively [5, 8, 15, 28, 31–34]. Conversely, gastrointestinal symptoms were prominent, with vomiting (30.8%), nausea (29.4%), and abdominal pain (12.8%) exceeding earlier findings [8, 34, 35]. This shift toward gastrointestinal predominance may reflect variations in *Borrelia recurrentis* virulence or differences in host nutritional status, which can modulate the inflammatory response. Respiratory symptoms such as cough (28.1%) and shortness of breath (14.2%) remained comparable to existing data [8, 32, 33, 35]. Neurological findings were less common in this study: altered mental status (4.7%), GCS < 15 (5.0%), and neck stiffness (1.7%) were substantially lower than the high frequencies (up to 42%) previously documented [5, 8, 15, 28, 31, 33–36] [32–34]. Hepatomegaly (3.1%) and splenomegaly (2.8%) were markedly less frequent than in Sudan and other Ethiopian cohorts, where rates reached 74% and 63%, respectively [5, 8, 15, 28, 32–36].

In this study, the haematological profile demonstrated considerable variability. Leukocyte abnormalities were distributed between leucopenia (23.8%) and leucocytosis (28.6%), a bimodal pattern consistent with previous reports of fluctuating white cell counts during clinical crises [35, 36]. Anaemia was present in 36.8% of patients, aligning closely with established findings and confirming it as a frequent sequela within this patient population [35]. Most notably, thrombocytopenia was a near-universal laboratory finding, occurring in 92.8% of participants. While this is consistent with the 84% to 93% reported in prior studies, the depth of depletion was particularly striking: 70.3% exhibited severe (<50,000/ μ L) or very severe (<20,000/ μ L) thrombocytopenia [35, 37, 38]. In the absence of jaundice and bleeding, this profound thrombocytopenia likely serves as a marker of high-grade spirochetaemia and splenic sequestration. These findings, in conjunction with elevated aspartate aminotransferase levels in 70.6% of subjects, corroborate existing evidence of hepatocellular involvement in advanced relapsing fever [32, 37, 39].

In this study, JHR occurred in 47.8% of patients, a rate substantially higher than the 7.4% reported among urban dwellers in Ethiopia's Arsi Zone, a discrepancy attributed to a lack of standardised diagnostic criteria [23]. Our findings align more closely with multicentre data from Gonder (31.6%) and Assela (43%), though they remain lower than the 75.5% incidence reported in Hossana [15, 21, 24]. These results are contextualised by a systematic review showing an overall JHR incidence of 55.8%, with rates climbing to 71.8% in studies primarily focused on the reaction [5, 40]. Regarding therapeutic induction, JHR occurred in 19.8% of patients treated with either tetracycline or penicillin, while 23.3% of those receiving combination therapy (penicillin and doxycycline) experienced the reaction. This observation deviates from established literature suggesting that intravenous tetracycline carries the highest risk (up to 100%), whereas low-dose penicillin is associated with fewer, albeit less curative, reactions [28]. Although combination therapy is traditionally favored for balancing efficacy with safety [41], our finding of a higher JHR frequency in the combination group compared to monotherapy cohorts warrants further investigation into the underlying mechanisms and clinical implications..

This study determined the hospital case fatality rate of LBRF to be 6.1%. This rate is comparable to those reported in other regions, including Sudan (5.5%), Addis Ababa (5%), and higher than a study from Gonder

(4.6%)[24, 28, 32]. However, it is notably lower than the 13.2 % fatality rate observed in adults at Gambo General Hospital, potentially attributable to the higher prevalence of coexistent malaria infection among those patients[25]. In contrast, the mortality rate reported in this study is higher than that of other studies, such as the 1.9% in Hossana and 3.6% in Assella[15, 21]. These disparities underscore the late-presenter phenomenon often observed in referral centers like ZMH, where patients arrive with established complications after failing initial treatment elsewhere. Historically, untreated patients during major epidemics have exhibited case fatality rates ranging from 30% to 80%, , but with antibiotic treatment mortality is reduced to 2% to 6% while Ethiopian studies typically report rates between 2% and 13% aligning with the findings from our study[5, 25, 27, 40].

The mortality predictors identified in this study align with established prognostic markers observed across a broad spectrum of severe febrile and viral haemorrhagic illnesses. Neurological impairment , defined as altered mentation or GCS < 15, was the strongest independent predictor of death (aOR = 26.60, 95% CI 6.66–106.30), consistent with its role as a marker of late-stage severity, direct CNS involvement, severe sepsis, or metabolic derangement [42–45]. Chest crepitations (aOR = 6.01, 95% CI 1.41–25.67) reflect respiratory compromise such as pneumonia, pulmonary oedema, or ARDS, which are common terminal pathways in systemic infection [45, 46]. Abdominal pain (aOR = 4.00, 95% CI 1.02–15.68) likely captures visceral pathology, including hepatic injury or splenic involvement, marking a subgroup with advanced systemic disease [45–47]. Notably, age was not retained in the primary model; in a sensitivity analysis including age alongside the four core predictors, the association was attenuated and no longer significant, suggesting that age may operate through clinical severity markers rather than as an independent predictor. The persistence of these four predictors across sensitivity models demonstrates their robustness and potential utility for triage and early escalation of care in resource-limited settings.

Louse-borne relapsing fever is a disease of poverty that thrives in settings of crowding, inadequate housing, and limited access to water and sanitation, conditions that facilitate person-to-person transmission of body lice. In our cohort, 64.7% of patients with documented housing status were homeless, and homeless patients were significantly younger than non-homeless patients (median 19 vs. 23 years), a pattern consistent with youth displacement, labour migration, and street involvement, all recognized drivers of LBRF outbreaks in the Horn of Africa. The higher mortality observed among homeless patients (8.2% vs. 3.8%) did not reach statistical significance in this underpowered subgroup, and homelessness was not independently associated with mortality after adjustment for clinical severity (aOR = 0.78, 95% CI 0.11–5.48, $p = 0.800$). This should not be interpreted as evidence that poverty is unimportant. Rather, it suggests that poverty operates upstream, increasing the risk of infection, delaying presentation, and driving severe disease, rather than acting as a proximate determinant of death once critical illness has developed. This distinction has direct implications for intervention: poverty-reduction efforts, housing provision, and improved access to primary care are likely to be most effective at the prevention end of the spectrum, while clinical severity markers should guide acute management.

Limitations of the Study

This study has several limitations. First, it was a retrospective, single-centre study conducted at ZMH, a tertiary referral hospital. Patients presenting there may be more severely ill than those managed at primary care facilities, which may inflate the observed case fatality rate and limit generalisability to other settings in Ethiopia. The retrospective design also relied on physician documentation rather than standardised research criteria for clinical complications, introducing potential information bias, and the cross-sectional design precludes causal inferences. Second, laboratory parameters had substantial missingness (AST: 54.7%; ALT: 56.9%; creatinine: 55.3%), and missingness was strongly associated with mortality: patients who died were more likely to have missing laboratory results because they died before investigations could be completed.

Third, housing status, the only socioeconomic variable available, was missing in 58.3% of patients. Although patients with known and unknown housing status did not differ significantly with respect to age, sex, or mortality, the small number of deaths among those with known housing status ($n = 10$) precluded reliable multivariable adjustment for homelessness. The dataset lacked income, education, water and sanitation access, food security, and distance to healthcare, all of which are important determinants of LBRF acquisition and outcome. Fourth, the small number of deaths ($n = 22$) limited statistical power. Although Firth's penalised regression was used to reduce small-sample bias, confidence intervals around some estimates remain wide, and the events-per-variable ratio of the primary model (5.5) is below the conventional threshold of 10. The association between antibiotic regimen and mortality is also confounded by indication, as patients with severe disease were more likely to receive parenteral therapy; this association should not be interpreted as evidence of a causal effect of antibiotic choice on mortality. We did not screen for co-infections (e.g., malaria, typhoid) or document time from admission to antibiotic administration, both of which may influence outcomes.

Finally, the absence of long-term follow-up data meant that post-discharge outcomes, including relapse and mortality, could not be assessed. The study period also included the COVID-19 pandemic years, during which healthcare-seeking and admission patterns may have been altered, although this impact could not be quantified in the present analysis

Conclusion and recommendation

This study confirms that LBRF continues to impose a substantial burden of severe illness in Addis Ababa, with a concerning upward trend in hospital admissions at ZMH between 2019 and 2024. The overall hospital mortality rate was 6.1%, with the majority of deaths occurring within 48 hours of admission, highlighting the rapid clinical deterioration characteristic of severe LBRF. Independent predictors of mortality included septic shock, abdominal pain, chest crepitations, and neurological impairment. Jarisch-Herxheimer reaction occurred in nearly half of all patients and was significantly more frequent among those receiving combined penicillin and doxycycline therapy. LBRF remains an important cause of preventable death in Ethiopia, and the rising case numbers demand urgent clinical and public health attention. We recommend implementing a triage system that incorporates the identified mortality predictors to identify high-risk patients immediately upon admission. Additionally, we recommend designating LBRF as a notifiable disease, integrating case-finding into existing febrile illness surveillance

systems, and launching targeted public health interventions. Furthermore, future research should include prospective, multicentre studies with complete laboratory and socioeconomic data, standardised treatment protocols, co-infection screening, long-term follow-up, and implementation research to evaluate triage and surveillance strategies in homeless and displaced populations.

Declarations

Authors' contributions

AE: conceptualization, methodology, project administration, formal analysis, visualization, writing of the original draft, review and editing RWY: writing the manuscript, visualization, review and editing MB: conceptualization, project administration, writing the proposal, writing the manuscript, review and editing AY: writing the proposal, methodology, review and editing KH: conceptualization, methodology, review and editing. AS and NM: writing of the original draft, review and editing FM: conceptualization, writing the proposal, writing the manuscript ZA: conceptualization, formal analysis, visualization, writing the manuscript, review and editing.

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Availability of data and materials

Supporting data for the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that there are no competing interests.

Ethical considerations

Ethical clearance was obtained from the institutional review boards of SPHMMC and Addis Ababa Public Health Research and Emergency Management Directorate. Subsequently, permission was obtained from Zewditu Memorial hospital administration. Participant details such as names or phone numbers was not included in the data extracted from the patient files.

Clinical trial number

Not applicable.

Consent for publication

Not applicable

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Figures

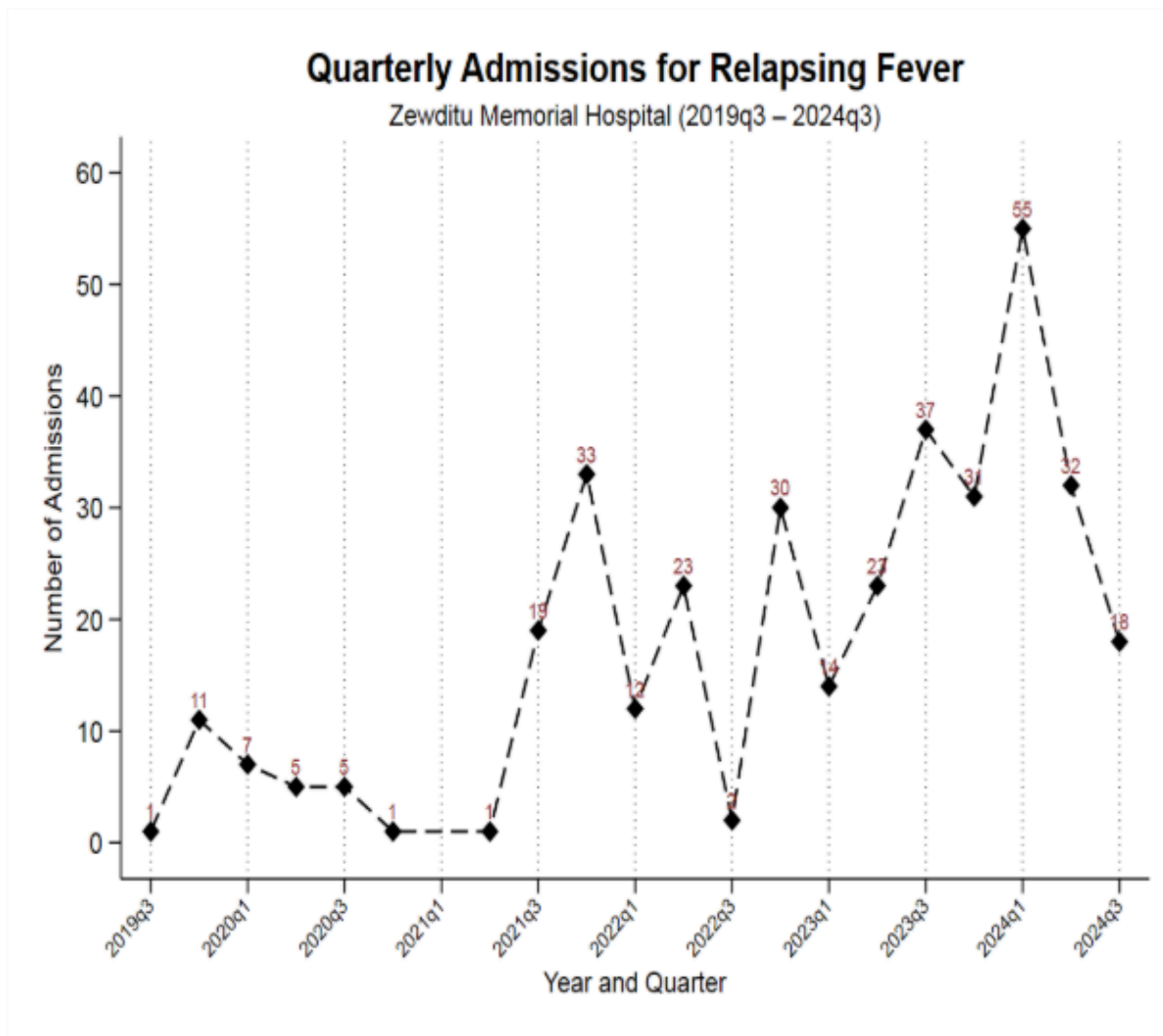


Figure 1

Quarterly admissions for louse-borne relapsing fever at Zewditu Memorial Hospital, Ethiopia, 2019–2024. Data points represent the number of patients admitted per quarter. Admission counts remained low until mid-2021, followed by a marked resurgence, with the highest number of admissions recorded in the first quarter of 2024 (n = 55).

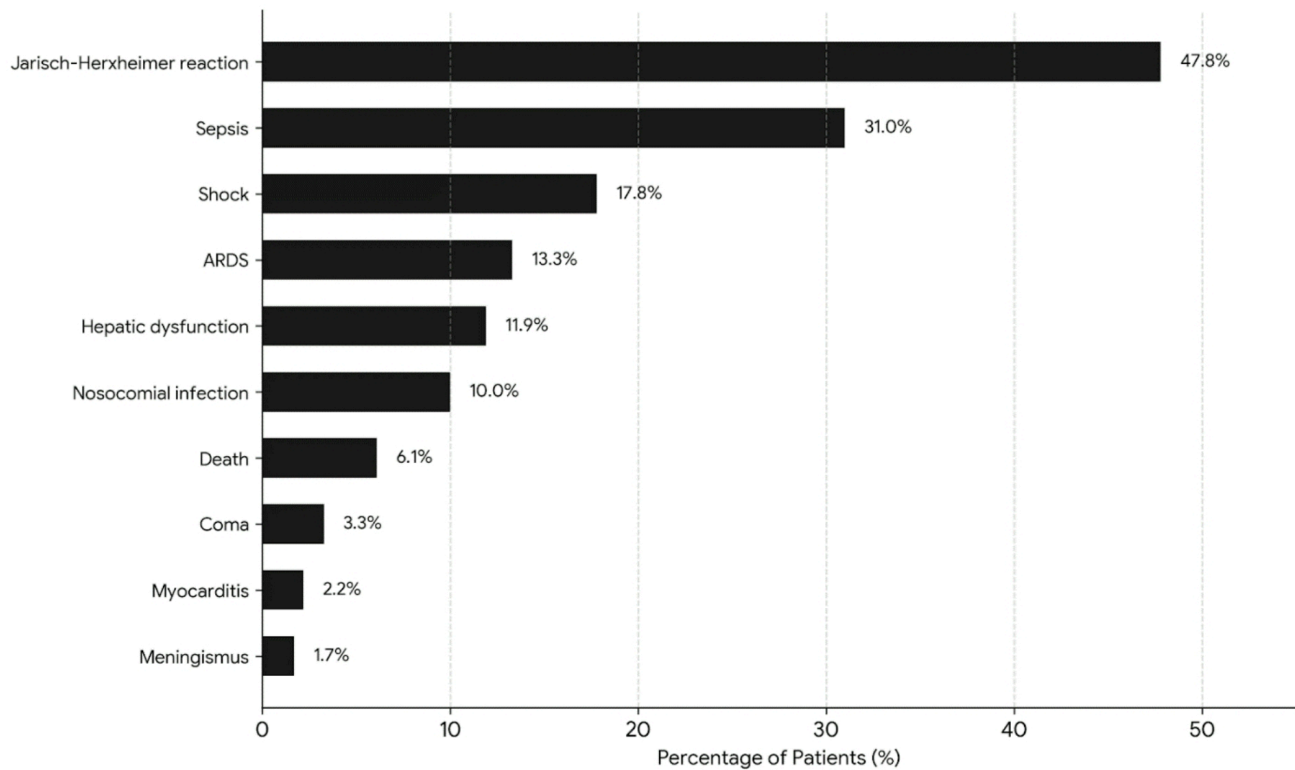


Figure 2

Prevalence of clinical complications and outcomes among patients with louse-borne relapsing fever at Zewditu Memorial Hospital, Ethiopia from 2019-2024 G.C (N = 360). Bars represent the percentage of patients who experienced each specific complication or outcome during their clinical course. Data are sorted in descending order of frequency.

Supplementary Files

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