

Frequency of Laboratory-Confirmed Malaria and Etiological Profile of Acute Febrile Syndromes among Hospitalized Adults in Kinshasa, Democratic Republic of the Congo: A Retrospective Evaluation

Madone Mandina

mandinamadone@gmail.com

Cliniques Universitaires de Kinshasa

Sephora Useni Salama

Cliniques Universitaires de Kinshasa

Ben Bepouka

Cliniques Universitaires de Kinshasa

Murielle Longokolo

Cliniques Universitaires de Kinshasa

Nadine Mayasi

Cliniques Universitaires de Kinshasa

Donat Mangala

Cliniques Universitaires de Kinshasa

Tuna Lukiana

Cliniques Universitaires de Kinshasa

Taylor Pindi

Cliniques Universitaires de Kinshasa

Ossam Odio

Cliniques Universitaires de Kinshasa

Marcel Mbula

Cliniques Universitaires de Kinshasa

Hippolyte Situakibanza

Cliniques Universitaires de Kinshasa

Roger Wumba

Cliniques Universitaires de Kinshasa

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Abstract

Background

In the Democratic Republic of the Congo (DRC), acute fever is historically and almost systematically equated with malaria. This deeply paradigm-driven clinical reflex ("Fever = Malaria") promotes massive over-diagnosis, inappropriate antimalarial overconsumption, and hazardous therapeutic delays for other severe life-threatening conditions, particularly bacterial infections. This study aimed to evaluate the true frequency of laboratory-confirmed malaria and determine the etiological landscape of acute febrile syndromes among adults admitted to a tertiary referral hospital in Kinshasa.

Methods

A retrospective cross-sectional and analytical study was conducted over a 24-month period (January 1, 2023, to December 31, 2024) at the Department of Internal Medicine (Infectious Diseases Service and Medical Intensive Care Unit) of the University Clinics of Kinshasa. Medical records of patients aged ≥ 16 years presenting with documented or reported fever at admission were exhaustively reviewed.

Results

A total of 135 febrile adult patients were included (mean age: 56.2 ± 21.6 years; 54.1% male). Alarming, only 56.3% ($n = 76$) of febrile patients received a biological diagnostic test for malaria (thick blood smear or rapid diagnostic test) at admission. Invasive bacterial sepsis and bacteremia emerged as the leading cause of hospitalization, accounting for 54.1% ($n = 73$) of the entire cohort, significantly outranking malaria (final diagnosis, 37.0%, $n = 50$) and central nervous system infections (26.7%, $n = 36$). Among malaria cases, 70.0% ($n = 35$) presented with severe clinical criteria. Furthermore, 16.7% ($n = 9$) of patients with a positive malaria test actually suffered from concurrent bacteriologically proven sepsis, representing incidental asymptomatic parasitemia. Conversely, 18.2% ($n = 4$) of patients with a negative malaria test were nevertheless diagnosed and treated as malaria. The overall in-hospital mortality rate was critically high at 60.7% ($n = 82$), and was significantly higher in the non-malarial febrile syndrome group than in the malaria group (69.4% vs. 46.0%; $p = 0.007$).

Conclusion

Bacterial sepsis is the dominant driver of severe febrile illness and mortality among hospitalized adults in this urban tertiary setting, far surpassing clinical malaria. Overreliance on empirical clinical diagnoses and the failure to systematically implement laboratory confirmation create severe diagnostic gaps, directly impacting patient survival. Systematic diagnostic screening for bacterial etiologies and immediate broad-spectrum antibiotic deployment for sepsis are urgently required.

Introduction

Malaria remains a monumental public health crisis globally, causing an estimated 249 million cases and over 600,000 deaths annually, with more than 95% of this burden concentrated in the World Health Organization (WHO) African region [1]. The Democratic Republic of the Congo (DRC) bears the second-highest global burden of malaria, immediately following Nigeria, where *Plasmodium falciparum* represents the predominant and most pathogenic species [2]. Nationally, malaria accounts for the leading cause of morbidity and mortality across all age groups [2].

However, in hyperendemic and holoendemic transmission zones such as Kinshasa, this heavy epidemiological footprint has deeply entrenched a historical clinical paradigm: "Fever equals Malaria" [3, 4]. Consequently, acute febrile adult patients are routinely prescribed empirical antimalarial therapies without systematic laboratory validation [5]. This deep-rooted practice incurs severe medical and socio-economic ramifications: it accelerates the selection pressure for artemisinin resistance, increases the direct out-of-pocket medical financial burden on households, and critically delays the administration of life-saving therapeutics for non-malarial febrile illnesses [4, 6].

Furthermore, an additional diagnostic challenge arises from the phenomenon of premunition [7, 8]. In high-transmission environments, a substantial proportion of adults maintain low-grade asymptomatic *P. falciparum* parasitemia [9]. When these individuals are hospitalized for an unrelated severe acute infection (e.g., bacterial pneumonia, pyelonephritis), routine rapid diagnostic tests (RDTs) or thick blood smears frequently return positive results [3, 10]. The classical diagnostic trap consists of attributing the fever solely to malaria based on this incidental biological positivity, thereby masking the primary life-threatening bacterial pathology [11]. At the University Clinics of Kinshasa (CUK), a premier tertiary referral hospital, contemporary data regarding the exact proportion of laboratory-verified malaria versus alternative bacterial etiologies in adults remain remarkably sparse. This study was designed to bridge this critical knowledge gap, providing precise quantification of diagnostic coverage, etiological distribution, and clinical outcomes.

Materials and Methods

Study Design and Setting

This was a retrospective, descriptive, and analytical cohort study spanning a 24-month consecutive period from January 1, 2023, to December 31, 2024. The study was conducted at the University Clinics of Kinshasa within the Department of Internal Medicine, specifically focusing on the Infectious and Tropical Diseases Service (MIT) and the Medical Intensive Care Unit (MISI).

Study Population and Eligibility Criteria

The target population comprised all adult patients hospitalized during the study period. To be eligible for inclusion, medical charts had to meet the following strict criteria: (1) patient age ≥ 16 years, (2) admission and overnight hospitalization within the MIT or MISI wards, and (3) a documented objective fever at admission (axillary or rectal temperature $\geq 38.0^{\circ}\text{C}$) or a distinct history of acute high-grade fever that directly prompted the emergency consultation [12, 13]. Charts with completely missing demographic, diagnostic, or clinical evolution data were excluded. Applying these criteria resulted in a final analytical cohort of 135 well-documented adult cases. The study protocol was reviewed and approved by the Institutional Review Board and Ethics Committee of the University Clinics of Kinshasa. Owing to the strictly retrospective design of this investigation and the exclusive use of fully de-identified, pseudonymized medical charts from routine clinical care, the requirement for individual patient informed consent was formally waived by the committee. Administrative permission to access the medical registries was granted by the hospital directorate.

Data Collection

Data collection was carried out using standardized extraction forms capturing socio-demographic variables, clinical parameters at admission (including respiratory rate, heart rate, Glasgow Coma Scale, and mucosal pallor), biological screening status (realization and results of thick blood smear or histidine-rich protein 2 [HRP2]-based RDTs), alternative microbiologic investigations (blood cultures, urine cultures [ECBU], and cerebrospinal fluid [CSF] analyses), therapeutic interventions initiated, duration of hospital stay, and final clinical outcomes (discharge, transfer, or in-hospital death).

Operational Definitions

- **Acute Febrile Syndrome:** Documented objective core temperature $\geq 38.0^{\circ}\text{C}$ at admission or a clear clinical history of recent high-grade fever driving hospital consultation [13, 14].
- **Laboratory-Confirmed Malaria:** Positive identification of asexual stages of *Plasmodium* via a thick blood smear examination or a positive rapid diagnostic test (RDT) at admission.
- **True Clinical Malaria-Disease:** Concomitance of an acute febrile syndrome and positive malaria biology (RDT or thick blood smear) in the complete absence of any alternative validated infectious focal points or alternative etiologies. We acknowledge that in hyperendemic transmission settings like Kinshasa, adult premunition ideally requires a quantitative parasite density threshold to formally differentiate clinical malaria-disease from incidental asymptomatic carriage. However, due to the retrospective nature of this study and routine clinical laboratory practices at the time, a quantitative cutoff could not be systematically applied, which represents a operational proxy definition [15].
- **Non-Malarial Febrile Syndrome:** Acute febrile presentation accompanied by strictly negative thick blood smear and RDT results [11].
- **Clinical Misclassification (False Malaria Diagnosis):** Empirical prescription of antimalarial regimens based purely on febrile clinical presentations despite documented negative parasite biology at

admission [16].

- **Etiological Misclassification (Incidental Parasitemia):** Detection of a positive malaria test (RDT/thick blood smear) in a severely ill febrile patient whose clinical state and fever are entirely driven by another confirmed primary source (e.g., bacterial sepsis or meningitis), reflecting the paradox of asymptomatic carriage in immune adults [17].
- **Invasive Bacterial Sepsis / Bacteremia:** Operationalized as an acute infection accompanied by systemic inflammatory response syndrome (SIRS) criteria or a quick Sequential Organ Failure Assessment (qSOFA) score ≥ 2 (e.g., respiratory rate ≥ 22 /min, altered mentation, or systolic blood pressure ≤ 100 mmHg), associated with either a microbiologically isolated pathogen (via blood, urine, or cerebrospinal fluid cultures) **OR** a highly probable, clinically and radiologically documented deep focal infection (such as severe lobar pneumonia or advanced pyelonephritis) requiring immediate intravenous broad-spectrum antibiotherapy.
- **Co-morbidities and Associated Chronic Conditions:** This category did not designate the primary acute etiology of the febrile syndrome that prompted admission. Instead, it operationalized the presence of underlying chronic diseases or co-morbidities documented in the patient's medical records at admission (including hypertension, diabetes mellitus, HIV infection, and obesity). These variables were collected to comprehensively characterize the baseline clinical profile and vulnerability of the study population.

Statistical Analysis

Statistical analyses were executed using SPSS version 25.0. Qualitative variables are presented as absolute numbers and percentages, while quantitative variables are reported as mean $\pm$ standard deviation (SD) or medians with interquartile ranges. Cross-tabulations were constructed to compare parameters between the malaria group (final diagnosis) and the non-malarial febrile syndrome group. Proportions were compared using the Pearson Chi-square test or Fisher's exact test, and continuous variables were evaluated using Student's t-test. Statistical significance was defined as $p < 0.05$.

Results

The comprehensive baseline characteristics, clinical presentation parameters, and admission triage pathways of the study cohort are presented at the outset of the findings in Table 1.

Table 1
Sociodemographic characteristics and admission parameters of patients according to the final diagnosis

Variables / Parameters	Total Cohort (n = 135)	Malaria Group (n = 50)	Non-Malaria Group (n = 85)	p-value
Mean Age, years ($\pm$ SD)	56.2 $\pm$ 21.6	53.4 $\pm$ 22.7	57.8 $\pm$ 20.8	0.258 ¹
Age Categories, n (%)				0.568 ²
≤ 30 years	25 (18.5%)	12 (24.0%)	13 (15.3%)	
31–45 years	18 (13.3%)	5 (10.0%)	13 (15.3%)	
46–60 years	23 (17.0%)	8 (16.0%)	15 (17.6%)	
> 60 years	69 (51.1%)	25 (50.0%)	44 (51.8%)	
Sex, n (%)				0.466 ²
Male	73 (54.1%)	25 (50.0%)	48 (56.5%)	
Female	62 (45.9%)	25 (50.0%)	37 (43.5%)	
Healthcare Seeking Delay, n (%)				0.790 ²
< 48 hours	13 (9.6%)	5 (10.0%)	8 (9.4%)	
2–7 days	49 (36.3%)	20 (40.0%)	29 (34.1%)	
> 7 days	72 (53.3%)	25 (50.0%)	47 (55.3%)	
Admission Ward Allocation, n (%)				0.003 ²
MIT (Infectiologie)	61 (45.2%)	32 (64.0%)	29 (34.1%)	
MISI (Medical Intensive Care Unit)	73 (54.1%)	18 (36.0%)	55 (64.7%)	
Other	1 (0.7%)	0 (0.0%)	1 (1.2%)	

¹ Student's t-test; ² Pearson's Chi-square test. Healthcare-seeking delay was not documented for one patient in the non-malaria group.

The socio-demographic profile of the 135 febrile patients revealed an older adult cohort, with a mean age of 56.2 $\pm$ 21.6 years (range: 16–93 years) and a slight male predominance (54.1% male, sex ratio 1.18:1). Crucially, a profound delay in seeking tertiary medical care was documented: 53.3% (n = 72) of the patients presented to the hospital only after more than 7 days of continuous fever, while a mere 9.6% (n = 13) sought care within 48 hours of symptom onset (Table 1).

At physical examination, signs of high systemic severity were highly prevalent: objective tachypnea/respiratory distress was observed in 89.6% (n = 121) of patients, tachycardia in 67.4% (n = 91), severe neurological impairment (altered consciousness or Glasgow Coma Scale < 15) in 59.3% (n = 80), and profound conjunctival/mucosal pallor in 45.9% (n = 62).

Diagnostic Coverage and Mismatches

A central finding of this investigation was the poor rate of biological diagnostic testing. Out of 135 patients admitted with acute fever, only 56.3% (n = 76) underwent a biological screening for malaria (thick blood smear or RDT) at admission, leaving 43.7% (n = 59) diagnosed and managed purely on empirical clinical suspicion. Among the 76 tested patients, 54 returned positive and 22 were negative. In the final clinical synthesis, combining laboratory workups and therapeutic response, 37.0% (n = 50) received a final diagnosis of malaria (of which 70.0% met the criteria for severe malaria), while 63.0% (n = 85) were classified as non-malarial febrile syndromes. This final malaria group comprised 45 patients with a positive test, 4 with a negative test and 1 who was not tested (Table 2).

Table 2 uncovers major clinical mismatches: 16.7% (n = 9) of patients with a biologically positive malaria test were ultimately proven to have a primary non-malarial infection. Among these 9 cases, 4 were strictly confirmed via positive cultures (blood or urine), while the remaining cases were validated based on robust clinical and biological syndromic criteria, including an altered qSOFA score (≥ 2), marked leukocytosis or leukopenia, and a clearly identified primary infectious focal point (e.g., severe pneumonia or soft tissue infection) requiring empiric broad-spectrum antibiotic therapy. Conversely, 18.2% (n = 4) of patients with a strictly negative biological malaria test were still fully treated with empirical antimalarial courses due to clinician distrust of laboratory results.

Table 2

Cross-tabulation between initial biological test results and the final verified clinical diagnosis

Initial Biological Test Result	Final Diagnosis: Non-Malaria	Final Diagnosis: Malaria	Total Patients
Test Positive	9 (16.7%)	45 (83.3%)	54
Test Negative	18 (81.8%)	4 (18.2%)	22
Not Performed / Not Documented	58 (98.3%)	1 (1.7%)	59
Total Cohort	85	50	135

Etiological Profile Distribution

The true etiological landscape was heavily dominated by bacterial infections rather than malaria. Invasive bacterial sepsis/bacteremia was documented as the primary final diagnosis in 54.1% (n = 73) of

cases. Central nervous system infections (bacterial or cryptococcal meningitis, meningoencephalitis) were identified in 26.7% (n = 36) of patients, while malaria (final diagnosis) ranked second overall at 37.0% (n = 50).

Figure 1 illustrates the distribution of overall final discharge diagnoses (cumulative diagnoses per patient record). Sepsis and bacteremia predominated as the leading acute etiologies, accounting for 54.1% of cases, followed by biological malaria at 37.0%. Additionally, 66.7% of the cohort presented with associated chronic co-morbidities (such as hypertension, diabetes, or HIV infection) underlying the acute febrile episode.

Comparative analysis between the malaria and non-malaria groups demonstrated distinct clinical pathways and patterns of healthcare utilization. While baseline demographics did not differ significantly, ward allocation was highly divergent (p = 0.003): malaria cases were primarily managed within the Infectious Diseases ward (MIT, 64.0%), whereas non-malarial syndromes—owing to their extreme septic shock or neurological presentations—required immediate admission to the Medical Intensive Care Unit (MISI, 64.7%) (Table 1).

Clinical Outcomes and Survival Disparities

The overall in-hospital mortality rate for the entire cohort reached a catastrophic 60.7% (n = 82), highlighting the advanced stage of disease at tertiary presentation. Strikingly, mortality was significantly more severe among patients suffering from non-malarial febrile syndromes than those with a final diagnosis of malaria (69.4% vs. 46.0%; p = 0.007), indicating that missing a bacterial diagnosis carries a significantly higher lethal risk (Figure 2, Table 3).

Table 3. Detailed clinical outcomes and in-hospital mortality analysis stratified by final diagnostic group

Clinical Outcomes	Total Cohort (n = 135)	Malaria Group (n = 50)	Non-Malaria Group (n = 85)	p-value
In-Hospital Death, n (%)	82 (60.7%)	23 (46.0%)	59 (69.4%)	0.007 ²
Discharged Improved, n (%)	50 (37.0%)	26 (52.0%)	24 (28.2%)	
Mean Stay, days (±SD)	8.6 ± 8.7	8.1 ± 6.4	8.9 ± 9.8	0.612 ¹

¹ Student's t-test; ² Pearson's Chi-square test.

Discussion

The findings of this retrospective study reveal critical gaps in the initial management of adult febrile illnesses at a premier tertiary hospital in Central Africa. Most notably, nearly 43% of patients presenting with acute fever did not receive any initial laboratory testing for malaria. This low screening rate directly illustrates the tenacity of the historical clinical reflex that assumes "Fever = Malaria," completely bypassing the mandatory biological confirmation advocated by both the WHO and the National Malaria Control Program (PNLP) [1, 2, 18].

Our data conclusively demonstrate an etiological landscape in hospitalized adults where invasive bacterial sepsis and bacteremia (54.1%) far surpass malaria (37.0%). This structural shift aligns with global evidence highlighting the high burden of non-malarial febrile illnesses in sub-Saharan Africa [19, 20]. In a tertiary facility like the University Clinics of Kinshasa, this pattern is amplified by referral bias. The high frequency of underlying chronic conditions (66.7%) reflects the typical recruitment pattern of a tertiary referral center like the University Clinics of Kinshasa. Patients typically present to this facility at an advanced stage, often after self-medicating with antimalarials at home or receiving empirical treatments in peripheral clinics [4]. This process effectively filters out uncomplicated malaria, leaving a pool of severe, undifferentiated bacterial pathologies or late-stage complications [19, 21]. The intersection of acute invasive bacterial infections (sepsis) with a frail baseline characterized by chronic co-morbidities likely acted as a major driver for the severe critical outcomes and the high in-hospital mortality rate (60.7%) observed in this cohort.

A major clinical risk highlighted by this study is the diagnostic trap of asymptomatic parasitemia. In Kinshasa, a hyperendemic region, a high percentage of the adult population exhibits immune-mediated premunition, carrying *Plasmodium* parasites without clinical symptoms [6, 7, 22]. Consequently, when an adult is admitted for severe bacterial sepsis, a positive malaria test can mislead clinicians into stopping further diagnostic investigations, attributing the entire clinical presentation to severe malaria [8, 23]. This error leads to dangerous delays in introducing targeted broad-spectrum antibiotics, contributing directly to the observed 69.4% mortality rate in the non-malaria group [4, 24]. Conversely, the practice of administering antimalarials to 18.2% of patients with documented negative tests underscores a profound distrust in laboratory results, a behavior driven by the fear of microscopic false negatives despite the high sensitivity of modern diagnostic tools [8, 25].

This study has several limitations. First, its single-center retrospective design relied on available medical chart records. Second, due to financial constraints and laboratory supply interruptions, systematic blood cultures and advanced molecular testing could not be performed for all patients. Nevertheless, the study provides a realistic assessment of the high mortality associated with febrile illnesses in urban tertiary settings in Central Africa.

Third, a major methodological limitation stems from the lack of systematic parasite density quantification (parasitemia thresholds). In holoendemic and hyperendemic areas such as Kinshasa, acquired semi-immunity (premunition) among adults frequently leads to low-grade asymptomatic *Plasmodium falciparum* carriage [6, 7, 16]. Although we strictly excluded cases with alternative obvious

infectious foci to refine our definition of "True Clinical Malaria-Disease," some misclassification due to incidental parasitemia remains possible.

Conclusion

This study confirms that invasive bacterial sepsis is the primary cause of acute febrile admission and mortality among adults at the University Clinics of Kinshasa, far outranking malaria. The traditional clinical assumption that "Fever = Malaria" is no longer sustainable and contributes to poor patient outcomes. To improve survival, clinicians must strictly adhere to mandatory biological screening, maintain high clinical suspicion for bacterial sepsis even when malaria tests are positive, and ensure the rapid deployment of empirical broad-spectrum antibiotics in patients showing signs of systemic sepsis.

Abbreviations

CSF	Cerebrospinal fluid
CUK	University Clinics of Kinshasa (Cliniques Universitaires de Kinshasa)
DRC	Democratic Republic of the Congo
ECBU	Cytobacteriological examination of urine (Examen Cytobactériologique des Urines)
HIV	Human immunodeficiency virus
HRP2	Histidine-rich protein 2
MISI	Medical Intensive Care Unit (Service de Réanimation Médicale)
MIT	Infectious and Tropical Diseases Service (Service de Maladies Infectieuses et Tropicales)
PNLP	National Malaria Control Program (Programme National de Lutte contre le Paludisme)
qSOFA	Quick Sequential Organ Failure Assessment
RDT	Rapid diagnostic test
SD	Standard deviation
SIRS	Systemic inflammatory response syndrome
SPSS	

Declarations

Ethics approval and consent to participate

This study was conducted in strict accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the University Clinics of Kinshasa, Faculty of Medicine, University of Kinshasa, Democratic Republic of the Congo. Administrative permission to access the patient registries was granted by the hospital directorate. Since this investigation involved an anonymized retrospective chart review where data were strictly pseudonymized prior to analysis, the requirement for written informed consent was waived by the ethics committee.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MMN and SUS conceived and designed the study. BB, ML, NM, DM, TL, TP and OO participated in data collection and cleaning. MM, HS, and RW analyzed the data and revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Figures

Etiological Profile of Acute Febrile Syndromes at Admission (N = 135)

(Cumulative final diagnoses per clinical record)

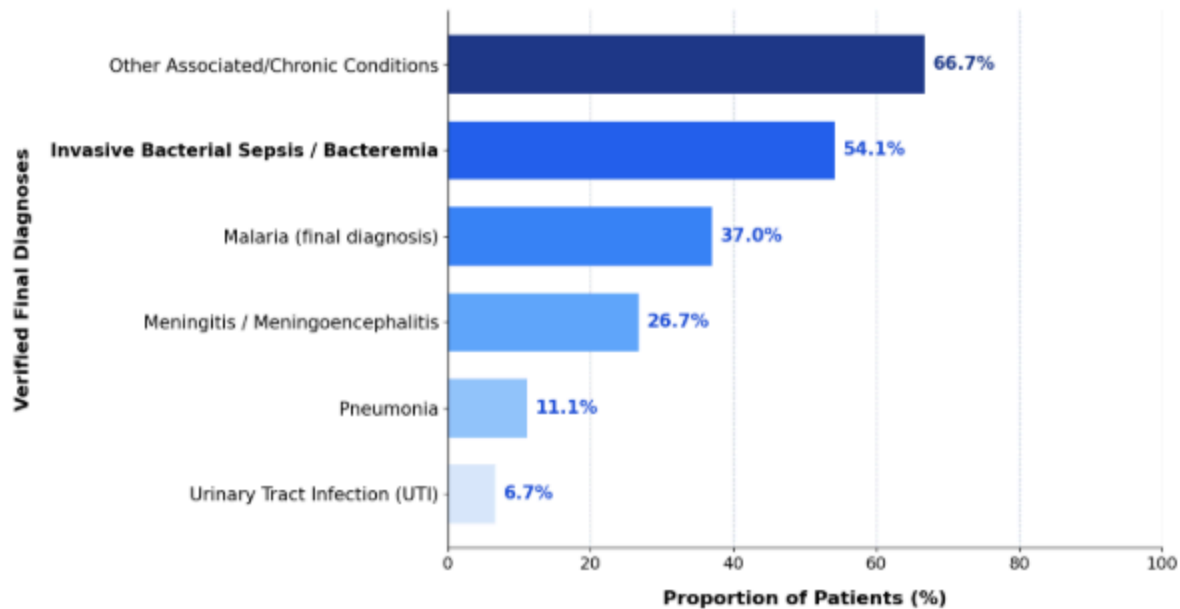


Figure 1

Detailed Etiological Profile of Acute Febrile Syndromes among Hospitalized Adults (n=135). Horizontal bar chart summarizing the cumulative proportions of verified final diagnoses across the study cohort. Sepsis and bacteremia predominated as the leading acute etiologies (54.1%), significantly outranking malaria (final diagnosis, 37.0%) and central nervous system infections (26.7%). Classification of invasive bacterial sepsis includes both microbiologically isolated pathogens and cases strictly validated based on robust clinical and biological syndromic criteria (including an altered qSOFA score ≥ 2 and clearly identified primary infectious focal points) to accurately account for diagnostic resource constraints and differentiate true severe bacterial illness from incidental asymptomatic plasmodial carriage. Total percentages exceed 100% due to cumulative concurrent diagnoses per clinical record (e.g., bacterial sepsis overlapping with incidental parasitemia)

In-Hospital Clinical Outcomes Stratified by Final Diagnostic Group

(Statistically significant mortality disparity: Chi-square $p = 0.007$)

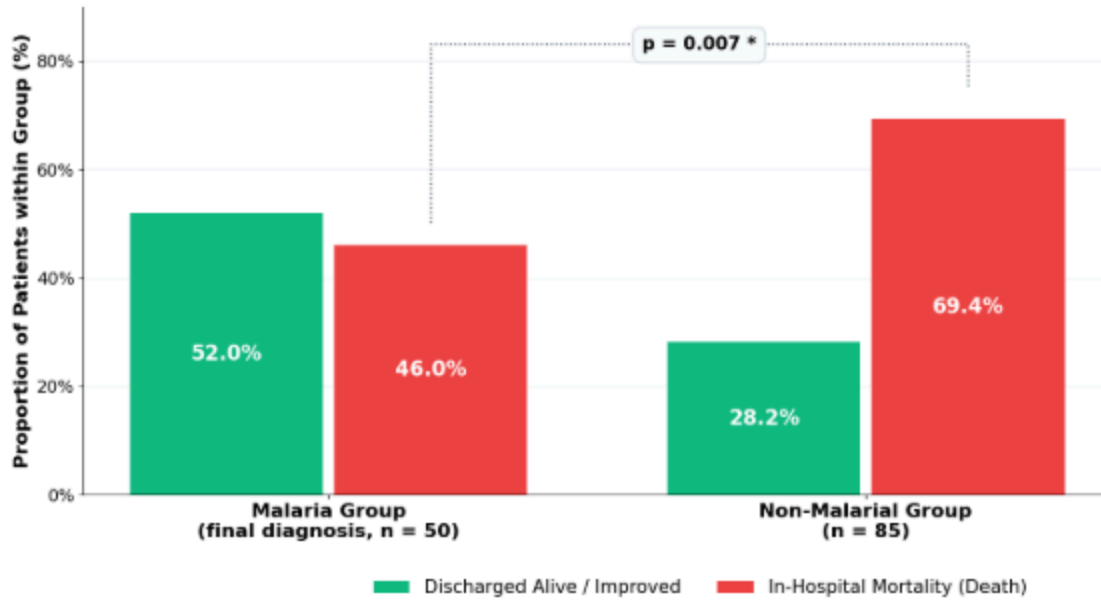


Figure 2

Comparison of In-Hospital Clinical Outcomes Between Malaria and Non-Malarial Groups. Clustered bar chart showing the breakdown of patient progression (survival with clinical improvement vs. mortality) stratified by final diagnosis. The in-hospital mortality rate is significantly higher in the non-malarial syndrome group (69.4%) compared to the malaria group (46.0%), as confirmed by Pearson's Chi-square test ($p = 0.007$). Note: percentages within each group may not total 100% due to minor documented rates of patient transfers or self-discharges (absconding).