

Pediatric Bloodstream Infections in Eastern Democratic Republic of the Congo: Epidemiology, Antimicrobial Resistance Patterns, and Predictors of Mortality

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Background: Bloodstream infections (BSI) are a major cause of pediatric morbidity and mortality in low- and middle-income countries, yet microbiological surveillance data remain limited in Central Africa. We aimed to characterize the epidemiology, microbiological spectrum, antimicrobial resistance (AMR) patterns, and predictors of mortality among children with culture-confirmed BSI in eastern Democratic Republic of the Congo (DRC).

Methods: We conducted a retrospective cohort study at Hôpital Provincial Général de Référence de Bukavu, a tertiary referral hospital in eastern DRC. Children aged 29 days to 18 years admitted with clinically suspected sepsis between June 2020 and December 2024 were eligible. Blood cultures classified as contaminants according to predefined microbiological criteria were excluded. Clinical, microbiological, and antimicrobial susceptibility data were extracted from hospital and laboratory records. Multivariable logistic regression was used to identify independent predictors of in-hospital mortality.

Results: Among 123 children with culture-confirmed bacteremia, 123 clinically significant bacterial isolates were identified and in-hospital mortality was 9.8% (12/123). Gram-negative bacteria predominated (84/123; 68.3%), with *Salmonella* spp. (27/123; 22.0%) and *Enterococcus* spp. (25/123; 20.3%) being the most frequently isolated pathogens. Among the main Gram-negative pathogens, resistance to amoxicillin-clavulanate was 100.0% in *Salmonella* spp. (24/24), *K. pneumoniae* (11/11), and *E. coli* (10/10), whereas amikacin resistance ranged from 0.0% (0/24) in *Salmonella* spp. to 23.1% (3/13) in *K. pneumoniae*; no meropenem resistance was detected among isolates tested. In multivariable analysis, altered level of consciousness was associated with higher odds of in-hospital mortality (aOR 12.83; 95% CI 1.54–107.09). Model discrimination was acceptable (AUROC 0.71; 95% CI 0.55–0.87).

Conclusion: Pediatric BSI in eastern DRC were predominantly caused by Gram-negative pathogens and showed substantial resistance to commonly used antibiotics. Altered level of consciousness was associated with higher odds of in-hospital mortality. Strengthening microbiological surveillance, diagnostic stewardship, and antimicrobial stewardship is essential to optimize empiric therapy and improve pediatric sepsis outcomes.

Keywords: pediatric sepsis, bloodstream infection, bacteremia, antimicrobial resistance, mortality, sub-Saharan Africa, Democratic Republic of the Congo

Introduction

Sepsis is a time-dependent medical emergency and remains a leading cause of preventable morbidity and mortality among children worldwide, disproportionately affecting low- and middle-income countries (LMICs). Recent global modelling analyses estimate that sepsis accounted for approximately 166 million cases and 21.4 million sepsis-related deaths worldwide in 2021, representing nearly one-third of all global deaths.^{1,2} Children and adolescents constitute a substantial proportion of this burden, with the highest sepsis-related mortality rates occurring in resource-limited regions such as sub-Saharan Africa (SSA).^{1–3}

Bloodstream infection (BSI) is one of the most severe manifestations of pediatric sepsis and plays a critical role in guiding antimicrobial therapy. However, microbiological confirmation of bacteremia remains challenging in many resource-constrained settings. Delayed healthcare access, prior antibiotic exposure, limited laboratory capacity, and insufficient blood culture volumes may reduce diagnostic yield.^{4–6} In addition, blood culture contamination can lead to diagnostic uncertainty and inappropriate antimicrobial escalation if not carefully distinguished from true infection.^{5,6}

The growing burden of antimicrobial resistance (AMR) has further complicated the management of invasive bacterial infections. Global analyses estimate that bacterial AMR was associated with nearly five million deaths worldwide in 2019 and continues to represent a major threat to global health.^{7,8} Surveillance data from the World Health Organization Global Antimicrobial Resistance and Use Surveillance System (GLASS) report persistently high resistance rates to third-generation cephalosporins among Enterobacterales isolates in many regions, including SSA.⁹ Recent systematic reviews also document a high prevalence of multidrug-resistant pathogens among pediatric bloodstream infections across the African continent.^{10,11} In the Democratic Republic of the Congo (DRC), inappropriate antimicrobial use, limited microbiological diagnostic capacity, and gaps in AMR surveillance may further complicate the management of bacterial infections.¹²

Available blood-culture surveillance data from the DRC highlight the importance of invasive *Salmonella* infections, although previous studies have not been restricted to pediatric populations. A 10-year multicenter blood-culture surveillance study involving patients across age groups documented the persistence of *Salmonella Typhi* BSI in the country, while hospital-based data from Bukavu similarly identified *Salmonella* spp. among the predominant bloodstream isolates and documented reduced susceptibility to several commonly used antibiotics.^{13,14} More recent pediatric data from Kisantu showed that non-typhoidal *Salmonella* BSI was diagnosed in 12.7% of children under five admitted with severe febrile illness, underscoring the importance of invasive salmonellosis specifically among Congolese children.¹⁵ Invasive non-typhoidal *Salmonella* is also an important cause of pediatric bacteremia across Africa, particularly among children with underlying vulnerabilities such as severe acute malnutrition (SAM), anemia, malaria, or immunosuppression.¹⁶ Malnutrition further increases susceptibility to invasive bacterial infection through impaired immune responses and has been associated with worse clinical outcomes among hospitalized children with severe infection.¹⁷

Despite this burden, contemporary hospital-based data describing the epidemiology, microbiological profile, AMR patterns, and outcomes of pediatric BSI remain scarce in eastern DRC. Available evidence is insufficient to define the local spectrum of bacterial pathogens, their antimicrobial susceptibility patterns, and the factors associated with adverse outcomes in affected children.^{10–15} Generating locally relevant evidence is therefore essential to inform empirical antibiotic strategies, strengthen microbiological diagnosis and antimicrobial stewardship, and improve outcomes for children with sepsis in this setting.

Therefore, we conducted a retrospective cohort study to characterize the epidemiology, microbiological spectrum, and AMR patterns of BSI among children older than 28 days admitted with suspected sepsis to a tertiary referral hospital in Bukavu, eastern DRC. We also sought to identify factors independently associated with in-hospital mortality, with particular attention to SAM. Finally, we compared the clinical characteristics of children with culture-confirmed bacteremia with those of children with culture-negative sepsis.

Methods

Study Design and Setting

This retrospective cohort study was conducted covering a five-year period (January 2020 to December 2024) at Hôpital Provincial Général de Référence de Bukavu (HPGRB), a principal public referral hospital in South Kivu Province, eastern DRC, designated within the national health system.¹⁸ South Kivu Province comprises 34 health zones coordinated by the Provincial Health Division and serves an estimated population of approximately 8.9 million inhabitants.¹⁹ As the main referral hospital located in the provincial capital, HPGRB provides tertiary pediatric care for Bukavu city and surrounding health zones.

The study was conducted within the Department of Pediatrics, which includes the General Pediatrics Unit (including pediatric intensive care beds) and the Saint Joseph Therapeutic Nutritional Centre (Centre Nutritionnel Saint Joseph, CNSJ) dedicated to children with SAM and associated complications. Children aged >28 days to 18 years admitted to the General Pediatrics Unit or CNSJ between 1 January 2020 and 31 December 2024 with clinically suspected sepsis were eligible. Neonates admitted to the Neonatology Unit were excluded. Reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²⁰

Study Population

All children aged 29 days to 18 years admitted to the pediatric department of HPGRB with clinically suspected sepsis were eligible for inclusion if a blood culture was obtained and hospital outcome (survival or in-hospital death) was documented. Children were excluded if they did not meet the clinical criteria for suspected sepsis, if no blood culture was performed, if hospital outcome data were missing, or if they were neonates (≤ 28 days of age). Neonates were excluded because they are managed in a separate Neonatology Unit at HPGRB and represent a clinically and epidemiologically distinct population, with specific risk factors, diagnostic considerations, and bloodstream infection profiles. The present study was therefore intentionally restricted to post-neonatal pediatric patients.

No a priori sample size calculation was performed because this retrospective study used a census approach, including all eligible records available during the predefined study period. The precision of the mortality estimates was therefore determined by the number of eligible culture-confirmed episodes and observed deaths, as reflected by the corresponding confidence intervals.

Clinically suspected sepsis was defined as a clinician-documented infectious syndrome and/or compatible clinical presentation associated with systemic features such as fever, altered mental status, respiratory distress, or hemodynamic instability at admission. In practice, suspected sepsis was identified from clinician-documented diagnoses and/or infectious syndromes recorded in medical charts. Blood cultures were obtained as part of routine clinical care at the discretion of treating clinicians.

Blood culture records were retrieved from the microbiology laboratory database and linked to clinical data extracted from hospital medical records. When multiple blood cultures were obtained during the same hospitalization and infectious episode, only the first blood culture episode was retained to avoid duplication.

Blood cultures classified as contaminants according to predefined microbiological criteria were excluded from analyses of bloodstream infections to minimize misclassification of clinically significant bacteremia. Only episodes with complete clinical and microbiological information were included in the final analytic dataset. The process used to identify eligible participants and blood culture episodes is summarized in [Figure 1](#).

Variable Definitions

Bacteremia was defined as the isolation of a pathogenic bacterial organism from at least one blood culture processed using standard microbiological techniques.^{21,22}

Coagulase-negative staphylococci (CoNS) and other skin commensals were classified as contaminants if isolated once, unless recovered repeatedly in a symptomatic child with compatible clinical features.^{22,23} Common contaminants included coagulase-negative staphylococci, *Corynebacterium* spp., *Bacillus* spp. (non-anthraxis), and *Micrococcus* spp. when isolated in a single culture without compatible clinical features.

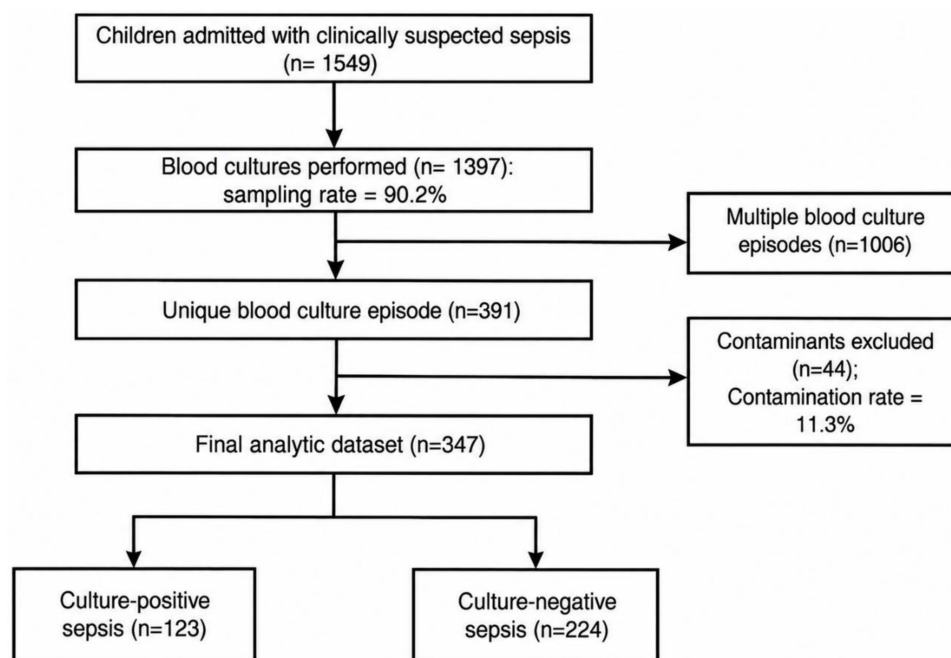


Figure 1 Flow diagram of the study population and blood culture episodes, including diagnostic stewardship indicators.

Sepsis was defined as suspected or confirmed infection associated with organ dysfunction according to the Surviving Sepsis Campaign pediatric guidelines.²¹ Organ dysfunction was defined using clinical and laboratory criteria consistent with this framework, including altered consciousness, respiratory distress, circulatory instability, or significant metabolic abnormalities documented at admission.²¹

SAM was defined according to World Health Organization (WHO) criteria as weight-for-height z-score <-3 , mid-upper arm circumference <115 mm in children aged 6–59 months, and/or the presence of bilateral pitting edema.²⁴

Multidrug resistance (MDR) was defined as non-susceptibility to at least one antimicrobial agent in three or more antimicrobial classes.²⁵ Extended-spectrum β -lactamase (ESBL) production was determined using phenotypic confirmatory methods according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute (CLSI) guidelines.^{26,27}

For the clinical interpretation of biological results, whole blood count abnormalities were defined according to age-adjusted pediatric reference ranges. Electrolyte abnormalities were interpreted according to standard pediatric laboratory thresholds. Hyperglycemia was defined as blood glucose >140 mg/dL and hypoglycemia as <70 mg/dL, in accordance with established pediatric clinical reference standards.²⁸

Microbiological Procedures

Blood cultures were collected under aseptic conditions and, whenever feasible, before initiation of antimicrobial therapy. Blood sampling was adapted to the child's weight, with a target blood volume of approximately 1 mL/kg according to the routine pediatric blood-culture procedure used at HPGRB. The actual volume inoculated could not be verified retrospectively because collection volumes were not systematically recorded in the laboratory registers. Blood-culture collection and processing followed routine laboratory procedures consistent with established principles for blood-culture practice.²⁸

At each blood-culture sampling time point, a single blood sample was collected from each patient and distributed between aerobic and anaerobic blood-culture bottles. A unique blood-culture episode was defined as a blood-culture sampling event performed for a clinically suspected infectious episode. When more than one blood-culture sampling event occurred during the same hospitalization for the same infectious episode, these were considered part of the same

episode and only the first episode was retained for analysis. Blood cultures obtained for a clinically distinct subsequent infectious episode were considered separate episodes.

Throughout the study period, blood cultures were processed using the Render blood-culture system, which had been implemented in the HPGRB bacteriology laboratory in 2019. Blood specimens were inoculated into commercially available aerobic and anaerobic Render blood-culture bottles and incubated at 37°C for up to five days in an incubator–shaker (Render Biotech Co., Shenzhen, China). Both aerobic and anaerobic blood cultures were routinely performed. Culture bottles were monitored for evidence of microbial growth according to the manufacturer’s procedures and routine laboratory practice. Bottles showing evidence of growth were subjected to Gram staining and appropriate subculture to obtain isolated bacterial colonies before definitive identification.

Bacterial identification and antimicrobial susceptibility testing were performed using the Render MA-120 automated system (Render Biotech Co., Shenzhen, China). The system provided bacterial identification and minimum inhibitory concentration (MIC) results for the antimicrobial agents tested. When automated MIC determination was unavailable, antimicrobial susceptibility testing was performed using the disk-diffusion method. Susceptibility results were interpreted according to the EUCAST and/or CLSI breakpoints applicable at the time of testing.^{25,26} High-level aminoglycoside resistance testing was not systematically performed. Breakpoints in use at the time of testing were retained, and no retrospective reclassification of susceptibility results using newer breakpoints was undertaken. All microbiological results were reviewed and validated by trained laboratory personnel according to routine laboratory procedures.

Diagnostic Stewardship Indicators

Three predefined diagnostic stewardship indicators were calculated: (i) blood culture sampling rate, defined as the proportion of children with clinically suspected sepsis who underwent blood culture testing; (ii) positivity rate, defined as the proportion of blood cultures yielding clinically significant bacterial pathogens; and (iii) contamination rate, defined as the proportion of blood cultures yielding organisms classified as contaminants.²³ Positivity and contamination rates were calculated using unique blood culture episodes after removal of duplicate samples obtained during the same infectious episode, thereby avoiding overestimation of microbiological yield.

Data Collection and Quality Control

Data were retrospectively abstracted from medical records and microbiology laboratory registers using a standardized electronic case report form. Variables of interest included sociodemographic characteristics (age, sex, referral status), clinical parameters at admission (fever, altered level of consciousness, respiratory distress, hemodynamic instability, and nutritional status including SAM), and laboratory results (hemoglobin level, platelet count, blood glucose, and serum electrolytes when available). Laboratory variables were interpreted using age-adjusted pediatric reference ranges. Microbiological variables included blood culture results, pathogen identification, and antimicrobial susceptibility profiles. The primary outcome was in-hospital mortality.

Data quality was ensured through double data entry of a randomly selected 10% subset of records. Discrepancies were resolved by verification against the original source documents. All data were anonymized prior to analysis.

Outcomes

The primary outcome was all-cause in-hospital mortality among children with culture-confirmed bacteremia. For outcome analyses, follow-up began during the index hospitalization in which the blood culture was obtained and continued until hospital discharge or in-hospital death. No post-discharge follow-up was performed. Secondary outcomes included the distribution of bacterial pathogens and antimicrobial resistance patterns among culture-confirmed episodes. Clinical and management-related factors associated with in-hospital mortality were also evaluated among children with culture-confirmed bacteremia.

Statistical Analysis

Culture-confirmed bacteremia was not treated as the primary exposure for the mortality model. Culture-positive and culture-negative children with clinically suspected sepsis were compared descriptively to characterize clinical differences

according to blood culture status; these comparisons were not intended to estimate the effect of bacteremia on mortality. The mortality analysis addressed a separate study objective and was restricted to children with culture-confirmed bacteremia to identify clinical and management-related factors associated with in-hospital death within this subgroup. Analyses of pathogen distribution and antimicrobial resistance patterns were likewise restricted to culture-confirmed episodes.

Statistical analyses were performed using Stata version 16.0 (StataCorp LLC, College Station, TX, USA). Continuous variables were summarized as medians with interquartile ranges (IQRs), whereas categorical variables were summarized as frequencies and percentages. Between-group comparisons were performed using the Mann–Whitney *U*-test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate.

Associations with in-hospital mortality were first explored using univariable analyses. Variables with more than 20% missing data were excluded from multivariable modelling. A complete-case analysis approach was used, and no imputation was performed because of the limited number of outcome events and the risk of model instability associated with multiple imputation in small samples.

Variables with a univariable *P* value <0.20 were considered for multivariable modelling, together with variables considered a priori clinically relevant to the study objectives. Given the limited number of deaths (*n*=12), the final model was intentionally restricted to three covariates: altered level of consciousness, lack of antibiotic adjustment after susceptibility testing, and severe acute malnutrition. Altered level of consciousness and lack of antibiotic adjustment met the prespecified univariable screening criterion, whereas severe acute malnutrition was retained because of its predefined clinical relevance to the study objective. Because the low number of outcome events raised concern about small-sample bias and model instability, penalized logistic regression using Firth's correction was performed as a sensitivity analysis using the same three covariates.

Multicollinearity was assessed using variance inflation factors (VIFs), with a threshold of >5 considered indicative of potential collinearity. All variables retained in the final model had VIF values below this threshold, indicating no evidence of problematic multicollinearity among predictors included in the final model ([Supplementary Table S1](#)).

Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Model discrimination was evaluated using the area under the receiver operating characteristic curve (AUROC).

Ethics

The study was approved by the Ethics Committee of Université Catholique de Bukavu (UCB/CIES/PB/GM/011/2026) and conducted in accordance with the principles of the Declaration of Helsinki.²⁹ As this was a retrospective analysis of routinely collected clinical data, the requirement for individual informed consent was waived. All extracted data were anonymized prior to analysis to preserve confidentiality and comply with ethical standards for research involving human participants.

Results

Results are presented in three complementary steps: (i) study population and diagnostic stewardship indicators, (ii) descriptive comparisons between children with culture-positive and culture-negative sepsis, and (iii) outcome modelling restricted to children with culture-confirmed bacteremia.

Study Population and Diagnostic Stewardship Indicators

The selection of study participants and blood culture episodes is summarized in [Figure 1](#). During the study period, 1549 children were admitted with clinical suspected sepsis, of whom 1397 underwent blood culture testing, corresponding to a sampling rate of 90.2%. After exclusion of records with incomplete clinical data and removal of duplicate cultures obtained during the same infectious episode, 391 unique blood culture episodes were identified. Among these episodes, 44 cultures were classified as contaminants (contamination rate 11.3%) and 123 yielded clinically significant bacterial pathogens, corresponding to a blood culture positivity rate of 31.5%, whereas the remaining 224 episodes were classified as culture-negative sepsis. After exclusion of 44 contaminated cultures, 347 episodes analyses.

Baseline characteristics according to blood culture results are summarized in Table 1. Children with culture-confirmed bacteremia were younger than those with culture-negative sepsis, with a median age of 20.0 months (IQR 8.0–40.0) compared with 24.5 months (IQR 11.0–50.2; $P=0.041$). Sex distribution, household size, referral status, vaccination coverage, and comorbid conditions including SAM, sickle cell disease, and HIV infection were similar between groups. Among presenting symptoms, fever was significantly less frequent among children with culture-confirmed bacteremia than among those with culture-negative sepsis (52.8% vs 67.0%; $P=0.013$). Other clinical manifestations, including cough, dyspnea, diarrhea, vomiting, and edema, did not differ significantly between groups.

The presumed sources of infection were also comparable between groups, with pneumonia and pyelonephritis representing the most frequently suspected foci. Biological abnormalities at admission were common but broadly similar

Table 1 Baseline Characteristics of Children with Suspected Sepsis Admitted to HPGRB, Democratic Republic of the Congo, According to Blood Culture Results

Characteristic	Blood Culture–Positive Sepsis (n = 123)	Blood Culture–Negative Sepsis (n = 224)	P-value
Demographic characteristics			
Age, months – median (IQR)	20.0 [8.0–40.0]	24.5 [11.0–50.2]	0.041
Age <24 months – n (%)	69 (56.1)	105 (46.9)	0.126
Male sex – n (%)	67 (54.5)	117 (52.2)	0.774
Household size – median (IQR)	6.0 [5.0–8.0]	7.0 [5.0–9.0]	0.440
Referral from another health facility – n (%)	44 (35.8)	87 (38.8)	0.654
Up-to-date vaccination – n (%)	73 (59.3)	151 (67.4)	0.160
Clinical presentation			
Fever – n (%)	65 (52.8)	150 (67.0)	0.013
Cough – n (%)	38 (30.9)	84 (37.5)	0.265
Dyspnea – n (%)	14 (11.4)	29 (12.9)	0.800
Diarrhea – n (%)	53 (43.1)	94 (42.0)	0.929
Vomiting – n (%)	51 (41.5)	87 (38.8)	0.717
Edema – n (%)	18 (14.6)	47 (21.0)	0.194
Severe acute malnutrition – n (%)	49 (39.8)	98 (43.8)	0.575
Sickle cell disease – n (%)	9 (7.3)	14 (6.2)	0.911
HIV infection – n (%)	2 (1.6)	4 (1.8)	1.000
Presumed source of infection			
Pneumonia – n (%)	55 (44.7)	106 (47.3)	0.748
Pyelonephritis – n (%)	47 (38.2)	72 (32.1)	0.329
Meningitis – n (%)	4 (3.3)	5 (2.2)	0.722
Biologically laboratory abnormalities			
Leukocytosis – n (%)	32 (26.0)	73 (32.6)	0.249
Leukopenia – n (%)	7 (5.7)	12 (5.4)	1.000
Anemia – n (%)	105 (85.4)	190 (84.8)	1.000
Thrombocytopenia – n (%)	20 (16.3)	44 (19.6)	0.527
Thrombocytosis – n (%)	45 (36.6)	68 (30.4)	0.287
Elevated C-reactive protein – n (%)	80 (65.0)	140 (62.5)	0.724
Hyponatremia – n (%)	53 (43.1)	91 (40.6)	0.740
Hypernatremia – n (%)	7 (5.7)	12 (5.4)	1.000
Hypokalemia – n (%)	17 (13.8)	33 (14.7)	0.943
Hyperkalemia – n (%)	8 (6.5)	9 (4.0)	0.443
Hyperglycemia – n (%)	34 (27.6)	84 (37.5)	0.083
Hypoglycemia – n (%)	1 (0.8)	2 (0.9)	1.000

Note: Data are presented as n (%) unless otherwise indicated. Continuous variables are expressed as median [interquartile range]. P values were calculated using the Mann–Whitney U-test for continuous variables and the chi-square or Fisher's exact test for categorical variables. IQR=interquartile range; HIV= Human Immunodeficiency Virus.

between groups. No statistically significant differences were observed for leukocytosis, leukopenia, anemia, thrombocytopenia, thrombocytosis, elevated C-reactive protein, electrolyte disturbances, or glycemic abnormalities. Hyperglycemia tended to be more frequent among culture-negative sepsis cases, although this difference did not reach statistical significance.

Microbiological Profile of Bloodstream Isolates

Among the 123 culture-positive episodes, 123 clinically significant bacterial isolates were identified. Gram-negative bacteria predominated, accounting for 84/123 (68.3%) isolates, whereas Gram-positive organisms accounted for 39/123 (31.7%). The most frequently isolated pathogens were *Salmonella* spp. (27/123; 22.0%), *Enterococcus* spp. (25/123; 20.3%), *Klebsiella pneumoniae* (17/123; 13.8%), and *Escherichia coli* (15/123; 12.2%). The complete distribution of Gram-negative and Gram-positive isolates is presented in Figures 2A and B, respectively.

Antimicrobial Resistance Patterns

The AMR profiles of the main Gram-negative pathogens are presented in Table 2. A heatmap visualization illustrating the resistance landscape across antibiotic classes is provided in the [Supplementary Figure S1](#).

Resistance estimates were calculated using the number of isolates tested for each organism–antimicrobial combination as the denominator. Among isolates with interpretable susceptibility results, resistance to amoxicillin–clavulanate was 100.0% in *Salmonella* spp. (24/24), *K. pneumoniae* (11/11), and *E. coli* (10/10). Resistance to third-generation cephalosporins varied across species: ceftriaxone resistance was 45.8% (11/24) in *Salmonella* spp., 66.7% (8/12) in *K. pneumoniae*, 54.5% (6/11) in *E. coli*, and 55.6% (5/9) in *Enterobacter* spp. Gentamicin resistance ranged from 41.7% (5/12) in *E. coli* to 84.6% (11/13) in *K. pneumoniae*. In contrast, amikacin resistance was lower, ranging from 0.0% (0/24) in *Salmonella* spp. to 23.1% (3/13) in *K. pneumoniae*. No meropenem-resistant isolate was identified among those tested, although estimates based on small numbers of tested isolates should be interpreted cautiously.

Antimicrobial resistance patterns among the main Gram-negative bloodstream isolates are presented in Table 2 and [Supplementary Figure S1](#). Among isolates with interpretable susceptibility results, resistance to amoxicillin–clavulanate was 100.0% in *Salmonella* spp. (24/24), *K. pneumoniae* (11/11), and *E. coli* (10/10). Ceftriaxone resistance ranged from 45.8% (11/24) in *Salmonella* spp. to 66.7% (8/12) in *K. pneumoniae*, whereas amikacin resistance ranged from 0.0% (0/24) in *Salmonella* spp. to 23.1% (3/13) in *K. pneumoniae*. No meropenem-resistant isolate was identified among those tested.

Resistance patterns among the main Gram-positive bloodstream isolates are summarized in Table 3. Among *S. aureus* isolates with available susceptibility results, resistance was 100.0% to penicillin (5/5) and trimethoprim–sulfamethoxazole (4/4), 50.0% to erythromycin (3/6), 40.0% to tetracycline (2/5), and 50.0% to oxacillin (1/2). Among *Enterococcus*

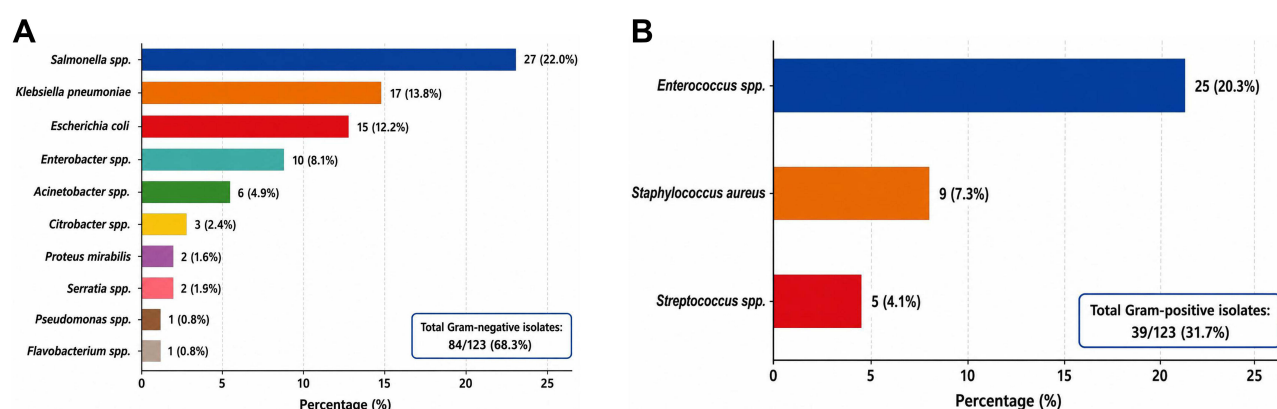


Figure 2 (A) Distribution of Gram-negative bacterial isolates among children with culture-confirmed bacteremia. Values are presented as number of isolates and percentage of all clinically significant bloodstream isolates (N=123). (B) Distribution of Gram-positive bacterial isolates among children with culture-confirmed bacteremia. Values are presented as number of isolates and percentage of all clinically significant bloodstream isolates (N=123).

Table 2 Antimicrobial Resistance Patterns Among the Main Gram-Negative Bloodstream Isolates

Antimicrobial Agent	<i>Salmonella</i> spp. (n=27)	<i>Klebsiella pneumoniae</i> (n=17)	<i>Escherichia coli</i> (n=15)	<i>Enterobacter</i> spp. (n=10)
Ampicillin	5/5 (100.0%)	—†	2/2 (100.0%)	—†
Amoxicillin–clavulanate	24/24 (100.0%)	11/11 (100.0%)	10/10 (100.0%)	—†
Cefotaxime	6/8 (75.0%)	4/4 (100.0%)	0/4 (0.0%)	4/5 (80.0%)
Ceftriaxone	11/24 (45.8%)	8/12 (66.7%)	6/11 (54.5%)	5/9 (55.6%)
Ceftazidime	5/17 (29.4%)	8/10 (80.0%)	4/7 (57.1%)	1/3 (33.3%)
Gentamicin	15/22 (68.2%)	11/13 (84.6%)	5/12 (41.7%)	5/9 (55.6%)
Amikacin	0/24 (0.0%)	3/13 (23.1%)	3/14 (21.4%)	1/10 (10.0%)
Ciprofloxacin	0/23 (0.0%)	9/12 (75.0%)	3/10 (30.0%)	4/8 (50.0%)
Levofloxacin	0/12 (0.0%)	6/12 (50.0%)	1/6 (16.7%)	4/8 (50.0%)
Trimethoprim–sulfamethoxazole	8/9 (88.9%)	6/6 (100.0%)	7/7 (100.0%)	0/1 (0.0%)‡
Chloramphenicol	12/22 (54.5%)	13/15 (86.7%)	5/11 (45.5%)	6/9 (66.7%)
Meropenem	0/9 (0.0%)	0/7 (0.0%)	0/1 (0.0%)‡	0/3 (0.0%)‡

Notes: Data are presented as number of resistant isolates/number of isolates tested (n/N [%]). Denominators vary across organism–antimicrobial combinations because antimicrobial susceptibility testing was not performed uniformly for all isolates. Percentages were calculated using only isolates with an available and interpretable susceptibility result for the corresponding antimicrobial agent. A dash (—) indicates that the result was not reported because the organism–antimicrobial combination is characterized by an expected resistant phenotype and was therefore excluded from the summary of acquired resistance. Results based on small numbers of tested isolates should be interpreted cautiously. † Results were not reported as acquired resistance for organism–antimicrobial combinations characterized by an expected resistant phenotype: ampicillin for *K. pneumoniae* and ampicillin and amoxicillin–clavulanate for *Enterobacter* spp. ‡ Estimate based on ≤3 tested isolates and therefore not considered representative of the corresponding species group.

Abbreviations: n, number of resistant isolates; N, number of isolates tested.

Table 3 Antimicrobial Resistance Patterns Among the Main Gram-Positive Bloodstream Isolates

Antimicrobial Agent	<i>Enterococcus</i> spp. (n=25)	<i>Staphylococcus aureus</i> (n=9)	<i>Streptococcus</i> spp. (n=5)
Penicillin	—	5/5 (100.0%)	2/3 (66.7%)
Ampicillin	2/6 (33.3%)	1/2 (50.0%)‡	—
Erythromycin	—	3/6 (50.0%)	2/4 (50.0%)
Clindamycin	—	2/8 (25.0%)	2/5 (40.0%)
Tetracycline	—	2/5 (40.0%)	2/2 (100.0%)‡
Gentamicin	0/1 (0.0%)§	0/6 (0.0%)	0/2 (0.0%)‡
Trimethoprim–sulfamethoxazole	—†	4/4 (100.0%)	1/1 (100.0%)‡
Cefoxitin	—	0/2 (0.0%)‡	—
Oxacillin	—	1/2 (50.0%)‡	0/1 (0.0%)‡
Vancomycin	0/22 (0.0%)	0/1 (0.0%)‡	0/1 (0.0%)‡
Fusidic acid	—	0/5 (0.0%)	—
Tigecycline	0/8 (0.0%)	0/4 (0.0%)	0/2 (0.0%)‡
Levofloxacin	11/16 (68.8%)	0/4 (0.0%)	1/2 (50.0%)‡

Notes: Data are presented as number of resistant isolates/number of isolates tested (n/N [%]). Denominators vary across organism–antimicrobial combinations because antimicrobial susceptibility testing was not performed uniformly for all isolates. Percentages were calculated using only isolates with an available and clinically interpretable susceptibility result. A dash (—) indicates that no clinically interpretable susceptibility result is reported. Results based on small numbers of tested isolates should be interpreted cautiously. † Trimethoprim–sulfamethoxazole susceptibility results for *Enterococcus* spp. were not reported because in vitro activity is not considered reliably predictive of clinical outcome; these results were therefore excluded from the acquired-resistance summary. ‡ Estimate based on ≤3 tested isolates and therefore not considered representative of the corresponding species group. § High-level aminoglycoside resistance testing was not systematically performed for *Enterococcus* spp.; conventional gentamicin susceptibility results should therefore not be interpreted as evidence of absence of high-level aminoglycoside resistance.

Abbreviations: n, number of resistant isolates; N, number of isolates tested.

spp., ampicillin resistance was 33.3% (2/6) and levofloxacin resistance was 68.8% (11/16), whereas no vancomycin resistance was detected among 22 isolates tested (0/22). Trimethoprim–sulfamethoxazole susceptibility results for *Enterococcus* spp. were not interpreted as acquired resistance. Resistance estimates for *Streptococcus* spp. were based on small numbers of tested isolates and should therefore be interpreted cautiously.

Table 4 Univariable and Multivariable Analyses of Factors Associated with in-Hospital Mortality Among Children with Culture-Confirmed Bacteremia

Variable	Deaths, n/N (%)	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Altered level of consciousness	2/4 (50.0)	10.90 (1.38–85.90)	0.023	12.83 (1.54–107.09)	0.018
No antibiotic adjustment after susceptibility testing	9/69 (13.0)	2.50 (0.64–9.73)	0.186	3.32 (0.75–14.78)	0.115
Severe acute malnutrition	6/49 (12.2)	1.58 (0.48–5.22)	0.452	1.97 (0.55–7.09)	0.298
Gram-negative isolate (vs Gram-positive)	9/84 (10.7)	1.44 (0.37–5.64)	0.601	—	—
Age (per month increase)	—	0.99 (0.97–1.01)	0.340	—	—

Notes: Crude ORs were estimated using univariable logistic regression. Adjusted ORs were estimated using the conventional multivariable logistic regression model. The multivariable model included three clinically prespecified variables: altered level of consciousness, no antibiotic adjustment after susceptibility testing, and severe acute malnutrition. Variables were not selected solely on the basis of statistical significance in univariable analysis. SAM was retained because of its established clinical relevance as a vulnerability factor in severe pediatric infection. Gram-negative isolate and age were not included in the multivariable model. A two-sided P value <0.05 was considered statistically significant. Dashes indicate that an adjusted estimate was not calculated.

Abbreviations: CI, confidence interval; OR, odds ratio; SAM, severe acute malnutrition.

Factors Associated with in-Hospital Mortality

Overall, in-hospital mortality among children with culture-confirmed bacteremia was 9.8% (12/123). In univariable analysis (Table 4), altered level of consciousness was associated with higher odds of in-hospital mortality (OR 10.90; 95% CI 1.38–85.90; $P=0.023$), whereas no antibiotic adjustment after susceptibility testing, SAM, Gram-negative isolate, and age were not significantly associated with mortality.

In the conventional multivariable model, altered level of consciousness remained independently associated with higher odds of in-hospital mortality (aOR 12.83; 95% CI 1.54–107.09; $P=0.018$), whereas no antibiotic adjustment after susceptibility testing (aOR 3.32; 95% CI 0.75–14.78; $P=0.115$) and SAM (aOR 1.97; 95% CI 0.55–7.09; $P=0.298$) were not independently associated with mortality. In a sensitivity analysis using Firth penalized logistic regression to reduce small-sample bias, altered level of consciousness remained associated with in-hospital mortality (aOR 10.97; 95% CI 1.55–80.27; $P=0.019$), whereas no antibiotic adjustment after susceptibility testing (aOR 2.88; 95% CI 0.80–13.60; $P=0.111$) and SAM (aOR 1.93; 95% CI 0.56–6.76; $P=0.290$) remained non-significant. Model discrimination was acceptable, with an area under the receiver operating characteristic curve of 0.71, as shown in Figure 3.

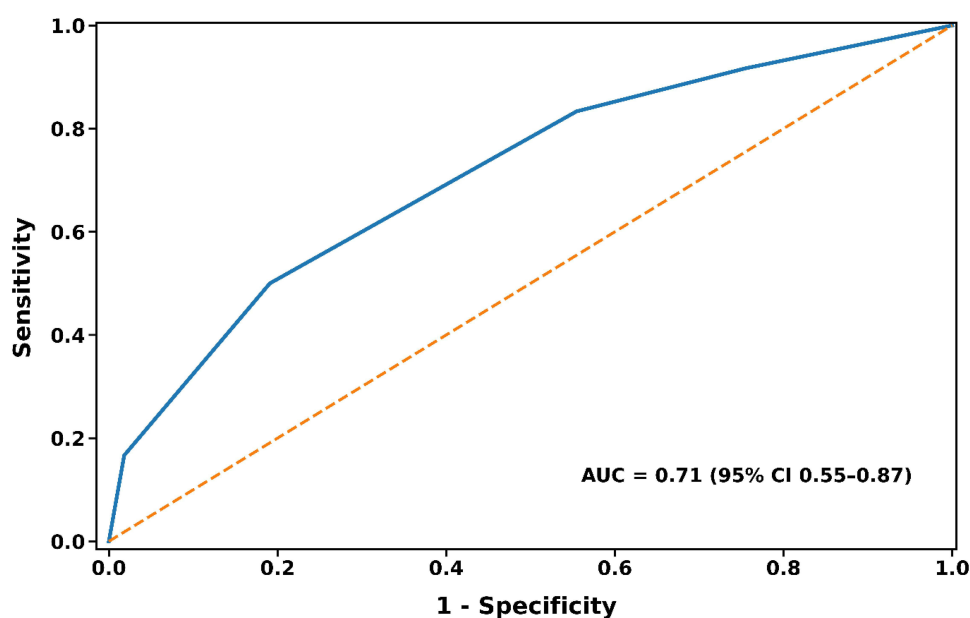


Figure 3 Receiver operating characteristic curve of the multivariable logistic regression model for in-hospital mortality among children with culture-confirmed bacteremia. The complete-case model included 122 children, including 12 in-hospital deaths, and yielded an AUROC of 0.71 (95% CI 0.55–0.87).

Discussion

This study provides contemporary data on the microbiological profile, antimicrobial resistance patterns, diagnostic stewardship, and outcomes of pediatric bloodstream infections in eastern DRC. Among 123 clinically significant bloodstream isolates, Gram-negative bacteria predominated (68.3%), with *Salmonella* spp. (22.0%) and *Enterococcus* spp. (20.3%) being the most frequently identified pathogens. Resistance to several commonly used antimicrobial agents was substantial among major Gram-negative pathogens, whereas amikacin resistance was comparatively low and no meropenem-resistant isolate was identified among those tested. Blood culture sampling, positivity, and contamination rates were 90.2%, 31.5%, and 11.3%, respectively. In-hospital mortality among children with culture-confirmed bacteremia was 9.8%, and altered level of consciousness was the only factor independently associated with mortality in the conventional multivariable model, a finding supported by Firth penalized logistic regression.

The high blood culture sampling rate suggests substantial use of microbiological investigation among children with suspected sepsis in this tertiary hospital. International guidelines recommend obtaining blood cultures before antimicrobial therapy whenever feasible, because microbiological confirmation can guide targeted treatment and antimicrobial stewardship.^{21,30} The positivity rate of 31.5% was higher than that reported in several hospital-based pediatric studies from sub-Saharan Africa, where positivity rates have often ranged from approximately 8% to 20%.^{16,31,32} This difference may reflect the selection of children with clinically suspected sepsis, differences in prior antimicrobial exposure, blood culture practices, and laboratory procedures. Conversely, the contamination rate of 11.3% was higher than generally recommended targets.^{6,23,30} This finding highlights an opportunity to improve specimen collection through standardized procedures, staff training, and routine monitoring of contamination rates.

Gram-negative organisms predominated, with *Salmonella* spp. representing the most frequently isolated pathogen. This is consistent with the recognized importance of invasive *Salmonella* infections in pediatric bacteremia in sub-Saharan Africa.^{16,31,32} However, species-level differentiation between typhoidal and non-typhoidal *Salmonella* was not systematically available; therefore, their respective contributions cannot be determined from our data. *K. pneumoniae* and *E. coli* were also prominent Gram-negative pathogens, consistent with reports from pediatric bloodstream infection studies elsewhere in the region.³² Among Gram-positive isolates, *Enterococcus* spp. predominated. The relatively high frequency of *Enterococcus* warrants further investigation, particularly because enterococcal bloodstream infections may be associated with healthcare exposure, underlying comorbidities, invasive procedures, and prior antimicrobial therapy.^{32,33}

The antimicrobial susceptibility findings raise concerns for empiric treatment in this setting. Substantial acquired resistance to commonly used agents, including third-generation cephalosporins, was observed among major Gram-negative pathogens, consistent with the increasing burden of antimicrobial resistance reported across sub-Saharan Africa.^{10,11,34} Importantly, organism–antimicrobial combinations with expected intrinsic resistance were excluded from the acquired-resistance summary; thus, ampicillin susceptibility was not clinically interpreted for *K. pneumoniae*, nor were ampicillin and amoxicillin–clavulanate susceptibility results for *Enterobacter* spp. This distinction avoids over-estimating acquired resistance and provides a more clinically meaningful representation of the susceptibility data.

Amikacin resistance was comparatively low among the major Gram-negative pathogens, and no meropenem-resistant isolate was identified among those tested. These findings indicate retained in vitro activity in this dataset but should not be interpreted as supporting routine empiric use of these agents. Susceptibility testing was not uniform across all organism–antimicrobial combinations, and some estimates were based on small denominators. Treatment decisions should therefore integrate clinical severity, local susceptibility data, drug availability, and antimicrobial stewardship principles. Regularly updated local antibiograms will be important for guiding empiric therapy while preserving agents with retained activity.

In-hospital mortality among children with culture-confirmed bacteremia was 9.8%. Altered level of consciousness was strongly associated with higher odds of mortality in the conventional multivariable analysis (aOR 12.83; 95% CI 1.54–107.09). Importantly, the association remained consistent in the Firth penalized sensitivity analysis (aOR 10.97; 95% CI 1.55–80.27), supporting the direction of the finding despite the small number of deaths. Altered consciousness

may reflect advanced systemic illness, impaired cerebral perfusion, metabolic disturbances, or central nervous system involvement and is recognized as a marker of severe pediatric infection.²¹

From a clinical perspective, systematic assessment of consciousness at admission and during hospitalization may provide a simple means of identifying children requiring urgent reassessment. When altered consciousness is detected, prompt evaluation for potentially reversible causes—including hypoglycemia, hypoxemia, shock, electrolyte disturbances, and central nervous system infection—together with timely antimicrobial therapy, close monitoring, and escalation of supportive care when indicated may facilitate earlier recognition and management of critically ill children. This approach is particularly relevant in resource-constrained settings where advanced monitoring may not always be available.

The mortality analysis nevertheless requires cautious interpretation. Only 12 deaths occurred, resulting in limited events per predictor and wide confidence intervals. Neither lack of antibiotic adjustment after susceptibility testing nor severe acute malnutrition was independently associated with mortality, and both remained non-significant in the Firth sensitivity analysis. The absence of an independent association with severe acute malnutrition should not be interpreted as evidence that malnutrition is clinically unimportant, given its established role as a vulnerability factor for severe pediatric infection.¹⁷ Rather, the limited number of outcome events reduced the precision with which moderate associations could be estimated. The mortality findings should therefore be considered hypothesis-generating and confirmed in larger prospective cohorts.

Taken together, these findings emphasize the complementary roles of diagnostic stewardship, antimicrobial stewardship, and early clinical recognition of severe illness. High blood culture utilization provides a useful foundation for microbiological diagnosis, but the elevated contamination rate indicates room for improvement in specimen collection. At the same time, substantial resistance to several commonly used antimicrobial agents reinforces the need for local resistance surveillance, periodically updated antibiograms, and timely integration of susceptibility results into clinical decision-making.

This study has several strengths, including the integration of clinical, microbiological, antimicrobial susceptibility, diagnostic stewardship, and outcome data from a setting where contemporary pediatric BSI surveillance remains limited. The use of organism-specific denominators for susceptibility estimates, explicit exclusion of expected intrinsic resistance from acquired-resistance summaries, and Firth penalized regression as a sensitivity analysis strengthened the interpretation of the findings. However, several limitations should be acknowledged. The retrospective design resulted in incomplete information for some variables and prevented verification of the actual blood volume inoculated into culture bottles. Prior antimicrobial exposure could not be reliably quantified. This was a single-center study, limiting generalizability. Susceptibility testing was not uniform across all organism–antimicrobial combinations, resulting in variable and occasionally small denominators. Species-level differentiation of *Salmonella* isolates was not systematically available, and detailed information needed to characterize the epidemiological context of *Enterococcus* bloodstream infections was limited. Finally, the small number of deaths constrained multivariable modelling and resulted in imprecise estimates despite the consistency of the Firth sensitivity analysis.

Overall, our findings support strengthening blood culture quality assurance, local antimicrobial resistance surveillance, and antimicrobial stewardship in eastern DRC. Improving specimen collection, routinely monitoring contamination, maintaining updated local antibiograms, and systematically assessing early clinical severity indicators—particularly altered level of consciousness—may help optimize the identification and management of children with severe bloodstream infections.

Conclusion

This study provides contemporary evidence on the microbiological profile, antimicrobial resistance patterns, diagnostic stewardship, and outcomes of pediatric BSI in eastern DRC. Gram-negative pathogens predominated, and substantial acquired resistance to several commonly used antibiotics was observed among major Gram-negative bloodstream isolates. Altered level of consciousness was independently associated with higher odds of in-hospital mortality, with consistent findings in the Firth penalized sensitivity analysis.

These findings support strengthening blood culture quality assurance, local AMR surveillance, and antimicrobial stewardship. Improving specimen collection to reduce contamination, maintaining regularly updated local antibiograms, and integrating microbiological results into clinical decision-making may help optimize empiric therapy. Systematic assessment of altered level of consciousness and prompt evaluation of potentially reversible causes may also facilitate early recognition and management of children at increased risk of poor outcomes.

Abbreviations

AMR, antimicrobial resistance; aOR, adjusted odds ratio; AUC, area under the curve; AUROC, area under the receiver operating characteristic curve; BSI, bloodstream infection; CI, confidence interval; CLSI, Clinical and Laboratory Standards Institute; CNSJ, Centre Nutritionnel Saint Joseph; CoNS, coagulase-negative staphylococci; DRC, Democratic Republic of the Congo; ESBL, extended-spectrum β -lactamase; EUCAST, European Committee on Antimicrobial Susceptibility Testing; GBD, Global Burden of Disease; GLASS, Global Antimicrobial Resistance and Use Surveillance System; HIV, human immunodeficiency virus; HPGRB, Hôpital Provincial Général de Référence de Bukavu; IQR, interquartile range; LMICs, low- and middle-income countries; MDR, multidrug resistance; OR, odds ratio; ROC, receiver operating characteristic; SAM, severe acute malnutrition; SSA, sub-Saharan Africa; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; UCB, Université Catholique de Bukavu; VIF, variance inflation factor; WHO, World Health Organization.

Data Sharing Statement

The findings of this study are derived from data collected and analyzed in accordance with the methods described. All relevant data are presented within the manuscript. The original dataset supporting these findings is available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

Ethical approval for this study was obtained from the Ethics Committee of Université Catholique de Bukavu (UCB/CIES/PB/GM/011/2026). The study adhered to the principles outlined in the Declaration of Helsinki. Given the retrospective nature of the study, based on routinely collected clinical data, the requirement for individual informed consent was waived. All data were anonymized prior to analysis to ensure confidentiality and to meet ethical requirements for research involving human participants.

Consent to Participate

Data were extracted from routine hospital records and analyzed anonymously. The need for informed consent was waived by the ethics committee due to the retrospective nature of the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests related to this work.

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