

Epidemiology and Antimicrobial Resistance Trends of Bloodstream Infections During and After the Implementation of the National Action Plan on Antimicrobial Resistance in Mwanza, Tanzania: A Comparative Cross-Sectional Study

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Background and Purpose: Bloodstream infections (BSIs) caused by antimicrobial-resistant pathogens, especially WHO-Bacterial-Priority-Pathogens (WHO-BPPs), contribute to significant mortality. The current study determined the prevalence of BSIs, causative bacterial pathogens and their antimicrobial susceptibility profiles, and factors associated with laboratory-confirmed BSIs by WHO-BPPs during and after National Action Plan on Antimicrobial Resistance (NAP-AMR) implementation in Mwanza, Tanzania.

Patients and Methods: A comparative cross-sectional study was conducted among sepsis patients in District, Regional, and Zonal Referral Hospitals from June 2019 to June 2020 (during NAP-AMR) and March to July 2023 (after NAP-AMR). Blood cultures were processed using conventional methods, while bacterial identification and antimicrobial susceptibility testing were performed using Vitek MS (MALDI-TOF-MS) and Vitek 2, respectively. STATA version 15.0 was used for data analysis.

Results: Among 1842 enrolled patients (median age: 5 years, IQR: 0–31), 51.4% were female. The overall prevalence of BSIs was 14.7% (271/1842). A total of 306 bacterial isolates were identified, with Gram-negative bacteria predominating during (92.4%) and after (73.5%) NAP-AMR. *Escherichia coli* was most common during (31.2%), whereas *Klebsiella pneumoniae* dominated after (43.4%) NAP-AMR. BSIs caused by WHO-BPPs rose significantly after NAP-AMR (43.5% vs 76.1%, $p < 0.001$), particularly extended-spectrum beta-lactamase producing Enterobacterales. *Klebsiella pneumoniae* resistance to cefotaxime (65.3% vs 93.2%, $p = 0.001$), gentamicin (63.3% vs 94.9%, $p = 0.001$), and ciprofloxacin (28.6% vs 76.3%, $p = 0.001$) increased significantly. Higher-tier hospitals (OR: 7.01; 95% CI: 1.58–31.05; $p = 0.010$) and after NAP-AMR enrollment (OR: 2.87; 95% CI: 1.33–6.19; $p = 0.007$) were linked to increased BSIs caused by WHO-BPPs.

Conclusion: We observed a high prevalence of BSIs with a rising proportion of BSIs caused by WHO-BPPs, particularly in higher-tier hospitals and after the implementation of NAP-AMR. Our findings highlight the need of hospital-specific antibiograms and reinforced infection prevention measures.

Keywords: antimicrobial resistance, bloodstream infections, epidemiology, National Action Plan, WHO bacterial priority pathogens

Introduction

Bloodstream infections (BSIs) impose a significant burden on healthcare systems globally, contributing to high morbidity and mortality rates.¹ Pathogens in the bloodstream can cause severe complications if not promptly diagnosed and treated.

The prevalence of BSIs varies across geographic regions and healthcare settings, influenced by factors such as patient demographics, medical practices, antibiotic usage, and antimicrobial resistance (AMR) patterns.²

Bacteria are the primary causative agents of BSIs, with Gram-negative bacteria (GNB) being the most prevalent.^{2,3} The growing AMR among GNB presents a major challenge in clinical management.⁴ Of particular concern is the emergence of pathogens included in the World Health Organization's Bacterial Priority Pathogens List (WHO-BPPL), first introduced in 2017,⁵ and updated in 2024.⁶ The WHO-BPPL classifies antibiotic-resistant (ABR) bacteria into critical, high, and medium priority levels, guiding research and public health interventions. Key pathogens on the WHO-BPPL, notably carbapenem-resistant and third-generation cephalosporin-resistant (3GC-R, notably extended-spectrum beta-lactamase (ESBL) producers) Enterobacterales (ESBL-PE; eg, *Escherichia coli* and *Klebsiella pneumoniae*), carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, and methicillin-resistant *Staphylococcus aureus* (MRSA), are frequently associated with BSIs globally.³ These pathogens are particularly devastating in low- and middle-income countries, where effective antibiotic treatments are limited.³

Tanzania, Mwanza region reported a prevalence of 14.2% of laboratory-confirmed BSIs among children below five years of age in 2016/2017 and 34.5% among neonates in 2018/2019.^{7,8} In Dar es Salaam, 11.4% of inpatients had laboratory-confirmed BSIs in 2020.⁹ These studies identified *K. pneumoniae*, *S. aureus*, *E. coli*, and *P. aeruginosa* as predominant pathogens.^{7–9} Notably, the proportion of 3GC-resistant GNB causing BSIs reached 79.0% in 2016/2017 and 93.2% in 2018/2019 in Mwanza.^{7,8} In Dar es Salaam, 46% of *P. aeruginosa* and 68% of Enterobacterales causing BSIs were carbapenem-resistant and ESBL-producing, respectively.⁹

In an effort to combat antimicrobial resistance (AMR), Tanzania implemented its first National Action Plan on AMR (NAP-AMR) for the period 2017–2022,¹⁰ adapted from the WHO Global Action Plan on AMR (GAP-AMR).¹¹ In partnership with the “Supporting the NAP-AMR” (SNAP-AMR) project, the plan was extended to district hospitals between June 2019 and June 2020 exclusively in Mwanza, Tanzania. Following this implementation, we conducted a follow-up study. Specifically, the study aimed to determine the prevalence of BSIs, identify causative bacterial pathogens and their antimicrobial susceptibility, and assess factors associated with laboratory-confirmed BSIs caused by WHO-Bacterial-Priority-Pathogens (WHO-BPPs) during and after NAP-AMR implementation in Mwanza, Tanzania. Understanding epidemiological trends and resistance patterns may strengthen infection prevention and control (IPC) measures, optimize antimicrobial therapy, and reinforce antimicrobial stewardship (AMS) strategies.

Materials and Methods

Study Design, Population, Duration, and Setting

This comparative cross-sectional hospital-based study, conducted in Mwanza, Tanzania, spanned two phases: the first (June 2019–June 2020) during and the second (March–July 2023) after the implementation of NAP-AMR. It involved five hospitals: Bugando Medical Centre (BMC), Sekou Toure Regional Referral Hospital (SRRH), Sumve (SDDH), Magu (MDH), and Misungwi (MisDH) District Hospitals. BMC, a zonal referral hospital with nearly 1,000 beds, serves approximately 18.8 million people across seven lake zone regions,¹² while SRRH (450 beds) caters to 3.6 million residents of Mwanza region. The district hospitals, SDDH, MDH, and MisDH (128–265 beds) serve 1.3 million people in Kwimba, Magu, and Misungwi, respectively.¹³ Ideally, the NAP-AMR was implemented in zonal and selected regional referral hospitals. However, between June 2019 and June 2020, its implementation was extended to three district hospitals in Mwanza, Tanzania. In these district hospitals (SDDH, MDH, and MisDH), the SNAP-AMR project not only pursued the core objectives of the NAP-AMR¹⁰ but also established bacteriology laboratories and strengthened the capacity of laboratory technologists. This included training in culture and sensitivity testing, as well as the detection and reporting of multidrug-resistant (MDR) pathogens, particularly key MDR phenotypes such as ESBL-PE, MRSA, and carbapenem-resistant GNB (CR-GNB). Referral hospitals were classified as higher-tier hospitals and district hospitals as lower-tier hospitals.

Criteria for Patients' Enrolment in the Study

Patients were enrolled based on a clinical diagnosis of sepsis upon admission or visit, identified using Systemic Inflammatory Response Syndrome (SIRS) or Sequential Organ Failure Assessment (SOFA) criteria.¹⁴ Blood samples were collected for culture and antimicrobial susceptibility testing. Upon receipt of blood samples in the laboratory, the research team was notified and followed up with the patients to obtain consent and collect additional data (eg, prior antibiotic use and hospitalization) using a standardized questionnaire. Patients were excluded if they declined participation, had incomplete data, died before data collection, or were discharged and unreachable. Sepsis diagnostic criteria remained consistent throughout the study.

Laboratory Procedures

Isolation, Identification, Antibiotic Susceptibility Testing, and Verification of Bacterial Pathogens Causing BSIs

The microbiology laboratories in respective hospitals carried out thorough procedures adhering to standardized protocols to ensure consistent and reliable results that informed patient therapy. The protocols were consistently applied in both study periods.

Manual blood culture¹⁵ was used to isolate bacteria from blood specimens. Pre-incubated (at 35 ± 2 °C for 20–24 hour) blood samples in brain heart infusion (BHI) broths (1:10) were subcultured on 5% sheep blood agar and MacConkey agar plates which were incubated aerobically at 35 ± 2 °C for 24 hours. In case where normal microbiota was isolated, a second blood culture was requested to verify the first results. Microbial growths were interpreted and recorded, the isolated pathogens were identified to genus or species level by in-house prepared biochemical identification tests documented previously.¹⁶ Antimicrobial susceptibility testing (AST) was conducted using the Kirby-Bauer disc diffusion method,¹⁷ with results interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines of 2019,¹⁸ 2020,¹⁹ and 2023.²⁰ Bacterial isolates were preserved in 1.5mL cryovials containing BHI broth with 20% glycerol, temporarily stored at -20°C in respective laboratory, and later transferred to -80°C at the Microbiology Laboratory at the Catholic University of Health and Allied Sciences (CUHAS), Mwanza, Tanzania.

Bacterial pathogens were further verified for identification and AST at the Institute for Hygiene and Microbiology, University of Würzburg, Germany, by MALDI-TOF on Vitek MST[™] (bioMérieux, Nürtingen, Germany), or with 16S rRNA sequencing for ambiguous identifications. Minimum inhibitory concentrations (MICs) were determined by Vitek 2 (bioMérieux, Nürtingen, Germany) using AST cards: AST-P654, AST-N214, AST-P655, and AST-N248 and interpreted per EUCAST 13.0 breakpoints (2023).²¹

Definitions and Detection of WHO-BPPs

1. Laboratory-confirmed BSI was defined as positive blood culture following clinical diagnosis of sepsis.
2. The WHO-BPPs included MRSA, ESBL-PE (*E. coli* and *K. pneumoniae*), and CR-GNB (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacterales) according to the WHO-BPPL of 2017.⁵

MRSA and ESBL-PE were identified using Vitek 2 AST cards (AST-P654 for MRSA and AST-N214 for ESBL). Additionally, GNB resistant to meropenem were classified as CR-GNB.

Quality Control

Culture media were prepared according to the manufacturer's guidelines and assessed for sterility and performance before use. *E. coli* ATCC 25922 and *S. aureus* ATCC 25923 were used as control organisms.

Data Management and Analysis

Data were documented, cleaned, and coded in Microsoft Excel before being analyzed using STATA 15.0. Categorical variables were examined through tabulation tests, with results presented as percentages and fractions. Descriptive statistics assessed the central tendency and variability of skewed continuous variables, reported as medians [IQR]. The Wilcoxon Rank Sum test compared medians of two independent continuous variables, and the double proportion test was used for categorical data comparisons. The Chi-square test assessed the distribution of independent categorical variables.

(eg, antibiotic use) against the dependent variable (BSIs by WHO-BPPs), and univariate logistic regression determined statistical associations. All independent variables were included in a multivariate logistic regression model due to their clinical significance and previous association with BSIs by WHO-BPPs,²² with final results reported as adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs) and p-values.

Results

Sociodemographic and Clinical Characteristics of Patients with Clinical Symptoms of Sepsis

A total of 1,842 patients (median age: 5 years [IQR: 0–31]) were enrolled, with 1,077 during and 766 after NAP-AMR. Patients enrolled during NAP-AMR were older (median: 5 [IQR: 1–28] vs 4 [IQR: 0–35], $p=0.007$). Enrollment was highest in pediatric wards/clinics during NAP-AMR (50.5%) and in medical wards/clinics after NAP-AMR (44.6%). Most patients (76.7%) were in higher-tier hospitals, and 68.3% were inpatients. Antibiotic use at enrollment was 43.1% (794/1,842), higher during NAP-AMR (46.6% vs 38.3%). Penicillins were more common during NAP-AMR (67.7% vs 38.9%), while aminoglycosides were more frequent after NAP-AMR (68.6% vs 27.7%), $p<0.001$. Co-morbidities were present in 11.2% of patients, with hypertension more frequent during NAP-AMR (33.5% vs 18.2%) and sickle cell disease after NAP-AMR (33.5% vs 53.0%), $p<0.001$ (Table 1).

Prevalence of Laboratory-Confirmed BSIs

The overall prevalence of laboratory-confirmed BSIs was 14.7% (271/1842; 95% CI: 13.1%–16.4%), with no significant difference between the NAP-AMR periods [13.7% (148/1076) vs 16.1% (123/766), $p=0.169$]. In lower-tier hospitals, the prevalence was 6.5% (28/430; 95% CI: 4.4%–9.3%), increased significantly from 4.8% (17/349) to 13.6% (11/81) after

Table 1 Sociodemographic and Clinical Characteristics of Patients with the Clinical Diagnosis of Sepsis During and After NAP-AMR in Mwanza, Tanzania

Characteristics	Categories	All (N=1842)	During NAP-AMR (N=1076)	After NAP-AMR (N=766)	Chi-square Analysis
		n(%)	n(%)	n(%)	P-value ^a
Median [IQR] age in years		5 [0–31]	5 [1–28]	4 [0–35]	0.007 ^b
Age groups	<1 year	522 (28.3)	218 (20.3)	304 (39.7)	<0.001
	1 – 5 years	425 (23.1)	322 (29.9)	103 (13.4)	
	>5 years	895 (48.6)	536 (49.8)	359 (46.9)	
Sex	Male	896 (48.6)	552 (51.3)	344 (44.9)	0.007
	Female	946 (51.4)	524 (48.7)	422 (55.9)	
Residency	Rural	669 (36.3)	404 (37.5)	265 (34.6)	0.194
	Urban	1173 (63.7)	672 (62.5)	501 (65.4)	
Education level	None	1072 (58.2)	646 (60.0)	426 (55.6)	0.182
	Primary	436 (23.7)	250 (23.2)	186 (24.7)	
	Secondary	205 (11.1)	110 (10.2)	95 (12.4)	
	Tertiary	126 (7.0)	70 (6.5)	56 (7.3)	
Occupation	None	1232 (66.9)	771 (71.7)	461 (60.2)	0.002
	Employed	167 (9.1)	78 (7.2)	89 (11.6)	
	Self-employed	443 (24.0)	227 (21.1)	216 (28.2)	
Level of healthcare facility	Higher-tier	1412 (76.7)	727 (67.6)	685 (89.4)	<0.001
	Lower-tier	430 (23.3)	349 (32.4)	81 (10.6)	
Patient category at enrollment	Outpatient	584 (31.7)	349 (32.4)	235 (30.7)	0.425
	Inpatient	1258 (68.3)	727 (67.6)	531 (69.3)	

(Continued)

Table 1 (Continued).

Characteristics	Categories	All (N=1842)	During NAP-AMR (N=1076)	After NAP-AMR (N=766)	Chi-square Analysis
		n(%)	n(%)	n(%)	P-value ^a
Ward or clinic of enrollment	Medical	710 (38.5)	368 (34.2)	342 (44.6)	<0.001
	Pediatric	649 (35.2)	544 (50.5)	105 (13.7)	
	Neonatology ^c	301 (16.3)	65 (6.0)	236 (30.8)	
	Surgical	96 (5.2)	68 (6.3)	28 (3.7)	
	AICU	45 (2.4)	24 (2.2)	21 (2.7)	
	Oncology	25 (1.4)	0 (0.0)	25 (3.3)	
	Gyn/Obs	16 (0.9)	7 (0.6)	9 (1.2)	
History of fever past 3 months	Yes	786 (42.7)	522 (48.5)	264 (34.5)	<0.001
	No	1056 (57.3)	554 (51.5)	502 (65.5)	
Hospital admission past 3 months	Yes	278 (15.1)	155 (14.4)	123 (16.1)	0.329
	No	1564 (84.9)	921 (85.6)	643 (83.9)	
History of antibiotic use past 3 months	Yes	642 (38.4)	395 (36.7)	247 (32.3)	0.047
	No	1200 (61.6)	681 (63.3)	519 (67.7)	
On antibiotic use at enrollment	Yes	794 (43.1)	501 (46.6)	293 (38.3)	<0.001
	No	1048 (56.9)	575 (53.4)	473 (61.7)	
Class of antibiotic use at enrollment	Penicillins	454 (57.2)	340 (67.7)	114 (38.9)	<0.001
	Cephalosporins	312 (39.3)	158 (31.5)	154 (52.5)	
	Aminoglycosides	340 (42.8)	139 (27.7)	201 (68.6)	
	Others ^d	138 (17.4)	107 (21.3)	31 (10.6)	
Chronic disease	Yes	206 (11.2)	140 (13.0)	66 (8.6)	0.003
	No	1636 (88.8)	936 (87.0)	700 (91.4)	
Types of chronic diseases	SCD	82 (39.8)	47 (33.5)	35 (53.0)	<0.001
	HTN	59 (28.6)	47 (33.5)	12 (18.2)	
	Diabetes	46 (22.3)	40 (28.6)	6 (9.1)	
	Others ^e	38 (18.4)	25 (17.8)	13 (19.7)	

Notes: ^aP-value by Chi-square test and ^bP-value by Rank Sum (Wilcoxon) test. During NAP-AMR: ^cNeonatology: Neonatology ward (2.7%; n=29) and NICU (3.3%; n=36). ^dOthers: Nitroimidazole (9.5%; n=48), Quinolone (8.9%; n=45), Macrolide (2.4%; n=12), and Carbapenem (0.4%; n=2). ^eOthers: HIV (13.6%; n=19), Asthma (0.7%; n=1), CHD (0.7%; n=1), HBV (0.7%; n=1), Leukemia (0.7%; n=1), Liver cirrhosis (0.7%; n=1), and SAM (0.7%; n=1). After NAP-AMR: ^cNeonatology: Neonatology ward (13.2%; n=101) and NICU (17.6%; n=135). ^dOthers: Nitroimidazole (5.8%; n=17), Macrolide (2.7%; n=8), Quinolone (1.7%; n=5), and Carbapenem (0.3%; n=1). ^eOthers: Cancer (9.1%; n=6) and HIV (10.6%; n=7). Given the distinct factors influencing hospitalization and antibiotic use in neonates (aged: 0–28 days; 72.5% born prematurely with median birthweight of 2000 [1300–2900] kilogram) and pediatric (aged: 1 month – 12 years) patients in our setting, we analyzed them separately.

Abbreviations: AICU, adult intensive care unit; CHD, congenital heart disease; Gyn/Obs, gynecology and obstetrics; HIV, human immunodeficient virus; HTN, hypertension; IQR, interquartile range; NAP-AMR, National Action Plan on antimicrobial resistance; NICU, neonatal intensive care unit; SAM, severe acute malnutrition; SCD, sickle cell disease.

NAP-AMR (p=0.004). In contrast, higher-tier hospitals had a prevalence of 17.2% (243/1412; 95% CI: 15.3%–19.3%), with no significant variation between periods [18.0% (131/727) vs 16.4% (112/685), p=0.406]. Overall, BSIs were more prevalent in higher-tier than lower-tier hospitals (17.2% vs 6.5%, p=0.072), [Figure 1](#).

The Proportions of Bacterial Species Causing BSIs During and After NAP-AMR

A total of 306 bacterial isolates were detected from 271 positive blood samples. During NAP-AMR, 170 isolates were detected from 148 samples, while 136 isolates were detected from 123 samples after NAP-AMR. GNB predominated in both periods, 92.4% (157/170) during and 73.5% (100/136) after NAP-AMR. *E. coli* (31.2%, 53/170) was most common during NAP-AMR, followed by *K. pneumoniae* (28.8%, 49/170) and *P. mirabilis* (12.4%, 21/170). After NAP-AMR, *K. pneumoniae* became predominant (43.4%, 59/136), followed by *E. coli* (8.8%, 12/136), and *E. faecalis* (7.4%, 10/136). Additionally, several rare bacterial species including *Acinetobacter calcoaceticus* and *Staphylococcus warneri* were exclusively identified after NAP-AMR ([Figure 2](#)).

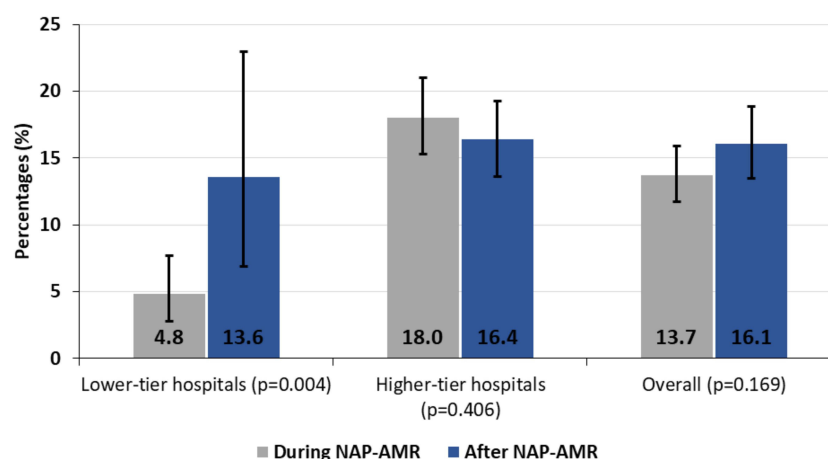


Figure 1 Prevalence of laboratory-confirmed bloodstream infections among patients with the clinical diagnosis of sepsis during and after NAP-AMR in Mwanza, Tanzania (P-value by Chi-square test).

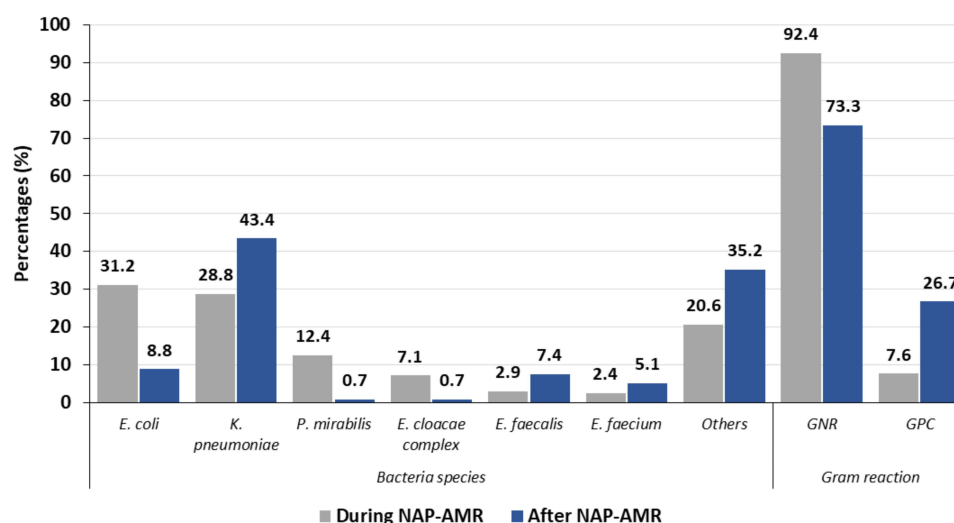


Figure 2 Comparison of proportions of bacteria species isolated from blood samples during and after NAP-AMR in Mwanza, Tanzania.

Notes: During NAP-AMR GNB: *Acinetobacter baumannii* (n=6), *Acinetobacter pittii* (n=1), *Citrobacter freundii* (n=1), *Enterobacter hormaechei* (n=2), *Enterobacter sakazakii* (n=1), *Morganella morganii* (n=1), *Proteus vulgaris* (n=3), *Pseudomonas aeruginosa* (n=6), and *Serratia marcescens* (n=1). GPB: *Lactococcus lactis* (n=1) and *Staphylococcus aureus* (n=3). After NAP-AMR GNB: *Acinetobacter baumannii* (3), *Acinetobacter calcoaceticus* (1), *Acinetobacter pittii* (1), *Acinetobacter radioresistens* (3), *Burkholderia cepacia* (2), *Citrobacter amalonaticus* (1), *Cupriavidus pauculus* (1), *Enterobacter hormaechei* (1), *Pantoea agglomerans* (2), *Proteus vulgaris* (2), *Pseudomonas aeruginosa* (3), *Pseudomonas septica* (1), *Serratia marcescens* (1), and *Stenotrophomonas maltophilia* (2). GPB: *Bacillus licheniformis* (1), *Exiguobacterium acetylicum* (2), *Lactococcus lactis* (1), *Micrococcus luteus* (1), *Rummeliibacillus stabekisii* (1), *Staphylococcus aureus* (6), *Staphylococcus epidermidis* (5), *Staphylococcus haemolyticus* (3), *Staphylococcus hominis* (1), and *Staphylococcus warneri* (1).

Abbreviations: GNR, Gram-negative rods; GPC, Gram-positive cocci.

Antimicrobial Resistance Trends of Bacteria Causing BSIs

Antibiotic resistance in GNB showed varying trends. *E. coli* resistance decreased slightly (4.4% for ceftazidime to 35.1% for gentamicin), though not significantly. Conversely, *K. pneumoniae* resistance significantly increased to cefuroxime, cefpodoxime, cefotaxime, ceftazidime, gentamicin, and ciprofloxacin ($p<0.05$), while resistance to piperacillin-tazobactam declined (63.3% vs 18.6%, $p=0.005$). Other GNB showed reduced resistance, notably to trimethoprim-sulfamethoxazole (70.9% vs 41.7%, $p=0.042$) and cefotaxime (61.8% vs 20.8%, $p=0.042$), (Table 2). Among GPB, emerging resistance after NAP-AMR was noted for clindamycin (10.5%), daptomycin (12.5%), and others, but no resistance to linezolid, rifampicin, tigecycline, or vancomycin was observed in either period (Table 3).

Table 2 Antimicrobial Resistance Trends of Gram-Negative Bacteria Causing Bloodstream Infections During and After NAP-AMR in Mwanza, Tanzania

Antibiotic agents tested	<i>Escherichia coli</i>			<i>Klebsiella pneumoniae</i>			Other Gram-negative bacteria		
	During NAP-AMR (N=53) %[95% CI]	After NAP-AMR (N=12) %[95% CI]	P value ^a	During NAP-AMR (N=49) %[95% CI]	After NAP-AMR (N=59) %[95% CI]	P value ^a	During NAP-AMR (N=55) %[95% CI]	After NAP-AMR (N=24) %[95% CI]	P value ^a
AMP	96.2[87.0–99.5]	83.3[51.6–97.9]	0.056	100[92.7–100]	100[93.9–100]	-	83.6[71.2–92.2]	87.5[67.6–97.3]	0.339
SXT	83.0[70.2–91.9]	75.0[42.8–94.5]	0.286	79.6[65.7–89.7]	83.1[71.0–91.5]	0.337	70.9[57.1–82.4]	41.7[22.1–63.4]	0.042
CXM	54.7[40.4–68.4]	50.0[21.1–78.9]	0.416	65.3[50.4–78.3]	93.2[83.5–98.1]	0.001	72.7[59.0–83.8]	50.0[29.1–70.9]	0.070
CPD	54.7[40.4–68.4]	41.7[15.2–72.3]	0.295	65.3[50.4–78.3]	93.2[83.5–98.1]	0.001	69.1[55.2–80.8]	45.8[25.5–67.2]	0.078
CTX	50.9[36.8–64.9]	41.7[15.2–72.3]	0.352	65.3[50.4–78.3]	93.2[83.5–98.1]	0.001	61.8[47.7–74.6]	20.8[7.1–42.1]	0.042
CAZ	37.7[24.8–52.1]	33.3[9.9–65.1]	0.433	48.9[34.4–63.7]	93.2[83.5–98.1]	0.001	23.6[13.2–37.0]	16.7[4.7–37.4]	0.385
GEN	43.4[29.8–57.7]	8.3[0.2–38.5]	0.243	63.3[48.3–76.6]	94.9[85.8–98.9]	0.001	60.0[45.9–72.9]	41.6[22.1–63.3]	0.152
CIP	54.7[40.4–68.4]	58.3[27.7–84.8]	0.431	28.6[16.6–43.3]	76.3[63.4–86.4]	0.001	32.7[20.7–46.7]	33.3[15.6–55.3]	0.488
TZP	20.7[10.8–34.1]	8.3[0.2–38.5]	0.382	63.3[48.3–76.6]	18.6[9.7–30.9]	0.005	30.9[19.1–44.8]	54.2[32.8–74.4]	0.099
TGC	16.9[8.0–29.8]	8.3[0.2–38.5]	0.412	NA	NA	-	64.5[51.4–77.8]	45.8[25.5–67.2]	0.122
MEM	0.0[0.0–6.7]	0.0[0.0–26.5]	-	0.0[0.0–7.3]	0.0[0.0–6.1]	-	3.6[0.4–12.5]	8.3[1.0–27.0]	0.421

Note: 95% CI=95% confidence interval. ^aP-value by double proportion test.

Abbreviations: AMP, ampicillin; CAZ, ceftazidime; CIP, ciprofloxacin; CPD, cefpodoxime; CTX, cefotaxime; CXM, cefuroxime; GEN, gentamicin; MEM, meropenem; NA, not applicable; NAP-AMR, National Action Plan on antimicrobial resistance; SXT, trimethoprim-sulfamethoxazole, TGC, tigecycline; TZP, piperacillin-tazobactam; and.

Proportions of WHO-BPPs Causing BSIs

The proportion of WHO BPPs (MRSA, n=9; ESBL-PE, n=155; CR-GNB, n=214) among tested isolates rose significantly from 43.5% (57/131) during NAP-AMR to 76.1% (70/92) after (p<0.001), driven by a sharp increase in ESBL-PE (58.3% [49/84] to 91.5% [65/71], p<0.001). MRSA rates remained stable (33.3%; 1/3 vs 33.3%; 2/6), while CR-GNB decreased slightly (5.5% [7/128] to 3.5% [3/86], p=0.446), (Figure 3). ESBL-producing *K. pneumoniae* was significantly more prevalent than ESBL-producing *E. coli* (85.2% [86/101] vs 51.8% [28/54], p<0.001).

Factors Associated with Laboratory-Confirmed BSIs by WHO-BPPs

BSIs caused by WHO-BPPs were significantly more common in younger patients (median age: 4.5 [0–21] vs 1 [0–19], p=0.019), especially infants under one year old (OR: 2.52; 95% CI: 1.37–4.65; p=0.003). Univariate logistic regression identified increased risks among inpatients (OR: 2.79; 95% CI: 1.53–5.07; p=0.001), patients in higher-tier hospitals (OR: 7.65; 95% CI: 2.15–27.28; p=0.002), receiving antibiotics at enrollment (OR: 1.91; 95% CI: 1.11–3.29; p=0.020), and those enrolled after NAP-AMR (OR: 4.13; 95% CI: 2.29–7.45; p=0.001). Conversely, lower odds were observed in patients from medical wards/clinics (OR: 0.38; 95% CI: 0.16–0.92; p=0.031), those with a history of fever (OR: 0.35; 95% CI: 0.20–0.61; p<0.001), and prior antibiotic users (OR: 0.53; 95% CI: 0.30–0.95; p=0.034).

Multivariable analysis confirmed that higher-tier hospitals (OR: 7.01; 95% CI: 1.58–31.05; p=0.010) and after NAP-AMR enrollment (OR: 2.87; 95% CI: 1.33–6.19; p=0.007) were independent risk factors. Although neonatology patients (OR: 3.36; p=0.129), those on antibiotics (OR: 1.82; p=0.102), and patients with co-morbidities (OR: 2.54; p=0.066) showed increased odds, however, not statistically significant. Interestingly, male patients had a significantly lower risk (OR: 0.52; 95% CI: 0.27–0.99; p=0.048), (Table 4).

Discussion

This study compared the epidemiology of BSIs and AMR trends of bacterial pathogens causing BSIs and determined factors associated with BSIs caused by WHO-BPPs during and after the implementation of NAP-AMR in Mwanza, Tanzania. The overall prevalence of laboratory-confirmed BSIs was 14.7%, consistent with previous findings of 14.2% in children under five,⁷ but lower than in neonates admitted in neonatal intensive care unit (NICU; 51.4% in 2009 and 34.5% in 2018–2019).^{8,23} The higher prevalence of BSIs among the neonatal population reported in previous studies from the same setting may be explained by the increased vulnerability of neonates, which is often associated with invasive procedures, prematurity, and congenital conditions.²⁴ Therefore, the neonatal population must be prioritized for

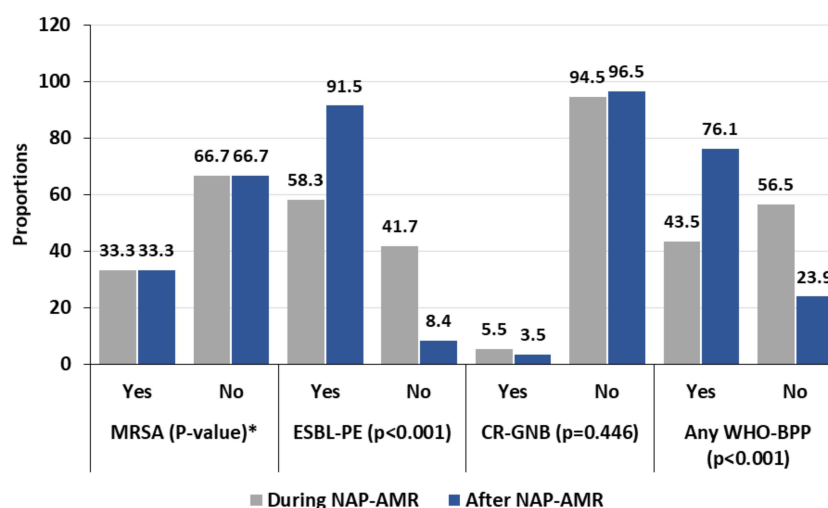
Table 3 Antimicrobial Resistance Trends of Gram-Positive Bacteria Causing Bloodstream Infections During and After NAP-AMR in Mwanza, Tanzania

Antibiotic Agent Tested	Gram-Positive Bacteria Causing BSIs		
	During NAP-AMR (N=13) % [95% CI]	After NAP-AMR (N=36) % [95% CI]	P value ^a
SXT	100 [29.2–100]	47.1 [22.9–72.2]	0.0541
GEN	50.0 [1.3–98.7]	20.0 [4.3–48.1]	0.2803
PEN	100 [15.8–100]	50.0 [11.8–88.2]	0.1160
ERY	66.7 [9.4–99.2]	63.2 [38.4–83.7]	0.4620
LVX	37.5 [8.5–75.5]	36.4 [20.4–54.9]	0.4859
TCY	66.7 [9.4–99.2]	42.1 [20.3–66.5]	0.2665
CLI	0.0 [0.0–70.8]	10.5 [1.3–33.1]	NA
LNZ	0.0 [0.0–36.9]	0.0 [0.0–10.3]	NA
DAP	0.0 [0.0–98.7]	12.5 [1.6–38.4]	NA
FOS	0.0 [0.0–84.2]	37.5 [15.2–64.6]	NA
FUS	0.0 [0.0–84.2]	18.6 [4.1–45.6]	NA
MUP	0.0 [0.0–84.2]	16.7 [0.4–64.1]	NA
RIF	0.0 [0.0–84.2]	0.0 [0.0–19.5]	NA
TGC	0.0 [0.0–40.9]	0.0 [0.0–10.6]	NA
TEC	0.0 [0.0–36.9]	15.2 [5.1–31.9]	NA
VA	0.0 [0.0–36.9]	0.0 [0.0–10.3]	NA

Note: 95% CI=95% confidence interval.^aP-value by double proportion test.

Abbreviations: CLI, clindamycin; DAP, daptomycin; ERY, erythromycin; FOS, fosfomycin; FUS, fusidic acid; GEN, gentamicin; LNZ, linezolid; LVX, levofloxacin; MUP, mupirocin; NA, not applicable; NAP-AMR, National Action Plan of antimicrobial resistance; PEN, penicillin; RIF, rifampicin; SXT, trimethoprim-sulfamethoxazole; TCY, tetracycline; TEC, teicoplanin; TGC, tigecycline; VA, vancomycin.

protection against BSIs through the rigorous implementation of IPC measures, minimizing non-essential invasive procedures, adhering to established protocols for the safe handling and care of preterm and low birth-weight infants, and exercising caution in the empirical use of antimicrobials to prevent resistance. Moreover, the current study revealed an overall higher prevalence of laboratory-confirmed BSIs in higher-tier hospitals compared to lower-tier hospitals

**Figure 3** Trends of pathogens on the WHO bacterial priority pathogens list causing bloodstream infections during and after NAP-AMR in Mwanza, Tanzania.

Notes: P-values by double proportion tests. *P-value: the small proportions of MRSA strains in both periods (33.3%; 1/3 vs 33.3%; 2/6) rendered statistical comparison and p-value computation unfeasible.

Abbreviations: CR-GNB, carbapenem-resistant Gram-negative bacteria; ESBL-PE, extended-spectrum beta-lactamase-producing Enterobacterales; MRSA, methicillin-resistant *S. aureus*.

Table 4 Factors Associated with Bloodstream Infections Caused by Pathogens on the WHO Bacterial Priority Pathogens List During and After NAP-AMR in Mwanza, Tanzania

Variables		Bloodstream Infections by Pathogens on the WHO Bacterial Priority Pathogens List					
		Negative	Positive	Univariable regression analysis		Multivariable Regression Analysis	
		N=96	N=127	cOR[95% CI]	P value	aOR[95% CI]	P value
Median [IQR] age in years		4.5[0–21]	1[0–19]		0.019 ^a	0.99[0.98–1.02]	0.963
Age groups	<1 year	25 (28.4)	63 (71.6)	2.52[1.37–4.65]	0.003	0.28[0.67–1.17]	0.081
	1 – 5 years	23 (59.0)	16 (41.0)	0.69 [0.33–1.48]	0.345	0.45[0.15–1.41]	0.174
	>5 years	48 (50.0)	48 (50.0)	1		1	
Sex	Female	52 (37.9)	85 (62.1)	1		1	
	Male	44 (51.2)	42 (48.8)	0.58[0.34–1.01]	0.053	0.52[0.27–0.99]	0.048
Residence	Rural	35 (49.3)	36 (50.7)	1		1	
	Urban	61 (40.1)	91 (59.9)	1.45[0.82–2.56]	0.199	1.33[0.63–2.78]	0.455
Patient category at enrollment	Outpatient	39 (60.9)	25 (39.1)	1		1	
	Inpatient	57 (35.8)	102 (64.2)	2.79[1.53–5.07]	0.001	1.56[0.62–3.90]	0.346
Ward or clinic of enrollment	Medical	36 (57.9)	24 (42.1)	0.41[0.17–0.98]	0.046	0.87[0.27–2.73]	0.806
	Pediatric	33 (55.9)	26 (44.1)	0.42[0.17–1.00]	0.051	1.46[0.43–4.98]	0.542
	Neonatology ^b	15 (21.1)	56 (78.9)	2.13[0.86–5.29]	0.103	3.36[0.70–16.01]	0.129
	Other ^c	12 (36.4)	21 (63.6)	1		1	
Facility level	Lower-tier	15 (83.3)	3 (16.7)	1		1	
	Higher-tier	81 (39.5)	124 (60.5)	7.65[2.15–27.28]	0.002	7.01[1.58–31.05]	0.010
History of fever	No	47 (33.6)	93 (66.4)	1		1	
	Yes	49 (59.0)	34 (41.0)	0.35[0.20–0.61]	0.001	0.55[0.27–1.14]	0.110
History of antibiotic	No	59 (38.3)	95 (61.7)	1		1	
	Yes	37 (53.6)	32 (46.4)	0.53[0.30–0.95]	0.034	0.75[0.34–1.69]	0.496
Current on antibiotic	No	62 (50.0)	62 (50.0)	1		1	
	Yes	34 (34.3)	65 (65.7)	1.91[1.11–3.29]	0.020	1.82[0.89–3.71]	0.102
History of admission	No	85 (43.2)	112 (56.8)	1		1	
	Yes	11 (42.3)	15 (57.7)	1.03[0.45–2.37]	0.935	1.35[0.46–3.93]	0.583
Chronic disease	No	86 (44.3)	108 (55.7)	1		1	
	Yes	10 (34.5)	19 (65.5)	1.51[0.67–3.42]	0.320	2.54[0.94–6.89]	0.066
Duration	During NAP-AMR	74 (56.5)	57 (43.5)	1		1	
	After NAP-AMR	22 (23.9)	70 (76.1)	4.13[2.29–7.45]	0.001	2.87[1.33–6.19]	0.007

Notes: 95% CI=95% confidence interval. ^aA p-value by Rank Sum (Wilcoxon) test. ^bConsidering the unique factors influencing hospitalization and antibiotic use in neonates and pediatric patients within our setting, neonates were analyzed separately. ^cFrom the overall small number of BSI cases in AICU (n=9), oncology (n=3), gynecology/obstetrics (n=4), and surgery (n=17), the wards/units were grouped into others. The adjusted odds ratios [95% CI] and p-values that were statistically significant were highlighted in bold.

Abbreviations: aOR, adjusted odds ratio; cOR, crude odds ratio; IQR, interquartile range; NAP-AMR, National Action Plan on antimicrobial resistance; WHO, World Health Organization.

(17.2% vs 6.5%). This difference is likely attributable to the greater severity of sepsis cases, which typically require specialized care and are therefore more frequently referred to higher-tier hospitals.

GNB remained the predominant pathogens, consistent with prior studies,^{7,8,23} underscoring their clinical significance and resistance to multiple antibiotics.²⁵ *E. coli* was the most common pathogen during NAP-AMR, but *K. pneumoniae* dominated after NAP-AMR. Additionally, *E. faecalis* and *E. faecium* replaced *P. mirabilis* and *E. cloacae* complex, likely due to antimicrobial selective pressure exacerbated by increased antibiotic use during the COVID-19 pandemic.²⁶ Rare species like *Lactococcus lactis*, *Cupriavidus pauculus*, and *Exiguobacterium acetylicus* were detected exclusively after NAP-AMR, highlighting the need for advanced diagnostics and vigilance in identifying opportunistic pathogens. While these bacteria may be considered common commensals, they have been documented as opportunistic pathogens, particularly in immunocompromised individuals or those with indwelling medical devices.²⁷ For example, *Lactococcus lactis*, *Micrococcus luteus*, *Bacillus licheniformis*, *Cupriavidus pauculus*, *Exiguobacterium acetylicus*, and *Rummeliibacillus stabekisii* have been associated with endocarditis^{28,29} and BSI³⁰ cases.

AMR trends varied among GNB. *E. coli* showed declining resistance, except to ciprofloxacin, while other GNB exhibited reduced resistance to trimethoprim-sulfamethoxazole and cefotaxime. The downward trend in AMR among *E. coli* and other GNB suggests that AMS and IPC strategies during NAP-AMR effectively curtailed resistant strain spread. However, routine surveillance is warranted to observe and prevent AMR escalation. Resistance to ampicillin, ciprofloxacin, piperacillin-tazobactam, and meropenem increased in other GNB, though not significantly. Additionally, *K. pneumoniae* demonstrated significant resistance increases to cephalosporins, aminoglycosides, and fluoroquinolones, likely due to heightened use of these antibiotics. Although, *K. pneumoniae* is recognized as a key trafficker of AMR genes, transferring them from environmental sources to clinically significant bacteria.³¹ The predominance of *K. pneumoniae* in BSIs at our setting,^{8,23} its intrinsic resistance towards ampicillin, and its growing AMR necessitate level-specific antibiograms in higher-tier hospitals. This is especially critical as ampicillin and gentamicin, and third-generation cephalosporins remain the first- and second-line treatments for BSIs in Tanzania.¹⁴ Notably, *K. pneumoniae* resistance to piperacillin-tazobactam declined, suggesting its preserved efficacy against MDR bacteria including ESBL-PE, as reported previously.³²

Among GPB, emerging resistance to clindamycin, daptomycin, fosfomycin, fusidic acid, mupirocin, and teicoplanin was observed after NAP-AMR, primarily in *S. haemolyticus* and other coagulase-negative Staphylococci, possibly due to change in species between the study periods. Unlike earlier study which reported no resistance to fusidic acid, mupirocin, and teicoplanin in *S. aureus*.³³ In the current study, key antibiotics like linezolid, rifampicin, tigecycline, and vancomycin remained effective, emphasizing the need for AMS to preserve their efficacy.

The proportion of WHO-BPPs, including MRSA, ESBL-PE, and CR-GNB, rose significantly, driven by a significant surge in ESBL-PE. ESBL-producing *K. pneumoniae* was significantly more prevalent than ESBL-producing *E. coli*, highlighting its role in AMR trafficking.³¹ Furthermore, the rising resistance to third-generation cephalosporins, particularly due to ESBL-PE, underscores the need for level-specific antibiograms.¹⁴ This is critical as MDR *K. pneumoniae* and *E. coli* continue to be the leading causes of BSIs in higher-tier hospitals.^{8,23}

Multivariable logistic regression revealed a significant link between BSIs caused by WHO-BPPs and patients in higher-tier hospitals and those enrolled after NAP-AMR. Though not statistically significant, increased odds were noted among neonates, antibiotic users at enrollment, and those with co-morbidities. This observation is due to the fact that, higher-tier hospitals manage severe cases, requiring broad-spectrum antibiotics and invasive procedures, raising MDR infection risks.³⁴ The COVID-19 pandemic (2020–2021) intensified AMR due to increased antibiotic use,²⁶ creating selective pressure for MDR bacteria.³⁵ Similarly to antibiotic use at enrollment.³⁵ Neonates are especially vulnerable due to immature immune systems and frequent antibiotic exposure.³⁶ Likewise, patients with co-morbidities face heightened risks from immune suppression, prolonged healthcare exposure, and prophylactic antimicrobial use, further increasing susceptibility to MDR infections.^{35,37}

Lastly, this study provides crucial evidence on the epidemiology of BSIs and AMR patterns during and after the implementation of the NAP-AMR in Mwanza, Tanzania. By comparing BSI prevalence, pathogen profiles, and resistance trends across hospital tiers and time periods, the study highlights the growing burden of MDR pathogens, particularly *K. pneumoniae* and ESBL-PE, in higher-tier hospitals. The findings emphasize the critical need for strengthened AMS, targeted IPC, and level-specific antibiograms. The emergence of rare and opportunistic pathogens underscores the importance of advanced diagnostic capacity and continuous surveillance. This study not only informs national AMR policy and clinical practice but also contributes valuable data to global AMR monitoring efforts, particularly in low-resource settings where such evidence is limited yet urgently needed.

Study Limitation

This study did not assess IPC practices, antibiotic usage, or distinguish healthcare-associated from community-acquired BSIs. Our findings may not generalize to regions with different healthcare systems, prescribing patterns, or AMR rates. Additionally, although the two study periods varied due to funding constraints, patient and isolate numbers supported robust statistical comparisons. Despite its limitations, this study offers valuable insights into the local epidemiology of infectious diseases and AMR, while also contributing to the broader global AMR surveillance efforts.

Conclusion

This study revealed a substantial prevalence of laboratory-confirmed BSIs among sepsis patients in Mwanza, Tanzania, with GNB, particularly *K. pneumoniae* and *E. coli*, as the predominant pathogens. WHO-BPPs were significantly more common in higher-tier hospitals and after NAP-AMR period. Increased odds of WHO-BPP-related BSIs were also observed among neonates, patients on antibiotics at enrollment, and those with underlying comorbidities. Although AMR trends varied, the observed reductions in resistance among *E. coli* and other GNB suggest a potential positive impact of NAP-AMR interventions, despite pressures from increased antibiotic use during the COVID-19 pandemic. These findings underscore the urgent need for context-specific strategies, including revised empiric treatment protocols, robust AMS programs, and enhanced IPC, especially in higher-tier hospitals. Notably, the decline in *K. pneumoniae* resistance to piperacillin-tazobactam merits further investigation to guide future therapeutic options.

Abbreviations

AMR, Antimicrobial Resistance; AST, Antimicrobial Susceptibility Testing; BMC, Bugando Medical Centre; BSIs, Bloodstream infections; CLSI, Clinical and Laboratory Standards Institute; CUHAS, Catholic University of Health and Allied Sciences; ESBL, Extended-spectrum beta-lactamase; GNB, Gram-negative bacteria; GPB, Gram-positive bacteria; IPC, Infection prevention and control; MRSA, Methicillin-resistant *Staphylococcus aureus*; NAP-AMR, National Action Plan on Antimicrobial Resistance; WHO-BPPs, World Health Organization bacterial priority pathogens.

Ethical Approval and Informed Consent

This study was ethically approved by the joint CUHAS/BMC Research Ethics and Review Committee and given certificate numbers: CREC/318/2018 (during NAP-AMR) and CREC/654/2023 (after NAP-AMR). Additionally, this study was ethically approved by the National Health Research Ethics Committee (NathREC) and given certificate numbers: NIMR/HQ/R.8a/Vol.IX/3017 (during NAP-AMR) and NIMR/HQ/R.8a/Vol.IX/4613 (after NAP-AMR). This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants, or from parents or legal guardians in the case of individuals under 18 years of age. Culture and AST results were timely communicated to guide patients' management.

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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 in this work.

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