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Original Article

Assessing the prevalence of antimicrobial resistance among pediatric patients at Kamuzu Central Hospital, Malawi

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Abstract

Introduction: Severe bacterial infections cause significant disease burden in developing countries, including Malawi. The situation is compounded by the scarcity of resources, inconsistent availability of antibiotics, and increasing antimicrobial resistance (AMR).

Methodology: This was a descriptive retrospective study where we analyzed blood culture results of pediatric patients admitted to Kamuzu Central Hospital (KCH), Lilongwe, Malawi. The data from January 2018 to January 2022 were compared with clinical metadata, and analyzed using the statistical software packages STATA version 16.1 and R version 4.2.

Results: The data of 272 isolates from blood culture were obtained; 47.8% (130/272) of participants presented with organisms resistant to first-line antibiotics; 13.4% (22/164) were resistant to second-line antibiotics which included resistance to piperacillin/tazobactam and meropenem. Gram-negative isolates constituted 54.3% (89/164) of the isolates, of which 32% (29/89) were *Acinetobacter* spp; while 45.7% (75/164) of the isolates were Gram-positive of which 42.7% (32/75) was *Staphylococcus aureus*. There were 12 *Escherichia coli* isolates, of which 50% (6/12) were highly resistant to piperacillin/tazobactam. The Fisher's exact test indicated that the antibiotic prescribed after a blood culture test result was significantly associated with the isolate observed ($p = 0.016$).

Conclusions: This study highlights high rates of AMR to commonly used antibiotics in the pediatric ward at KCH, and calls for the need to revise treatment guidelines in the wake of empiric antibiotic choices for pediatric patients, including intensification of maximal use of blood culture tests as part of management of febrile illnesses and reinforcement of antimicrobial stewardship in pediatric patient care.

Key words: susceptibility; isolate; blood culture.

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Introduction

Antimicrobial resistance (AMR) is a global public health problem. An estimated 4.9 million deaths globally were associated with AMR in 2019, of which 1.27 million (25.9%) were directly attributed to bacterial AMR. Low- and middle-income countries (LMICs) are disproportionately affected with the highest rates of AMR deaths (27.3 deaths per 100,000) occurring in western sub-Saharan Africa in 2019 [1]. This excess burden in LMICs is due to factors such as limited resources, and overuse and misuse of antibiotics; and these are a growing problem in Africa due to the huge burden of infectious diseases [1,2]. These estimates have, however, been based on scant microbiological data from Africa [3].

One of the leading causes of morbidity and mortality in sub-Saharan Africa is bacterial infections, which are worsened by inadequate antibiotic supply and inappropriate antimicrobial therapy choices [4]. In addition to the continuous challenges of inconsistent antibiotic availability and scarcity of consumption data in Africa [5], uncertainty over susceptibility and resistance patterns, combined with the changing etiology of bacterial infections are longstanding

challenges [6]. Understanding these patterns through establishing infectious disease surveillance platforms is key to informing local antibacterial treatment practices, such as, empiric antibiotic therapy and guided public health interventions aimed at controlling the spread of AMR [7,8]. This challenge was illustrated in Malawi by a recent study describing these trends in under-5-year-old children admitted at the Queen Elizabeth Central Hospital in Blantyre, Malawi; that reported a substantial increase in the resistance of Gram-negative pathogens to all first-line antibiotic treatments from 3.4% in 1998 to 30% in 2017, and the importance of *Klebsiella pneumoniae* as a cause of neonatal sepsis [9]. A different study conducted in 2020 showed that out of all bloodstream infections, 67% were resistant to third-generation cephalosporins, compared to 33% that were susceptible [10]. Optimal and timely empiric treatment is key to achieving good outcomes for patients, especially the most vulnerable (neonates or patients with immunosuppression). This is enabled, through surveillance of the common infectious pathogens, and defining local antibiograms [11]. However, no specific antibiograms were available for pediatric patients in Kamuzu Central Hospital (KCH) in Malawi.

A surveillance study on the trends in AMR at Queen Elizabeth Central Hospital in Malawi, analyzed blood cultures of adult and pediatric patients with fever in suspicion of sepsis from 1998–2016. The results showed that most isolates were resistant to the commonly prescribed antibiotics like amoxicillin and penicillin, with 63% being Gram-negative bacteria and 6.6% being Gram-positive bacteria [6]. This enabled the establishment of an antimicrobial stewardship program which successfully reduced ceftriaxone consumption [12]. The challenge of AMR has also been identified in a study conducted in the Central Hospitals in Malawi. The Gram-positive bacteria isolates dominated this study with the most prevalent isolate being *Staphylococcus aureus* (34.7%) and showed an increase in the prevalence of AMR in all major isolates over the study period [13].

These findings are important, but only reflective of trends in these institutions, and we cannot assume that they are representative of the picture in different regions and cities in Malawi. It is vital to have quality-assured diagnostic microbiology laboratory data aggregated to consistently guide clinicians in the development of locally relevant antibiotic usage guidelines to ensure effective antimicrobial therapy [14].

Although these results can be used by clinicians and health workers to get an idea on the common pathogens found in the institution, whether geographically or hospital-based, they do not provide complete and accurate unit-based results that are tailored towards patients that present there [15]. Today, few facilities in Malawi have been able to conduct AMR surveillance regularly. For example, antibiotic treatment in the pediatric ward at KCH is entirely empirical and the etiology of infections is rarely confirmed before initiating antimicrobial treatment. This study aimed to describe pathogens' susceptibility and resistance patterns in the pediatric ward at KCH, and to compare the common isolates identified in the wards with the common antibiotics prescribed.

Methodology

We undertook a descriptive retrospective study, by using diagnostic microbiology, data and linking it to available clinical data from patients admitted to the pediatric ward, to address this knowledge gap at KCH. We compared the antibiogram from these isolates with the antibiotics prescribed in the hospital.

Study setting

This study was conducted at KCH in Lilongwe, Malawi, where most severe pediatric infections are treated. It is one of the largest referral hospitals in Malawi. The hospital has 708 beds, although the number of patients frequently exceeds the number of beds available. KCH serves approximately 25,000 pediatric admissions annually. This hospital also serves as a teaching facility for doctors, nurses, and other healthcare professionals.

The pediatric ward at KCH is divided into 10 units, including the Children's Ward High Dependency Unit and the Pediatric Hematology-Oncology Unit. Conducting routine blood culture tests was a challenge prior to 2021; however, there has since been a substantial increase in the number of blood culture tests conducted.

The inclusion criteria for this study were pediatric patients (≤ 18 years old) with a clinically significant fever (≥ 37.5 °C) or neutropenia (absolute neutrophil count < 1000 cells), who had blood culture collected and who received antibiotics. The details of the inclusion criteria for the study have been presented elsewhere [16].

Data collection and analysis

The blood culture data recorded in the period between January 2018 and January 2022 were extracted from the laboratory database at KCH and the University of North Carolina (UNC) laboratories at KCH. The laboratory results were linked to the clinical files using

unique patient identification numbers for accurate matching of the results obtained. Blood cultures during this period were only taken when there was a clinical reason to suspect septicemia. The blood culture collection criteria at KCH specify that blood cultures should be taken before administration of antibiotics; however, blood cultures are still indicated for patients on antibiotics when the patients show symptoms of a temperature of > 38 °C or new onset of confusion.

The blood cultures were taken using the aseptic technique and incubated using the automated Becton Dickson continuous blood culture monitoring system (BACTEC, USA). The culture in bottles that were flagged as positive, were Gram stained and microscopically observed; and, based on the results they were incubated at 37 °C aerobically for 18–24 hrs. Identification and antimicrobial susceptibility testing were performed for all growth observed. When no growth was observed on media, the culture bottles were re-incubated, and no growth after re-incubation was reported as "negative." Antimicrobial susceptibility was undertaken using disc diffusion according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines breakpoints [17].

For the purposes of this study, antimicrobial resistance was defined as lack of susceptibility to more than one antimicrobial drug in more than or equal to three antimicrobial categories. All blood culture results between January 2018 and January 2022 were reviewed and followed up with a review of each patient file for diagnosis and prescribing information. The patient demographics with complete records of bacteriological culture and resistance patterns were retrieved from the laboratory database and reviewed. The data were analyzed using STATA V.16 (StataCorp LLC, College Station, TX, USA) and R version 4.2.1 software after checking for completeness and consistency.

Ethical considerations

Ethical approval for conducting this study was obtained from the College of Medicine Research Ethics Committee at Kamuzu University of Health Sciences (COMREC P.04/22/3613) and the Health Research Ethics Committee (HREC S22/04/060). The study was granted a waiver for patient consent for the use of the laboratory and patient file data due to the retrospective nature of the study.

Results

Demographic and clinical characteristics

Out of the 272 records included in the study, 53% (145) were female and 47% (127) were male. The median age of the patients was 3 years (range 0–18 years), and 64% (175) were less than 5 years of age (Figure 1). Each patient had at least one blood culture collected.

Most participants (69%) were from the Lilongwe district; followed by neighboring central region districts such as Dedza (6%), Dowa (4%), and Mchinji (3%). A minority came from the northern region districts such as Mzimba, Mzuzu, and Karonga (Figure 2). Most patients were admitted to the pediatric oncology ward (52%), followed by the Ethel Mutharika (EM) nursery ward (22%) and the Children's Ward A (CWA; 13%) (Figure 3).

Out of 272 records which had blood culture samples collected, 63.2% cultures showed growth of at least 1 organism, while 36% resulted in no growth, and 15.6% were contaminants.

Summary of the diagnoses

Out of the 272 records included, 191 had the clinical

Figure 1. Distribution of study sample by age group and gender.

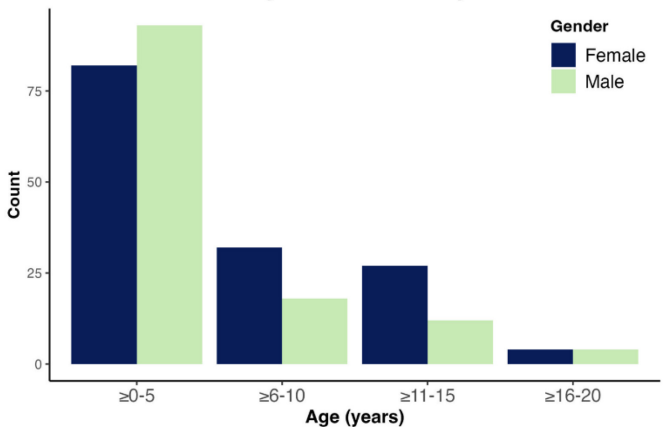


Figure 2. Distribution of study participants by geographical location.

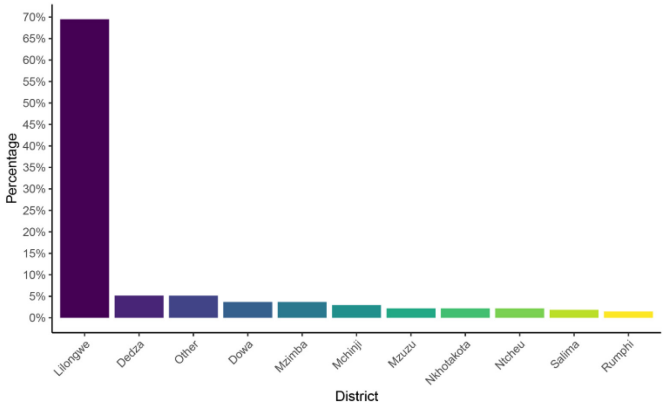
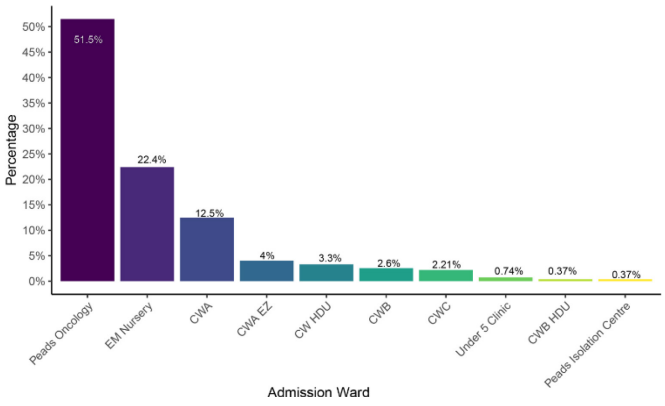


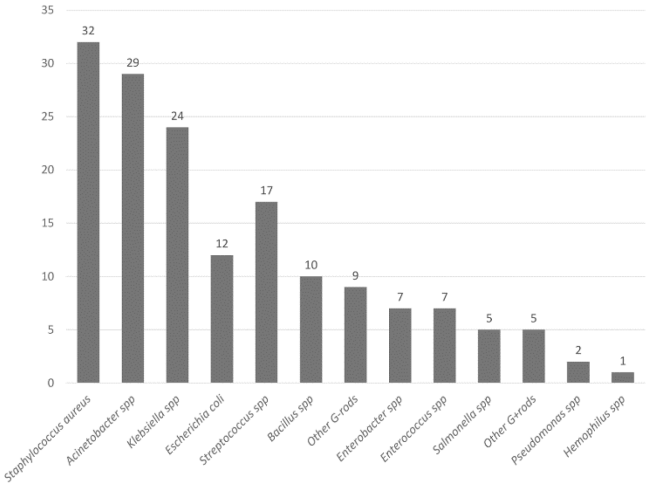
Figure 3. Distribution of study participants by admission ward in the hospital.



Peads oncology: pediatric oncology; EM nursery: Ethel Mutharika nursery; CWA: children's ward A; CWA EZ: children's ward A - emergency zone; CW HDU: children's ward high-dependency unit; CWB: children's ward B; CWC: children ward C; CWB HDU: children's ward B high-dependency unit; Peads isolation center: pediatric isolation center.

diagnosis clearly stated in the patient file and database. The most common clinical diagnosis was of febrile neutropenia (in oncology patients) in 35% (95/272) of the patients. The second most common diagnosis was pneumonia representing 12.6% (34/272) of the patients. Conditions such as sepsis (with undiagnosed infection) also dominated, representing 6.3% (17/272) of the patients' diagnoses. Severe aplastic anemia represented 2.6% (7/272), meningitis constituted 2% (6/272), and typhoid and liver cysts both represented 1% (3/272) of all diagnoses. Other conditions such as malaria constituted less than 1% (1/272) of the diagnoses. Among all the patients included in the study, 70.2% (191/272) had a clear diagnosis stated in the patient file, while 29.8% (81/272) of the patients had no clear diagnosis indicated.

Figure 4. Commonly isolated bacteria in the pediatric ward from January 2018-January 2022.



G- rods: Gram positive rods; G- rods: Gram negative rods.

Bacteriology results

The prevalence of antimicrobial resistance was 47.8%. Out of the 272 records included in the study, 130 had a blood culture isolate that was resistant to at least 1 commonly prescribed antibiotic. There were no cases from which multiple bacterial isolates were recovered. The most isolated bacteria were *S. aureus* (32), followed by *Acinetobacter* spp. (29), and *Klebsiella* spp. (24); while the least isolated bacteria in the pediatric wards were *Pseudomonas* spp. (2) and *Hemophilus* spp. (1) (Figure 4).

Gram-negative isolates represented 54.3%, while Gram-positive isolates represented 45.7% of the records. The most common Gram-negative isolate was *Acinetobacter* spp. (32.6%); followed by *Klebsiella*

Table 1. Resistance of Gram-negative isolates to common antibiotics at the Kamuzu Central Hospital pediatric ward (January 2018 to January 2022).

Gram-negative isolates		Antibiotics, n (%)														
		AMP	CEF	CIP	SXT	CN	CEM	PTZ	CEX	CEN	CRO	MRP	TBR	CHR	AMC	IMI
Acinetobacter spp. n = 29	*R*	8 (88.9)	9 (69.2)	6 (30)	15 (78.9)	11 (57.9)	5 (71.4)	3 (33.3)	3 (37.5)	2 (28.6)	3 (75)	7 (30.4)	9 (64.3)	5 (83.3)	2 (50)	1 (50)
Enterobacter spp. n = 7	*R*	2 (100)	1 (100)	2 (50)	3 (100)	5 (100)	4 (100)	*	1 (50)	*	2 (66.7)	1 (16.7)	1 (100)	*	3 (100)	1 (100)
Escherichia coli. n = 12	*R*	7 (100)	6 (66.7)	6 (54.55)	6 (85.7)	4 (57.1)	5 (83.3)	4 (50)	2 (100)	1 (50)	4 (80)	*	*	*	2 (50)	1 (100)
Haemophilus spp. n = 1	*R*	1 (100)	1 (100)	*	*	*	*	*	*	*	*	*	*	1 (100)	*	*
Klebsiella spp. n = 24	*R*	8 (100)	11 (78.6)	11 (55)	9 (90)	12 (70.6)	7 (87.5)	3 (23.1)	7 (87.5)	1 (12.5)	5 (71.4)	*	*	3 (37.5)	11 (68.8)	1 (12.5)
Other Gram-negative rods. n = 9	*R*	1 (33.33)	4 (66.7)	3 (50)	3 (42.9)	3 (60)	2 (100)		4 (100)	1 (100)	*	1 (33.3)	*	2 (40)	2 (66.7)	2 (66.7)
Pseudomonas spp. n = 2	*R*	*	*	1 (100)	*	1 (50)	*	*	*		*	*	1(100)	*	*	*
Salmonella spp. n = 5	*R*	*	1 (33.3)	*	2 (66.7)	1 (25)	*	1 (50)	*	1 (33.3)	*	1 (25)	*	*	*	*

AMP: ampicillin; CEF: ceftriaxone; CIP: ciprofloxacin; SXT: trimethoprim/sulfamethoxazole; CN: gentamicin; CEM: ceftazidime; PTZ: piperacillin/tazobactam; CEX: cefotaxime; CEN: cefoxitin; CRO: cefuroxime; MRP: meropenem; TBR: tobramycin; CHR: chloramphenicol; AMC: amoxicillin/clavulanate; IMI: imipenem; *not tested; n = number of bacteria isolated.

Table 2. Resistance patterns of Gram-positive isolates observed in the pediatric wards at the Kamuzu Central Hospital, Lilongwe, Malawi (January 2018 to January 2022).

Gram positive isolates		Antibiotics; n (%)																	
		AMP	CEF	CIP	SXT	CN	CEM	CEX	CEN	CRO	LIN	TBR	P	CLY	ERY	OXA	TET	VAN	CHR
Coagulase (-) *Staphylococcus*	*R*	*	*	*	*	*	*	*	*	*	*	1 (100)	*	*	*	*	*	*	*
Enterococcus spp	*R*	3 (75)	2 (100)	7 (100)	1 (50)	2 (100)	1 (100)	*	*	1 (100)	1 (100)				*	*	*	*	*
Staphylcoccus aureus	*R*	*	*	4 (40)	5 (83.3)	6 (27.3)	*	1 (50)	2 (33.3)	*	*	1 (100)	9 (100)	8 (30.8)	17 (73.9)	3 (30)	4 (57.1)	*	5 (23.8)
Streptococcus spp	*R*	2 (66.7)	3 (50)	*	3 (100)	*	*	*	*	*	*	*	4 (80)	5 (71.4)	6 (75)	*	2 (100)	2 (40)	1 (20)

AMP: ampicillin; CEF: ceftriaxone; CIP: ciprofloxacin; SXT: trimethoprim/sulfamethoxazole; CN: gentamicin; CEM: ceftazidime; CEX: cefotaxime; CEN: cefoxitin; CRO: cefuroxime; LIN: linezolid; TBR: obramycin; P: penicillin; CLY: clindamycin; ERY: erythromycin; OXA: oxacillin; TET: tetracycline; VAN: vancomycin; CHR: chloramphenicol; *not tested.

spp. (26.9%), *Escherichia coli* (13.5%), *Enterobacter* spp. (7.9%), *Salmonella* spp. (5.6%), *Pseudomonas* spp. (2.3%), and other Gram-negative isolates (11.2%). *S. aureus* was the most common Gram-positive isolate representing 55.5%, followed by *Streptococcus* spp. comprising of 14.7% of the isolates observed. In addition, *Enterococcus* spp. constituted 9.3%. Numerous likely contaminants were isolated, including *Bacillus* spp. and coagulase-negative *Staphylococci*, both comprising of 13.3%; and other Gram-positive rods constituting 6.7%. A total of 15.6% isolates represented contaminants.

Out of 29 *Acinetobacter* spp. isolated, not all were tested against every antibiotic. Nineteen of the 29 isolates were tested for gentamicin, and 11 (57.8%) of those were found to be resistant. Similarly, 13 isolates were tested for ceftriaxone susceptibility, and 9/13 (69%) of the *Acinetobacter* spp. isolated showed resistance to ceftriaxone, one of the most prescribed antibiotics at KCH. Nine isolates of *Acinetobacter* spp. were tested for ampicillin, and 8/9 (89%) were resistant to ampicillin (Table 1).

Amongst the Enterobacterales, unsurprisingly, all *Klebsiella* spp. (n = 24) were resistant to ampicillin, 90% were resistant to trimethoprim/sulfamethoxazole, 71% were resistant to gentamicin, and 78.5% were resistant to cefotaxime. Another common Gram-negative isolate was *E. coli* with 8 out of 12 (66.7%) of the isolates identified showing resistance to ceftriaxone. In addition, 85.7% of *E. coli* were resistant to cotrimoxazole, and 50% of the *E. coli* isolates were resistant to piperacillin/tazobactam.

The most common Gram-positive isolate *S. aureus* (n = 32) showed the highest rates of resistance to penicillin (100%), cotrimoxazole (83%), and erythromycin (73.9%), and more than half of the organisms identified showed resistance to erythromycin. *Streptococcus* spp. (n = 11) was the second most common Gram-positive isolate observed. The majority of *Streptococcus* spp. were resistant to penicillin (80%), followed by clindamycin (71%), and cotrimoxazole (100%). In addition, half of the *Streptococcus* spp isolates showed resistance to ceftriaxone (Table 2). Amongst other Gram-negative organisms, all *Hemophilus* spp. were resistant to ampicillin and ceftriaxone. A few isolates of *Pseudomonas* spp. were identified warranting profiling for antimicrobial susceptibility.

The results showed that up to 70% of the isolates observed were highly resistant to commonly used antibiotics such as ceftriaxone, ciprofloxacin, gentamicin, and trimethoprim/sulfamethoxazole. However, 78.2% of the isolates observed maintained susceptibility to meropenem, a less commonly used antibiotic agent.

According to the AWaRe classification of antibiotics introduced by the World Health Organization (WHO) in 2017, 64.2% (9/14) of the antimicrobial drugs tested in this study were antibiotics classified under the Access category, while 35.7% (5/14) were antibiotics classified under the Watch category [18].

Analysis of clinical and microbiological data

Table 3. Association between demographic characteristics and isolates of bacterial pathogens observed in patients at the Kamuzu Central Hospital pediatric ward (January 2018 to January 2022).

Characteristics	Isolates observed; n (%)		Association
	Gram (-) Bacteria	Gram (+) Bacteria	
Gender			
Female	42 (47.7)	34 (44.7)	
Male	46 (52.3)	42 (55.2)	
Total	88	76	$\chi^2 = 0.038$, $p = 0.8$
Age			
0–5 years	46 (76)	69 (66.3)	
6–10 years	6 (10)	16 (15.4)	
11–15 years	6 (10	13 (12.5)	
16–20 years	2 (3.3)	6 (5.8)	
Total	60	104	$\chi^2 = 43.12$, $p = 0.4$

Table 4. Association between the common isolates observed and the antibiotics prescribed before blood culture test at the Kamuzu Central Hospital pediatric ward (January 2018 to January 2022).

Isolates observed	Drugs prescribed before blood culture test result												
	AMX n (%)	CEF n (%)	CN n (%)	MRP n (%))	MET n (%)	PTZ n (%)	X-PEN n (%)	CRO n (%)	FLU n (%)	VAN n (%)	CLY n (%)	CLO n (%)	SXT n (%)
Acinetobacter spp	1 (8.3)	4 (33.3)	2 (16.7)	1 (8.3)	1 (8.3)	1 (8.3)	2 (16.7)	0	0	0	0	0	0
Bacillus spp	0	1 (33.3)	0	1 (33.3)	0	1 (33.3)	0	0	0	0	0	0	0
Coagulase (-) *Staphylococcus*	1 (9.1)	3 (27.3)	0	1 (9.1)	0	3 (27.3)	0	1 (9.1)	1 (9.1)	1 (9.1)	0	0	0
Enterobacter spp	0	4 (36.4)	0	0	4 (36.4)	0	0	0	0	0	1 (9.1)	1 (9.1)	1 (9.1)
Enterococcus spp	0	2 (33.3)	1 (16.7)	0	0	0	2 (33.3)	0	1 (16.7)	0	0	0	0
Escherichia spp	0	0	2 (28.6)	0	0	2 (28.6)	3 (42.9)	0	0	0	0	0	0
Klebsiella spp	0	5 (41.7)	2 (16.7)	0	2 (16.7)	1 (8.3)	2 (16.7)	0	0	0	0	0	0
Other spp	1 (7.1)	7 (50)	2 (14.3)	0	1 (7.1)	1 (7.1)	1 (7.14)	0	0	0	1 (7.1)	0	0
Salmonella spp	0	1 (20)	1 (20)	0	1 (20)	0	1 (20)	1 (20)	0	0	0	0	0
Staphylococcus spp	2 (7.1)	6 (21.5)	6 (21.4)	1 (3.6)	3 (10.7)	2 (7.1)	6 (21.4)	0	1 (3.6)	0	1 (3.6)	0	0
Streptococcus spp	1 (50)	1 (100)	0	0	0	0	0	0	0	0	0	0	0

AMX: amoxycillin; CEF: ceftriaxone; CN: gentamicin; MRP: meropenem; MET: metronidazole; PTZ: piperacillin/tazobactam; X-PEN: benzylpenicillin; CRO: ciprofloxacin; FLU: flucloxacillin; VAN: vancomycin; CLY: clindamycin; CLO: cloxacillin; SXT: trimethoprim/sulfamethoxazole; p value = 0.0507.

There was no association between gender and positive blood culture ($p = 0.8$). Similarly, there was no statistically significant association between the age of the patient and the group isolate observed ($p = 0.4$) (Table 3).

It is crucial that the antibiotics prescribed are effective against the isolate observed. Whilst there was no association between the antibiotics prescribed before the blood culture test results with the isolates observed (Table 4, $p = 0.0507$), antibiotics that were prescribed after blood culture results were available did correlate (Table 5, $p = 0.002$). This suggests that the blood culture results positively influenced the antibiotics prescribed to the patient.

Following logistic regression analysis, it was noted that younger patients were at a slightly higher risk of presenting with an isolate that showed resistance to commonly used antibiotics than the older patients (odds ratio (OR) 0.9; 95% CI 0.8–1.0). Additionally, adding cancer diagnosis to the multivariable model and holding age as a constant, resulted in the OR of 0.3 (95% CI 0.18–0.76) risk of a cancer patient presenting with an isolate that showed resistance to commonly used antibiotics. This further indicated that cancer-diagnosed pediatric patients were more likely to present with a resistant isolate than others.

Discussion

This study was conducted at the KCH pediatric wards and 47.8% prevalence of AMR to first-line antibiotics was noted, consistent with AMR prevalence data from elsewhere in Malawi and highlighting the rise of bloodstream infections that are untreatable with commonly available antibiotics [6]. The lack of effective antibiotics for treating conditions like neonatal sepsis, which accounted for 6.3% of patients in this study, poses a significant challenge in treating these cases [19]. The limited availability of alternatives to ineffective antibiotics, coupled with scarce resources, appears to be contributing to high AMR prevalence rates in Africa [20].

Out of the 54.4% Gram-negative isolates observed, over 60% *Acinetobacter* spp. showed resistance to cephalosporins, which are the common drug of choice for bloodstream infections. This further highlights the increase in resistance of Gram-negative bacteria to commonly used and readily available antibiotics in most African countries, as reported by Kumwenda *et al.* [13]. Hence, accuracy in the drug choice prescribed to

Table 5. Association between the observed isolates of bacterial pathogens and the antibiotic prescribed after a blood culture test at the Kamuzu Central Hospital (January 2018 to January 2022).

Isolates observed	Drugs prescribed after blood culture test result														
	AMX n (%)	CEF n (%)	MRP n (%)	MET n (%)	PTZ n (%)	CRO n (%)	FLU n (%)	VAN n (%)	CLO n (%)	SXT n (%)	X-PEN n (%)	AMC n (%)	CN n (%)	AZT n (%)	CLY n (%)
Acinetobacter spp	1 (10)	5 (50)	2 (20)	1 (10)	1 (10)	0	0	0	0	0	0	0	0	0	0
Bacillus spp	0	0	1 (50)	0	1 (50)	0	0	0	0	0	0	0	0	0	0
Coagulase (-) *Staphylococcus*	0	1 (12.5)	2 (25)	0	2 (25)	1 (12.5)	1 (12.5)	1 (12.5)	0	0	0	0	0	0	0
Enterobacter spp	0	3 (33.3)	1 (11.1)	1 (11.1)	0	0	0	0	1 (11.1)	1 (11.1)	0	0	0	0	0
Enterococcus spp	0	2 (50)	0	0	0	0	1 (25)	1 (25)	0	0	1 (25)	0	0	0	0
Escherichia spp	0	0	1 (12.5)	0	1 (12.5)	0	0	0	0	0	2 (25)	1 (12.5)	2 (25)	0	0
Klebsiella spp	0	3 (27.3)	1 (9.1)	2 (18.2)	1 (9.1)	0	0	0	0	0	2 (18.2)	0	2 (18.2)	0	0
Other spp	1 (7.1)	4 (28.5)	0	1 (7.1)	1 (7.1)	1 (7.1)	0	0	0	0	1 (7.1)	1 (7.1)	2 (14.3)	1 (7.1)	1 (7.1)
Salmonella spp	0	2 (50)	0	1 (25)	0	1 (25)	0	0	0	0	0	0	0	0	0
Staphylococcus spp	1 (5.6)	7 (38.9)	0	0	1 (5.6)	0	1 (5.6)	0	0	0	3 (16.7)	1 (5.6)	3 (16.7)	0	1 (5.6)
Streptococcus spp	1 (50)	1 (50)	0	0	0	0	0	0	0	0	0	0	0	0	0

AMX: amoxycillin; CEF: ceftriaxone; MRP: meropenem; MET: metronidazole; PTZ: piperacillin/tazobactam; CRO: ciprofloxacin; FLU: flucloxacillin; VAN: vancomycin; CLO: cloxacillin; SXT: trimethoprim/sulfamethoxazole; X-PEN: benzylpenicillin; AMC: amoxicillin/clavulanate; CN: gentamicin; AZT: azithromycin; CLY: clindamycin; p value = 0.01635.

patients needs to be improved to avoid the increase and spread of AMR in these organisms at the KCH pediatric ward. In this study, the species of *Acinetobacter* were not identified; hence it is unknown whether the species present *was Acinetobacter baumannii*, or an environmental contaminant. Such judgements are even harder to make in immunosuppressed patients, which was one of the limitations of the study.

The results clearly show that there is a growing resistance to third-generation cephalosporins and broad-spectrum antibiotics such as piperacillin and tazobactam amongst the Enterobacterales and *Acinetobacter* spp., which can make it difficult to treat common infections, and increase the costs needed to effectively manage these infections [6,11]. *Hemophilus* spp., another Gram-negative isolate, was 100% resistant to ampicillin and ceftriaxone. *S. aureus* isolates were remarkably resistant, with 30% being methicillin-resistant *Staphylococcus aureus* (MRSA). This trend appears to be prevalent in African settings, as studies in Zambia and Zimbabwe identified *S. aureus* as one of the most frequently occurring species with AMR [21,22]. The spread of MRSA would be a serious challenge as vancomycin is not commonly available and therapeutic drug monitoring is rarely conducted at KCH. Previous study findings in Malawi have shown a similar increasing rate of MRSA and emphasized that it can be difficult to treat these infections [6]. The high rate of use of penicillin and third-generation cephalosporins (3GCs) upon admission at the pediatric ward and the alarming rate of resistance of the infecting organisms to commonly prescribed drugs should be considered when establishing antimicrobial usage guidelines. A study in the Rumphi District Hospital, Malawi, found that over 50% of patients were prescribed ceftriaxone (3GCs) empirically, without microbiological justification [23]. In addition, ceftriaxone has been the main drug prescribed in the surgery department in Malawi [24]. Similar high resistance rates to commonly used antibiotics have been reported in South Africa, where resistance trends in drugs such as ciprofloxacin was shown to be high and increasing [25].

This study showed that there is a significant association between the antibiotics that were prescribed after a blood culture test was used to identify the isolate (p = 0.016), which suggests that frequent and timely blood culture tests can improve the choice of antibiotics administered to the patient. It also shows that there is some concordance between empiric antimicrobials and the susceptibility test. Hence, if all patients had blood culture test results available, we may have concluded that the antibiotics administered before the blood culture test results were not appropriate to treat the isolate that was infecting the patient. Prescribing antibiotics based on blood culture results can significantly decrease the number of patients receiving commonly prescribed drugs when not needed. This can decrease the rate of prescribing of antibiotics and reduce bacterial resistance to penicillin and other commonly prescribed drugs, as observed in nearly all species in this study. This study also showed that younger patients are more likely to acquire AMR bacteria, and there are multiple possible explanations for this [26].

Monitoring and frequent surveillance of AMR trends found in each setting can improve the local management of pediatric patients with different infectious diseases that require antimicrobial therapy. This can improve prescribing patterns, and reduce hospital and healthcare costs due to AMR in Africa [27]. Implementation of antimicrobial stewardship programs as an intervention to improve the use of antibiotics in pediatric settings, as recommended by the Infectious Diseases Society of America (IDSA), resulting in activities such as administering the correct treatment is a crucial step for achieving effective treatment outcomes [28]. Identification of the bacterial pathogens through blood culture tests guarantees a dependable guide on the appropriate selection of antimicrobial agents that are effective against the organisms in the setting. Routine blood culture tests can be used to identify the organisms causing infection in pediatric patients in hospitals [29].

The majority of the antibiotics that most isolates were resistant to in this study were those in the WHO AWaRe Access category. This further alludes to the importance of AMR surveillance in pediatric hospitals. These antibiotics are classified as first or second empiric treatment options for pediatric infectious diseases and it is crucial to continuously monitor antimicrobial susceptibility [30]. Similarly, most common diagnoses in this study, such as pneumonia, febrile neutropenia, and conditions related to sepsis, require that blood cultures be performed before initiating antibiotic treatment. This further solidifies the importance of obtaining blood cultures and frequent testing of the access and watch category antibiotics to improve detection of AMR [18].

This study had some limitations. The ratio of participants in the different pediatric departments was in favor of the pediatric oncology department, making the sample biased towards patients with complex underlying diseases. This was largely because these

patient files were kept separate from the other pediatric wards, making it easier to locate patient files and recorded data. Other pediatric wards lacked adequate resources such as files, file cabinets, and computerized systems to store records of the patients who were receiving antibiotics [31]. Routine blood cultures were a challenge, especially before 2021. This could have resulted in underestimation of the infection rates observed prior to 2021. This study had a small sample size due to the lack of available resources to conduct blood culture tests regularly, and the lack of a computerized patient information system to accurately record the results and patient demographics. A prospective study in this group of patients on AMR that includes analyzing newly collected blood culture results is required using the WHO framework for assessing the burden of AMR. However, the high level of contaminants (15.6%) shows that a high proportion of blood culture tests were not performed with adequate aseptic precautions. Further investigations are needed on personnel, equipment use, reagents used, and the environment in which the tests are conducted to improve the outcome of blood cultures.

Conclusions

An increase in the resistance of the isolates to commonly used antimicrobials in the pediatric ward at KCH is a growing concern. Pediatric patients presenting with fever and infection are prescribed gentamicin, ceftriaxone, and penicillin; as an empiric treatment before any blood cultures are taken. This study has shown that most isolates are resistant to these drugs. There is a need for revision of the current guidelines for empiric antimicrobial treatment choices. In addition, blood culture tests should be conducted upon presentation of fever and infection to ensure that the correct antimicrobial treatment is administered to the patient. This study has highlighted the susceptibility patterns of the isolates to most antimicrobials prescribed in this setting to help guide on the appropriate antibiotics to administer to the patients for optimal treatment results.

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Conflict of interests

No conflict of interests is declared.

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