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ORIGINAL ARTICLE

Divergent epidemiology and antimicrobial resistance of bloodstream pathogens: a comparative study in a general tertiary care and a specialized cardiac institute

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ABSTRACT

Background: Bloodstream infections (BSIs) are a critical cause of mortality globally, yet the profile of causative pathogens and their antimicrobial resistance (AMR) patterns vary dramatically across different healthcare settings. This study critically compared the BSI landscape between a specialized cardiac center (Peshawar Institute of Cardiology, PIC), which deals with high-risk nosocomial infections, and a general tertiary care hospital (Khyber Teaching Hospital, KTH), which handles a broad spectrum of community-acquired illnesses.

Methods: In total, 7,330 blood culture specimens (6,765 from KTH and 565 from PIC) were processed and rigorously identified. Antimicrobial Susceptibility Testing (AST) was performed using the VITEK 2 Compact Automated System and Kirby-Bauer disc diffusion, interpreted according to CLSI guidelines.

Results: The study revealed a bipartite epidemiology of BSIs. At Cardiac Center, the positivity rate was significantly higher (26.9%) and was overwhelmingly dominated by Gram-positive cocci (75%), characteristic of healthcare-associated infections. The principal pathogen was Staphylococcus aureus (48.7%). At General Hospital, the profile was a near-monomicrobial outbreak, with Gram-negative rods predominating (99%). The primary pathogen was Salmonella species (95.7%), reflecting a severe regional burden of community-acquired extensively drug-resistant enteric fever. All tested Gram-positive isolates retained 100% susceptibility to Linezolid, Vancomycin, and Teicoplanin. Similarly, Salmonella isolates showed 100% susceptibility to Carbapenems and Azithromycin. Salmonella exhibited near-universal resistance to Ciprofloxacin (0–2.2% susceptibility) and very poor susceptibility to Ceftriaxone.

Conclusion: This study provides a definitive, comparative profile of BSI pathogens in KP, demonstrating that the microbial threat is fundamentally linked to the healthcare environment. The reliance on last-line antibiotics is critical yet threatened by high resistance rates among common oral agents. Immediate clinical and policy action, informed by these institution-specific antibiograms, is urgently required to strengthen Antimicrobial Stewardship Programs and contain the spread of high-priority Multidrug-Resistant organisms.

Keywords: Antimicrobial Resistance, Bloodstream Infections, Healthcare Associated Infections

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Introduction

Bloodstream infections (BSIs) remain a major global health threat, contributing significantly to morbidity, mortality, and increased healthcare costs, particularly in hospitalized patient cohorts (1). Prompt and accurate etiological identification via blood cultures is the definitive standard for guiding specific antimicrobial therapy (2). However, the therapeutic landscape is critically threatened by the escalating global crisis of Antimicrobial Resistance (AMR), which compromises the efficacy of empirical regimens, especially in low- and middle-income countries (LMICs) (3). In Pakistan, and specifically within the Khyber Pakhtunkhwa (KP) province, the confluence of high BSI incidence and rapidly rising AMR rates constitutes a profound public health emergency, underscoring the necessity for targeted, localized surveillance data (4).

The spectrum of organisms causing BSI is highly heterogeneous, commonly featuring both Gram-positive organisms (e.g., *Staphylococcus aureus*, Coagulase-negative Staphylococci) and Gram-negative bacilli (e.g., *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) (5). Crucially, the dominant pathogen profile is not static; it is intrinsically linked to the specific healthcare setting, patient population, and geographic locale. Recent evidence highlights a worrying global shift toward a predominance of Gram-negative pathogens in many lower-middle-income countries (LMIC), frequently exhibiting more complex, multidrug-resistant (MDR) phenotypes in critical care environments (5). The global burden of bacterial AMR is estimated to cause over 4.95 million deaths annually, with the highest rates concentrated in South Asia and sub-Saharan Africa, emphasizing the urgency of regional data (6, 7).

The emergence and dissemination of resistance mechanisms, such as Extended-Spectrum Beta-Lactamases (ESBLs), Methicillin-Resistant *Staphylococcus aureus* (MRSA), and, critically, Carbapenemase-Producing Enterobacterales (CPE), have rendered numerous conventional antibiotics ineffective (8, 9). Within Pakistan, surveillance studies have persistently reported alarmingly high resistance rates, particularly among *E. coli*, *Klebsiella spp.*, and *Acinetobacter spp.* (10). This problem is exacerbated by systemic factors, including the unregulated, over-the-counter access to antibiotics, inconsistent stewardship, and pervasive deficits in infection control practices (11).

A significant research gap exists concerning the comparative epidemiology of BSI across diverse healthcare typologies in KP. Most available data stem from single-center reports, lacking the necessary generalizability to inform regional policy. This study addresses that deficit by directly comparing data from a general tertiary care hospital (KTH), which primarily handles community-acquired infections, with a specialized cardiac center (PIC), which faces high-acuity nosocomial challenges. Understanding the divergence in pathogen distribution and resistance patterns between these settings is crucial for developing highly granular, institution-specific antibiograms to optimize empirical therapy and strengthen regional antimicrobial stewardship efforts (12).

Methods

This was a descriptive, cross-sectional study conducted over 06 months from January 2025 to June 2025, analyzing blood culture specimens from two major tertiary care facilities in Peshawar, Khyber Pakhtunkhwa: the Khyber Teaching Hospital (KTH) and the Peshawar Institute of Cardiology (PIC). A total of 7,330 blood culture specimens were processed for the study (6,765 from KTH and 565 from PIC), collected from both admitted (inpatient) and outpatient department (OPD) patients. Initial processing utilized automated continuous monitoring systems: the VersaTREK™ Automated Microbial Detection System (Thermo Scientific, USA) was used at KTH, while the BACT/ALERT 3D System (bioMérieux, France) was employed at PIC-MTI. Blood culture bottles flagged as positive by either system were immediately removed from the incubator and subjected to aseptic sub-culturing onto a panel of solid media, including Sheep Blood Agar, MacConkey's Agar, and Chocolate Agar (Oxoid, UK), which were subsequently incubated aerobically at 37°C for 18–24 hours. Bacterial isolates were identified from pure colonies using a rigorous protocol involving Gram staining and conventional biochemical tests, with final species-level confirmation, particularly for Enterobacterales and other clinically significant organisms, achieved using the API 20E and relevant API identification kits (bioMérieux, France).

Antimicrobial susceptibility testing (AST) was performed using a combined methodological approach, with all results interpreted according to the Clinical and Laboratory Standards Institute (CLSI) M100 guidelines, 33rd Edition (2023). The Kirby-Bauer disc diffusion method was employed as the primary screening tool, utilizing a bacterial inoculum standardized to a 0.5 McFarland Standard and lawned onto Muller-Hinton Agar plates. Crucially, all clinically significant isolates, especially those exhibiting intermediate or resistant phenotypes by disc diffusion, were subjected to quantitative Minimum Inhibitory Concentration (MIC) determination. These quantitative MIC values for a comprehensive panel of recommended antibiotics were determined using the bioMérieux VITEK 2 Compact Automated System (bioMérieux, France), utilizing specific AST cards (AST-GN and AST-GP) to provide quantitative resistance profiles essential for guiding clinical management of bloodstream infections. All collected culture, identification, and quantitative antimicrobial susceptibility data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 22 (IBM Corp., USA).

Results

A total of 6765 blood samples were processed at Khyber Teaching Hospital (KTH), out of which 740 (10.9%) yielded positive cultures. In contrast, 565 samples were analyzed at the Peshawar Institute of Cardiology (PIC), with 152 (26.9%) that yielded growth. At KTH, the spectrum of organisms was narrow and heavily skewed toward Gram-negative pathogens. Gram-negative rods predominated (99%), with only 1% of BSIs caused by Gram-positive cocci. Salmonella species were the overwhelmingly dominant pathogen, comprising 95.7% of all isolates. Enterobacterales other than accounted for 3.2%, while Staphylococcus aureus made up only 1 % of the isolates. In contrast, the microbial profile at PIC was notably diverse, attributed mainly to Gram-positive cocci (75%). The most frequent organism was Staphylococcus aureus (48.7%). Other notable isolates included Streptococcus species (20.4%) and Enterococcus species. Among

gram-negative rods (25%), Salmonella species (14.5%), Enterobacterales (7.2%), and Pseudomonas (3.3%) were isolated from blood cultures. Table 1.

Table 1: Blood Culture Positivity and Organism Distribution

Hospital	Total Samples Processed	Positive Cultures (n)	Positivity Rate (%)	Dominant Organism	n (Hospital)	% of Total (Hospital)
Khyber Teaching Hospital (KTH)	6,765	740	10.90%	Salmonella spp.	708	95.70%
				Enterobacterales	24	3.30%
				Staphylococcus aureus	8	1.00%
Peshawar Institute of Cardiology (PIC)	565	152	26.90%	Staphylococcus aureus	74	48.70%
				Streptococcus spp.	31	20.40%
				Salmonella spp.	22	14.50%
				Enterobacterales	11	7.20%
				Enterococcus spp.	9	5.90%
				Pseudomonas spp.	5	3.30%

The antibiotic resistance profile of Salmonella *spp*., the dominant pathogen at KTH and a key isolate at PIC, was analyzed. At KTH, Salmonella exhibited excellent susceptibility to Imipenem and Meropenem (100%), and Azithromycin (100%), suggesting carbapenems and macrolides remain highly effective. However, very poor susceptibility was observed to Ciprofloxacin (2.2%), Ampicillin (6.7%), Cefotaxime (13.99%), and Ceftriaxone (15.3%), indicating significant resistance to commonly used oral and third-generation cephalosporins. Susceptibility to Co-trimoxazole (30.2%) and Chloramphenicol (10.9%) remained moderate to low. While at PIC, although the sample size was smaller (n=22), the Salmonella isolates mirrored similar resistance patterns. No sensitivity to Ciprofloxacin (0%) was observed, and only 30% were susceptible to Ceftriaxone. Encouragingly, 100% susceptibility to Imipenem, Meropenem, and Azithromycin was preserved, while Co-trimoxazole showed 60% sensitivity, and Chloramphenicol demonstrated 35% sensitivity, as shown in Figure 1. This figure illustrates the percentage susceptibility of key organisms, specifically Salmonella spp., Enterobacterales, and Staphylococcus aureus, to a panel of tested antibiotics as determined by the Kirby-Bauer and VITEK 2 MIC methods.

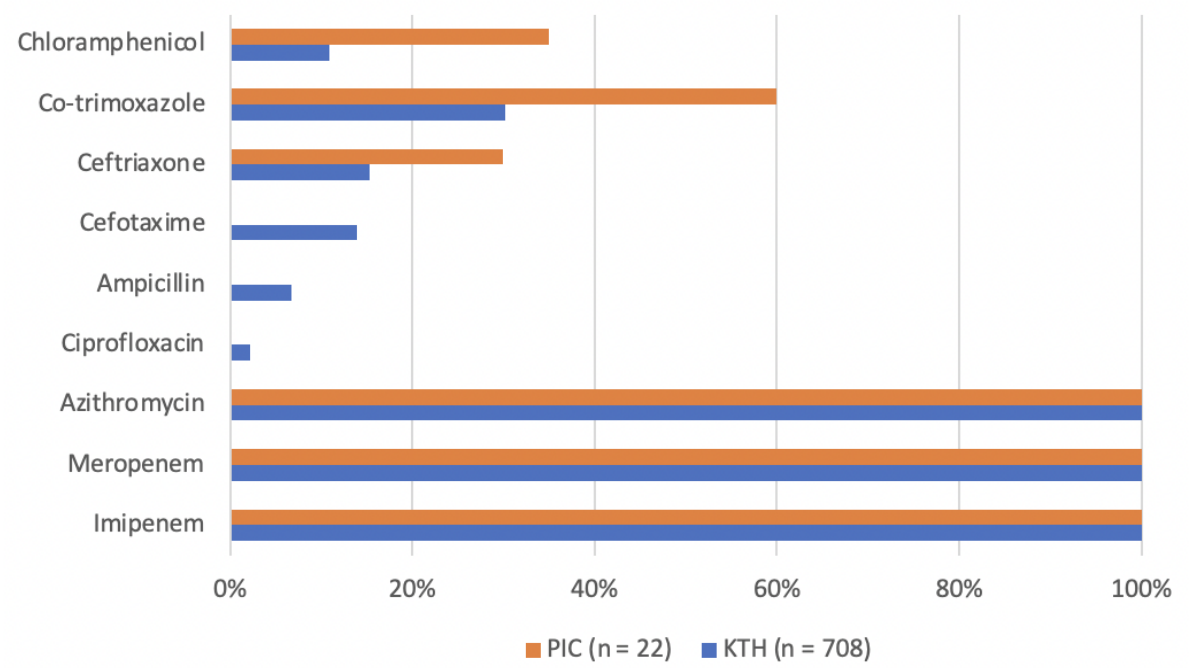

Figure 1: Antibiotic Susceptibility Profiles of Key Bacterial Isolates at KTH and PIC

The antibiotic profiles for other Enterobacterales isolated from PIC and KTH were also analyzed. A total of 11 and 28 Enterobacterales were recovered from blood specimens at PIC and KTH, respectively. A uniform susceptibility pattern was observed at both healthcare facilities, showing a susceptibility rate of 100% to Imipenem, Meropenem, Piperacillin–Tazobactam, Tigecycline, and Colistin, indicating these agents remain highly effective against resistant Gram-negative organisms. Additionally, Amikacin and Gentamicin demonstrated 80% sensitivity, whereas Ciprofloxacin showed 40% susceptibility, suggesting moderate fluoroquinolone resistance. However, Ampicillin resistance was universal 0% susceptibility and third-generation cephalosporins such as Ceftriaxone/Cefotaxime (10-20%), Cefepime (20-30%), Ceftazidime (20%), Co-trimoxazole (20-30%), and amoxicillin-clavulanate (10—20%) showed poor activity against Enterobacterales. Antibiotic susceptibility of Enterobacterales at PIC and KTH is shown in Table 2. This table illustrates the percentage susceptibility of Enterobacterales isolates recovered from blood specimens at both KTH and PIC, highlighting their susceptibility to agents like Carbapenems (Imipenem, Meropenem), Piperacillin–Tazobactam, and third-generation cephalosporins (Ceftriaxone/ Cefotaxime).

Table 2: Antibiotic Susceptibility Profiles of *Enterobacterales* at KTH and PIC

	AMP	AMC	CN 10	CIP	CRO	FEP	CAZ	DOX	TZP	SXT	AK	MEM	C	CT	TGC
PIC	0%	10%	80%	40%	20%	20%	20%	10%	100%	20%	80%	100%	60%	100%	100%
KT H	0%	20%	50%	25%	10%	30%	20%	15%	88%	30%	75%	88%	50%	100%	100%

Ampicillin (AMP), Amoxicillin Clavulanate (AMC)+ Gentamicin (CN), Ciprofloxacin (CIP), Ceftriaxone (CRO), Cefepime (FEP), Ceftazidime (CAZ), Doxycycline (DOX), Piperacillin-Tazobactam (TZP), Cotrimoxazole (SXT), Amikacin (AK), Imipenem (IMP), Meropenem (MEM), Chloramphenicol (C), Sulbactam-Cefoperazone (SCF), Tigecycline (TGC), Colistin (CT)

Despite the variable frequency of Staphylococcus aureus at PIC and KTH, 100% susceptibility was observed for Linezolid, Teicoplanin, cefoxitin, Amoxicillin-clavulanate, Vancomycin, and Tigecycline, confirming their continued reliability for Gram-positive bacteremia. Rifampin and Doxycycline also showed good activity with sensitivities of 100% and 100%, respectively. However, susceptibility dropped considerably for first-line oral agents. Ciprofloxacin and cotrimoxazole demonstrated only 33% susceptibility; Erythromycin was effective against 20%. Amikacin (90%) and Gentamicin (83%) retained relatively high efficacy. Predictably, Ampicillin and Penicillin resistance were near-universal. Antibiotic susceptibility of Staphylococcus aureus is shown in Table 3. This figure illustrates the percentage susceptibility of *Staphylococcus aureus* isolates to a panel of tested antibiotics, including Glycopeptides (Vancomycin, Teicoplanin), Oxazolidinones (Linezolid), and common oral agents (Ciprofloxacin, Co-trimoxazole), across both healthcare facilities.

Table 3: Antibiotic Susceptibility Profile of *Staphylococcus aureus* at KTH and PIC

	P	AMC	CIP	E	DA	SXT	DOX	RIF	CN 10	AK	TEC	FOX	VA	LZD	TGC
PIC	0%	100%	33%	20%	25%	33%	100%	100%	75%	83%	100%	100%	100%	100%	100%
KTH	0%	100%	30%	17%	20%	46%	84%	100%	83%	81%	100%	100%	100%	100%	100%

Penicillin (P), Amoxicillin Clavulanate (AMC), Gentamicin (CN. Ciprofloxacin (CIP), Doxycycline (DOX), Clindamycin (DA), Vancomycin (VA), Cefoxitin (FOX), Linezolid (LZD), Teicoplanin (TEC), Cotrimoxazole (SXT), Amikacin (AK), Tigecycline (TGC)

Of the 31 Streptococcus species isolates at PIC, 100% were susceptible to Penicillin, Ampicillin, Vancomycin, Teicoplanin, Linezolid, and Tigecycline, underlining the high efficacy of beta-lactams and glycopeptides. Moderate activity was observed for Erythromycin (33%) and Clindamycin (40%), whereas susceptibility to Ciprofloxacin was limited to 16%, indicating poor oral treatment options for streptococcal bacteremia. Chloramphenicol and Ceftriaxone both showed full activity (100%), supporting their use in severe systemic infections. Among the 9 Enterococcus isolates identified at PIC, resistance to multiple agents was apparent. However, 100% susceptibility was retained for Linezolid, Vancomycin, Teicoplanin, and Chloramphenicol, making them the most effective choices. Ampicillin showed 66% susceptibility, while Ciprofloxacin was only effective against 20% of isolates. Activity of Minocycline (66%) and Levofloxacin (25%) was variable. The aminoglycosides fared moderately, with Gentamicin (CN120) showing 50% susceptibility and Amikacin not consistently tested. These results reflect typical multidrug resistance among enterococci, with preserved susceptibility to key last-line agents.

For all Gram-negative isolates, carbapenems (Imipenem and Meropenem) remained highly effective, while fluoroquinolones like Ciprofloxacin demonstrated declining efficacy, especially among Salmonella and Enterobacterales. Among Gram-positive organisms, glycopeptides (Vancomycin, Teicoplanin) and oxazolidinones (Linezolid) consistently showed 100% efficacy against *S. aureus*, *Streptococcus, and Enterococcus species.* However, increasing resistance to oral agents such as Ampicillin, Erythromycin, Ciprofloxacin, and Co-trimoxazole was evident across all pathogen classes.

Discussion

This comparative analysis reveals significant differences in the burden, diversity, and antibiotic sensitivity of organisms causing bloodstream infections (BSIs) at two distinct tertiary care institutions, Khyber Teaching Hospital (KTH) and the Peshawar Institute of Cardiology (PIC). The clear divergence in the microbial etiology between the two facilities underscores the influence of specific patient risk factors and the broader community epidemiology on BSI acquisition, necessitating a highly granular approach to antimicrobial policy.

Among 26.9% of positive blood culture isolates at the Peshawar Institute of Cardiology (PIC), a Gram-positive etiology was dominant, accounting for 75% of all the BSIs. Notable isolates included *Staphylococcus aureus* (48.75%), *Streptococcus spp* (20.4%), and *Enterococcus spp* (5.9%). This pathogen profile is pathognomonic for Healthcare-Associated Bloodstream Infections (HA-BSIs). Patients at PIC, undergoing high-risk cardiac interventions such as surgery, stenting, and valve replacement, are critically reliant on central venous access and prosthetic devices. Prolonged hospital stays in intensive care environments, which are typical for this patient cohort, provide a high-selective pressure environment that favours the colonization and systemic invasion of the bloodstream by commensal gram-positive cocci. These findings are consistent with earlier epidemiological studies, both local and international, where the presence of invasive procedures and indwelling vascular devices was identified as a potent predictor of Healthcare-Acquired Infections (HAIs) and BSI (13, 14). Previous studies have also documented an increased risk of postoperative infection by *Staphylococcus aureus* in cardiac patients, specifically linked to perioperative nasal colonization and longer operative times (15, 16). The historical context of MRSA emergence, dating to 1992 in cardiac surgical units through nosocomial horizontal transfer (17), underscores the persistent threat of multidrug-resistant Gram-positives in specialized cardiac settings. Regional studies from similar cardiac units consistently show that Gram-positive BSIs are highly prevalent in heart surgery patients, strongly agreeing with the finding of a relatively higher percentage of *S. aureus* in blood culture specimens of PIC (18).

The spectrum of BSI observed at KTH, Peshawar, revealed a significant epidemiological variation, characterized by an overwhelming monomicrobial predominance of gram-negative rods, notably *Salmonella* species (95.5%). As a general tertiary-care hospital, KTH serves a diverse catchment area and manages varied pathologies, including community-acquired febrile illnesses, abdominal infections, and emergency admissions. The high burden of community-acquired Gram-negative infections, particularly *Salmonella Typhi* and *Paratyphi*, is a well-documented public health crisis in Pakistan (19). The observation of Gram-negative sepsis at KTH is primarily

explained by the influx of Community-Acquired Bloodstream Infections (CA-BSIs). The extremely high prevalence of *Salmonella* isolates (95.5%) at KTH is quantitatively consistent with the ongoing regional epidemic of Extensively Drug-Resistant (XDR) and Multi-Drug Resistant (MDR) enteric fever in Pakistan (20, 21). This epidemiological shift reflects a profound breakdown in basic Water, Sanitation, and Hygiene (WASH) infrastructure, which facilitates the faecal-oral transmission of *Salmonella* in endemic regions (22). The relatively low percentage of Gram-positive organisms and the limited diversity of isolates at KTH strongly point towards a dominant community-acquired etiology, in contrast to the nosocomial drivers at PIC.

We also observed differences in the distribution of other Gram-positive organisms. *Streptococcus* species and *Enterococcus* species were exclusively isolated at the cardiac care facility (PIC), accounting for 20.4% and 5.9% of the cases, respectively. This difference reflects the microbial tropism associated with specific procedural risks and associated comorbid conditions. Early studies have documented the increasing risk of streptococcal and enterococcal bacteremia in patients exposed to catheter-based interventions and valvular surgeries. *Streptococcus viridans* is often linked to underlying valvular heart diseases, while *Enterococcus faecalis* and *Enterococcus faecium* are critical pathogens in healthcare-associated bacteremia, particularly due to their capability for biofilm formation and their association with prolonged hospitalization and prior antibiotic exposure in cardiac units (23, 24). The global increase in *Enterococcus* BSI, coupled with the risk of progressing to Infective Endocarditis (IE), is highly pertinent to the PIC patient cohort (25). The absence or low detection of these strains at KTH may reflect genuine epidemiological differences, variations in specimen submission practices, or differences in laboratory detection sensitivities. Findings from the present study highlight the need for targeted surveillance, institution-based antibiograms derived from robust quantitative methods, and effective infection prevention and control interventions.

The quantitative resistance profiles, rigorously assessed via the VITEK 2 Compact System MIC determination, revealed a concerning frequency of resistant isolates. At both centers, *Salmonella* isolates demonstrated an alarming lack of susceptibility to Ciprofloxacin and third-generation cephalosporins (Ceftriaxone) (4), a signature of the XDR phenotype. This resistance pattern is likely driven by the unregulated use of over-the-counter antibiotics and incomplete treatment courses. However, the confirmed preserved susceptibility to carbapenems (Imipenem, Meropenem) and Azithromycin is a critical finding, validating their status as the last-line therapeutic reserves for severe, systemic enteric fever (26). A similar resistance pattern was observed in Salmonella isolates in previous studies in our region, demanding strengthening of ongoing surveillance, public awareness, and preventive strategies (27–29).

The Enterobacterales isolates from PIC also exhibited a multidrug-resistant phenotype, with high rates of resistance to Ampicillin, cephalosporins, and fluoroquinolones, consistent with global reports from tertiary care hospitals (30, 31). The continued efficacy of Carbapenems, Tigecycline, Colistin, and β-lactam/β-lactamase inhibitor combinations (like Piperacillin–Tazobactam) positions them as essential empirical therapeutic options in this high-acuity setting.

Continuous surveillance using quantitative MIC methods is imperative to detect the emergence of highly concerning resistance mechanisms, such as Carbapenemase-Producing Enterobacterales (CPE), including those harboring OXA-48-like enzymes, a rapidly expanding global threat (32). In the PIC setting, Gram-positive organisms, particularly *Staphylococcus aureus*, demonstrated 100% susceptibility to Glycopeptides (Vancomycin, Teicoplanin) and Oxazolidinones (Linezolid), affirming their indispensable role as the first-line agents for suspected MRSA and other resistant Gram-positive infections. Conversely, the widespread resistance to traditional oral agents like Ciprofloxacin, Erythromycin, and Co-trimoxazole severely compromises options for oral step-down therapy and outpatient management, often associated with prosthetic device infections due to biofilm formation (33). The *Streptococcus* and *Enterococcus* species isolated at PIC showed susceptibility patterns generally consistent with established resistance literature. Beta-lactams and glycopeptides remained largely effective for *Streptococcus*, whereas resistance in *Enterococcus* was more heterogeneous, with only Linezolid, Vancomycin, and Teicoplanin offering reliable coverage (34). This reflects the inherent and acquired resistance mechanisms in *Enterococcus* species and the selective clinical utility of oxazolidinones and glycopeptides.

In summary, this study highlights a severe and geographically distinct pattern of emerging Multidrug Resistance (MDR) across both Gram-positive (PIC) and Gram-negative (KTH) pathogens. The high-level Ciprofloxacin resistance in *Salmonella* and the declining efficacy of common oral antibiotics pose significant challenges to clinical de-escalation and resource management. The reliance on last-line agents (carbapenems, glycopeptides, oxazolidinones) mandates their protection through intensified Antimicrobial Stewardship Programs (ASPs), stringent IPC measures, and targeted policy interventions to curb antibiotic misuse. The results emphatically underscore the necessity for highly granular, facility-specific antibiograms to inform empirical treatment and guide focused public health efforts aimed at containing the spread of high-priority MDR organisms.

Limitations

While this study offers critical comparative insights into the microbial epidemiology of bloodstream infections (BSIs), it is constrained by several limitations that affect the generalizability and depth of the analysis.

Firstly, the geographic-specific, cross-sectional design—confined to a single general hospital and one specialized cardiac center—limits the external validity of the findings. The observed divergence in BSI profiles and resistance patterns may not be fully generalizable to other healthcare facilities with different patient demographics, infection control policies, or antibiotic stewardship programs across the region.

Secondly, the reliance on retrospective data from routine microbiology records restricts the control over potential confounding variables. Crucial patient-level data, such as comorbidity burdens, clinical severity scores, metrics on invasive device utilization (e.g., central line days), and precise details of prior antimicrobial exposure, were absent. The lack of these variables precludes a robust multivariate analysis to definitively link specific clinical factors to BSI risk or resistance phenotypes.

Finally, while phenotypic resistance determination via the VITEK 2 system

provided essential Minimum Inhibitory Concentration (MIC) data, the study lacks molecular characterization (e.g., identification of resistance genes like blaN-D-M-1 or mecA). Molecular typing is crucial for establishing the clonal relationship of the XDR Salmonella isolates or accurately characterizing specific staphylococcal strains, which is necessary to fully elucidate the transmission dynamics of these high-threat pathogens. Future research must prioritize prospective surveillance and molecular epidemiology.

Conclusion

This study establishes a bipartite epidemiology of Bloodstream Infections (BSIs), which is fundamentally driven by the distinct patient populations at the two centers. The Gram-negative dominance (99%) at KTH, characterized by XDR Salmonella spp., confirms a severe burden of Community-Acquired BSI, challenging treatment with oral antibiotics. Conversely, the Gram-positive dominance (75%) at PIC highlights the persistent threat of nosocomial, device-associated MDR organisms. Immediate clinical and policy action, including institution-specific antibiograms and strengthened Antimicrobial Stewardship Programs (ASPs), is urgently required to preserve the efficacy of last-line antibiotics and protect patient outcomes across the region.

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References

1. Di Franco S, Alfieri A, Pace MC, Sansone P, Pota V, Fittipaldi C, et al. Blood Stream Infections from MDR Bacteria. Life. 2021 Jun 18;11(6):575.
2. Liu TP, Wu HF, Chang PL. Direct identification and antimicrobial susceptibility testing of microorganisms from positive blood culture bottles using a membrane filtration method. BMC Microbiol. 2025 Oct 2;25(1):606.
3. Chinemerem Nwobodo D, Ugwu MC, Oliseloke Anie C, Al-Ouqaili MTS, Chinedu Ikem J, Victor Chigozie U, et al. Antibiotic resistance: The challenges and some emerging strategies for tackling a global menace. J Clin Lab Anal. 2022 Sep 10;36(9).
4. Safdar N, Saleem S, Salman M, Tareq AH, Ishaq S, Ambreen S, et al. Economic burden of antimicrobial resistance on patients in Pakistan. Front Public Health. 2025 Feb 25;13.
5. Kalayci Cekin Z. Bloodstream Infections Caused by Multidrug Resistant Bacteria: Clinical and Microbiological Features and Mortality. SiSli Etfal Hastanesi Tip Bulteni / The Medical Bulletin of Sisli Hospital. 2023;416–25.
6. Naghavi M, Vollset SE, Ikuta KS, Swetschinski LR, Gray AP, Wool EE, Aguilar GR, Mestrovic T, Smith G, Han C, Hsu RL. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. The Lancet. 2024 Sep 28;404(10459):1199-226
7. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, Han C, Bisignano C, Rao P, Wool E, Johnson SC. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The lancet. 2022 Feb 12;399(10325):629-55.)
8. Ahmed SK, Hussein S, Qurbani K, Ibrahim RH, Fareeq A, Mahmood KA, et al. Antimicrobial resistance: Impacts, challenges, and future prospects. Journal

of Medicine, Surgery, and Public Health. 2024 Apr;2:100081.
9. Oliveira M, Antunes W, Mota S, Madureira-Carvalho Á, Dinis-Oliveira RJ, Dias da Silva D. An Overview of the Recent Advances in Antimicrobial Resistance. Microorganisms. 2024 Sep 21;12(9):1920.
10. Bilal H, Khan MN, Rehman T, Hameed MF, Yang X. Antibiotic resistance in Pakistan: a systematic review of past decade. BMC Infect Dis. 2021 Dec 6;21(1):244.
11. Chitedze AC, Mzikamanda RR, Maida T, McAtee CL, Mapahla L, Feasey N, et al. Assessing the prevalence of antimicrobial resistance among pediatric patients at Kamuzu Central Hospital, Malawi. The Journal of Infection in Developing Countries. 2025 Aug 31;19(08):1172–81.
12. Paintsil EK, Adu-Asiamah CK, Kronsten VT, Ntuli Y, Shawcross DL. Global Trends in Antimicrobial Resistance Among Cirrhosis Patients with Bacteremia: A Systematic Review and Meta-Analysis. Clinical Gastroenterology and Hepatology. 2025 Jul 23.
13. Dadi NCT, Radochová B, Vargová J, Bujdáková H. Impact of Healthcare-Associated Infections Connected to Medical Devices—An Update. Microorganisms. 2021 Nov 11;9(11):2332.
14. Weiner-Lastinger LM, Abner S, Edwards JR, Kallen AJ, Karlsson M, Magill SS, et al. Antimicrobial-resistant pathogens associated with adult healthcare-associated infections: Summary of data reported to the National Healthcare Safety Network, 2015–2017. Infect Control Hosp Epidemiol. 2020 Jan 26;41(1):1–18.
15. Allen KB, Fowler VG, Gammie JS, Hartzel JS, Onorato MT, DiNubile MJ, et al. Staphylococcus aureus Infections After Elective Cardiothoracic Surgery: Observations From an International Randomized Placebo-Controlled Trial of an Investigational S aureus Vaccine. Open Forum Infect Dis. 2014 Sep 1;1(2).
16. Tadros MA, Williams VR, Plourde S, Callery S, Simor AE, Vearncombe M. Risk factors for Staphylococcus aureus surgical site infection during an outbreak in patients undergoing cardiovascular surgery. American journal of infection control. 2013 Jun 1;41(6):509-12.
17. Carrier M, Marchand R, Auger P, Hébert Y, Pellerin M, Perrault LP, et al. Methicillin-resistant Staphylococcus aureus infection in a cardiac surgical unit. J Thorac Cardiovasc Surg. 2002 Jan;123(1):40–4.
18. Sousa-Uva* M, Head SJ, Milojevic M, Collet JP, Landoni G, Castella M, et al. 2017 EACTS Guidelines on perioperative medication in adult cardiac surgery. European Journal of Cardio-Thoracic Surgery. 2018 Jan 1;53(1):5–33.
19. Ullah A, Shabil M, Abdulsamad SA, Jan A, Naeem AA, Ullah H, et al. Prevalence of the Antibiotic Resistance of Salmonella typhi and Salmonella paratyphi in Pakistan: A Systematic Review and Meta-analysis. Open Forum Infect Dis. 2025 Mar 27;12(4).
20. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al. Extensively Drug-Resistant (XDR) Typhoid: Evolution, Prevention, and Its Management. Biomed Res Int. 2020 Jan 2;2020(1).
21. Zhu Q, Yue Y, Zhu L, Cui J, Zhu M, Chen L, et al. Epidemiology and

microbiology of Gram-positive bloodstream infections in a tertiary-care hospital in Beijing, China: a 6-year retrospective study. Antimicrob Resist Infect Control. 2018 Sep 3;7(1):107.
22. Ullah A, Shabil M, Abdulsamad SA, Jan A, Naeem AA, Ullah H, Khattak M, Zakiullah. Prevalence of the Antibiotic Resistance of Salmonella typhi and Salmonella paratyphi in Pakistan: A Systematic Review and Meta-analysis. InOpen Forum Infectious Diseases 2025 Apr (Vol. 12, No. 4, p. ofaf131). US: Oxford University Press
23. Rapti V, Giannitsioti E, Spernovasilis N, Magiorakos AP, Poulakou G. The Evolving Landscape of Infective Endocarditis: Difficult-to-Treat Resistance Bacteria and Novel Diagnostics at the Foreground. J Clin Med. 2025 Mar 19;14(6):2087.
24. Chamat-Hedemand S, Dahl A, Østergaard L, Arpi M, Fosbøl E, Boel J, et al. Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species. Circulation. 2020 Aug 25;142(8):720–30.
25. Hernández RB, Juliá MB. Enterococcus spp. and Streptococcus spp. bloodstream infections: epidemiology and therapeutic approach. Revista Española de Quimioterapia. 2023 Nov 27;36(Suppl 1):2.
26. Irfan Z, Afridi FI, Fatima A, Zafar H, Pervaiz YM, Farooq L. Prevalence of Extensively Drug Resistant Salmonella typhi and its susceptibility against meropenem, tigecycline, fosfomycin and azithromycin among clinical isolates from a tertiary care hospital laboratory: Susceptibility in Extensively Drug Resistant Salmonella typhi. Pakistan Journal of Health Sciences. 2024 Aug 31:49-54.
27. Khan M, Khattak MT, Gul A, Riaz M, Zahra FT. A comparable risk of extensively drug-resistant typhoid fever in the pediatric cohort during the COVID-19 pandemic. Int J Health Sci (Qassim). 2024;18(1):24–8.
28. Nizamuddin S, Ching C, Kamal R, Zaman MH, Sultan F. Continued Outbreak of Ceftriaxone-Resistant Salmonella enterica Serotype Typhi across Pakistan and Assessment of Knowledge and Practices among Healthcare Workers. Am J Trop Med Hyg. 2021 Jan 25;104(4):1265–70.
29. Ahmad J, Khan MA, Atif M, Rahman ZU, Nasir A, Ahmad HM, et al. Incidence and antimicrobial resistance profile of multi-drug resistant Salmonella typhi isolated from blood samples in Khyber Pakhtunkhwa, Pakistan. Diagn Microbiol Infect Dis. 2026 Feb;114(2):117122.
30. Lee YL, Wang WY, Ko WC, Hsueh PR. Global epidemiology and antimicrobial resistance of Enterobacterales harbouring genes encoding OXA-48-like carbapenemases: insights from the results of the Antimicrobial Testing Leadership and Surveillance (ATLAS) programme 2018–2021. Journal of Antimicrobial Chemotherapy. 2024 Jul 1;79(7):1581–9.
31. Fadlallah M, Salem Sokhn E. Epidemiology and resistance profiles of Enterobacterales in a tertiary care hospital in Lebanon: a 4-year retrospective study. The Journal of Infection in Developing Countries. 2023 Jul 27;17(07):986–93.
32. Lee YL, Wang WY, Ko WC, Hsueh PR. Global epidemiology and antimicrobial

resistance of Enterobacterales harbouring genes encoding OXA-48-like carbapenemases: insights from the results of the Antimicrobial Testing Leadership and Surveillance (ATLAS) programme 2018–2021. Journal of Antimicrobial Chemotherapy. 2024 Jul;79(7):1581-9.

33. Epstein L, Mu Y, Belflower R, Scott J, Ray S, Dumyati G, et al. Risk Factors for Invasive Methicillin-Resistant Staphylococcus aureus Infection After Recent Discharge From an Acute-Care Hospitalization, 2011–2013. Clinical Infectious Diseases. 2016 Jan 1;62(1):45–52.
34. Farsi S, Salama I, Escalante-Alderete E, Cervantes J. Multidrug-Resistant Enterococcal Infection in Surgical Patients, What Surgeons Need to Know. Microorganisms. 2023 Jan 17;11(2):238.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	