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FREQUENCY OF GRAM-NEGATIVE BACTERIA AND THEIR ANTIBIOTIC SUSCEPTIBILITY OF BLOOD-STREAM INFECTION IN CHILDREN OF KHYBER PAKHTUNKHWA

Original Research

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ABSTRACT

Background: Bloodstream infections (BSIs) caused by Gram-negative bacteria (GNB) pose a significant global health concern, particularly due to their increasing resistance to antibiotics. The rapid emergence of multidrug-resistant (MDR) strains has complicated treatment strategies, leading to increased morbidity and mortality. Surveillance of antimicrobial susceptibility patterns is essential to guide effective therapeutic interventions and curb the spread of resistant bacterial strains.

Objective: To determine the frequency of Gram-negative bacteria in bloodstream infections among pediatric patients and assess their antibiotic susceptibility patterns.

Methods: A cross-sectional study was conducted over eight months in two tertiary care hospitals in Peshawar, Pakistan. A total of 2,247 blood samples from suspected bloodstream infection cases were collected and cultured on MacConkey agar for bacterial isolation. Identification of bacterial species was performed using standard morphological and biochemical methods. Antibiotic susceptibility testing was conducted using the Kirby-Bauer disk diffusion method, following Clinical and Laboratory Standards Institute (CLSI) 2020 guidelines. The resistance and susceptibility patterns were analyzed.

Results: Among the 2,247 blood samples, 117 (5.2%) tested positive for Gram-negative bacteria. Males accounted for 72 (61.5%) of the cases, while females constituted 45 (38.5%). Salmonella typhi was the most frequently isolated pathogen (97 cases, 82.9%), followed by Pseudomonas aeruginosa (4 cases, 3.4%), Klebsiella pneumoniae (4 cases, 3.4%), and Escherichia coli (3 cases, 2.5%). High resistance was observed against Ciprofloxacin, Chloramphenicol, Ampicillin, and Cefepime, whereas Meropenem, Imipenem, and Azithromycin showed the highest sensitivity.

Conclusion: The study highlights the increasing prevalence of antibiotic-resistant Gram-negative bacteria in bloodstream infections, emphasizing the urgent need for antimicrobial stewardship programs. The widespread resistance to commonly used antibiotics necessitates continuous surveillance and stringent policies to regulate antibiotic use in clinical settings.

Keywords: Antibiotic Resistance, Bloodstream Infections, Gram-negative Bacteria, Multidrug Resistance, Pediatric Infections, Salmonella typhi, Susceptibility Testing.

INTRODUCTION

Bloodstream infections (BSIs) represent a significant public health challenge worldwide, with an increasing prevalence and a substantial risk of morbidity and mortality, particularly in pediatric populations. These infections are caused by various bacterial pathogens, among which Gram-negative bacteria play a crucial role due to their ability to develop resistance to commonly used antibiotics. The transmission of bacterial infections occurs through multiple routes, including airborne droplets, direct contact, contaminated food and water, and vectors. Humans often serve as the primary or sole natural hosts for many bacterial pathogens, contributing to their widespread impact on global health (1). Gram-negative bacteria pose a serious clinical concern, especially in healthcare settings where immunocompromised individuals, such as those admitted to intensive care units (ICUs), are at heightened risk. The majority of clinically relevant Gram-negative bacteria belong to the Enterobacteriaceae family and non-fermenters, with additional pathogenic species such as Neisseria spp., Haemophilus spp., Helicobacter pylori, and Chlamydia trachomatis also contributing to significant infections (2). The burden of Gram-negative bloodstream infections is further exacerbated by rising antimicrobial resistance, which limits treatment options and complicates patient management. Surveillance data from Korea (2016–2017) identified Escherichia coli and Staphylococcus aureus as the predominant pathogens in BSIs, a trend similarly observed in European antimicrobial resistance surveillance reports spanning from 2002 to 2009. In contrast, regions such as Malawi report Salmonella typhi, non-typhoidal Salmonella, and Streptococcus pneumoniae as common causative agents of BSIs, emphasizing the geographical variability in pathogen distribution (3).

Antimicrobial resistance patterns differ across regions, significantly impacting treatment efficacy. Gram-negative bacteria, including carbapenem-resistant Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter baumannii, and Stenotrophomonas maltophilia, pose a considerable therapeutic challenge. Resistance to carbapenems and third-generation cephalosporins is particularly alarming, necessitating the development and clinical use of novel antimicrobial agents such as ceftolozane-tazobactam, imipenem-colistin-tazobactam, meropenem-vaborbactam, plazomicin, eravacycline, and cefiderocol (4). The emergence of these resistant pathogens underscores the need for continuous surveillance and updated treatment strategies tailored to regional epidemiological trends. Despite the growing threat of Gram-negative bloodstream infections, there is limited regional data on their prevalence and antibiotic susceptibility patterns, particularly in pediatric populations. Understanding the antimicrobial resistance trends in these infections is essential for optimizing treatment guidelines and improving patient outcomes. This study was conducted at referral hospitals in Khyber Pakhtunkhwa to determine the frequency of Gram-negative bacterial bloodstream infections in children and assess their antibiotic susceptibility patterns. The findings will contribute to the growing body of knowledge on antimicrobial resistance, providing valuable insights for clinical management and guiding future research efforts in the region (5).

METHODS

This cross-sectional study was conducted in 2022 at Rahman Medical Institute Hospital and Hayat Abad Medical Complex, Peshawar, over a period of eight months following ethical approval from the institutional review board. The study aimed to determine the frequency of Gram-negative bacterial bloodstream infections and assess their antibiotic susceptibility patterns in pediatric patients. Informed consent was obtained from the legal guardians of all participants prior to sample collection (6). A total of 2,247 blood samples were collected from patients under the age of 18 who were suspected of having bloodstream infections. The study included hospitalized patients and inpatients with clinical suspicion of bacterial infections who had not received any antibiotic treatment in the preceding 48 hours. Patients with conditions such as diabetes, leukemia, thalassemia, or other severe systemic illnesses were excluded to minimize confounding variables related to underlying immunosuppressive states (7).

Blood samples ranging from 1 mL (for neonates) to 5 mL (for children) were obtained through venipuncture under aseptic conditions and immediately transferred into two separate resin-containing bottles—one for aerobic and one for anaerobic bacterial culture. Sodium polyanethol sulfonate (SPS), a commonly used anticoagulant, was employed to facilitate bacterial growth. The samples were subsequently incubated and cultivated for the isolation of Gram-negative bacterial strains. Standard morphological and biochemical tests were performed to identify bacterial species, including subculturing on blood agar and MacConkey agar (Oxoid, UK) followed by overnight aerobic incubation at 37°C. The colony morphology and culture characteristics were analyzed to confirm bacterial identification (8,9). Antimicrobial susceptibility testing was conducted using the Kirby-Bauer disk diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) 2020 guidelines. The bacterial isolates were inoculated on Mueller-Hinton agar (Oxoid, UK), and the zone of inhibition around antimicrobial discs was measured to determine susceptibility patterns. The findings were interpreted based on CLSI standards to categorize the isolates as susceptible, intermediate, or resistant (10,11).

The selection of antimicrobial agents for susceptibility testing was based on commonly prescribed antibiotics for Gram-negative bacterial infections, following the Clinical and Laboratory Standards Institute (CLSI) 2020 guidelines. A panel of broad-spectrum and targeted antibiotics, including β-lactams, carbapenems, aminoglycosides, fluoroquinolones, and polymyxins, was utilized to assess resistance patterns. The exclusion of patients with diabetes, leukemia, and thalassemia was primarily due to their altered immune responses and pre-existing risk of bloodstream infections, which could introduce variability in antimicrobial susceptibility patterns. These patients often present with multidrug-resistant infections due to recurrent hospitalizations and prolonged antibiotic exposure, which may not reflect the resistance trends in the general pediatric population. However, future studies focusing on these high-risk groups could provide valuable insights into the specific resistance mechanisms and tailored treatment strategies for immunocompromised patients (12).

RESULTS

A total of 2,247 blood samples from pediatric patients suspected of bloodstream infections were analyzed, of which 117 (5.2%) tested positive for Gram-negative bacterial infections. Among these, 72 (62%) cases were observed in males, while 45 (38%) were in females. Age-wise distribution of positive cases revealed that the highest prevalence was among children aged 0 to 3 years, with 32 cases. In children aged 4 to 6 years, 22 cases were identified, while 23 cases were observed in those aged 7 to 9 years. The number of positive cases decreased with age, with 18 cases in the 10 to 12-year group, 14 cases in the 13 to 15-year group, and the lowest incidence of 8 cases among those aged 16 to 18 years. Among the isolated bacterial species, Salmonella typhi had the highest positivity rate, accounting for 97 cases (4.3%), followed by Pseudomonas aeruginosa and Klebsiella with 4 cases each (0.17%). Other detected pathogens included Escherichia coli (3 cases, 0.13%), Acinetobacter (3 cases, 0.13%), Citrobacter freundii (2 cases, 0.08%), Salmonella paratyphi (1 case, 0.04%), Burkholderia cepacia (1 case, 0.04%), Stenotrophomonas maltophilia (1 case, 0.04%), and Enterobacter vulneris (1 case, 0.04%).

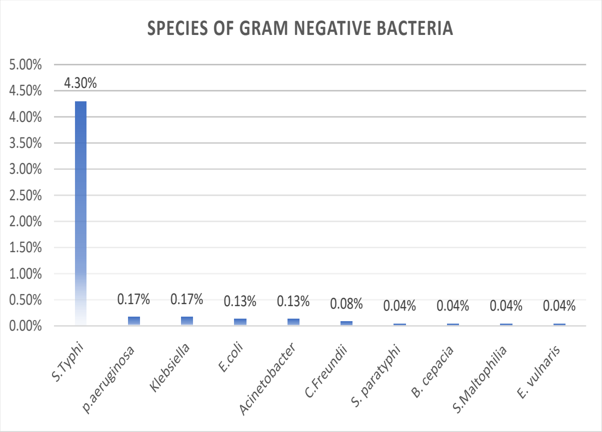

Fig: Species of Gram negative Bacteria

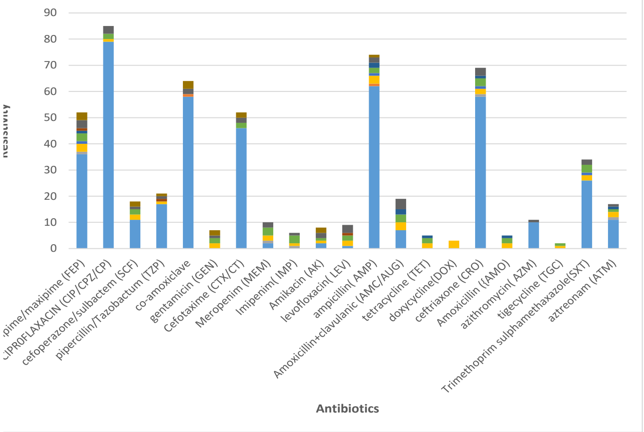

Figure 1.3. Resistivity Shown to Antibiotics

Antimicrobial susceptibility testing of the Gram-negative bacterial isolates demonstrated the highest sensitivity to Meropenem, Azithromycin, Imipenem, Trimethoprim-sulfamethoxazole (SXT), Amikacin, Tigecycline (TGC), and Gentamicin (GEN). In contrast, high resistance was observed against Ciprofloxacin (CIP), Chloramphenicol (C), Ampicillin (AMP), Co-amoxiclav, Ceftriaxone (CRO), Cefotaxime (CTX), Cefepime (FEP), and Trimethoprim-sulfamethoxazole (SXT). A detailed resistance spectrum revealed that Salmonella typhi exhibited notable resistance to Ceftriaxone, Ampicillin, Ciprofloxacin, and Co-amoxiclav, while Pseudomonas aeruginosa demonstrated resistance to Cefepime, Piperacillin-Tazobactam, and Ciprofloxacin. Klebsiella showed resistance to Ceftriaxone, Ampicillin, and Cefotaxime, whereas E. coli exhibited resistance to Ampicillin, Ciprofloxacin, and Trimethoprim-sulfamethoxazole. Acinetobacter and Citrobacter freundii displayed resistance to multiple beta-lactam antibiotics, including Ceftriaxone and Cefotaxime. Statistical analysis of antimicrobial resistance patterns across different age groups and genders revealed no significant difference in resistance prevalence ($p > 0.05$), indicating a uniform distribution of resistance trends among pediatric patients. Comparative analysis showed that males exhibited a slightly higher prevalence of antimicrobial resistance than females, though this difference was not statistically significant. Additionally, a substantial proportion of isolated Gram-negative bacteria demonstrated multi-drug resistance (MDR), with Salmonella typhi, Klebsiella, Pseudomonas aeruginosa, and Acinetobacter exhibiting resistance to at least three or more major antibiotic classes. Notably, MDR Salmonella typhi strains displayed concurrent resistance to Ceftriaxone, Ciprofloxacin, and Co-amoxiclav, while MDR Pseudomonas aeruginosa showed resistance to Cefepime, Piperacillin-Tazobactam, and Ciprofloxacin. The high prevalence of MDR strains underscores the urgent need for targeted antimicrobial stewardship strategies to optimize treatment protocols and mitigate the spread of resistant pathogens in pediatric bloodstream infections.

Table 1: Age wise distribution

Species of Gram Negative Bacteria											
Age (Years)	**S. typhi**	**Klebsiella**	**P.aeruginosa**	**E.coli**	**Acinetobacter**	**C.freundii**	**S. paratyphi**	**B.Cepecia**	**S.Maltophilia**	**E.vulneris**	**Total**
0 to 3	18	3	2	3	2	1	-	1	-	1	31
4 to 6	22	-	-	-	-	1	1	-	-	-	24
7 to 9	21	-	-	-	-	-	-	-	-	-	21
10 to 12	15	-	1	-	-	-	-	-	1	-	17
13 to 15	13	1	-	-	1	-	-	-	-	-	15
16 to 18	8	-	1	-	-	-	-	-	-	-	9
Total	97	4	4	3	3	2	1	1	1	1	117

Table 2: Antibiotic Resistant spectrum of Gram-negative bacteria

Gram negative bacteria's																				
Bacteria	***S. typhi***		***S. paratyphi***		***S. Maltophilia***		***E. coli***		***E. Vulnaris***		***Acinetobacter***		***C. freundii***		***B. Cepecia***		***Klebsiella***		***P.aeruginosa***	
Antimicrobials	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
cefipime/maxipime (FEP)	1	36	1	0	0	1	0	3	0	1	0	3	1	1	0	1	1	3	1	3
CIPR0FLAXACIN (CIP/CPZ/CP)	17	79	1	0	-	-	2	1	-	-	1	2	1	1	-	-	1	3	2	2
cefoperazone/sulbactem (SCF)	20	11	1	0	1	0	1	2	1	0	1	2	2	0	1	0	3	1	1	2
pipercillin/Tazobactum (TZP)	18	17	1	0	1	0	2	1	1	0	-	-	2	0	0	1	3	1	2	1
co-amoxiclave	1	58	0	1	-	-	-	-	1	0	-	-	-	-	-	-	2	2	1	3
gentamicin (GEN)	23	50	1	0	1	0	0	2	1	0	1	2	2	0	1	0	2	1	1	2
Cefotaxime (CTX/CT)	3	46	1	0	1	0	1	0	1	0	1	2	2	0	0	1	2	2	1	2

Bacteria	***S. typhi***		***S. paratyphi***		***S. Maltophilia***		***E. coli***		***E. Vulnaris***		***Acinetobacter***		***C. freundii***		***B. Cepecia***		***Klebsiella***		***P.aeruginosa***	
Meropenim (MEM)	86	2	1	0	0	1	1	2	1	0	0	3	2	0	1	0	2	2	3	1
Imipenim(IMP)	43		1	0	0	1	2	1	1	0	0	3	2	0	1	0	3	1	3	1
Amikacin (AK)	27	2	1	0	1	0	2	1	1	0	2	1	2	0	1	0	2	2	1	2
levofloxacin(LEV)	36	1	-	-	-	-	1	2	1	0	1	2	1	1	0	1	1	3	2	2
ampicillin(AMP)	1	62	0	1	-	-	0	3	0	1	1	2	0	2	-	-	2	2	3	1
Amoxicillin+clavulanic (AMC/AUG)	11	7	1	0	1	0	0	3	1	0	0	3	0	2	1	0	0	4	1	3
tetracycline (TET)	11	11	-	-	1	0	1	2	1	0	1	2	0	1	1	0	1	3	2	2
doxycycline(DOX)	14	13	-	-	-	-	0	3	-	-	1	2	1	1	0	1	2	2	0	0
ceftriaxone (CRO)	2	58	1	0	0	1	0	2	0	1	0	3	1	1	1	0	1	3	0	4
Amoxicillin ({AMO)	-	-	0	1	1	0	1	2	0	1	1	2	1	1	1	0	3	1	-	-
azithromycin(AZM)	80	10	0	1	1	0	-	-	0	1	-	-	-	-	1	0	3	1	2	2
tigecycline (TGC)	24	5	1	0	1	0	2	1	1	0	2	1	-	-	1	0	4	0	-	-
Trimethoprim sulphamethaxazole(SXT)	33	26	1	0	1	0	1	2	0	1	0	3	2		1	0	2	2	-	-
aztreonam (ATM)	1	11	1	0	1	1	1	2	1	0	2	1	1	1	1	0	3	1	-	-

***n*: Number, S: Sensitive strains, R: Resistant strains**

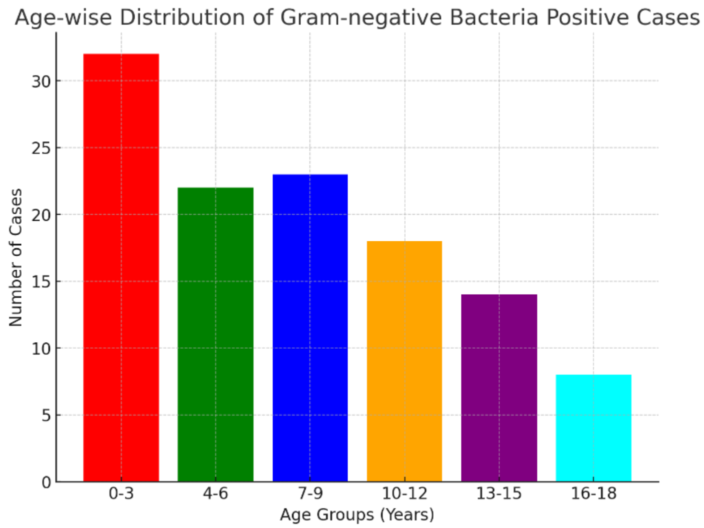

Figure 2 Age Wise Distribution of Gram-Negative Bacteria Positive Cases

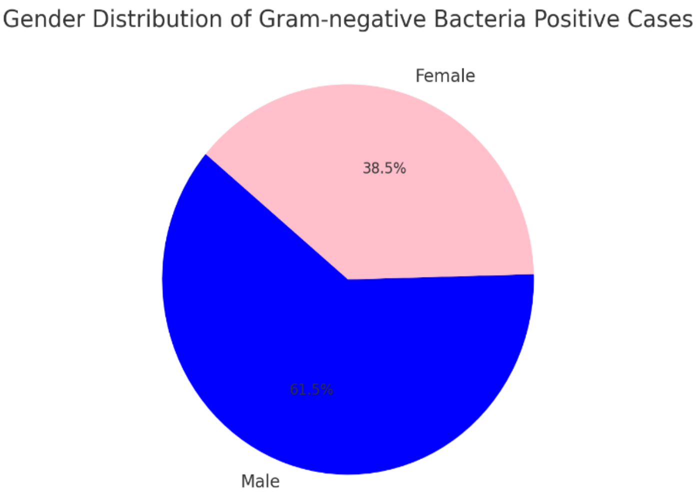

Figure 1 Gender Distribution of Gem-Negative Bacteria Positive Cases

DISCUSSION

The study investigated the prevalence and antimicrobial resistance patterns of Gram-negative bloodstream infections in pediatric patients under 18 years of age in hospitals across Peshawar. Out of 2,247 blood cultures, 117 (5.2%) tested positive for Gram-negative bacteria, with a higher prevalence observed in males (61.5%) compared to females (38%). The most frequently isolated pathogen was *Salmonella typhi*, accounting for 82% of positive cases, followed by *Pseudomonas aeruginosa* and *Klebsiella* (3.4% each), and *Escherichia coli* (2.5%). These findings align with previous studies that reported *Salmonella typhi* as the predominant pathogen in bloodstream infections, though variations in prevalence rates can be attributed to differences in study populations and sample sizes. A similar study conducted in a tertiary care hospital in Peshawar reported a higher positivity rate of 19.6%, which may be due to differences in study settings and patient selection criteria. Despite variations, both studies consistently highlight the significance of Gram-negative pathogens in bloodstream infections and their increasing antimicrobial resistance (13). Comparative analysis with other international studies reveals differences in bacterial distribution and resistance patterns, largely influenced by geographical and demographic factors. A study conducted in Saudi Arabia reported a much higher number of positive Gram-negative bacterial cases, with *Pseudomonas aeruginosa* and *Klebsiella* being the most commonly isolated pathogens. The broader age range of participants in that study, spanning from infancy to over 80 years, makes direct comparisons challenging. However, findings related to *Pseudomonas aeruginosa* resistance align with the current study, demonstrating high resistance to third-generation cephalosporins and beta-lactam antibiotics. Another study from a tertiary care hospital in Tanzania found *Pseudomonas aeruginosa* to be the most prevalent Gram-negative organism, contrasting with the current study where *Salmonella typhi* was the dominant pathogen. Differences in bacterial prevalence may be influenced by regional epidemiological factors, antibiotic prescription practices, and specific inclusion criteria, such as the Tanzanian study's focus on malnourished children (14,15).

Antimicrobial resistance trends observed in this study further emphasize the growing concern of multi-drug resistance (MDR) in bloodstream infections. The findings indicate a high degree of resistance to *Ciprofloxacin, Chloramphenicol, Ampicillin, Co-amoxiclav, Ceftriaxone, and Cefotaxime*, while susceptibility remained highest to *Meropenem, Azithromycin, Imipenem, and Amikacin*. A study conducted in a similar setting identified *Salmonella typhi* as a highly resistant pathogen, supporting the current findings that indicate its significant resistance to *Ceftriaxone, Ciprofloxacin, and Co-amoxiclav*. In contrast, *Pseudomonas aeruginosa* exhibited resistance to *Cefepime, Piperacillin-Tazobactam, and Ciprofloxacin*, consistent with reports from other studies conducted in both regional and international settings. The widespread use of empirical and prophylactic antibiotic therapy, particularly in developing countries, contributes significantly to this resistance crisis (16,17). The study has several strengths, including a relatively large sample size and a focus on pediatric patients, which remains an underreported population in antimicrobial resistance research. However, certain limitations must be acknowledged. The study was limited to specific hospitals in Peshawar, restricting the generalizability of findings to other regions. The lack of molecular characterization of resistance genes limits a deeper understanding of the underlying mechanisms driving antimicrobial resistance. Additionally, the exclusion of immunocompromised patients, such as those with diabetes, leukemia, and thalassemia, may have led to an underestimation of the true burden of resistant bloodstream infections in high-risk pediatric populations. Future studies should consider including these patient groups to provide a more comprehensive assessment of antimicrobial resistance trends (18,19).

The increasing prevalence of MDR strains observed in this study underscores the urgent need for antibiotic stewardship programs. The implementation of mandatory antibiotic susceptibility testing before prescribing antimicrobials can help optimize treatment strategies and reduce resistance development. Regular surveillance studies are essential to monitor resistance trends and guide empirical antibiotic therapy. Strengthening policies on antibiotic use in healthcare facilities and regulating over-the-counter sales of antibiotics is necessary to combat the rising threat of antimicrobial resistance. Additionally, increasing awareness among healthcare professionals and the general public regarding the risks associated with the indiscriminate use of antibiotics is crucial to curbing the antibiotic resistance crisis (20,21).

CONCLUSION

The findings of this study highlight the alarming rise in antibiotic resistance among Gram-negative bacterial bloodstream infections in pediatric patients, posing a significant threat to public health. The predominance of Salmonella typhi, followed by Pseudomonas aeruginosa and Escherichia coli, underscores the urgent need for targeted surveillance and antimicrobial stewardship strategies. High resistance to commonly used antibiotics, particularly fluoroquinolones, beta-lactams, and aminopenicillins, raises concerns about the diminishing efficacy of standard treatment options. In contrast, susceptibility to carbapenems and select aminoglycosides provides some therapeutic alternatives, though their overuse could further accelerate resistance. The growing burden of antimicrobial resistance necessitates stricter policies on antibiotic use, routine susceptibility testing before prescribing, and public awareness initiatives to curb the indiscriminate use of antibiotics. Immediate action is required to prevent the further escalation of resistance and safeguard the effectiveness of available antimicrobial therapies for future generations.

AUTHOR CONTRIBUTIONS

Author	Contribution
Shah Faisal Jamal	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Shabir Ahmad*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Noman Khan	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Yasir	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Miraj Ud Din	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Nayab Gul	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Lee M, Scardina T, Zheng X, Patel SJ. Clinical Performance and Impact of Accelerate Pheno for Gram-negative Bacteremia in Hospitalized Children. Clin Ther. 2020;42(9):1630-6.

2. Martora F, Pagliuca C, Della Pepa ME, Della Rocca MT, Curto S, Iovene MR, et al. Campylobacter jejuni bacteremia in Italian pediatric patients with acute lymphoblastic leukemia: Report of two cases. New Microbiol. 2020;43(2):96-8.

3. Abebe W, Tegene B, Feleke T, Sharew B. Bacterial Bloodstream Infections and their Antimicrobial Susceptibility Patterns in Children and Adults in Ethiopia: a 6-Year Retrospective Study. Clin Lab. 2021;67(11).

4. Grigorova EV, Nemchenko UM, Voropaeva NM, Belkova NL, Noskova OA, Savilov ED. Effect of Disinfectants with Different Active Ingredients on Biofilm Formation in Pseudomonas aeruginosa. Bull Exp Biol Med. 2021;171(6):745-9.

5. Miloudi M, El Kamouni Y, Oulhadj H, Arsalane L, Zouhair S. Comamonas testosteroni appendicitis: About a case and review of the literature. Infect Dis Now. 2021;51(4):395-7.

6. Negash AA, Asrat D, Abebe W, Hailemariam T, Wubete A, Aseffa A, et al. Etiology, antibiotic susceptibility and prognostic factors of pediatric community-acquired sepsis in Addis Ababa, Ethiopia. J Infect Dev Ctries. 2021;15(1):113-22.

7. Cook A, Sharland M, Yau Y, Group P, Bielicki J. Improving empiric antibiotic prescribing in pediatric bloodstream infections: a potential application of weighted-incidence syndromic combination antibiograms (WISCA). Expert Rev Anti Infect Ther. 2022;20(3):445-56.

8. Godfrey E, Majaliwa E, Assenga EN. Aetiology, antimicrobial susceptibility and outcome of children with sepsis, admitted at Muhimbili National Hospital, Dar es Salaam. Pan Afr Med J. 2022;42:167.

9. Stokes W, Peirano G, Matsumara Y, Nobrega D, Pitout JDD. Population-based surveillance of Enterobacter cloacae complex causing blood stream infections in a centralized Canadian region. Eur J Clin Microbiol Infect Dis. 2022;41(1):119-25.

10. Tiewsoh JBA, Gupta P, Angrup A, Ray P. Haemophilus influenzae bacteremia: A 5-year (2016-2020) retrospective study analysing the clinical and laboratory features. Indian J Med Microbiol. 2022;40(3):436-9.

11. Wang J, Lv Y, Yang W, Zhao P, Yin C. Epidemiology and clinical characteristics of infection/colonization due to carbapenemase-producing Enterobacterales in neonatal patients. BMC Microbiol. 2022;22(1):177.

12. Worku M, Belay G, Tigabu A. Bacterial profile and antimicrobial susceptibility patterns in cancer patients. PLoS One. 2022;17(4):e0266919.

13. Gumus DD, Demir OO, Aykac K, Hazirolan G, Avci H, Ceyhan M, et al. Gram-negative bacteremia, the risk factors, and outcome in children. Diagn Microbiol Infect Dis. 2024;109(3):116324.

14. Kumaresan M, Manoharan M, Sugumar M, Sistla S. Species distribution and antimicrobial susceptibility of Burkholderia cepacia complex isolates in clinical infections: Experience from a tertiary care hospital, Southern India. Indian J Med Microbiol. 2024;49:100613.

15. Mareković I, Vujnović T, Radanović J, Herljević Z, Kuliš T, Pavlović M, et al. Bloodstream Infections in Pediatric Oncology Patients: Bacterial Pathogen Distribution and Antimicrobial Susceptibility at the University Hospital Centre Zagreb, Croatia-A 5-Year Analysis. J Pediatr Hematol Oncol. 2024;46(2):e156-e63.

16. Rezk S, Ashraf N, Heshmat H, Elsawaf G, Elsheredy A. Rapid detection of carbapenemase-producing gram-negative bacteria directly from blood culture bottles for a reliable guided empiric therapy. Acta Microbiol Immunol Hung. 2024;71(2):140-7.

17. Sajedi Moghaddam S, Mamishi S, Pourakbari B, Mahmoudi S. Bacterial etiology and antimicrobial resistance pattern of pediatric bloodstream infections: a 5-year experience in an Iranian referral hospital. BMC Infect Dis. 2024;24(1):373.

18. Shao H, Zhang X, Li Y, Gao Y, Wang Y, Shao X, et al. Epidemiology and drug resistance analysis of bloodstream infections in an intensive care unit from a children's medical center in Eastern China for six consecutive years. Int Microbiol. 2024;27(5):1345-55.

19. Wen SCH, Harris PNA, Forde B, Permana B, Chatfield MD, Lau CL, et al. Characterization of Gram-negative Bloodstream Infections in Hospitalized Australian Children and Their Clinical Outcomes. Clin Infect Dis. 2024;79(3):734-43.

20. Mahmood, Waqas, Majida Khan, Sher Alam Khan, Mohammad Ali Siddiqui, Abdul Sami Shaikh, Muhammad Jamal, and Maryam Ehsan. "Review of Pharmacological Strategies for Reducing Antibiotic Resistance in Healthcare Settings." Insights-Journal of Life and Social Sciences, Volume 3 Issue 1 2025 Life (Health & Biology Studies) https://doi.org/10.71000/nm39hg89.

21. Koh MCY, Ngiam JN, Chew KL, Smitasin N, Lum LH, Allen DM. Clinical presentation and outcomes of bloodstream infection with intrinsically carbapenem-resistant non-fermenting gram-negative organisms: Stenotrophomonas maltophilia, Elizabethkingia spp. and Chryseobacterium spp. in Singapore, from 2012 to 2024. BMC Infect Dis. 2025;25(1):273.