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Bacterial Pathogens and Antimicrobial Resistance in Pediatric Leukemia: Implications for Infection Control in Immunocompromised Children

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ABSTRACT

The present study examined bacterial profiles and antimicrobial resistance in children with leukemia to understand how underlying malignancy influences therapeutic response to severe infections. Thirty pediatric patients aged 1–16 years (18 males, 12 females) were retrospectively analyzed. Clinical cultures identified 13 bacterial species, including both Gram-positive (n = 8) and Gram-negative (n = 5) organisms. The cohort included patients with different leukemia subtypes: most girls were diagnosed with B-cell acute lymphoblastic leukemia (ALL). In contrast, cases of acute myeloid leukemia were observed in one boy and one girl. Among boys, T-cell ALL and pre-B ALL were also recorded. The dominant pathogens were methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *S. aureus* (MSSA), *Klebsiella* spp., and *Staphylococcus epidermidis*. Because of severe immunosuppression, many patients required intensive care and treatment with potent antibiotics such as linezolid, vancomycin, and ertapenem, which generally retained activity despite variable resistance patterns. The study highlights the clinical importance of defining pathogen distribution and resistance characteristics in pediatric leukemia. A precise understanding of local antimicrobial susceptibility is essential for guiding targeted therapy and improving outcomes in immunocompromised children with serious bacterial infections.

Keywords: multidrug-resistant infections, Antibiotic resistance, Infection Management, Antimicrobial Susceptibility, Pediatric leukemia, Immunocompromised patients

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Introduction

Acute lymphoblastic leukemia in pediatrics: epidemiology, outcomes, and challenges in resource-limited settings

Acute lymphoblastic leukemia (ALL) represents the most frequently diagnosed malignancy in children, accounting for roughly 80% of pediatric cancer cases managed in oncology practice [1]. Over recent decades, therapeutic advances have led to substantial improvements in outcomes, with complete remission rates now exceeding 90% in many developed settings [2, 3]. Nevertheless, relapse still occurs in approximately 20% of cases, and disease-related mortality remains around 15% [2, 3]. In contrast, survival outcomes in low- and middle-income countries are considerably lower, ranging from 50% to 75%, largely due to diagnostic delays and limited access to standardized treatment protocols [4]. ALL is most commonly diagnosed between 3 and 6 years of age and shows a slight male predominance, with a reported male-to-female ratio of approximately 1.4:1 [5]. Because pediatric leukemia patients are profoundly immunocompromised, they are highly susceptible to infectious complications, which represent a major cause of morbidity and treatment-related mortality during intensive chemotherapy. These infections are further complicated by the rising prevalence of antimicrobial resistance,

which reduces therapeutic effectiveness and increases clinical risk. Therefore, understanding pathogen distribution alongside resistance patterns is essential for optimizing antimicrobial strategies and improving outcomes in this high-risk population.

The critical role of addressing antimicrobial resistance in pediatric leukemia: challenges and strategies

The rise of antimicrobial resistance (AMR) continues to undermine the effectiveness of standard therapies and contributes to recurrent, difficult-to-treat infections in vulnerable patients [6]. On a global scale, drug-resistant bacterial infections are responsible for an estimated 700,000 deaths annually, and this number could exceed 10 million per year by 2050 if no effective interventions are implemented [7, 8]. These projections highlight the need for coordinated action under the One Health framework, integrating human, animal, and environmental health strategies to limit the spread of resistant organisms [9]. This issue is particularly pressing in low- and middle-income countries, where surveillance systems and infection control resources remain limited [10, 11]. In Romania, AMR was linked to approximately 4,300 direct deaths and 16,500 associated deaths in 2019, underscoring its growing clinical burden.

In the present study, 30 pediatric leukemia patients were analyzed (18 males and 12 females), with ages ranging from early infancy to adolescence; the youngest case was a girl aged 1 year and 10 months. Due to intensive chemotherapy regimens involving cytotoxic agents, most patients required additional supportive therapy, including liver-protective medications to manage treatment-related toxicity.

Because leukemia and its treatment profoundly impair immune function, even minor infections may rapidly progress to severe or fatal outcomes. This underscores the importance of timely pathogen identification and appropriate antimicrobial selection in clinical management. The aim of this study was therefore to identify the predominant bacterial agents in pediatric leukemia cases and to evaluate therapeutic responses, thereby improving infection control strategies in this high-risk group.

Fungal infections also represent a significant complication in immunocompromised pediatric patients, particularly those caused by *Candida albicans* and *Candida parapsilosis*. These pathogens are frequently associated with bloodstream infections and invasive disease, requiring prompt antifungal intervention. Fluconazole was widely used in this cohort due to its established antifungal activity against *Candida* species and its favorable safety profile.

Bridging pediatric leukemia and antimicrobial resistance: insights from pathogen distribution and treatment response

The emergence of multidrug-resistant bacteria, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), poses a serious challenge in the management of infections in children with leukemia. Because these patients are severely immunocompromised, infectious complications can escalate quickly, making rapid microbiological diagnosis and appropriate antimicrobial selection critical for survival. However, pediatric-specific data remain limited, especially in resource-constrained settings. In Romania, where antimicrobial resistance represents an increasing public health concern, pediatric oncology patients constitute a particularly high-risk population, underscoring the need for region-specific epidemiological evidence to guide therapy.

In the present cohort, 13 bacterial pathogens were identified, with MRSA being the most frequently isolated organism (11 cases, 36.6%), followed by methicillin-sensitive *S. aureus* (MSSA, 6 cases, 20%). When empirical treatment was ineffective, antimicrobial susceptibility testing became essential for guiding therapy modification. Linezolid was the most commonly used agent for MRSA infections, administered either as monotherapy or in combination regimens. Other antibiotics applied based on clinical severity and susceptibility results included gentamicin, meropenem, vancomycin, amikacin, ceftriaxone, and ertapenem.

Treatment decisions were adjusted according to both microbiological findings and patient condition, with linezolid and several broad-spectrum β-lactams showing the most reliable clinical response after initial treatment failure.

Given the extreme vulnerability of pediatric leukemia patients, even minor infections can progress rapidly to severe disease. This highlights the importance of timely pathogen identification and continuous monitoring of local resistance patterns to support rational antimicrobial use. The aim of this study was therefore to describe bacterial distribution and resistance characteristics in pediatric leukemia patients from a single Romanian center and to evaluate their impact on treatment outcomes.

Overall, continuous surveillance of antimicrobial resistance is essential, particularly in countries with a high AMR burden such as Romania [12]. Improving diagnostic speed, optimizing antibiotic stewardship, and tailoring

therapy to local resistance profiles are key strategies to enhance outcomes and reduce infection-related mortality in this vulnerable population.

Materials and Methods

This investigation focused on children with acute lymphoblastic leukemia (ALL) treated in the Pediatric Oncology Department of the County Emergency Clinical Hospital of Craiova from January 2022 to January 2024. All included patients experienced severe infectious complications associated with intensive oncological therapy, occurring in the context of marked bone marrow suppression. Clinical manifestations included profound neutropenia, thrombocytopenia, anemia, and increased circulating blast cells.

Microbiological evaluation was based on a wide array of clinical specimens collected from different anatomical sites. These included bloodstream samples, upper respiratory tract swabs (nasal and pharyngeal), tracheobronchial aspirates, ocular secretions, cutaneous samples, and cultures obtained from central venous catheters.

The study cohort consisted of 30 pediatric patients aged between 1 and 15 years. The gender distribution included 18 boys and 12 girls. Regarding residence, most patients originated from urban areas (n = 20), while the remainder originated from rural areas (n = 10).

For antimicrobial susceptibility testing, standardized laboratory procedures were applied using commercially sourced antibiotics and antifungal agents, including ampicillin, vancomycin, and fluconazole, obtained from certified manufacturers. All reagents were stored according to the manufacturer's specifications until use.

Phenotypic antimicrobial testing was performed using the Kirby–Bauer disk diffusion method on Mueller–Hinton agar, and minimum inhibitory concentrations (MICs) were determined by broth microdilution. Automated identification and susceptibility interpretation were performed using the VITEK 2 Compact system (bioMérieux, France).

Result interpretation followed the EUCAST 2024 standards for breakpoint classification. Data acquisition and analysis were conducted using the integrated software provided with the automated system, ensuring standardized reporting across all isolates.

Clinical management of these patients required coordinated multidisciplinary care. Treatment strategies were guided by antimicrobial susceptibility results and combined with intensive supportive measures, including blood product transfusions. Drug selection and dosing were individualized based on patient weight and renal function to optimize efficacy and minimize toxicity. In high-risk cases, antifungal and antiviral prophylaxis was also considered due to the elevated risk of opportunistic infections in severely immunocompromised hosts.

Tested antibiotics

Cephalosporins

- Cefepime
- Ceftriaxone
- Cefoxitin
- Cefuroxime
- Ceftazidime
- Ceftaroline
- Cefazolin
- Cefotaxime

Penicillins

- Ampicillin
- Augmentin (Amoxicillin with clavulanic acid)
- Oxacillin
- Ampicillin with Sulbactam
- Penicillin
- Piperacillin/Tazobactam

Fluoroquinolones

- Ciprofloxacin
- Levofloxacin

- Moxifloxacin
- Ofloxacin

Tetracyclines

- Minocycline
- Tigecycline
- Doxycycline
- Tetracycline

Carbapenems

- Ertapenem
- Meropenem
- Imipenem with Cilastatin

Aminoglycosides

- Gentamicin
- Amikacin
- Tobramycin

Macrolides

- Clarithromycin (Clacid)
- Erythromycin

Glycopeptides

- Vancomycin
- Teicoplanin

Oxazolidinones—Linezolid
Lipopeptides—Daptomycin
Folate Pathway Inhibitors—Trimethoprim/Sulfamethoxazole (Biseptol)
Nitrofurans—Nitrofurantoin
Polymyxins—Colistin

- Streptogramins—Quinopristin/Dalfopristin
- Rifamycins—Rifampicin
- Lincosamides—Clindamycin

Others—Chloramphenicol, Fusidic acid

Results and Discussion

The objective of this study was to determine the predominant infectious agents in pediatric patients diagnosed with leukemia. A total of 30 cases, ranging in age from infancy to 16 years, were evaluated. Microbiological analysis identified 13 pathogens, comprising 11 bacterial species and 2 fungal organisms: *Candida albicans* and *Candida parapsilosis*.

To manage fungal infections, fluconazole was administered as the primary antifungal therapy, particularly for infections caused by Candida species, which are well recognized as common causes of bloodstream infection in immunocompromised children.

The bacterial spectrum included both common and less frequently encountered organisms. While major pathogens such as methicillin-resistant Staphylococcus aureus (MRSA), methicillin-sensitive S. aureus (MSSA), Escherichia coli, and Klebsiella spp. were predominant, sporadic isolates such as Staphylococcus hominis and Staphylococcus warneri were also detected. This diversity reflects the complexity of infection management in pediatric leukemia patients and underscores the variability of opportunistic pathogens in this population **(Table 1).**

Table 1. Clinical characteristics and microbial distribution in pediatric leukemia patients with confirmed infections. Abbreviations: M, male; F, female; U, urban; R, rural; Y, years; M (age), months; M (diagnosis), leukemia subtype.

Nr	Age	Sex	Place of residence	Diagnosis	Pathogen
1.	10 Y	M	U	ALL B2	MRSA
2.	10 Y	M	R	ALL L1-T4	*S. pneumoniae*

3.	3 Y 7 M	M	R	ALL pre-B	*Klebsiella* spp.
4.	6 Y 5 M	M	U	ALL B	MRSA
5.	3 Y 9 M	M	R	ALL T	*Staphylococcus warneri*
6.	4 Y 11 M	M	U	ALL B	MRSA
7.	4 Y 8 M	M	R	ALL L1	*Acinetobacter* spp.
8.	3 Y	M	R	AML M1	MRSA
9.	9 Y	F	U	ALL B	MRSA
10.	5 Y	F	U	ALL B	MSSA, *Candida albicans*
11.	3 Y 5 M	M	U	ALL B	MRSA, MSSA
12.	2 Y	M	U	ALL B	MRSA, *S. epidermidis*, *Candida parapsilosis*
13.	7 Y	M	U	ALL B	*E. coli*
14.	15 Y	F	U	ALL B	MSSA, *S. homini*
15.	5 Y	M	R	ALL pre-B	MRSA
16.	5 Y 8 M	F	U	ALL B	*Candida albicans*
17.	3 Y 8 M	F	R	ALL B	E. Coli, recurrent infection
18.	6 Y	M	U	ALL pre-B	MRSA, *P. aeruginosa*
19.	11 Y	F	R	ALL B	MSSA, *Enterobacter* spp., *S. epidermidis*
20.	1 Y 10 M	F	U	ALL B	*Klebsiella* spp.
21.	4 Y 1 M	F	U	AML	*Acinetobacter baumani*
22.	4 Y 5 M	M	U	ALL B	*Klebsiela* spp.
23.	8 Y	M	R	ALL B	MRSA
24.	1 Y 10 M	F	U	ALL B	*Klebsiella pneuminiae*
25.	7 Y	M	U	ALL T	MRSA
26.	15 Y 10 Y	M	U	ALL B	*Pseudomonas aeruginosa*
27.	13 Y 8 M	F	R	ALL B	*S. epidermidis*
28.	8 Y	F	U	ALL B	E coli
29.	4 Y	F	U	ALL B	MSSA
30.	3 Y 10 M	M	U	ALL B	MSSA

The cohort included children aged 1 to 16 years, with most patients (n = 21) falling within the 3–10-year age range, while only a small proportion (n = 3) were younger than 3 years.

Regarding leukemia classification, a relatively uniform pattern was observed among female patients, the majority of whom were diagnosed with B-lineage acute lymphoblastic leukemia (ALL), except for a single case of acute myeloid leukemia (AML). In contrast, male patients displayed greater heterogeneity in disease subtypes, including pre-B ALL (n = 3), T-lineage ALL (n = 3), L1-type ALL (n = 1), and AML-M1 (n = 1).

This variation in leukemia subtypes, particularly among male patients, reflects the overall heterogeneity of disease presentation within the study population **(Figure 1).**

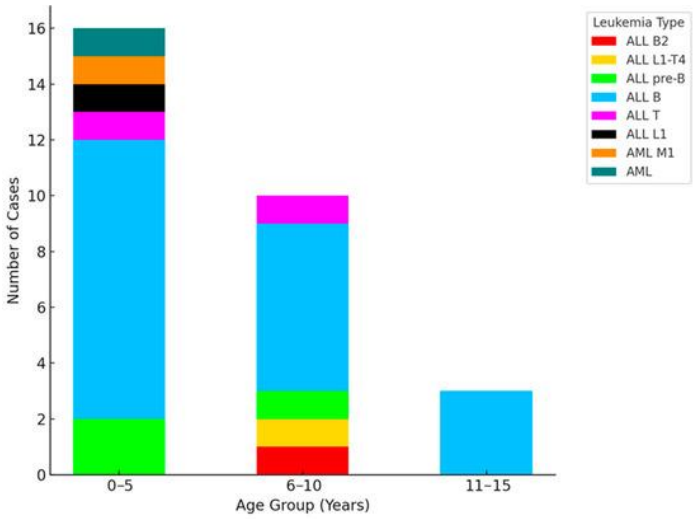


Figure 1. Age distribution and leukemia subtype breakdown within the pediatric study population.

Microbiological testing revealed 13 different microbial species, including eight Gram-positive and five Gram-negative isolates **(Figure 2).** Overall, Gram-positive pathogens were responsible for infections in 18 patients (60%), while Gram-negative organisms were identified in 12 cases (40%) **(Figure 3).**

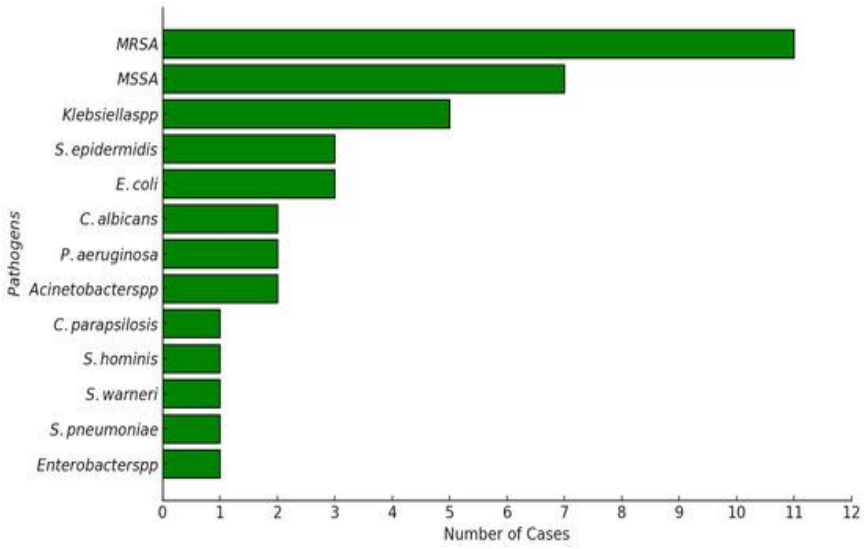


Figure 2. Distribution of detected pathogens among children with leukemia.

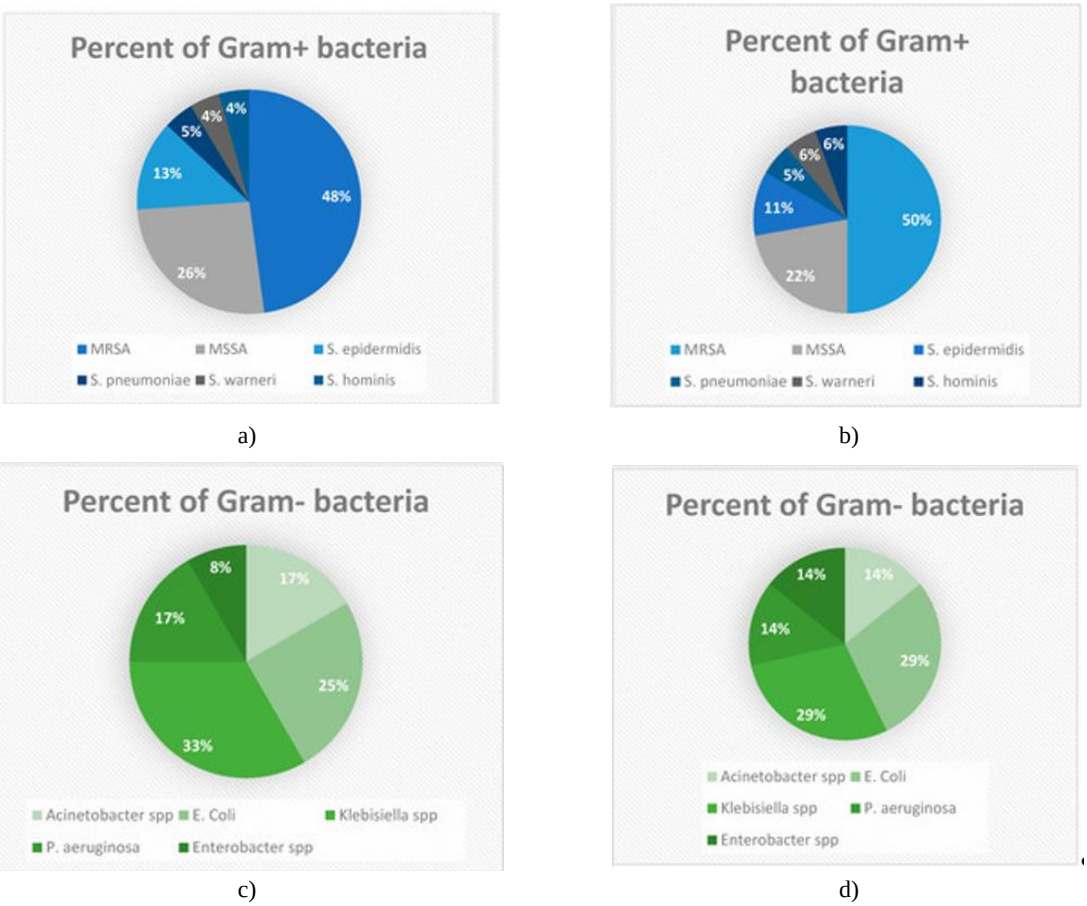
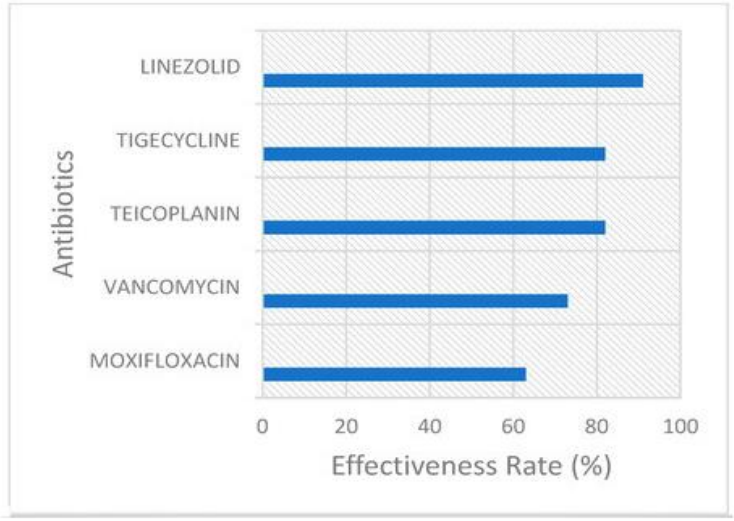


Figure 3. Breakdown of bacterial infections by Gram type in children with leukemia.

MRSA was the most common pathogen identified, with 11 cases (10 boys, 1 girl—Patient 9). A range of antibiotics was tested against these MRSA isolates: ciprofloxacin, daptomycin, levofloxacin, gentamicin, linezolid, moxifloxacin, norfloxacin, ofloxacin, trimethoprim-sulfamethoxazole (Biseptol), teicoplanin,

tigecycline, and vancomycin. These agents were selected for their known activity against MRSA in young and immunocompromised patients.

The most successful drugs were linezolid, teicoplanin, tigecycline, vancomycin, and moxifloxacin. Linezolid was effective in 10 of 11 cases (≈91%), demonstrating strong efficacy. Teicoplanin and tigecycline were each effective in 9 of 11 patients (≈82%), making them strong candidates for first-line therapy. Vancomycin was effective in 8 cases (73%), and moxifloxacin in 57 cases (63%). Gentamicin was susceptible in five cases, offering an option for some but with less reliability than linezolid or tigecycline. These results help prioritize treatment, highlighting linezolid and teicoplanin as key drugs against MRSA in pediatric oncology **(Figure 4).**



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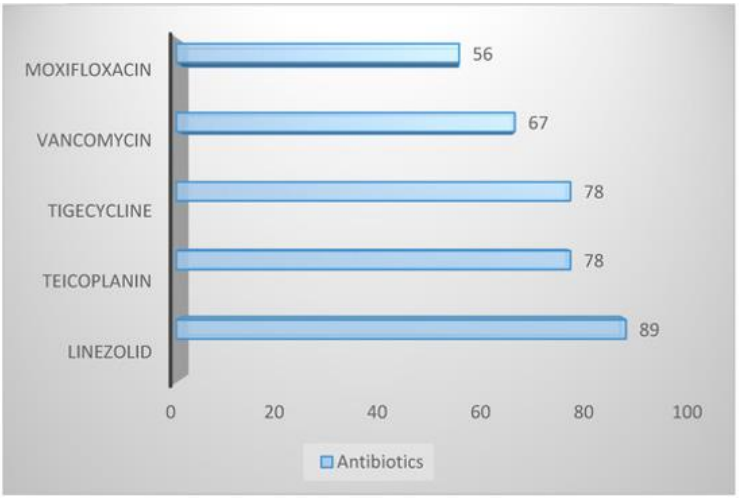
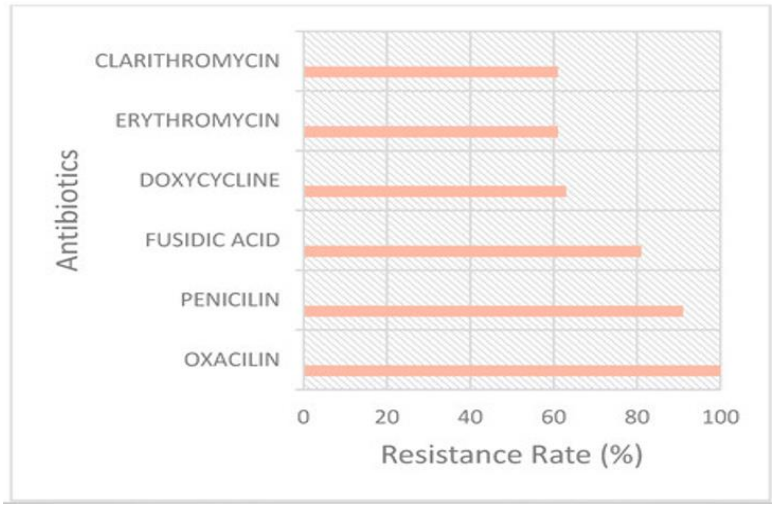


b)

Figure 4. Therapeutic response of selected antimicrobial agents against MRSA isolates in pediatric leukemia patients.

Analysis of resistance profiles revealed clear limitations in the effectiveness of several commonly used antibiotics. High resistance rates were observed for oxacillin, penicillin, erythromycin, clarithromycin, and fusidic acid. Notably, all MRSA isolates were oxacillin-resistant (100%), with MIC values exceeding 4.0 µg/mL, confirming the ineffectiveness of β-lactam agents against these strains in immunocompromised patients.

Fusidic acid also showed reduced activity, with resistance detected in the majority of isolates (9/11 cases), restricting its clinical applicability in severe infections. Similarly, clarithromycin and erythromycin demonstrated substantial resistance levels (approximately 76% and 81%, respectively), with MIC values ranging from 4.0–16.0 µg/mL for clarithromycin and around 2.0–4.0 µg/mL for fusidic acid. Doxycycline resistance was also notable, affecting 7 of 11 cases (63%), further limiting its role in empirical treatment strategies **(Figure 5).**



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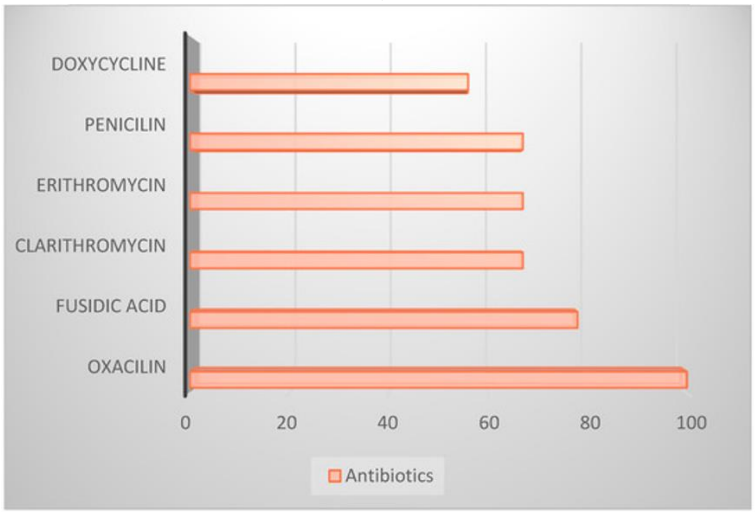
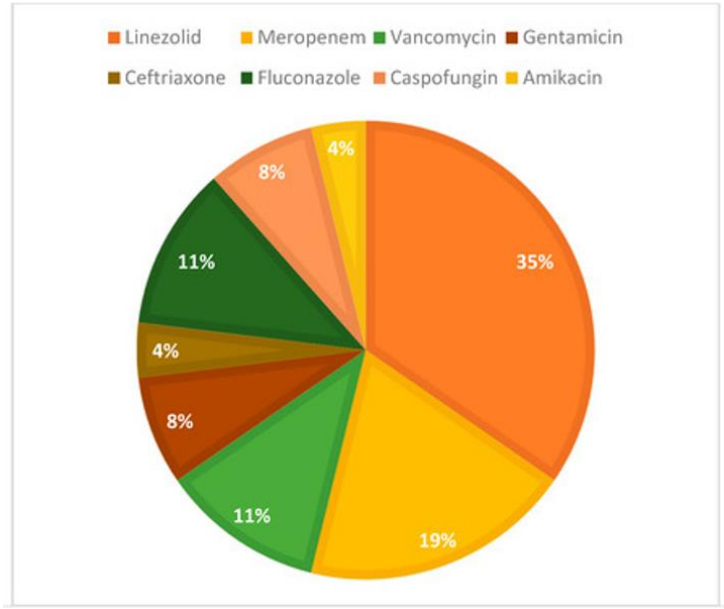


b)

Figure 5. Antimicrobial resistance profiles of MRSA isolates in pediatric leukemia patients.

Regarding therapeutic management, linezolid was the most frequently administered agent, used in 10 out of 11 MRSA cases, and served as monotherapy in 6 patients. Intravenous linezolid was given for 10 days in two male patients (Patients 1 and 8), while a 7-day regimen was applied in three cases (Patients 4 and 6, both male, and Patient 9, female).

More complicated infections required combination therapy. For example, Patient 11, a male case with MRSA detected in blood culture and MSSA in wound exudate, developed febrile pneumonia and received sequential antimicrobial treatment. Initial therapy with meropenem and gentamicin was escalated to vancomycin and linezolid, with antifungal coverage switched from fluconazole to caspofungin, resulting in clinical improvement **(Figure 6).**



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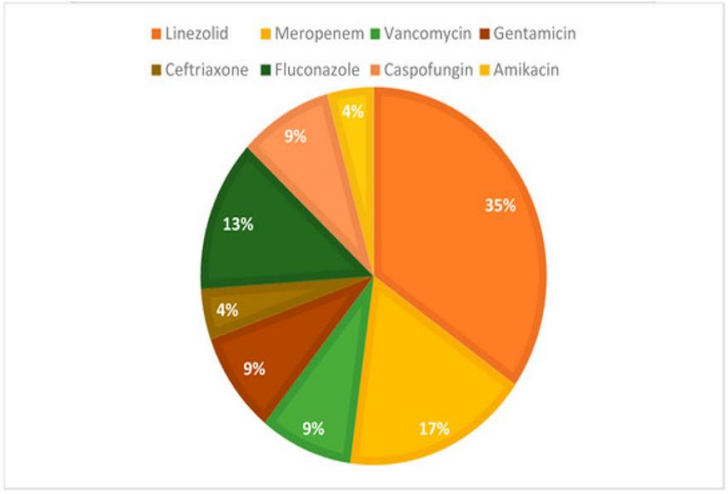

b)

Figure 6. Distribution of antibiotic regimens used in pediatric leukemia patients with severe infections.

Patient-specific therapeutic strategies reflected substantial variability depending on infection severity and pathogen spectrum. Patient 12 (male), co-infected with *Candida parapsilosis* and *Staphylococcus epidermidis*, required intensive care management. The initial regimen included meropenem, linezolid, and fluconazole, which was later modified to caspofungin-based antifungal therapy to achieve improved clinical response.

Another critical case, Patient 15 (male), presented with severely compromised clinical status and required an expanded multidrug regimen comprising meropenem, gentamicin, vancomycin, amikacin, linezolid, and fluconazole.

In contrast, Patient 18, the only case not treated with linezolid, had a favorable outcome with a simplified regimen of meropenem and ceftriaxone, without the need for additional agents.

These cases illustrate the individualized nature of antimicrobial therapy in pediatric oncology, where treatment selection is guided by infection severity, microbial profile, and patient condition **(Figure 6).**

A wide panel of antibiotics was further evaluated for activity against methicillin-sensitive *Staphylococcus aureus* (MSSA) isolates obtained from four pediatric patients. Tested agents included aminoglycosides, fluoroquinolones, macrolides, tetracyclines, glycopeptides, and β-lactams, among others.

Amikacin demonstrated consistent activity, with full susceptibility observed in multiple cases (Patients 10, 11, 29, and 30), supporting its potential role in targeted therapy. Ciprofloxacin demonstrated universal effectiveness against all tested isolates, indicating high in vitro activity against MSSA **(Figure 7).**

Clarithromycin also demonstrated substantial efficacy, being active against most isolates (5 of 6 cases), although with slightly lower consistency than ciprofloxacin. These findings suggest that, while clarithromycin may be useful in selected cases, susceptibility testing remains important before clinical use.

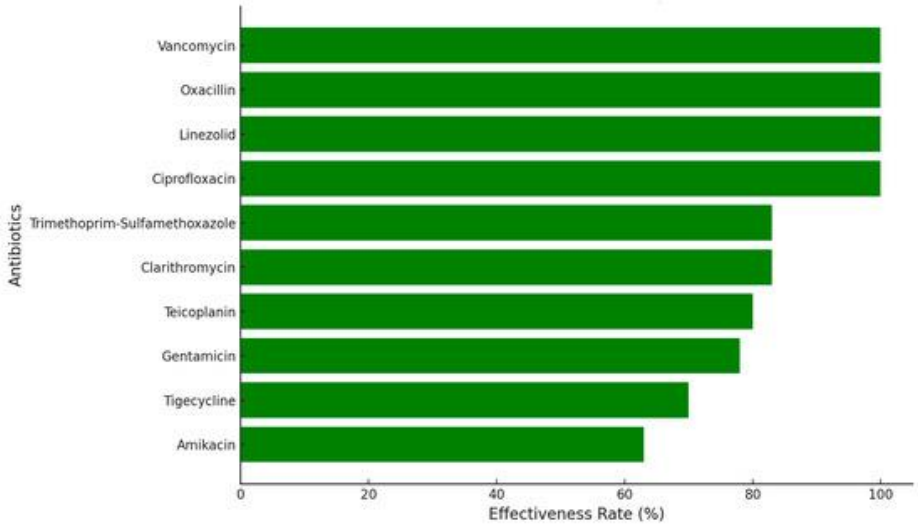

Figure 7. Antimicrobial activity of selected antibiotics against MSSA isolates in pediatric leukemia patients.

Among the tested agents, clindamycin showed inconsistent activity, with susceptibility observed in three cases (Patients 10, 19, and 29) and resistance in Patient 14. This variability indicates that clindamycin may be suitable only for selected MSSA infections and should ideally be guided by susceptibility testing before use.

Doxycycline demonstrated activity in three isolates (Patients 10, 11, and 14), suggesting potential utility as an alternative or adjunctive option in cases where first-line agents are not suitable.

Linezolid demonstrated complete in vitro efficacy against all tested isolates, highlighting its strong, reliable activity against MSSA, particularly in severe or refractory infections. Likewise, oxacillin showed uniform susceptibility in all isolates, supporting its role as a primary therapeutic option for MSSA infections in pediatric patients, given its established clinical effectiveness and tolerability.

Trimethoprim–sulfamethoxazole also demonstrated good overall performance, with effectiveness in most cases (5/6), indicating its potential as an alternative treatment option when standard therapies are limited. Vancomycin, tested in a single case, retained full activity, suggesting its value as a reserve agent in severe or unresponsive infections.

Resistance analysis revealed complete penicillin resistance across all isolates **(Figure 8),** confirming its lack of clinical utility for MSSA management in this cohort. High resistance rates were also observed with several β-lactam and cephalosporin antibiotics, including ceftazidime, ceftriaxone, and ceftaroline, with resistance ranging from approximately 85% to 90% and MIC values frequently exceeding therapeutic thresholds.

Moderate resistance was observed for tetracycline-class agents, including minocycline, with resistance rates around 60–65%. These findings collectively indicate limited effectiveness of conventional β-lactam antibiotics and certain cephalosporins in immunocompromised pediatric patients, reinforcing the importance of β-lactamase-stable agents such as oxacillin for MSSA treatment.

Therapeutic regimens varied according to disease severity and co-infections. In most MSSA cases, meropenem was included in the treatment backbone. Patient 10 received a relatively simplified regimen including oxacillin, ciprofloxacin, and fluconazole due to clinical stability.

More complex infections required escalation of therapy. For instance, Patient 11, with concurrent MSSA and MRSA infection, required broad-spectrum combination therapy including meropenem, gentamicin, vancomycin, linezolid, and antifungal adjustment to caspofungin due to persistent fever. Similarly, Patient 14 was treated with meropenem, teicoplanin, and caspofungin, while Patient 19 required meropenem combined with vancomycin, linezolid, and fluconazole to ensure adequate coverage against bacterial and fungal pathogens.

These cases emphasize the need for individualized antimicrobial strategies in pediatric leukemia, where infection severity, polymicrobial involvement, and patient fragility require flexible, adaptive therapeutic decision-making.

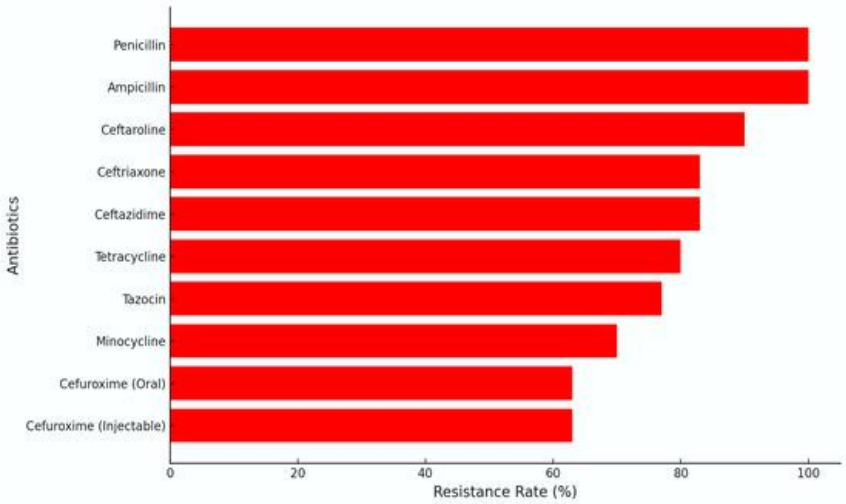

Figure 8. Antimicrobial resistance profiles of MSSA isolates in pediatric leukemia patients.

Three cases of *Staphylococcus epidermidis* infection demonstrated heterogeneous but partially overlapping susceptibility patterns. Patient 12 (male) showed broad in vitro susceptibility to multiple antimicrobial classes, including fluoroquinolones, glycopeptides, aminoglycosides, tetracyclines, rifampicin, linezolid, and trimethoprim–sulfamethoxazole. However, resistance to oxacillin, penicillin, and erythromycin was observed. Due to concomitant infections with MRSA and *Candida parapsilosis*, this patient required ICU-based management with a combination regimen including meropenem, linezolid, and caspofungin, with antifungal therapy escalated to better control fungal involvement.

Patient 19 (female) exhibited a somewhat different susceptibility profile, remaining sensitive to several agents, including clindamycin, fluoroquinolones, daptomycin, linezolid, rifampicin, trimethoprim–sulfamethoxazole, tetracycline derivatives, and vancomycin, while showing resistance to nitrofurantoin. Her treatment regimen incorporated broad-spectrum antibacterial and antifungal coverage, including meropenem, linezolid, vancomycin, and fluconazole, reflecting a similarly intensive therapeutic strategy.

Patient 27 (female, 13 years and 8 months) with bloodstream infection caused by *S. epidermidis* demonstrated susceptibility to a wide range of antibiotics, including fluoroquinolones, tetracyclines, rifampicin, glycopeptides, aminoglycosides, and tigecycline. Resistance was noted against several β-lactam combinations, including amoxicillin–clavulanate and ampicillin-based regimens, limiting conventional treatment options.

For *Escherichia coli*, two pediatric cases required individualized therapeutic approaches due to complex resistance patterns. Patient 13 showed susceptibility to carbapenems, aminoglycosides, nitrofurantoin, fluoroquinolones, tetracyclines, and several broad-spectrum agents, while exhibiting resistance to multiple cephalosporins and penicillins, indicating reduced efficacy of β-lactam therapy.

Patient 17 presented with a recurrent *E. coli* infection and displayed susceptibility to ciprofloxacin, colistin, gentamicin, imipenem, and trimethoprim, but resistance to several aminoglycosides and β-lactam antibiotics. Subsequent exudate testing confirmed sensitivity to carbapenems and selected aminoglycosides, guiding adjusted therapy with ertapenem and gentamicin following relapse.

Patient 28, diagnosed with urinary tract infection due to *E. coli*, showed susceptibility to aminoglycosides, certain cephalosporins, carbapenems, fluoroquinolones, and colistin. However, resistance and intermediate susceptibility were observed across multiple β-lactams, fosfomycin, nitrofurantoin, and trimethoprim–sulfamethoxazole, significantly restricting therapeutic options.

Therapeutically, Patients 13 and 28 received combination treatment including meropenem and supportive probiotic therapy, along with antifungal coverage using caspofungin when indicated. Patient 17 initially received chloramphenicol and cefoperazone–sulbactam during hospitalization, followed by ceftriaxone maintenance therapy. Upon recurrence eight months later, treatment was escalated to ertapenem and gentamicin based on updated susceptibility results.

Klebsiella infections were detected in four patients (Patients 3, 20, 22, and 24), including both male and female cases, with Patient 20 being the youngest in the cohort.

Patient 3 showed susceptibility to linezolid, tigecycline, vancomycin, nitrofurantoin, and quinupristin/dalfopristin, while demonstrating resistance to multiple fluoroquinolones, aminoglycosides, macrolides, penicillin, tetracycline, and trimethoprim–sulfamethoxazole. Based on this profile, linezolid was administered intravenously for 7 days, resulting in effective infection control **(Figures 9 and 10).**

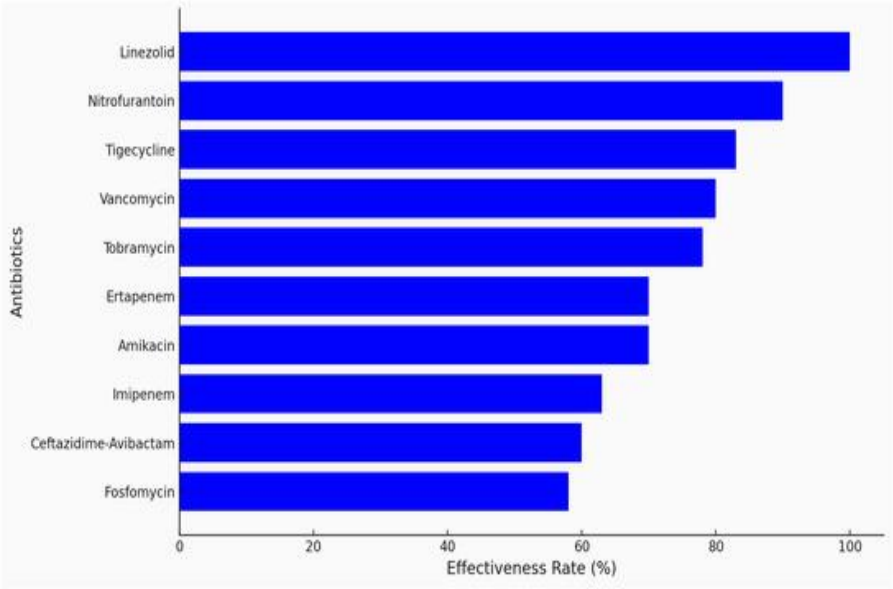

Figure 9. Antimicrobial susceptibility profile of *Klebsiella* spp. isolates from pediatric leukemia patients.

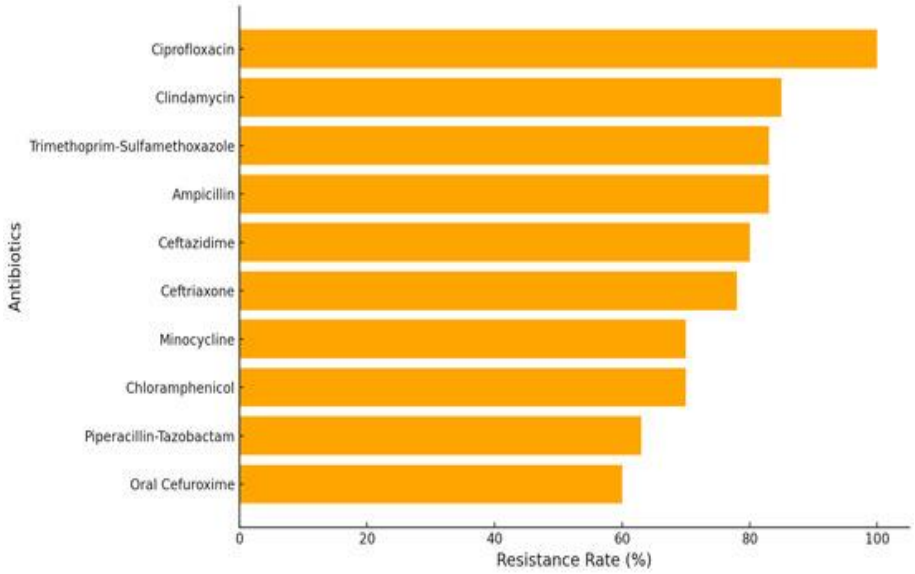

Figure 10. Antimicrobial resistance patterns of *Klebsiella* spp. isolates in pediatric leukemia patients.

The antibiogram obtained for Patient 20 indicated a resistance landscape of greater complexity, in which susceptibility was preserved to Amikacin, Aztreonam, Ceftazidime, Ertapenem, Imipenem/Cilastatin, Tigecycline, and Tobramycin, all of which could therefore be considered valid treatment options. By contrast, the cultured organism lacked susceptibility to Augmentin, Ampicillin, Cefazolin, Cefepime, Cefotaxime, Cefuroxime, Ciprofloxacin, Chloramphenicol, Gentamicin, Trimethoprim-sulfamethoxazole, Imipenem, and Meropenem. Guided by these laboratory findings, clinical care was based on a three-drug protocol comprising Linezolid, Amikacin, and Ertapenem, a comprehensive strategy made essential by the patient's pediatric age and the pathogen's extensive resistance profile.

A urinary tract infection stemming from Klebsiella spp. was diagnosed in Patient 22, a male. The recovered organism tested susceptible to Ampicillin-Sulbactam, Ceftibuten, Ciprofloxacin, Colistin, Piperacillin-Tazobactam, Imipenem, Nitrofurantoin, Cefotaxime, Fosfomycin, and Tobramycin. Meropenem, Ceftazidime, and orally administered Cefuroxime were classified as having intermediate susceptibility. Nonetheless, resistance to Ampicillin and Trimethoprim-Sulfamethoxazole constrained certain treatment pathways. Patient 24, a female whose illness was ascribed to Klebsiella spp., harbored an isolate responsive to Amoxicillin, Amoxicillin-Clavulanic acid, Cefoxitin, Ceftazidime-Avibactam, Chloramphenicol, Ertapenem, Gentamicin, Imipenem, Meropenem, Moxifloxacin, Nitrofurantoin, Ofloxacin, Tigecycline, and Tobramycin. In contrast, resistance was observed against Ceftaroline, Ceftazidime, Ceftriaxone, Minocycline, injectable Cefuroxime, Trimethoprim-Sulfamethoxazole, Tetracycline, Piperacillin-Tazobactam, and oral Cefuroxime. This pattern considerably reduced the list of viable antimicrobial choices.

Among the fungal organisms encountered in this series, *Candida albicans* accounted for one of the two non-bacterial infections, the other being Candida parapsilosis. This yeast species was identified in two female subjects: Patient 10, whose infection was polymicrobial and included MSSA, and Patient 16, from whom *Candida albicans* was the only pathogen isolated.

In managing Patient 10, the anti-Candida component of therapy consisted of Fluconazole, which aligned with the concurrent anti-MSSA regimen already described. Antifungal sensitivity assays demonstrated that the isolate was sensitive to Amphotericin B, Clotrimazole, Econazole, Fluconazole, Itraconazole, Ketoconazole, Miconazole, and Voriconazole, suggesting a broad-spectrum antifungal agent menu with potential utility against this strain.

With respect to Patient 16, whose infection involved *Candida albicans* alone, Fluconazole was similarly selected as the antifungal agent of choice. The sensitivity pattern in this case covered Amphotericin B, Caspofungin, Fluconazole, Flucytosine, Voriconazole, and Micafungin, revealing a broad palette of active therapeutic options. Both patients enjoyed favorable clinical outcomes with Fluconazole. This drug retained consistent potency in both instances, a finding that bolsters its position as a cornerstone of therapy for *Candida albicans* within the studied population.

Streptococcus pneumoniae, detected in a male patient (Patient 2), exhibited a sensitivity profile that featured multiple effective antibiotics, namely Ertapenem, Cefixime, Chloramphenicol, Doxycycline, Levofloxacin, Linezolid, Moxifloxacin, Rifampicin, Tigecycline, and Vancomycin. Conversely, the organism proved resistant to Clindamycin, Erythromycin, Penicillin, Trimethoprim-Sulfamethoxazole (Biseptol), and Tetracycline. Such a susceptibility-resistance configuration underscores the imperative to resort to newer or more potent agents, such as Ertapenem, Linezolid, or Vancomycin, when treating Streptococcus pneumoniae to ensure adequate disease control, a consideration made all the more pressing by the documented ineffectiveness of traditional first-line agents like Penicillin.

S. warneri, cultured from a male subject (Patient 5), was susceptible to Ciprofloxacin, Clindamycin, Daptomycin, Erythromycin, Levofloxacin, Linezolid, Moxifloxacin, Nitrofurantoin, Quinupristin/Dalfopristin, Rifampicin, Trimethoprim-Sulfamethoxazole (Biseptol), Tetracycline, and Tigecycline. Resistance was documented solely for Gentamicin, Oxacillin, and Penicillin. The therapeutic intervention comprised intravenous Linezolid administered over 7 days, a choice presumably dictated by the drug's well-established clinical efficacy and the high in vitro susceptibility of the S. warneri isolate.

Acinetobacter spp. was recovered from two individuals, Patient 7 (male) and Patient 21 (female). Antimicrobial sensitivity testing verified that Gentamicin, Tetracycline, Ceftazidime, Cefotaxime, Ampicillin, Piperacillin/Tazobactam, Meropenem, and Ceftriaxone retained activity. The initial regimen combined Gentamicin and Ampicillin, followed by a switch to Meropenem, ultimately yielding a favorable therapeutic response.

For Candida parapsilosis, which was present in a male patient (Patient 12) together with MRSA and Staphylococcus epidermidis, the therapeutic approach was outlined in earlier sections. It involved administering Caspofungin, selected for its reliable anti-Candida activity. Sensitivity testing confirmed the organism's susceptibility to Caspofungin, Flucytosine, Miconazole, and Voriconazole.

Staphylococcus hominis, isolated from a female patient (Patient 14) who also carried MSSA, showed robust susceptibility to Ciprofloxacin, Daptomycin, Tigecycline, Vancomycin, Levofloxacin, Linezolid, Moxifloxacin, Ofloxacin, and Teicoplanin. Substantial resistance was nonetheless evident for Fusidic acid, Clarithromycin, Clindamycin, Erythromycin, Gentamicin, Oxacillin, and Penicillin, a resistance pattern that appreciably limited the armamentarium of effective treatments against this S. hominis strain. Turning to *Pseudomonas aeruginosa*

recovered from a male subject (Patient 18) with concurrent MRSA, the sensitivity panel demonstrated pronounced activity for Aztreonam, Ceftazidime, Meropenem, Ciprofloxacin, Ertapenem, Linezolid, and Vancomycin. Resistance to Tigecycline was, however, observed, precluding its deployment in managing this particular case.

Lastly, an *Enterobacter* spp. isolate obtained from a female patient (Patient 19), whose co-infecting organisms included MSSA and Staphylococcus epidermidis, proved sensitive to Amikacin, Augmentin (Amoxicillin plus Clavulanic acid), Ampicillin combined with Sulbactam, Cefotaxime, Cefoxitin, Cefazolin, Cefuroxime, Chloramphenicol, Colistin, Ertapenem, Gentamicin, Levofloxacin, Meropenem, and Trimethoprim-Sulfamethoxazole (Biseptol). Even with this broad susceptibility range, the isolate showed resistance to both Ampicillin and Nitrofurantoin, ruling out a role for these agents in the treatment plan.

Acute lymphoblastic leukemia (ALL) occurs approximately five times more frequently than acute myeloid leukemia (AML), accounting for nearly 75% of pediatric leukemia cases [13]. In line with this epidemiological pattern, the present cohort was predominantly composed of ALL patients (n = 19, 95%), whereas AML was observed in only one case (5%).

Previous studies by S.P. Hunger *et al*. [14] and M.S. Christensen *et al*. [15] have reported that treatment-related mortality in pediatric ALL ranges from 2% to 4%, with infections being the leading cause of death. In a large cohort of 1652 children with ALL, Christensen *et al*. reported a 3.4% mortality rate related to therapy complications, of which 68% were attributed to infections [16]. These findings highlight the critical importance of infection prevention and management in improving survival outcomes in pediatric leukemia.

Although antibiotic therapy was generally effective in controlling infections in our cohort of 320 patients, the intensity of treatment reflects the severity of infectious complications in immunocompromised children. Similar concerns have been raised in previous studies, emphasizing the need to reassess infection risk in ALL patients. In high-risk cases, prophylactic strategies against bacterial and fungal infections may be considered to reduce the need for aggressive antimicrobial therapy [17-19]. However, according to ECIL-8 guidelines, routine antibacterial prophylaxis is not recommended in pediatric acute leukemia (recommendation 1; grade D, level III evidence) [20].

Polymicrobial infections are associated with higher infection-related mortality in pediatric leukemia patients compared with single-pathogen infections [21]. This is consistent with our findings, where persistent fever was observed in cases with suspected fungal involvement and resolved only after targeted antifungal therapy. Similarly, the 2012 systematic review by Sung *et al*. emphasized the importance of identifying high-risk pathogens in AML to guide appropriate therapy [22].

Comparable antimicrobial effectiveness has been reported in other studies. For instance, David *et al*. demonstrated that linezolid and ertapenem were effective against multidrug-resistant strains in pediatric infections in China [23], findings that align with ours. *Staphylococcus* species were also the most commonly isolated pathogens, consistent with our cohort, in which 9 patients had MRSA, and 4 had MSSA infections. Lehrnbecher *et al*. reported that cefepime alone or in combination with vancomycin is effective for bacterial infections in pediatric oncology patients [18]. Although these were used in our study, linezolid was administered more frequently, often in combination with vancomycin.

The high prevalence of MRSA in our study is consistent with findings from Jones *et al*., who identified linezolid as one of the most effective treatments for pediatric MRSA infections [24]. Similarly, Njoungang *et al*. reported higher resistance rates among *S. aureus* isolates from cancer patients than from non-cancer patients [25]. This aligns with our results, where MRSA accounted for 69% of S. aureus infections and MSSA for 31%, highlighting the predominance of resistant strains in vulnerable populations.

We also observed strong resistance to penicillin, consistent with reports by Gurung *et al*. [26], Williams *et al*. [27], and Lee *et al*. [28], all of whom documented widespread resistance to β-lactam antibiotics in pediatric isolates. In our study, linezolid, meropenem, vancomycin, and gentamicin were primarily used, which is consistent with findings by Kim *et al*., who highlighted the importance of carbapenems and linezolid in treating severe pediatric infections such as sepsis [29]. This is further supported by Garcia *et al*. and Lyu *et al*., who demonstrated the efficacy of linezolid and ertapenem against resistant organisms [30, 31], as well as by Wu *et al*., who emphasized the use of linezolid and teicoplanin in treating Staphylococcus aureus infections in children [32]. Collectively, these studies underscore the importance of linezolid and carbapenems as key therapeutic options in immunocompromised pediatric patients.

This study has several limitations. The relatively small sample size of 30 pediatric leukemia patients may limit the generalizability of the findings. As a single-center study, the results may reflect local microbial patterns that

are not representative of other regions. The retrospective design also introduces potential bias due to reliance on existing medical records and variability in clinical documentation. In addition, the study primarily focused on bacterial infections, limiting evaluation of viral and fungal contributions. Finally, the absence of long-term follow-up data prevents assessment of recurrence rates and long-term outcomes.

Despite these limitations, our findings reinforce the critical role of linezolid in treating resistant Gram-positive infections in pediatric leukemia patients, consistent with previous studies in immunocompromised populations [23, 30, 32]. The high prevalence of MRSA and β-lactam resistance observed in this cohort is consistent with global trends, including those reported in Eastern Europe [25, 26]. These results highlight the importance of continuous antimicrobial surveillance, implementation of stewardship programs, and use of antibiogram-guided therapy. They also support the use of carbapenems and glycopeptides in empirical treatment of high-risk patients [18, 20].

Conclusion

In immunocompromised pediatric patients, prompt microbiological assessment, including antibiogram testing at the onset of fever, is essential to guide timely and targeted antimicrobial therapy. In the present study, febrile episodes were generally managed using an intensive empirical approach, most commonly involving broad-spectrum and anti–Gram-positive agents such as linezolid, meropenem, vancomycin, and gentamicin.

Overall, Gram-positive organisms were more frequently identified than Gram-negative bacteria. Among Gram-negative isolates, Klebsiella spp., Escherichia coli, and Acinetobacter spp. were detected, typically as single-pathogen infections. In contrast, Gram-positive bacteria were more often found in polymicrobial contexts or in association with additional infectious agents.

All cases of *Candida albicans* infection were observed exclusively in female patients. Although these fungal infections were generally responsive to standard antifungal therapy, persistent febrile episodes occurred when treatment was not sufficiently potent. In such cases, symptom resolution was achieved only after escalation to more effective antifungal agents, particularly caspofungin.

These findings emphasize the importance of rapid pathogen identification and resistance profiling in immunocompromised hosts, as well as the need for appropriately potent antimicrobial and antifungal regimens to achieve effective control of infection-related fever.

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