ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Microbiological profile and antibiotic susceptibility of body fluids or swabs of acute leukemia patients with sepsis in a tertiary care hospital

Arka Karmakar[1], Atreyi Chakraborty[2], Krishnendu Bandyopadhyay[3], Biswajit Biswas[4], Sankar Kumar Das[5], Atanu Roy[6], Sayan Chatterjee[7], Mayank K Vidyarthi[8], Chayanik Ghosh[9], Pradip K Bej[10], Jeker Ali[11], Akashleena Datta[12]

[1]Senior Resident, [3]Assistant Professor, [4]Professor, [7]Associate Professor, [8,9,12]Junior Resident, [10,11]Medical Officer, Department of Pediatrics, Prafulla Chandra Sen Government Medical College and Hospital, Arambag, Hooghly, West Bengal, India, [2]Assistant Professor, Department of Microbiology, [5]Professor, Department of Pediatrics, Medical College and Hospital, Kolkata, West Bengal, India, [6]Professor, Department of Pediatrics, IPGMER, Kolkata; and Ex Associate Professor, Department of Pediatrics, Medical College and Hospital, Kolkata, West Bengal, India

Submission: 24-04-2025 Revision: 03-06-2025 Publication: 01-07-2025

ABSTRACT

Background: Therapeutic approach to children with acute leukemia and sepsis involves identification of the causative organism and institution of appropriate antimicrobial therapy. The pattern of local flora and antibiotic susceptibility should guide empirical antimicrobial therapy. **Aims and Objectives:** To identify the bacteria and fungi causing sepsis in children with acute leukemia and study their antimicrobial profile. **Materials and Methods:** This descriptive observational study with a cross-sectional study design involved 100 consecutive children admitted to the inpatient department with acute leukemia and clinical sepsis with an acute rise of pediatric sequential organ failure assessment score of more than 2. All possible samples, including blood, urine, and pus were sent for culture and sensitivity. Data were analyzed using the Statistical Package for the Social Sciences 23 software. **Results:** All children had fever. Most common form of infection was pneumonia (27%). Positive microbial growth was found in 23.18% of all the samples (n = 220). Gram-negative bacteria were most commonly (49.01%) isolated followed by Gram-positive (27.45%) organisms and fungi (23.52%). Overall, the most common organism was *Klebsiella* (15.68%). *Klebsiella* showed 50% sensitivity toward tigecycline and colistin and 37.5% sensitivity toward meropenem, amikacin, and levofloxacin each. Gram-positive organisms showed 100% sensitivity toward vancomycin, linezolid, daptomycin, and tigecycline. We got 23.52% pan resistant organisms. **Conclusion:** Sepsis is the leading cause of morbidity and mortality among children with acute leukemia. The major causative agents were Gram-negative rods followed by Gram-positive microbes and fungi. Appropriate antimicrobial therapy must be initiated as per the culture sensitivity pattern of the local area to improve outcome and to reduce emergence of drug resistance.

Key words: Acute leukemia; Sepsis; Microbes; Antibiotics

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i7.4578

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Acute leukemia is the most common Indian childhood cancer with a relative proportion between 25% and 40% of all childhood cancers. These patients are prone to develop life-threatening infections caused by various bacteria and fungi. The overall prognosis depends upon timely institution of appropriate antibiotic and antifungal

Address for Correspondence:
Dr. Biswajit Biswas, Ulhas Mini Township, 1st Avenue, 11th Street, House - 23, Bardhaman East, West Bengal - 713104, India.
Mobile: +91-9874179931. **E-mail:** drbiswazeetbiswas@gmail.com

drugs. Emergence of drug resistance is a matter of concern. Currently, antimicrobial drugs are chosen based on guidelines given in standard textbooks and national and international journals. However, it should be guided by the prevalence of local flora and antimicrobial susceptibility patterns of the institution. No recent study in this regard is available in our hospital, especially in children with leukemia. Hence, this study may provide valuable inputs in guiding the treatment of such patients.

Aims and objectives

To identify organisms responsible for sepsis in children with leukemia and to study their antimicrobial sensitivity pattern.

MATERIALS AND METHODS

This descriptive observational study with cross-sectional study design was carried out in the Department of Pediatrics, Medical College and Hospital, Kolkata, India. The total study period was 2 years (October 2021–September 2023). Children with acute leukemia, between 1 month and 12 years of age, who presented with sepsis and were admitted to ward were included. A total of 100 consecutive patients were included in the study.

Inclusion criteria

Patients of acute leukemia, between 1 month and 12 years of age, who were admitted with clinical sepsis, and had an acute rise of 2 or more pediatric sequential organ failure assessment score (pSOFA) points.[1]

The pSOFA score is a tool used to assess the severity of illness in critically ill children. This is a modified version of the SOFA score, adapted for the pediatric population. The pSOFA score assesses six organ systems: respiratory, hematological, hepatic, cardiovascular, neurological, and renal. It helps predict mortality and other outcomes in critically ill children.

Exclusion criteria

a. Diagnosed cases of chronic systemic diseases
b. Patient with dysmorphic features
c. Patients who had received intravenous antibiotics 48 hours before hospital admission
d. Patients of leukemia who had achieved complete remission and were free of any anticancer chemotherapy.

Necessary permission from the institutional ethics committee, and written informed consent from all parents were taken. Consecutive 100 patients of acute leukemia and sepsis with an acute rise of 2 or more pSOFA points were selected from the pediatric general ward, pediatric intensive care unit and high dependency unit. All of them were subjected to thorough history taking and meticulous clinical examination. Investigations such as complete blood count including peripheral blood smear; liver function test; renal function tests; serum electrolytes; tumour lysis syndrome markers; markers of infection such as C-reactive protein, erythrocyte sedimentation rate and procalcitonin; and urine analysis were done. Ultrasound and computed tomography scan were done when deemed necessary. Calculation of pSOFA score was done for each case. Five ml of venous blood was collected and injected into blood culture collection bottles from each patient by phlebotomy after adequate dressing of the skin surface with isopropyl alcohol and povidone iodine. Urine samples were taken from patients in pre-sterile glass test tubes, maintaining proper asepsis. Swabs were taken from the throat when patients had signs or symptoms suggestive of oral or oropharyngeal infections. Swabs were also taken from pustules, abscesses and wounds as per the clinical profile of the patients. The samples thus collected were sent to the department of microbiology and were examined for bacterial and fungal culture, and antibiotic susceptibility. Viral studies were not done due to financial and technical constraints. Blood cultures were processed by the BACTEC system, whereas all other specimens were processed by the VITEK system. Results were available after 5 days. Blood culture was considered to be negative if there was no growth after 5 days, and urine culture was considered to be negative if there was no growth after 3 days. All the data were entered into the MS Excel sheet, and appropriate statistical analysis was done.

Statistical methods

Data were maintained in Microsoft Excel 2010. Statistical Package for the Social Sciences software version 23 was used for the statistical analysis of the data. Quantitative data were expressed as mean, standard deviation, ratio, etc. Categorical data were expressed in terms of number, percentage, and ratio. Quantitative continuous variables were compared between groups using Mann–Whitney's nonparametric tests when the variable had a non-normal distribution. Unpaired t-test was used when the variable had a normal distribution. Qualitative variables were compared using the Chi-square test and Fisher exact test. A two-sided $P<0.05$ was considered statistically significant for all the tests.

RESULTS

Consecutive 100 children admitted in the pediatric inpatient department with leukemia and sepsis were included into the study during the period from October 2021 to September 2023 when study parameters were fulfilled. The mean age of presentation was 4.32 years±2.50 years. Sixty-eight patients were boys and 32 patients were girls, with the boy: girl ratio of 2.1:1.

Clinical and laboratory parameters (Table 1)

Most of the patients (76%) belonged to the B acute lymphoblastic leukemia (B-ALL) group, followed by T ALL (15%) and acute myeloid leukemia (AML) (9%). Sepsis was found in 20 patients even before the initiation of chemotherapy. Organisms could be isolated in only 6 of those patients. 45 patients were in the induction phase, 25 in the consolidation and 10 in the maintenance phase of chemotherapy when they were included in the study. Microbes could be isolated in 29, 16, and 2 patients, respectively.

65 patients developed hospital-acquired infections. Fever was present in all patients. 25 patients were found to have no obvious focus, although they had fever. The most common site of infection was the respiratory system; with pneumonia comprising 27%. Other respiratory complications, such as lung abscess, empyema, fungal ball, etc., comprised 10% of the cases. Absolute neutrophil count (ANC) was <200 in 70 patients. Six patients did not fulfil the criteria of neutropenia (i.e., they had ANC more than 500). The mean pSOFA score was 9.98±1.50 at the time of inclusion of the subjects into the study. Microbes could be isolated in 52 out of 70 patients (74.28%) in severely neutropenic patients. The duration of neutropenia was more than 7 days in 56% of cases. The focus of infection could not be documented by clinical and radiological methods in 23 patients.

Table 1: Clinical and laboratory parameters

Parameter	Frequency			
Subtypes of acute leukemia		**(n=100)**		
B ALL		76		
T ALL		15		
AML		9		
Timing of detection of sepsis	**Total (%) (n=100)**	**Microbe isolated (%)**		**Microbe not isolated (%)**
Before initiation of chemotherapy	20	6		14
Phase of chemotherapy				
Induction	45	29		16
Consolidation	25	16		09
Maintenance	10	02		08
Type of infection		**(n=100)**		
Community acquired		35		
Hospital acquired		65		
Symptomatology		**(n=100)[#]**		
Fever without obvious focus		25		
Dysuria		10		
Respiratory distress		35		
Vomiting		19		
Pain abdomen		20		
Shock		12		
Bone pain		2		
Catheter site abscess		3		
Pus discharge from sinus		2		
Hepatomegaly±splenomegaly		35		
Site of infection	**Total (n=100)**	**ANC <200 (%)**	**ANC 200–500 (%)**	**ANC >500 (%)**
UTI	10	6 (6)	2 (2)	2 (2)
Pneumonia	27	20 (20)	5 (5)	2 (2)
Fever without focus	23	20 (20)	2 (2)	1 (1)
Mucositis	8	5 (5)	3 (3)	0
Neutropenic enterocolitis	11	5 (5)	6 (6)	0
Empyema	3	3 (3)	0	0
Other non-pneumonia lung infections	7	5 (5)	2 (2)	0
Abscesses	11	6 (6)	4 (4)	1 (1)
Focus of infection		**(n=100)**		
Found		77		
Not found		23		
Absolute neutrophil count	**Total (n=100)**	**Microbe isolated (%)**		**Microbe not isolated (%)**
>500	6	02		04
200–500	24	18		06
<200	70	52		18
Duration of neutropenia		**(n=100)**		
<7 days		44		
More than or equal to 7 days		56		

ANC: Absolute neutrophil count, ALL: Acute lymphoblastic leukemia, AML: Acute myeloid leukemia, UTI: Urinary tract infections. [#]Some children had two or more symptoms.

Table 2: Types of organisms in culture positive samples

Group of organism	Type of organism	Total positive culture (n=51)	Blood culture (n=28)	Urine culture (n=12)	Pus culture (n=8)	Others (ET aspirate, BAL) (n=3)
Gram negative organisms (n=25)	*Escherichia coli*	5	1	3	1	0
	Pseudomonas	7	3	2	1	1
	Klebsiella	8	3	2	2	1
	Acinetobacter	3	2	0	0	1
	Salmonella	2	2	0	0	0
Fungi (n=12)	*Candida albicans*	2	2	0	0	0
	Candida non-albicans	3	3	0	0	0
	Aspergillus	4	3	1	0	0
	Mucor	3	3	0	0	0
Gram positive organisms (n=14)	Methicillin sensitive *Staphylococcus aureus*	3	2	0	1	0
	Methicillin resistant *Staphylococcus aureus*	5	3	0	2	0
	Enterococcus	6	1	4	1	0

Microbiological profile of patients (Table 2)

Blood and urine cultures were sent from all patients and had a positivity rate of 28% and 12%, respectively. Pus was sent from patients with empyema (n=3) and abscess (n=11). Pus culture was positive in 57.14% of the cases out of a total of 14 samples tested. Endotracheal tube aspirate and bronchoalveolar lavage were sent for culture in 3 cases each and were positive in 100% of cases. Hence, out of a total of 220 samples sent for analysis, 51 (23.18%) samples turned out to be positive for microbial growth. Gram-negative organisms were found most commonly (49.01%, 25 out of 51). Gram-positive organisms and fungi were found in 14 and 12 samples, respectively.

Klebsiella (8 out of 25, 32%) and *Staphylococcus aureus* (8 out of 14, 57.14%) were the most common Gram-negative and Gram-positive organisms respectively. *Candida* comprised 41.66% (5 out of 12) of all fungus positive samples. *Klebsiella* accounted for 10.71% of all blood isolates (n=28), 16.67% of all urine isolates (n=12) and 27.27% of isolates from other sites (n=11). *S. aureus* (both Methicillin-sensitive *S. aureus* [MSSA] and Methicillin-resistant *S. aureus* [MRSA]) accounted for 17.85% of all blood isolates (n=28) and 37.5% of isolates from pus (n=8). *Candida* (both albicans and non-albicans) accounted for 17.85% of all blood cultures (n=28). *Enterococcus* was the most common (33.33%) isolate from urine cultures (n=12).

Antimicrobial susceptibility profile and therapeutic considerations (Table 3)

Table 3 shows the pattern of antimicrobial usage on the empirical basis to the patients under the study. Antimicrobial drugs were used empirically mostly in various combinations or singly, depending on the clinical status of the patients as per the departmental policy.

In 61% of cases, a combination of different antibiotics was used. Third-generation cephalosporin, such as ceftriaxone was used in 51% of cases (n=100). Vancomycin, a glycopeptide antibiotic, was used in 40% of cases (n=100). Beta-lactam with beta-lactamase inhibitors such as piperacillin tazobactam, and carbapenem group of drugs such as meropenem were used in 25% and 24% of cases (n=100), respectively. Oxazolidinone drugs such as linezolid have been used in 12% cases (n=100). Aminoglycosides such as amikacin; fluoroquinolones such as levofloxacin; and lincosamides such as clindamycin were used in only 2%, 7%, and 4% cases (n=100), respectively. Fourth-generation cephalosporins such as cefepime and polypeptide antibiotics, such as colistin, were never used empirically. Antifungals such as caspofungin were used in 8% of cases (n=100).

Table 3: Empirical use of antimicrobial drugs

Characteristics	Frequency
Type of antimicrobial therapy	(n=100)
Monotherapy	39
Combination therapy	61
Empirical antibiotics used	(n=100)[#]
3rd Generation Cephalosporin (ceftriaxone)	51
4th Generation cephalosporin (cefepime)	0
Beta lactam with beta lactamase inhibitor (Piperacillin-tazobactam)	25
Carbapenem (Meropenem)	24
Aminoglycosides (Amikacin)	2
Lincosamide (Clindamycin)	4
Glycopeptide (Vancomycin)	40
Oxazolidinone (Linezolid)	12
Polypeptide (Colistin)	0
Fluoroquinolone (Levofloxacin)	7
Antifungal (Caspofungin)	8
Change of antibiotics	(n=100) (%)
Changed	80
Not changed	20

[#]More than 1 antibiotic was used

Table 4 shows the antibiotic susceptibility pattern as per culture and sensitivity reports. It is important to note

Table 4: Antibiotic sensitivity pattern as per culture sensitivity reports

Organism	Ceftriaxone	Cefepime	Piperacillin tazobactam	Meropenem	Amikacin	Vancomycin	Linezolid	Colistin	Levofloxacin	Tigecycline	Daptomycin	No drug sensitivity
Escherichia coli (n=5)	1	0	2	3	3	xxx	xxx	3	3	3	xxx	2
Pseudomonas (n=7)	1	1	2	3	3	xxx	xxx	3	3	3	xxx	4
Acinetobacter (n=3)	1	0	1	1	1	xxx	xxx	1	1	1	xxx	2
Klebsiella (n=8)	1	0	2	3	3	xxx	xxx	4	3	4	xxx	4
Salmonella (n=2)	2	2	xxx	2	xxx	xxx	xxx	xxx	2	xxx	xxx	0
MSSA (n=3)	3	3	1	3	3	3	3	xxx	2	3	3	0
MRSA (n=5)	0	0	0	0	0	5	5	xxx	xxx	5	5	0
Enterococcus (n=6)	1	1	1	1	1	6	6	xxx	2	6	6	0
Total	10	7	9	16	14	14	14	11	16	24	14	12

MSSA: Methicillin-sensitive *Staphylococcus* aureus, MRSA: Methicillin-resistant *Staphylococcus* aureus

that different antibiotics were tested for susceptibility to different organisms.

Vancomycin was tested for susceptibility in case of Gram-positive organisms only, whereas colistin was tested for Gram-negative organisms. For drugs such as levofloxacin with dual coverage, it was tested for both Gram-positive and Gram-negative organisms. Gram-negative organisms showed maximum sensitivity toward meropenem, amikacin, levofloxacin, tigecycline, and colistin. *Escherichia coli* (n=5) showed 60% sensitivity toward the aforementioned drugs. *Klebsiella* (n=8) showed 50% sensitivity toward tigecycline and colistin and 37.5% sensitivity toward meropenem, amikacin and levofloxacin each. *Pseudomonas* (n=7) showed 42.85% sensitivity toward meropenem, amikacin, tigecycline and colistin each. *Acinetobacter* (n=3) showed 33.33% sensitivity toward almost all the antibiotics we tested for. It showed the highest degree of pan-resistance (66.67%). We got very low degrees of sensitivity among Gram-negative organisms toward ceftriaxone (12.5% in case of *Klebsiella*, n=8) and cefepime (14.2% in case of *Pseudomonas*, n=7). Gram-positive organisms such as *S. aureus* (both methicillin sensitive, n=3 and methicillin resistant, n=5) and *Enterococcus* (n=6) showed 100% sensitivity toward vancomycin, linezolid, daptomycin, and tigecycline. However, *Enterococcus* (n=6) showed very low sensitivity toward ceftriaxone, cefepime, piperacillin-tazobactam, meropenem and amikacin (16.67% each). Pan resistance was manifested by 12 organisms, all of which were Gram-negative rods.

In 80% of the cases, empirically used antibiotics had to be changed either because of non-response to initially used antibiotics or as per culture sensitivity reports.

DISCUSSION

Out of the total 220 samples sent for analysis in our study, 51 (23.18%, n=220) samples turned out to be positive for microbial growth. *Klebsiella, S. aureus* and *Candida* comprised 32% (n=25), 57.14% (n=14) and 41.66% (n=12) of all Gram-negative, Gram-positive and fungal growths respectively. Gram-negative organisms showed maximum sensitivity toward meropenem, amikacin, levofloxacin, tigecycline, and colistin. Gram-positive organisms showed 100% sensitivity toward vancomycin, linezolid, daptomycin and tigecycline. Organisms could not be isolated in 49 of the study subjects in our study. In 23 patients, the focus of infection could not be documented by clinical and radiological methods.

Roy et al.,[2] showed in their study involving 40 children that organisms were isolated in 60.66% cases. Zengin et al.,[3] in a retrospective study on children with AML in Turkey found 6.89% of pathogenic growth in their clinical samples. Rajeswari et al.,[4] (Thiruvananthapuram, India) and Abdollahi et al.,[5] (Tehran) found culture positivity in 30.6% and 22.5 % respectively (Table 5). The frequency of culture-positive samples in the latter was 18.95%, 22.96%, and 36% in blood, urine, and wound cultures respectively.

The study by Ruth et al.,[6] conducted in Kenya involving 80 children with ALL, showed 30% growth in blood cultures. Segulja et al.,[7] from Croatia were able to isolate causative agents in 64.4% of infectious events in their study involving 23 children with ALL. Yao et al.,[8] observed 23.5% blood culture positivity results out of 2365 blood samples analysed.

Gram-negative microbes were the major cause of sepsis in most of the studies.[3-5,8] While *Klebsiella* was the major Gram-negative microbe in our study, *E. coli* was the most common Gram-negative microbe in studies conducted by Zengin et al.[3] and Abdollahi et al.[5] *Pseudomonas* was found as a major Gram-negative microbe by Rajeswari et al.[4] and Yao et al.[8]

Among Gram-positive organisms, *S. aureus* was the major pathogen in all the studies,[3-8] however the proportion of coagulase positive and coagulase negative *Staphylococcus* varied amongst different studies.[3-8] The *Viridans* group of *Streptococci* was the major Gram-positive microbe in the study conducted by Zengin et al.[3]

Candida species were the major isolated fungi in different studies.[9-11] Yao et al.,[8] however, mentioned *Trichosporon asahii* as the major fungal growth. A study by Lin et al.,[12] showed 20.5% cases of invasive fungal infections in a cohort of 78 AML children admitted in a hospital in Taiwan with proven, probable, and possible infections. *Candida* caused 59.1% of the invasive fungal infections in this study. Sezgin Evim et al.,[13] stated the incidence of invasive fungal infections as 39.4% in a retrospective analysis of 307 children with acute leukemia from Turkey. Invasive Aspergillosis (81.9%) was the most frequent invasive fungal infection followed by invasive candidiasis (13.4%).

Different studies have given mixed reviews regarding the efficacy of antimicrobial monotherapy versus combination therapy to treat sepsis. Segulja et al.,[7] have shown that in 46.1% of cases, a combination of different antibiotics was started on an empirical basis compared to 61% in our study.

We found a high degree of resistance among Gram-negative microbes toward cephalosporins, both 3rd and 4th generation. Among Gram-negative bacteria, only 1 species of *Pseudomonas* was sensitive toward cefepime. Sensitivity toward ceftriaxone was as low as 12.5% in *Klebsiella* species. There was moderate sensitivity among Gram-negative bacteria toward beta-lactam/beta-lactamase inhibitors (30.43%) and aminoglycosides (43.47%). Highest sensitivity was observed among Gram-negative rods toward tigecycline (47.82%), colistin (47.82%), fluoroquinolones (48%), and carbapenems (48%). We got 12 species (23.53% of all bacteria) which were sensitive to none of the drugs we tested, and all of them were Gram-negative rods. 2 species of *Salmonella* showed sensitivity toward all the drugs we tested.

Oztekin Guntas et al.,[14] (Ankara, Turkey) demonstrated more than 50% resistance to 3rd and 4th generation cephalosporins, 21.5% carbapenem resistance, and 38.2% fluoroquinolone resistance. Colistin was the most sensitive drug (93.3%) for Gram-negative rods, whereas

Table 5: Comparison with similar studies regarding microbiological profile of the cases

Parameters	Our study	Roy et al.[2]	Rajeswari et al.[4]	Zengin et al.[3]	Yao et al.[8]	Abdollahi et al.[5]
No. of samples sent for cultures	220	47	147	682	2635	3366
Positive cultures (%)	51 (23.18)	45 (95.74)	45 (30.61)	47 (6.89)	619 (23.49)	760 (22.57)
Negative cultures (%)	163 (76.82)	02 (4.26)	102 (69.39)	635 (93.11)	2016 (76.51)	2606 (77.43)
Most common microbes isolated						
Overall	*Klebsiella*	CONS	*Pseudomonas*	*Escherichia coli*	*Pseudomonas*	*E. coli*
Gram-positive	*Staphylococcus* (MRSA)	CONS	*Staphylococcus* (Both types)	Viridans streptococci	*Staphylococcus*	*Staphylococcus* epidermidis
Gram-negative	*Klebsiella*	*Klebsiella*	*Pseudomonas*	*E. coli*	*Pseudomonas*	*E. coli*
Fungus	*Candida* non albicans	*Candida*	*Candida*	XXXX	*Trichosporon asahii*	XXXX

MRSA: Methicillin-resistant *Staphylococcus aureus*, CONS: Coagulase-negative staphylococci

the least sensitive was ceftazidime (46.3%). The study by Ahmadzadeh et al.,[15] a multicentric retrospective study conducted at four centres in Tehran and Iran on 89 neutropenic patients in postchemotherapy acute leukemia patients, showed the highest sensitivity of Gram-negative rods toward aminoglycosides, moderate sensitivity toward carbapenems, and lowest sensitivity toward 3rd generation cephalosporins. Abdollahi et al.,[5] have demonstrated good sensitivity among Gram-negative rods toward ciprofloxacin. However, more than 50% of Gram-negative rods were resistant to cefepime, ceftriaxone and imipenem. Yao et al.,[8] showed high carbapenem resistance among Gram-negative rods.

In our study, Gram-positive bacteria showed 14.28% sensitivity toward beta-lactam/beta-lactamase inhibitors and 28.57% sensitivity each toward 3rd and 4th generation cephalosporins, carbapenems, fluoroquinolones and aminoglycosides. There was 100% sensitivity among Gram-positive bacteria toward vancomycin, linezolid, tigecycline, and daptomycin. The results were comparable to other studies showing 100% sensitivity among Gram-positive organisms toward vancomycin.[2,4-8]

Roy et al., have shown that *Staphylococcus* had 72–75% sensitivity to Cloxacillin and Amikacin; whereas vancomycin and linezolid had 100% sensitivity, making it a good option for resistant *Staphylococcus* infection.[2] Third-generation cephalosporins (cefepime, ceftazidime) had 75–100% efficacy against Gram-negative organisms. Levofloxacin has an excellent and wide sensitivity against both Gram-positive and Gram-negative organisms.

Sjahruddin et al.,[16] found more than 90% sensitivity among Gram-negative bacteria toward piperacillin, carbapenems and aztreonam. There was moderate sensitivity toward chloramphenicol, cefazolin and cefotaxime and the lowest sensitivity toward ampicillin and amoxicillin. Gram-positive organisms showed high sensitivity toward cefoxitin, gentamicin and oxacillin and lower sensitivities toward clindamycin and penicillin Taneja and Sharma[17] described in their review article on Indian scenario that more than 70% isolates of *E. coli*, *Klebsiella pneumoniae* and *Acinetobacter* and nearly half of all *Pseudomonas aeruginosa* were resistant to fluoroquinolones and third generation cephalosporins. The resistance to the drug combination of piperacillin tazobactam was <35% for *E. coli* and *P. aeruginosa* each. As 65% *K. pneumoniae* and 71% *Acinetobacter* are resistant to carbapenems, colistin is the last resort antimicrobial. The rate of colistin-resistant *Klebsiella* was <1%. Among the Gram-positive organisms, 42.6% of *S. aureus* were methicillin-resistant and 10.5% of *Enterococcus faecium* were vancomycin-resistant.[17]

Another review article by Wattal and Goel[18] from India on pediatric blood cultures and antibiotic resistance has shown that for Gram-positive organisms, MRSA has a prevalence of 46%, and clindamycin resistance has been found to be 23%. There were significantly higher rates of resistance in MRSA (erythromycin: 70.8%, clindamycin: 46.6%, gentamicin: 58.3%) as compared to MSSA (erythromycin: 26.3%, clindamycin: 14.7%, gentamicin: 17.4%). There was no documented resistance to vancomycin, teicoplanin and linezolid. For Gram-negative bacteria, a very low susceptibility of 3rd generation cephalosporins ranging from 7% to 33% was observed. Similarly, they observed a low susceptibility to beta-lactam and beta-lactamase inhibitors like piperacillin-tazobactam, and cefoperazone/sulbactam (16–67%) and quinolones (13–64%). Carbapenems, considered as the last resort drugs, showed low susceptibility in *Acinetobacter* (21%) and *K. pneumoniae* (42%). Resistance to colistin in Gram-negative bacteria, except in *Klebsiella* (2%) and *Enterobacter* spp. (4%) has not been seen.

In our study, antibiotics had to be changed in 80% of cases as per culture sensitivity reports and in cases of nonresponse of the patients to initial empirical antibiotics. In cases of pending or negative antibiotic susceptibility reports, antibiotics had to be upgraded when the patient had become hemodynamically unstable, a fresh focus of infection was found or in the face of rising inflammatory markers. This has been done in accordance with the guidelines by IAP on febrile neutropenia.[19]

Limitations of the study

This was a single-center, descriptive type of observational study with cross-sectional study design. There was no control group; and follow-up of the patients could not be done. The study was conducted in in-patient settings and included critically ill cases mostly. Outpatient Department cases were missed. Tests for anaerobic organisms, viruses and protozoa could not be done due to time and resource constraints. Antifungal susceptibility could not be tested due to the same reason.

CONCLUSION

Sepsis is the leading cause of morbidity and mortality in children with acute leukemia. Gram-negative followed by Gram-positive bacteria, and fungi were the leading causes of sepsis in our study. *Klebsiella* and *Pseudomonas* were the major Gram-negative bacteria, whereas *S. aureus*

and *Enterococcus* were the major Gram-positive organisms. Among fungi, *Candida, Aspergillus* and *Mucor* were common organisms. Resistance to carbapenems, beta lactams with beta lactamase inhibitors and cephalosporins was high in our study. Drugs like aminoglycosides, colistin, tigecycline and fluoroquinolones were sensitive in many cases. Drugs like vancomycin and linezolid has shown good sensitivity.

Findings from this study will help to judiciously choose antibiotics in such settings to achieve maximum therapeutic benefit and to prevent emergence of drug-resistance as well. We strongly recommend continued surveillance and periodical monitoring to determine the susceptibility profile of the commonly isolated infectious microorganisms to enhance the clinical approach and antibiotics treatment among children with acute leukemia.

ACKNOWLEDGMENT

The authors are immensely thankful to the Department of Paediatrics and Department of Microbiology, Medical College, Kolkata, for generous support and encouragement toward successful accomplishment of this study.

REFERENCES

1. Matics TJ and Sanchez-Pinto LN. Adaptation and validation of a pediatric sequential organ failure assessment score and evaluation of the sepsis-3 definitions in critically Ill children. JAMA Pediatr. 2017;171(10):e172352.
https://doi.org/10.1001/jamapediatrics.2017.2352
2. Roy B, Biswas A, Chatterjee A, Pan A and Basu K. Infections in acute leukemia in Indian Children. J Coll Med Sci Nepal. 2014;9(1):40-47.
https://doi.org/10.3126/jcmsn.v9i1.9672
3. Zengin E, Sarper N, Gelen SA, Demirsoy U, Karadogan M, Kilic SC, et al. High infection-related mortality in pediatric acute myeloid leukemia without preventive antibiotics and antifungals: Retrospective cohort study of a single center from a middle-income Country. Turk J Hematol Infect. 2017;(34):340-344.
https://doi.org/10.4274/tjh.2017.0052
4. Rajeswari B, Nair RK, Guruprasad CS, Nair M, Thankamony P and Parukutty K. Infections during induction chemotherapy in children with acute lymphoblastic leukemia - profile and outcomes: Experience from a cancer center in South India. Indian J Med Paediatr Oncol. 2018;(39):188-192.
https://doi.org/10.4103/ijmpo.ijmpo_95_17
5. Abdollahi A, Hakimi F, Doomanlou M and Azadegan A. Microbial and antibiotic susceptibility profile among clinical samples of patients with acute leukemia. Int J Hematol Oncol Stem Cell Res. 2016;10(2):61-69.
6. Ruth RC, Salinah RJ and Moses NM. Antimicrobial susceptibility status of bloodstream infections in children presenting with acute lymphoblastic leukemia at moi teaching and referral hospital in Kenya. Afr J Educ Sci Technol. 2023;7(3):938-944.
https://doi.org/10.13140/RG.2.2.34602.63688
7. Segulja S, Vranešević K, Đorđević A and Roganović J. Infections in children with acute lymphoblastic leukemia. Medicina (Kaunas). 2024;60(9):1395.
https://doi.org/10.3390/medicina60091395
8. Yao JF, Li N and Jiang J. Clinical characteristics of bloodstream infections in pediatric acute leukemia: A singlecenter experience with 231 patients. Chin Med J (Engl). 2017;130(17):20762081.
https://doi.org/10.4103/03666999/213411
9. Gal Etzioni TR, Fainshtain N, Nitzan-Luques A, Goldstein G, Weinreb S, Temper V, et al. Invasive fungal infections in children with acute leukemia: Epidemiology, risk factors, and outcome. Microorganisms. 2024 Jan 11;12(1):145.
https://doi.org/10.3390/microorganisms12010145
10. Garcia-Vidal C, Cardozo-Espinola C, Puerta-Alcalde P, Marco F, Tellez A, Aguero D, et al. Risk factors for mortality in patients with acute leukemia and bloodstream infections in the era of multiresistance. PLoS One. 2018;13(6):35-40.
https://doi.org/10.1371/journal.pone.0199531
11. Sung L, Lange BJ, Gerbing RB, Alonzo TA and Feusner J. Microbiologically documented infections and infection-related mortality in children with acute myeloid leukemia. Blood. 2007;110(10):3532-3539.
https://doi.org/10.1182/blood-2007-05-091942
12. Lin GL, Chang HH, Lu CY, Chen CM, Lu MY, Lee PI, et al. Clinical characteristics and outcome of invasive fungal infections in pediatric acute myeloid leukemia patients in a medical center in Taiwan. J Microbiol Immunol Infect. 2018;51(2):251-259.
https://doi.org/10.1016/j.jmii.2016.08.011
13. Sezgin Evim M, Tüfekçi Ö, Baytan B, Ören H, Çelebi S, Ener B, et al. Invasive fungal infections in children with leukemia: Clinical features and prognosis. Turk J Haematol. 2022;39(2):94-102.
https://doi.org/10.4274/tjh.galenos.2021.2021.0203
14. Oztekin Guntas Ş, Köse V, Koca Yozgat A, Çulha V, Özbek NY, Parlakay A, et al. Microbiologically documented infection-related mortality in children with acute leukemia: A single-center experience. J Pediatr Acad. 2023;4(4):122-127.
https://doi.org/10.4274/jpea.2023.222
15. Ahmadzadeh A, Varnasseri M, Jalili MH, Maniavi F, Valizadeh A, Mahmoodian M, et al. Infection pattern of neutropenic patients in post-chemotherapy phase of acute leukemia treatment. Hematol Rep. 2013;5(4):e15.
https://doi.org/10.4081/hr.2013.e15
16. Sjahruddin DD, Husada D and Ugrasena ID. Microbiological profile and antibiotic susceptibility pattern in children with malignancy and febrile neutropenia. Int J Health Sci. 2022;6(S1):7866-7880.
https://doi.org/10.53730/ijhs.v6nS1.6792
17. Taneja N and Sharma M. Antimicrobial resistance in the environment: The Indian scenario. Indian J Med Res. 2019;149(2):119-128.
https://doi.org/10.4103/ijmr.IJMR_331_18
18. Wattal C and Goel N. Pediatric blood cultures and antibiotic resistance: An overview. Indian J Pediatr. 2020;87(2)125-131.
https://doi.org/10.1007/s12098-019-03123-y
19. Raj R, Jain R and Kharya G. Febrile neutropenia. In: Standard Treatment Guidelines. Vol. 28. Mumbai: Indian Academy of Pediatrics; 2022. p. 1-9.

Authors' Contributions:
AK, SKD, AC, AR- Patient management, planning of the study, data collection; **AK, BB**- Manuscript writing and critical revision; **KB, AC, SKD, AR, SC, PKB, JA**- Compilation of records, review of literature; **AK, MKV, CG, AD**- Manuscript editing.

Work attributed to:
Department of Pediatrics and Department of Microbiology, Medical College and Hospital, Kolkata, West Bengal, India.

Orcid ID:
Dr. Biswajit Biswas - https://orcid.org/0000-0002-9179-3098
Dr. Sayan Chatterjee - https://orcid.org/0000-0002-6879-3751

Source of Support: Nil, **Conflicts of Interest:** None declared.