



(RESEARCH ARTICLE)



## Bacterial and fungal etiology of bloodstream infections in leukemic children under chemotherapy

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### Abstract

Bloodstream infections are severe complications in children with leukemia during chemotherapy and represent a major public health problem. The purpose of this study is to investigate patterns of bacterial and fungal bloodstream infection in children with leukemia during chemotherapy and to provide a rational basis for the use of antibiotics to reduce bacterial resistance. This study was conducted at the Centre for Hematology and Oncology of the children's Protection Teaching Hospital in the Medical City in Baghdad between January and December 2021. We registered children aged under 18 with leukemia and undergoing chemotherapy. A total of 197 bloodstream infection episodes were diagnosed in 165 children. Gram-positive bacteria are the most frequent pathogens (58%) (Staphylococcus aureus 22.8% was the predominant pathogen followed by Staphylococcus epidermidis 13.7%). Among Gram-negative isolates (38%), E. coli 15.2% was the most prevalent isolate followed by pseudomonas aeruginosa 11.7%). The most common isolate of fungi (4%) was candida. albicans 2%. During testing the bacterial pathogen to empirical antibiotics we did find multidrug resistance among bacterial groups. The Gram-positive isolates showed a high resistance rate to oxacillin (99%) and a low resistance rate to Linezolid (6%) while Gram-negative isolates exhibited (100%) resistance to Ampicillin and the least resistance (5%) to cefoxitin. The incidence of bloodstream infection in children with leukemia is caused by multidrug-resistant organisms, without changes during different chemotherapy phases. Further study is needed to reduce this infection and antibiotic sensitivity tests are essential to avoid bacterial resistance and improve advanced therapeutic prophylaxis strategies.

**Keywords:** Blood Cancer; Children; Chemotherapy; Pathogenic microorganism

### 1. Introduction

Over the last decade, various studies demonstrated that children with leukemia are at particularly high risk of developing infection complications [1]. Bloodstream infection is a life-threatening disease that occurs as a response to a viral, bacterial, and fungal pathogen. The symptoms of infection in children may not be clear in many cases, and many children do not show the usual symptoms that can be seen in adults. Symptoms may appear according to the age of the child, the location of the infection, and the pathogens causing it [2]. Some studies have reported that the initial levels of mortality rates up to 42% [3] Children with leukemia often have prolonged neutropenia, suppression in the immune system, skin damage, and alteration in nature of the gastrointestinal mucosa as a result of blood cancer, administration of chemotherapy, radiotherapy, and prolonged hospitalization. All these factors make these patients vulnerable to high-risk bloodstream infections by multiple microbiological agents [4,5]. Although, in this time of problems caused by multidrug-resistant bacterial and fungal etiology, limited information has been previously recorded on epidemiology and risk factors for mortality of bloodstream infection in children with leukemia, especially during induction treatment. This study aimed to evaluate the pattern of bacterial and fungal bloodstream infections with leukemia in children

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throughout the all different phases of chemotherapy and provide a rational basis for the use of antibiotics to reduce bacterial resistance.

## 2. Material and methods

This study was conducted at the Centre for Hematology and Oncology of the Children's Protection Teaching Hospital in the Medical City in Baghdad between January and December 2021.

We registered children aged under 18 with leukemia and undergoing chemotherapy. Blood samples from 165 child patients (94 male and 71 female) were cultured with incubation for 5 days at 37 °C.

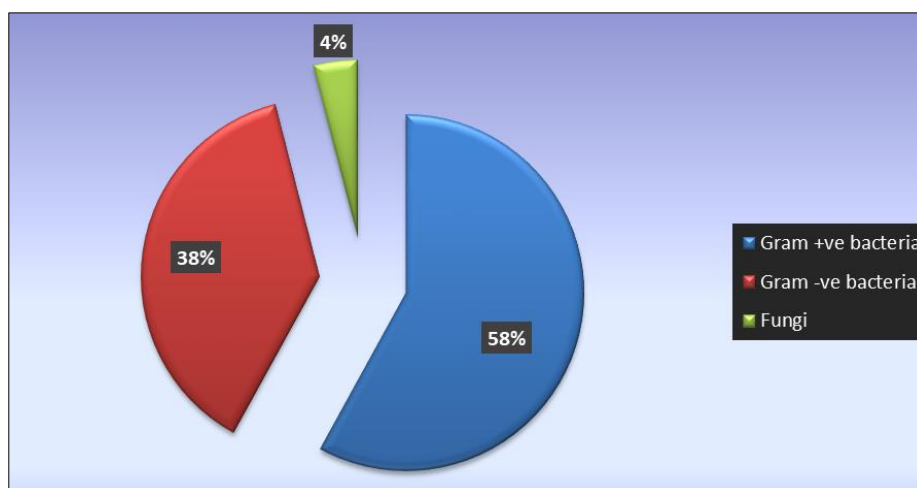
Positive blood cultures were subjected to Gram-staining followed by chocolate, blood, and MacConkey agar plates. Chocolate and blood agar plates were incubated aerobically in 5% CO<sub>2</sub> at 37 °C for 24 - 72 h. MacConkey agar plates were incubated aerobically at 37 °C for 24h. Isolates of bacteria were identified using standard bacteriological and biochemical tests [6].

For fungal cultures, Sabouraud dextrose agar plates were inoculated and incubated at 28°C 5-7days. Identification of fungal isolates was detected according to microscopic findings, colony morphology, and standard laboratory methods [7].

Kirby - Bauer's disk diffusion method was used to perform antimicrobial sensitivity tests for bacterial isolates to different antibiotics [8]. The results were analyzed according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) 2018 [9].

## 3. Results

During the period of study, 197 bloodstream infection episodes were diagnosed in 165 child Patients under 18 years of age and undergoing chemotherapy (94 males and 71 females). A total of 197 positive blood culture monomicrobial infections accounted for 63%(125/197) of all samples and Polymicrobial infections 37% (72/197). Figure 1 shows the isolation ratio of Gram+ve bacteria, Gram-ve bacteria, and fungi are 58% 38%, and 4%, respectively.



**Figure 1** Distribution of percentages of isolates according to pathogens

Table 1 shows that *Staphylococcus aureus* (22.8%) is the most frequent Gram-positive isolate followed by *staphylococcus epidermidis* (13.7%), Coagulase Negative staph. (8.1), *streptococcus sp.* (5.6%), *Enterococcus sp.* (4.6), *micrococcus sp.* (2.5%), and *corynebacterium sp.* (1%).

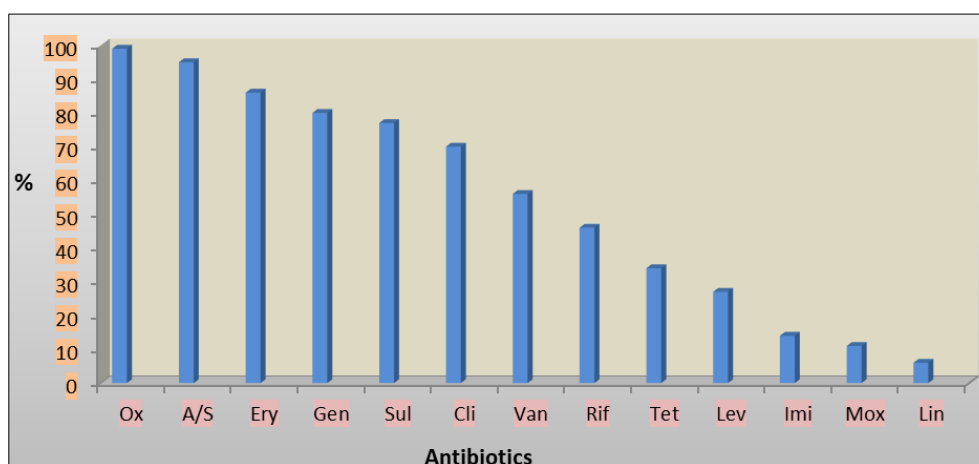
The predominant Gram-negative bacteria were *E.coli* (15.2%) 2 followed by *Pseudomonas aeruginosa* (11.7%), *Klebsiella pneumoniae* (5.6%), *Enterobacter sp.* (3.6%) and *Acinetobacter baumannii* (1.5%).

The most common isolate of fungi was *Candida albicans* (2%) followed by *Candida tropicalis* (1%), *Candida parapsilosis* (0.5%) and *Fusarium sp.* (0.5%).

**Table 1** Distribution of most frequent pathogens caused bloodstream infections in children with leukemia

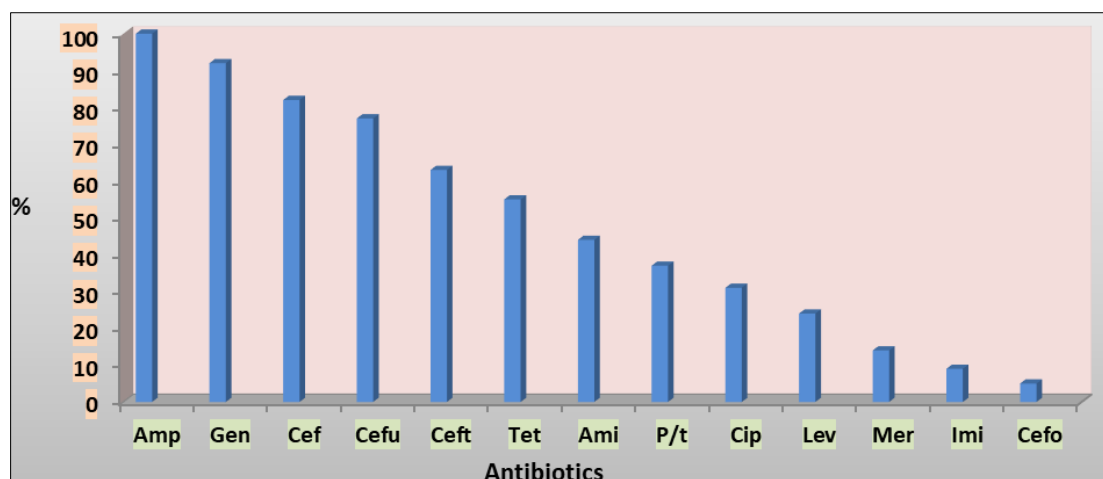
Etiology	Number of isolates	Percentage (%)
<b>Gram-positive</b>		
<i>Staphylococcus aureus</i>	45	22.8
<i>Staphylococcus epidermidis</i>	27	13.7
Coagulase Negative staph.	16	8.1
<i>Streptococcus sp.</i>	11	5.6
<i>Enterococcus sp.</i>	9	4.6
<i>Micrococcus sp.</i>	5	2.5
<i>Corynebacterium sp.</i>	2	1
<b>Gram-negative</b>		
<i>E.coli</i>	30	15.2
<i>Pseudomonas aeruginosa</i>	23	11.7
<i>Klebsiella pneumoniae</i>	11	5.6
<i>Enterobacter sp.</i>	7	3.6
<i>Acinetobacter baumannii</i>	3	1.5
<b>Fungi</b>		
<i>Candida albicans</i>	4	2
<i>Candida. tropicalis</i>	2	1
<i>Candida parapsilosis</i>	1	0.5
<i>Fusarium sp</i>	1	0.5
Total	197	100

All bacterial isolates exhibited resistance to antibiotics used in this study. The Gram-positive bacteria have shown high resistance to Oxacillin (99%) followed by Ampicillin/Sulbactam (95%), Erythromycin (86%), Gentamicin (80%), Sulfamethoxazole (77%), Clindamycin (70%), Vancomycin (56%), Rifampicin (46%), Tetracyclin (34%), Levofloxacin (27%), Imipenem (14%), Moxifloxacin (11%) and Linezolid(6%) Figure (2).



**Figure 2** The percentage of Gram-positive resistance to antibiotics: Ox(Oxacillin), A/S(Ampicillin/Sulbactam), Ery(Erythromycin), Gen(Gentamicin), Sul(Sulfamethoxazole), Cli(Clindamycin), Van(Vancomycin), Rif(Rifampicin), Tet(Tetracyclin), Lev(Levofloxacin), Imi(Imipenem), Mox(Moxifloxacin), Lin(Linezolid)

The percentage of Gram-negative resistance to antibiotics revealed a high resistance to Ampicillin (100%) followed by Gentamicin (92%), Cefotaxime (82%), Cefuroxime (77%), Ceftazidime(63%) Tetracyclin (55%), Amikacin (44%), Piperacillin/tazobactam (37%), Ciprofloxacin (31%) Levofloxacin (24%), Meropenem (14%), Imipenem (9%) and Cefoxitin (5%) Figur(3).



**Figure 3** The percentage of Gram-positive resistance to antibiotics: Amp(Amicillin),Gen(Gentamicin) Cef(Cefotaxime),Cefu(Cefuroxim),Ceft(Ceftazidime),Tet(Tetracyclin),Ami(Amikacin), P/T(Piperacillin/Tazobctam), Cip(Ciprofloxacin),Lev(Levofloxacin),Mer(Meropenem), Imi(Imipenem),Cefo(Cefoxitin).

#### 4. Discussion

Bloodstream infections are a major cause of mortality rate in children with leukemia during chemotherapy treatment due to a deficient immune system and susceptibility to infection complications [10]. The incidence of bloodstream infection was increased in patients with immunosuppressive agents, mucosal barrier damage, corticosteroids, and long-term neutropenia after chemotherapy [11]. Our study showed that a group of Gram+ve bacteria play a leading role in infections more than Gram-negative bacteria and fungi. Celkan *et al.* [12] reported that Gram +ve bacteria accounted for 60% of the pathogens from the positive blood culture of 132 patients with leukemia. These results are consistent with the results of our study. Among Gram-ve isolates, *Staphylococcus aureus* (22.8) was the most predominant pathogen, followed by *staphylococcus epidermidis*(13.7%). Among Gram-negative isolates, *E.coli* (15.2%) was the most prevalent isolate followed by *Pseudomonas aeruginosa* (11.7%). These results are compatible with those demonstrated by others [13,14.] Our current results showed the most causative agent of fungemia was *Candida albicans*. These findings are similar to past studies, the candida species play role in the development of bloodstream infections among newborns and children [15, 16].

Through the results of the antibiotic sensitivity test of bacterial isolates, we found multidrug resistance among bacterial groups. The Gram-positive isolates showed high resistance to Oxacillin (99%) and low resistance rate to Linezolid (6%), while Gram-negative isolates exhibited 100 % resistance to Ampicillin and the least resistance was 5%to Cefoxitin. These findings are concerted with other studies involving patients with blood cancer [17, 18, 19]. Information interacts with a present epidemiologic and outcome of multidrug-resistant bacteria in patients who have blood cancer scare [20,21] and there includes a loss of data on leukemic patients. The incidence of infections produced by multidrug-resistant organisms became a serious global health problem [22, 23].

#### 5. Conclusion

In our study, we found that multidrug-resistant organisms are widespread in bloodstream infections in children with leukemia, and Gram-positive bacteria are the most frequent pathogens, without changes during different chemotherapy phases .further study is needed to reduce the risk factors of this infection and antibiotic sensitivity test are essential to avoid bacterial resistance and improve advanced therapeutic prophylaxis strategies.

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## Compliance with ethical standards

### *Acknowledgments*

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### *Disclosure of conflict of interest*

There are no conflicts of interest for any of the authors.

### *Statement of ethical approval*

The present research work does not contain any studies performed on animal/human subjects by any of the authors.

### *Statement of informed consent*

This study was done with the consent of the patients or the parents.

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