

## REVIEW ARTICLE

## Bloodstream infections in patients with acute leukemia: A review

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## Abstract

**Introduction:** Acute leukemia (AL) is a life-threatening hematologic malignancy marked by the rapid expansion of immature blood cells and profound immune suppression. This immunocompromised state renders patients highly susceptible to bacterial infections, particularly bloodstream infections, which occur in 11% to 38% of cases and are a leading cause of morbidity and mortality.

**Objective:** This review provides an in-depth analysis of the bacterial infection burden in AL patients, focusing on common pathogens, risk factors, diagnostic hurdles, and clinical management.

**Results:** Gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus*, coagulase-negative staphylococci, and enterococci, along with Gram-negative pathogens like *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*, represent the most frequently isolated organisms. Both nosocomial and community-acquired infections are examined, with particular attention to the rise of multidrug-resistant strains. Risk factors for infection include prolonged neutropenia, chemotherapy, central venous catheters, and extended hospitalization. Diagnostic complexity arises from non-specific symptoms and delayed pathogen identification, making timely, accurate diagnosis critical. Advances in culture-independent testing and imaging are improving detection but remain underused. The cornerstone of effective management includes prompt empirical antibiotic therapy, targeted prophylaxis, and rigorous infection control. Adjunct strategies, such as vaccination and nutritional optimization, play supportive roles.

**Conclusion:** In conclusion, tackling infection-related complications in AL requires a multifaceted, proactive approach. Future priorities include developing unified diagnostic algorithms, enhancing antimicrobial stewardship, and tailoring interventions to individual risk profiles to improve survival and quality of life in this vulnerable population.

**Keywords:** Acute leukemia; Bloodstream infections; Neutropenia; Chemotherapy; Antimicrobial resistance; Immunocompromised patients

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## 1. Introduction

Acute leukemia (AL) is a complex disease with diverse clinical symptoms and molecular features.<sup>1</sup> It is characterized by the infiltration of abnormal, poorly differentiated, proliferating hematopoietic stem cells. The symptom spectrum is determined by the affected lineage: lymphoid, myeloid, or mixed.<sup>2</sup> There are two primary types of AL: acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). The incidence of AML increases steadily after the age of 40, with a median age of around 65 years,<sup>3</sup> whereas the incidence of ALL peaks between ages 2 and 4, declines in late childhood and early adulthood, and then rises again in older age.<sup>4</sup> In AML, abnormal proliferation and impaired differentiation of myeloid stem cell clones are core features. Chromosomal translocations such as t(8;21) impair the normal maturation of myeloid progenitors.<sup>5</sup> Although AML was once linked to genome-damaging factors such as chemical exposure, recent research has not confirmed the role of these agents; instead, AML is hypothesized to arise from various genetic mutations and chromosomal abnormalities.<sup>6</sup>

Additionally, ALL involves the malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow and bloodstream. Genetic factors significantly influence the risk of genetic alterations. These alterations, such as fusions, rearrangements, and mutations, disrupt the normal function of T or B cells and contribute to each ALL classification.<sup>7</sup>

Various environmental factors have been proposed to contribute to the development of leukemia.<sup>8</sup> Most involve exposure to carcinogenic substances at different life stages, including during infections. Leukemia has been associated with bacterial, viral, and fungal infections either alone or in conjunction with genetic abnormalities. Infectious agents, such as Epstein-Barr virus, herpesviruses, human immunodeficiency virus, severe acute respiratory syndrome, COVID-19, and human T-lymphotropic virus, have been suggested to influence leukemia's etiology and have been extensively investigated.<sup>9</sup> Bloodstream infections (BSIs) are common among individuals with hematological malignancies, with an incidence ranging from 11% to 38%.<sup>10</sup>

Sepsis is a life-threatening organ dysfunction resulting from a systemic response to infection.<sup>11</sup> In AL patients, the severity of sepsis symptoms is influenced by factors such as chemotherapy-induced mucosal damage, the duration of neutropenia or prolonged humoral immune impairment, and prior antibiotic use.<sup>12</sup> Age also affects survival outcomes,<sup>13</sup> with some research indicating that children are more prone to severe sepsis and often experience moderate to severe neurocognitive deficits.<sup>14</sup> The risk

and severity of infection tend to escalate if sepsis occurs during treatment, leading to significant deterioration in AL patients' condition.<sup>15</sup>

In this narrative review, we aim to summarize common bacterial infections, risk factors, and their pathophysiology in patients with AL. We describe clinical diagnosis and laboratory tests, emphasizing the most common management approaches for these infections in this patient population.

## 2. Common bacterial infections in acute leukemia patients

Patients with hematological malignancies face a higher risk of BSIs, with prevalence rates ranging from 11% to 38%.<sup>16</sup> Their compromised immune systems make them more susceptible, particularly after chemotherapy and during prolonged neutropenia. Some studies report attributable mortality rates of up to 30%, while overall mortality ranges from 12% to 42%. The most common bacterial infections are caused by Gram-positive and Gram-negative organisms, including both nosocomial and community-acquired infections (Table 1).<sup>17</sup>

Patients with AML typically have a higher prevalence and increased severity of bacterial infections compared to those with ALL.<sup>18</sup> This disparity is chiefly ascribed to the extended and severe neutropenia linked to AML induction chemotherapy, increased impairment of innate immune defenses, and prolonged hospitalization lengths.<sup>19</sup> Gram-negative bacteria, notably *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, are the primary pathogens implicated in BSIs in AML.<sup>20</sup> Gram-positive organisms, such as coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus*, are commonly isolated in both AML and ALL, especially in relation to central venous catheters.<sup>21</sup> Numerous studies have shown that individuals with AML have a markedly elevated incidence of BSIs, febrile neutropenia, intensive care unit admissions, and infection-related death in comparison to those with ALL. Kuo *et al.*<sup>22</sup> indicated that BSIs were more prevalent in pediatric AML patients compared to those with ALL (79.3% vs. 61.8%), highlighting the increased intensity of myelosuppressive therapy and prolonged neutropenic durations in AML.<sup>22</sup> Rolston<sup>23</sup> also highlighted that bacterial infections are the most prevalent and initial infectious consequences in AL, with the greatest risk occurring during extended neutropenia, a condition more commonly seen in AML than in ALL.<sup>23</sup> These data highlight the need for disease-specific infection surveillance, immediate empirical antibiotic treatment, and enhanced preventive efforts, especially for patients with AML who face a significantly elevated risk of severe

bacterial infections.

### 2.1. Gram-positive bacteria

The most common Gram-positive pathogens are *S. aureus* and coagulase-negative staphylococci (CoNS) (Table 1).<sup>24</sup> CoNS frequently causes catheter-related bacteremia with persistent infection treated with antimicrobial agents if the catheter is not removed.<sup>25</sup> A study of AL in pediatric patients revealed a high prevalence of Gram-positive bacterial infections, with methicillin-resistant *S. aureus* emerging as a significant concern.<sup>16</sup> Alpha-hemolytic or viridans group streptococci are also significant pathogens in AL patients, particularly during periods of neutropenia.<sup>26</sup> These organisms can cause severe septicemia and are associated with the development of acute respiratory distress syndrome in some cases. In addition, *Enterococci*, especially *Enterococcus faecalis* and *faecium*, are important pathogens in leukemia patients.<sup>27</sup> Intrinsic antibiotic resistance and the ability to acquire new resistance mechanisms are major obstacles to treating these infections.<sup>28</sup> *Bacillus* species, *Corynebacterium* species, and *Micrococcus* species are other Gram-positive bacteria that commonly colonize human skin and contribute to infections in AL patients with catheter-related bacteremia.<sup>29</sup> The increasing prevalence of Gram-positive infections is attributed to factors such as the use of intravascular devices and antibiotic prophylaxis strategies that may inadvertently select for resistant strains. Infections generated by *S. aureus* exhibit heightened pathogenicity and are linked to significant morbidity and mortality.<sup>30</sup> The rise of multidrug-resistant strains complicates treatment options and emphasizes the importance of antibiotic stewardship in clinical settings. In summary, the prevalence of Gram-positive bacterial infections, especially multidrug-resistant strains, illustrates the importance of stringent infection control practices and targeted antibiotic strategies to protect vulnerable leukemia patients.

### 2.2. Gram-negative bacteria

Gram-negative bacteria are significant contributors to BSIs in AL patients (Table 1).<sup>31</sup> The gastrointestinal tract is an essential source of these infections. In some centers, the use of antibiotic prophylaxis in AL patients has led to a reduction in the incidence of Gram-negative infections.<sup>32</sup> The common Gram-negative bacteria isolated from neutropenic patients include *Pseudomonas aeruginosa*, *E. coli*, and *K. pneumoniae*.<sup>33</sup> In a retrospective study conducted in Saudi Arabia, *K. pneumoniae* (33.3%), *P. aeruginosa* (23.5%), and *E. coli* (17.6%) were identified as the most prevalent Gram-negative pathogens among adult leukemia patients.<sup>34</sup> However, less common Gram-negative pathogens include *Acinetobacter* species and *Enterobacter*

species, which can also cause serious infections in immunocompromised patients. Non-fermentative Gram-negative bacilli such as *P. aeruginosa* and *Acinetobacter baumannii* are particularly concerning due to their ability to resist multiple antibiotics, often requiring more aggressive and targeted therapeutic approaches. The development of Gram-negative bacteria, especially in febrile neutropenia, can increase the risk of morbidity and mortality because the ability to combat these infections is reduced.<sup>35</sup> Furthermore, indwelling catheters can facilitate these pathogens' entry into the bloodstream.<sup>36</sup> Together, Gram-negative bacteria represent a critical challenge in leukemia patients, which points to the need for rigorous infection control and prompt treatment interventions.

### 2.3. Nosocomial infections

Acute leukemia patients are frequently hospitalized and exposed to healthcare settings for extended periods. As a result, nosocomial infections pose a substantial risk to these patients. There is a growing prevalence of multidrug-resistant pathogens in this population, including vancomycin-resistant *Enterococcus* and methicillin-resistant *S. aureus* (Table 1). A study indicated that up to 52.6% of BSIs were nosocomially acquired, emphasizing the critical need for stringent infection control measures within healthcare facilities.<sup>37</sup> The emergence of these resistant strains complicates treatment options and demonstrates the value of early detection and appropriate empirical therapy. Implementing effective infection control protocols is crucial for reducing the incidence of nosocomial infections in this vulnerable group. Nosocomial infections not only increase treatment complexity but also contribute to higher mortality rates in AL patients.<sup>38</sup> In summary, strengthening infection prevention and timely intervention strategies is essential for safeguarding patient health and improving clinical outcomes.

### 2.4. Community-acquired infections

While nosocomial infections dominate, community-acquired bacterial infections also present risks for AL patients. They can arise from various sources, such as the respiratory, urinary, or gastrointestinal systems,<sup>39</sup> including *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *E. coli*, which can lead to severe outcomes in immunocompromised patients (Table 1).<sup>40</sup> Effective management strategies must incorporate knowledge of prevalent organisms, resistance mechanisms, and the unique vulnerabilities of this patient population. The management requires a comprehensive approach that includes empirical antibiotic therapy based on the patient's clinical status and local epidemiological data. Understanding local patterns of resistance can guide

effective treatment strategies and reduce morbidity and mortality in these patients.

### 3. Pathophysiology of bacterial infections in hematologic cancer patients

Bacterial infection in AL patients can present differently because persistent neutropenia limits the ability to mount an adequate inflammatory response.<sup>41,42</sup> Around 60% of febrile patients show no specific symptoms during infection due to fever of unknown origin. These febrile episodes can progress rapidly into bacterial infection if not diagnosed correctly. Chemotherapy is a risk factor for prolonged neutropenia, which can lead to recurrent bacterial infections.<sup>43</sup> AML is the most prominent type of leukemia and often experiences multiple episodes of symptoms when undergoing invasive chemotherapy.<sup>44</sup> It is most common in childhood.<sup>45</sup> Children diagnosed with AML exhibit more susceptibility to disseminated infections; this suggests a consequence of chemotherapy treatment during phases 1 and 2 of the treatment course.<sup>46</sup> On the other hand, ALL is associated with recurrent neutropenia episodes and persistent infection during phase 2 of treatment in children with an average age of 9.9 years.<sup>47</sup> This provides a possible similarity of bacterial infection manifestations in ALL and AML within the same age group. Antibiotic prophylaxis can prevent bacterial invasion; however, it may mask BSI-related symptoms and delay diagnosis and proper treatment planning.<sup>48</sup> During the treatment plan, when the underlying cause of symptoms cannot

be identified due to the masking effect, chemotherapy will be discontinued, which is suggested to be one of the possible risk factors for febrile neutropenia and infections. In addition, antibacterial tolerance may cause antibiotics to be unable to penetrate the cell wall and stop bacterial dissemination.<sup>49</sup> Blinatumomab, the targeted therapy for B cells in ALL, is another factor contributing to bacterial dissemination. It significantly changes immunoglobulin G (IgG) levels and decreases immunoglobulin A (IgA) levels, which contributes to bacterial dissemination, toxin production, and reduced neutralization at the mucosal surface membrane. Patients treated with blinatumomab were found to have significantly changed IgG levels and decreased IgA levels; this is due to the production of toxins that enhance bacterial distribution, in addition to impairment of neutralization and bacterial control, which is the key function of IgA at the mucosal surface.<sup>50,51</sup> IgG is the most abundant serum subtype and travels to mucosal surfaces to complement the function of IgA,<sup>52,53</sup> and both are crucial for fighting infection.<sup>54</sup> Moreover, ALL treatments have been significantly associated with increased immunosuppression, which causes less effective memory cells in younger patients. The mechanism behind opportunistic bacterial infection is explained in CD19-targeted cell therapy. The bacterial infection can worsen during the first stage of infection and is exacerbated by anti-inflammatory treatment, which induces neutropenia. Patients in this stage are prone to BSI, gastritis, and pneumonia, and their humoral immunity can remain

**Table 1. Common types of bacterial infections in acute leukemia**

| Pathogen type                 | Examples                                                                                                                                              | Characteristics                                                                                                          | Clinical implications                                                                                                                                                               |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gram-positive bacteria        | <i>Staphylococcus aureus</i> , coagulase-negative staphylococci, <i>Streptococcus</i> species (including viridans group), <i>Enterococcus</i> species | Commonly isolated; increasing prevalence; often associated with indwelling catheters; potential for multidrug resistance | High rates of morbidity; MRSA poses significant treatment challenges; viridans streptococci can cause severe septicemia; enterococci show intrinsic resistance to many antibiotics  |
| Gram-negative bacteria        | <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>                                                                | High virulence; frequent cause of severe BSIs; mortality rates up to 40%                                                 | Associated with febrile neutropenia; requires aggressive management; <i>K. pneumoniae</i> most common (33.3%), followed by <i>P. aeruginosa</i> (23.5%), and <i>E. coli</i> (17.6%) |
| Nosocomial infections         | MRSA, vancomycin-resistant <i>Enterococci</i> , multidrug-resistant Gram-negative bacteria                                                            | Multidrug-resistant; significant treatment challenges                                                                    | Increased risk during hospitalization; necessitates strict infection control measures; complicates treatment options                                                                |
| Community-acquired infections | Various pathogens including less virulent organisms                                                                                                   | Can lead to severe outcomes in immunocompromised patients; requires tailored management                                  | Important consideration in outpatient settings; needs prompt treatment based on local epidemiology and resistance patterns                                                          |

Abbreviations: BSIs: Bloodstream infections; MRSA: Methicillin-resistant *Staphylococcus aureus*.

resistant for up to one year due to rising cytokine levels.<sup>55,56</sup> In summary, multiple factors contribute to changes in the immune system of patients diagnosed with AL, but intensive chemotherapy is regarded as a primary cause of the inflammatory response that results in a poor response to vaccination and challenges in eliminating infections.<sup>57,58</sup>

#### 4. Risk factors for bacterial infections in acute leukemia patients

Bacterial infections pose a significant threat to patients with hematologic malignancies, contributing to increased morbidity and mortality rates. In this section, we discuss the key risk factors predisposing these patients to bacterial infections, focusing on disease, patient, and treatment-related factors (Figure 1).

##### 4.1. Disease-related factors

The immunocompromised status is one of the disease-related risk factors in AL patients. The underlying leukemia compromises the immune system, rendering patients more susceptible to infections.<sup>59</sup> Leukemia is associated with neutropenia, a condition defined by low neutrophil counts, which greatly increases the risk of infection. When the absolute neutrophil count drops below 500 cells per microliter, the immune system is unable to establish a sufficient defense against infection. Regarding infection risk, the severity and duration of neutropenia are directly correlated, with prolonged neutropenia (more than seven days) being more harmful. Moreover, gastrointestinal tract disturbance constitutes a disease-related risk factor, as leukemia can influence the gastrointestinal tract, which is a significant source of Gram-negative infections.<sup>60</sup>

##### 4.2. Patient-related factors

Advanced age of patients is a significant patient-related risk factor, since older individuals are more susceptible to age-related immunological disorders and comorbidities.<sup>61</sup> Comorbidities and pre-existing health disorders can further undermine the immune system.<sup>62</sup> Furthermore, dietary problems, such as malnutrition, are prevalent among cancer patients and can compromise immunological defenses. The extended hospitalization of AL patients may elevate the risk of exposure to nosocomial infections. Hospital settings include antibiotic-resistant microorganisms, posing risks of exposure to hazardous infections for patients. Research suggests that 52.6% of BSIs in these individuals are acquired nosocomially.<sup>63</sup>

##### 4.3. Treatment-related factors

Chemotherapy is a cytotoxic treatment that suppresses the immune system and increases infection risk. Chemotherapy-induced neutropenia is a common

complication, leaving patients vulnerable to various bacterial infections.<sup>64</sup> Central venous catheters provide a direct entry point for pathogens into the bloodstream. Gram-positive bacteria, primarily CoNS, cause up to 60% of catheter-related infections. While antibiotic prophylaxis reduces some infections, these procedures can lead to the selection of resistant strains. Stem cell transplantation and subsequent immunosuppression may elevate the risk of infection in AL patients. Chemotherapy-induced mucositis can cause mucosal barrier injury and allow bacterial translocation.<sup>65</sup>

##### 4.4. Multifactorial risk

The complex interplay of these factors significantly increases the risk of bacterial infections in AL patients. Figure 1 illustrates the multifactorial nature of BSI risk in this population, highlighting the combined contribution of prolonged neutropenia, mucosal barrier injury, central venous catheter use, antimicrobial exposure, and host-related vulnerabilities. The figure emphasizes that BSIs in AL do not arise from a single cause, but rather from the interaction between disease-related, patient-related, and treatment-related factors. This integrated view supports the need for individualized preventive and therapeutic strategies in clinical practice. Neutropenia, particularly when prolonged, is a critical risk factor.<sup>66</sup> The use of central venous catheters, while necessary for treatment, substantially increases infection risk.<sup>67</sup> The emergence of multidrug-resistant organisms further complicates treatment options. Elderly patients face unique challenges due to age-related immune decline, comorbidities, and increased frailty.<sup>68</sup> Comprehensive geriatric assessments can help identify these vulnerabilities and guide treatment decisions.

In summary, managing infection risk in AL patients requires a multifaceted approach that addresses disease-, patient-, and treatment-related factors. Strategies such as careful neutropenia management, judicious use of invasive procedures, strict infection control practices, and comprehensive patient assessments are crucial for improving outcomes in this vulnerable population. Understanding these risk factors is essential for developing effective prevention and management strategies to reduce infection rates and improve patient outcomes.

#### 5. Diagnosis of infections in leukemia

Diagnosing bacterial infection in leukemia patients requires multiple steps of clinical investigation, including clinical evaluation and laboratory testing. Relying on a single parameter alone can cause a non-specific diagnosis due to similarities with other diseases that require a differential diagnosis.<sup>69</sup> Additionally, some types of bacteria

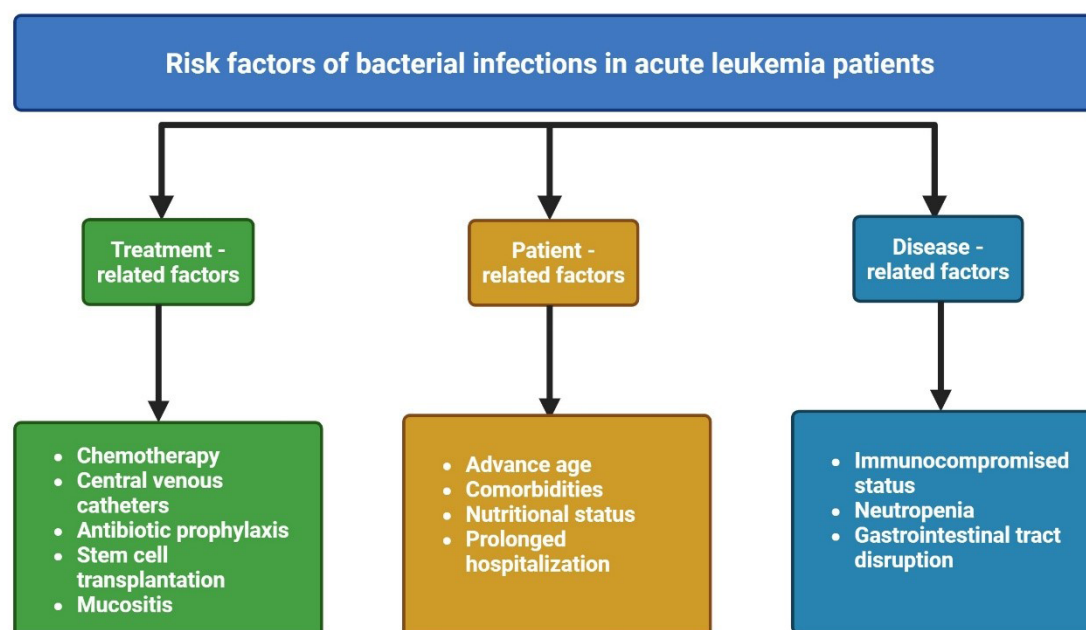


Figure 1. Risk factors for bacterial infections in acute leukemia patients

are characterized by specific clinical outcomes, and others can cause a wide range of diseases. In AL patients, the diagnosis is considered more challenging because of the confounding risk of the disease. The laboratory workflow starts with choosing the best specimen, which is a crucial part of the analysis.<sup>70</sup> The gold standard practice for bacterial identification and specification is the culture procedure followed by biochemical methods. However, these methods are prone to errors, which may compromise the accurate identification of the pathogenic species.<sup>71</sup> Automated processes with high sensitivity have been introduced to improve test quality, effectively detecting low concentrations of bacteria, especially in BSI cases.<sup>72</sup> Overall, the automated method achieved greater microorganism recovery than conventional methods and provided a variety of culture media with reliable results.<sup>73</sup>

### 5.1. Imaging techniques used to identify infections

Radiological diagnosis plays a vital role in indirectly managing several microbial infections. It can assist in the diagnosis of *Mycobacterium tuberculosis* infection and also locate the source of infection using techniques like ultrasonography and computed tomography, which helps in choosing the appropriate sample for collection.<sup>74</sup> Although radiological imaging cannot reliably differentiate bacterial infection from sterile fluid accumulation, a novel approach has suggested that biofilms may appear as microdroplets on ultrasound images.<sup>75</sup> In AL cases, early

detection of bacterial infection is essential, particularly when evaluating abdomen- and pelvis-related pathology.<sup>76</sup> Rather than conventional methods, using radiolabeled substances improves overall resolution in cases of infection. However, poor differentiation between infection and malignancy has been shown. Positron emission tomography using <sup>18</sup>F-fluorodeoxyglucose is a known technique used in clinical infectious and inflammatory diseases.<sup>77</sup>

### 5.2. Challenges in the early diagnosis of infections in immunocompromised patients

Diagnosing bacterial infection in AL cases is considered different because it requires an in-depth investigation and a diagnostic panel covering a broad spectrum of possible microorganisms. Another aspect to consider is the emergence of new treatments and uncommon pathogens during treatment, which introduces additional factors that can make diagnosis more challenging.<sup>78</sup> Although the symptoms related to drug toxicity are less common, they should be considered to help exclude non-infectious causes.<sup>79</sup> One microbiology report notes that conventional testing methods such as culture are not suitable for more invasive samples and suggests using metagenomic sequencing in advanced infection. However, despite advances in testing techniques, obtaining invasive samples from immunocompromised patients remains challenging.<sup>80</sup> From a radiology perspective, when a patient is suspected

of having an infection, antibiotics are administered immediately, causing interference with advanced imaging techniques like positron emission tomography scans.<sup>81</sup>

## 6. Management of bacterial infection in leukemia patients

Patients with AL are highly vulnerable to bacterial infections due to profound immunosuppression caused by both the malignancy itself and the effects of chemotherapy. Effective infection management in this population requires a structured approach that includes prompt antimicrobial therapy, targeted prophylaxis, and rigorous infection control measures.

### 6.1. Risk stratification

Initial management should begin with formal risk assessment using the Multinational Association for Supportive Care in Cancer risk index,<sup>82</sup> which incorporates burden of illness, presence of hypotension, chronic obstructive pulmonary disease, tumor type, dehydration, outpatient status, and age. A score  $\geq 21$  identifies low-risk patients who may be candidates for oral or early step-down therapy, whereas high-risk patients—including those with anticipated profound neutropenia (ANC  $\leq 100$  cells/ $\mu$ L) lasting more than seven days, hemodynamic instability, or significant comorbidities—require inpatient intravenous therapy.<sup>83</sup>

### 6.2. Empirical antimicrobial therapy

High-risk febrile neutropenic patients should receive empirical monotherapy with an anti-pseudomonal  $\beta$ -lactam—cefepime, piperacillin-tazobactam, or a carbapenem (meropenem or imipenem-cilastatin)—administered within one hour of presentation, even before pathogen identification. Aminoglycosides and fluoroquinolones should not be used as monotherapy. Combination therapy, adding an aminoglycoside to the  $\beta$ -lactam, may be considered in complicated presentations such as septic shock, pneumonia, or suspected carbapenem-resistant organisms.<sup>84</sup>

### 6.3. Prophylactic antibiotics

Prophylactic antibiotic use is another widely implemented strategy, particularly during anticipated periods of prolonged neutropenia. Fluoroquinolones, such as levofloxacin, have been shown to reduce the incidence of bacterial infections in high-risk patients. However, their use must be carefully balanced against the potential for selecting multidrug-resistant organisms.

### 6.4. Addition of Gram-positive coverage

Empirical vancomycin, or an alternative such as linezolid

or daptomycin, is not recommended routinely but should be added when there is hemodynamic instability or septic shock, clinically suspected catheter-related infection, skin or soft-tissue infection, severe mucositis in patients receiving fluoroquinolone prophylaxis, known colonization with methicillin-resistant *S. aureus*, or radiographically confirmed pneumonia. If empirical vancomycin is started and cultures at 48–72 hours do not confirm a resistant Gram-positive organism, it should be discontinued.<sup>85</sup>

### 6.5. Source control and catheter management

Blood cultures should be drawn from both the catheter and a peripheral site to help localize the source of infection. Catheter removal is generally indicated for bacteremia due to *S. aureus*, *P. aeruginosa*, *Candida* species, rapidly growing non-tuberculous mycobacteria, tunnel or port-pocket infection, septic thrombosis, endocarditis, or bacteremia persisting beyond 72 hours of appropriate therapy.<sup>86</sup> In contrast, catheter salvage using systemic antibiotics combined with antibiotic-lock therapy can be attempted for CoNS and selected Gram-negative or enterococcal infections in clinically stable patients, with close monitoring for treatment failure.<sup>87</sup>

### 6.6. Treatment of resistant Gram-negative organisms

Extended-spectrum  $\beta$ -lactamase-producing organisms are generally treated with a carbapenem. For carbapenem-resistant *Enterobacterales* or carbapenem-resistant *P. aeruginosa*, options include ceftazidime-avibactam, meropenem-vaborbactam, or cefiderocol, guided by susceptibility testing; polymyxins such as colistin remain a last-resort option where newer agents are unavailable.<sup>88</sup> Local antibiograms and prior colonization data should guide empirical antibiotic selection in settings with a high prevalence of resistant organisms.<sup>89</sup>

### 6.7. De-escalation

Once a causative pathogen is identified and susceptibility results are available, therapy should be narrowed to the most targeted effective agent, and empirical broad-spectrum or Gram-positive coverage discontinued if not clinically indicated.<sup>90</sup> De-escalation reduces selection pressure for resistant organisms without compromising outcomes in clinically stable patients.<sup>91</sup>

### 6.8. Duration of therapy

Recent findings also suggest that short-course antibiotic therapy, typically seven days or less, may be sufficient for uncomplicated BSIs, provided the patient is clinically stable. This approach minimizes antibiotic exposure without compromising treatment efficacy.<sup>92</sup>

### 6.9. Infection control practices

Preventive measures extend beyond medications. Strict infection control practices within healthcare settings are vital, including practicing hand hygiene, using high-efficiency particulate air filtered environments, and minimizing invasive procedures. During periods of hospital construction or renovation, environmental safeguards are especially critical to prevent exposure to airborne pathogens.<sup>93</sup>

### 6.10. Vaccination strategies

In addition to antibiotics, vaccinations represent an important preventive layer. Although immunosuppression can limit vaccine efficacy, administering pneumococcal and influenza vaccines during remission or before chemotherapy is encouraged when feasible. These vaccines help reduce the incidence of severe respiratory infections, which are common in immunocompromised patients.<sup>94</sup>

### 6.11. Nutritional and supportive care

Supportive measures such as nutritional optimization also play a role in strengthening host defenses. Malnutrition is prevalent in cancer patients and is associated with increased susceptibility to infection; therefore, early dietary intervention is recommended as part of comprehensive care.<sup>95</sup>

Effective infection control in AL is not limited to reactive treatment; it must include anticipatory, preventative, and individualized strategies. By aligning antimicrobial protocols with patient-specific risks and maintaining high standards of hospital hygiene, clinicians can significantly reduce infection-related morbidity and improve patient outcomes.<sup>96</sup>

## 7. Conclusion

In conclusion, AL is a complex disease that presents different clinical manifestations depending on leukemia lineage. Underlying pathophysiological alterations in immune response and genetic background are among the factors that lead to increased infection risk. Bacterial infections can be introduced throughout the treatment plan, including chemotherapy, antibiotics, and nosocomial infections during hospitalization and invasive procedures. Managing and understanding all factors contributing to the overall outcome of disease helps decrease the infection rate and improve prognosis. Early detection of the disease through highly sensitive and specific automated testing can prevent the need for invasive sample procedures at advanced stages of infection by effectively identifying the targeted pathogen at the onset of the disease. Antibiotic resistance is considered one of the significant challenges in

treatment when Gram-negative or Gram-positive infection is associated with intravascular devices or catheterization because of its ability to produce resistance during empiric therapy. Bacteria that can resist multiple antibiotics often require more aggressive antibiotics, which can increase mortality and morbidity in immunocompromised patients. The suggested future perspective is to establish a clear, guided protocol to identify potential strategies to control and prevent infection in AL patients, and to study the effectiveness of the established diagnostic protocol for detecting pathogens from laboratory and radiology perspectives. Additionally, the effects of multifactorial factors on disease outcomes and quality of life in patients with AL should be considered.

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The authors declare that they have no competing interests.

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