

ANTIMICROBIAL RESISTANCE PATTERNS IN HEMATO-ONCOLOGY: A COMPREHENSIVE REVIEW

Justy Babu¹, Sathasivam Sivamalar^{2*}

¹Department of Research, Meenakshi Academy of Higher Education and Research (MAHER), Chennai, 600078, Tamil Nadu, India.

^{2*}Department of Research, Meenakshi Academy of Higher Education and Research (MAHER), Chennai, 600078, Tamil Nadu, India. Email ID: drsivamalar@maher.ac.in

ABSTRACT:

Background: Hematological malignancies and their therapies have improved survival outcomes, yet infections remain a major cause of morbidity and mortality. Immunosuppression, invasive devices, and prolonged hospitalizations predispose patients to antimicrobial-resistant pathogens. With rising prevalence of multidrug-resistant organisms (MDROs), effective infection management in hemato-oncology is increasingly complex.

Methods A systematic search of PubMed, Scopus, and Google Scholar was conducted for studies published between 2014 and 2025. Eligible studies included observational cohorts, clinical trials, and case reports reporting antimicrobial resistance (AMR) in hemato-oncology populations. Data extraction focused on study characteristics, pathogens, resistance patterns, and clinical outcomes. Methodological quality was assessed using the Newcastle–Ottawa Scale, and findings were synthesized narratively.

Results: Gram-negative organisms, particularly *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, accounted for the majority of bloodstream infections, with extended-spectrum β -lactamase (ESBL) and carbapenem resistance highly prevalent. Among Gram-positive bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA), coagulase-negative staphylococci, and vancomycin-resistant *Enterococcus* (VRE) were frequently reported. Emerging fungal resistance, including azole-resistant *Aspergillus* and multidrug-resistant *Candida auris*, further compromised management. Resistant infections were associated with prolonged hospitalization, ICU admission, and high mortality, with multidrug-resistant Gram-negative bacteremia showing mortality rates up to 42%. Resistance trends varied geographically, with higher prevalence in low- and middle-income countries.

Conclusion: Antimicrobial resistance significantly worsens clinical outcomes in hemato-oncology patients. Local resistance surveillance, robust antimicrobial stewardship, infection control, and tailored empiric therapy are essential to mitigate morbidity and mortality. Multicenter prospective studies are needed to strengthen global evidence and inform policy.

KEYWORDS: Hemato-oncology, antimicrobial resistance, multidrug-resistant organisms, bloodstream infections, antimicrobial stewardship

INTRODUCTION

The screening of microbial secondary metabolites is becoming successful aspirants for innovation of antibiotic and non-

Hematological malignancies and their treatments have advanced considerably, with chemotherapy, hematopoietic stem cell transplantation (HSCT), and targeted therapies improving patient survival. Despite these achievements, infectious complications remain a major cause of morbidity and mortality in hemato-oncology patients. Neutropenia, disruption of mucosal barriers, indwelling devices, and immunomodulatory regimens create a vulnerable state where opportunistic and healthcare-associated infections thrive [1,4]. These infections frequently delay cancer therapy, compromise transplant outcomes, and contribute significantly to non-relapse mortality [10,17].

The rise of antimicrobial resistance (AMR) has further complicated infection management in this high-risk group. The World Health Organization has declared AMR a critical public health threat, and hemato-oncology patients are disproportionately affected. Multidrug-resistant organisms (MDROs) such as extended-spectrum β -lactamase (ESBL)-producing Enterobacterales, carbapenem-resistant *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant *Enterococcus* (VRE) are increasingly reported [18,16,15]. These pathogens are often implicated in bloodstream infections, pneumonia, urinary tract infections, and intra-abdominal infections, all of which are associated with elevated morbidity, prolonged hospitalization, and mortality rates that may reach 40–60% in severe sepsis [2,7].

Beyond bacterial resistance, invasive fungal infections represent an emerging threat. *Candida auris* has demonstrated resistance to multiple antifungal classes, while azole-resistant *Aspergillus* species complicate prophylaxis and therapy in transplant recipients [8]. The therapeutic options for such infections are limited, and resistance to echinocandins or amphotericin B has been documented. These developments underscore the converging challenge of bacterial and fungal resistance in immunocompromised populations [3].

Several factors contribute to the heightened risk of resistance in hemato-oncology settings. Prolonged and recurrent exposure to broad-spectrum antibiotics exerts selective pressure that drives resistance. Central venous catheters, long hospitalizations, and ICU admissions facilitate colonization and transmission of MDROs [1,10]. Immunosuppression provides ecological niches for resistant organisms, while inconsistent infection control and stewardship practices further fuel dissemination [15,18]. Importantly, resistance trends vary geographically, shaped by local antimicrobial policies, stewardship programs, and resource availability [5,6].

Reports from low- and middle-income countries (LMICs) consistently describe higher rates of resistance, including carbapenem-resistant Gram-negative bacteria, compared with high-income regions [4,18]. Contributing factors include unrestricted antibiotic access, limited diagnostic capacity, and weaker infection prevention infrastructure. Temporal analyses suggest that resistance rates have escalated globally over the past two decades, with increasing detection of ESBL-producing and carbapenemase-producing strains [16,10]. Such heterogeneity highlights the need for contextualized evidence to guide empirical therapy and policy interventions.

The clinical and economic consequences of AMR in cancer care are substantial. Resistant infections are associated with higher rates of treatment failure, longer hospital stays, intensive care admissions, and higher healthcare costs [18,17]. Delays in initiating effective therapy increase the risk of complications, and inadequate coverage during febrile neutropenia may be fatal [14,6]. Colonization or infection with MDROs in transplant recipients can jeopardize graft success and long-term survival. The cumulative burden not only affects individual patients but also strains health systems by increasing the cost and complexity of oncology care [10,15].

Despite numerous single-center and regional studies documenting AMR in oncology wards, evidence remains fragmented. Most reports focus on bacterial resistance, while data on antifungal resistance particularly for *Candida auris* and non-albicans *Candida* remain limited [8,3]. Pediatric populations, though highly vulnerable, are underrepresented in existing literature [1,17]. Moreover, methodological differences in study designs and inconsistent reporting standards make it challenging to compare findings across regions. Without systematic synthesis, clinicians lack robust evidence to inform empirical therapy, infection prevention strategies, and stewardship policies tailored to hemato-oncology [18,10].

This Comprehensive review aims to consolidate global evidence on antimicrobial resistance in hemato-oncology patients, characterizing multidrug-resistant pathogens, geographic and temporal trends, and their impact on outcomes. By highlighting resistance to last-resort agents and gaps in pediatric and resource-limited populations, it supports clinical decision-making, stewardship, and policy strategies.

METHODS

Search Strategy and Study Selection

A comprehensive literature search was performed in PubMed, Scopus, and Google Scholar, covering studies published between 2014 and 2025. The strategy combined controlled vocabulary (MeSH/Emtree) and free-text terms related to antimicrobial resistance, hemato-oncology conditions, and infectious complications. The core Boolean query was ((“antimicrobial resistance” OR “AMR” OR “drug resistance”) AND (“hemato-oncology” OR “leukemia” OR “lymphoma” OR “myeloma” OR “bone marrow transplant” OR “stem cell transplant”) AND (“infection” OR “bacteremia” OR “sepsis” OR “fungal infection”)). Reference lists of included studies were screened manually to identify additional eligible studies. Grey literature and preprints were excluded to ensure methodological rigor and peer-reviewed evidence quality.

Study Inclusion and Screening Process

Eligibility for study inclusion was determined using the Population–Exposure–Outcome (PEO) framework. The population of interest comprised hemato-oncology patients of any age undergoing chemotherapy, stem cell or bone marrow transplantation, or other immunomodulatory therapies. Titles and abstracts were independently screened by two reviewers to determine relevance to the study objectives. Articles that met the inclusion criteria were subsequently assessed at the full-text level to confirm eligibility. Studies reporting antimicrobial resistance patterns in hemato-oncology patients, including observational studies, randomized controlled trials, case series, and case reports, were included. Non-empirical studies, those lacking extractable AMR data, or not specific to hemato-oncology populations were excluded. Discrepancies regarding study inclusion were resolved through discussion, and when necessary, by consulting a third reviewer to ensure impartiality. To enhance transparency and reproducibility, the study selection process was documented in accordance with PRISMA 2020 guidelines and presented as a flow diagram (Figure 1), showing the number of studies screened, excluded, and included at each stage.

Data Extraction

Data were extracted using a standardized, pilot-tested form in Microsoft Excel. Two independent reviewers collected information across several domains, including study characteristics (author, year, country, design, and sample size), patient information (demographics, hematologic diagnosis, and treatment regimen), pathogen characteristics (species, site of infection, and diagnostic methods), antimicrobial resistance patterns (resistance rates, prevalence of multidrug resistance, and resistance to last-resort agents), clinical outcomes (mortality, treatment failure, length of hospital stay, and ICU admissions), and methodological details (study setting, funding source, blinding, and follow-up duration). Inter-rater agreement was assessed, and any discrepancies

were resolved through discussion or, if necessary, by consulting a third reviewer. Additionally, study authors were contacted for missing or unclear information to ensure completeness and accuracy of the extracted data.

Quality Assessment

The methodological quality of the included observational studies was independently assessed by two reviewers using the Newcastle–Ottawa Scale (NOS). Each study was assigned a risk of bias rating of low, moderate, or high based on NOS criteria. Discrepancies between reviewers were resolved through discussion or, when necessary, consultation with a third reviewer.

Discussion

Burden of Infections in Hemato-Oncology Patients

Infections remain a major cause of morbidity and mortality among both pediatric and adult hemato-oncology patients. Chemotherapy-induced immunosuppression, including neutropenia, lymphopenia, and mucosal injury, significantly predisposes these patients to bloodstream infections (BSIs) and other nosocomial infections. Invasive devices such as central venous catheters (CVCs) and prolonged hospitalization further elevate infection risk. Al-Mulla et al., (2014) [1] in Qatar and Dhingra et al. (2020). [4] in India reported that infection-related mortality, while relatively low in some pediatric cohorts, is closely associated with multidrug-resistant organism (MDRO) infections.

Evolving Microbial Epidemiology

Gram-Positive vs. Gram-Negative Bacteria

The distribution of Gram-positive (GP) and Gram-negative (GN) bacteria in BSIs is dynamic, with regional variations influencing empirical therapy decisions.

- **Gram-Positive Dominance:** Coagulase-negative Staphylococcus (CoNS) consistently emerges as the most frequent GP isolate across pediatric and adult cohorts. Ilmi et al. (2022). [3] in Indonesia reported that CoNS comprised 50% of isolates, while Al-Mulla et al., (2014) et al. [1] highlighted the prevalence of *S. epidermidis*, *S. hominis*, and *S. haemolyticus*. Gram-positive cocci dominate in certain multicenter pediatric studies in Italy, accounting for more than 60% of BSIs [10,17].
- **Gram-Negative Prevalence:** In contrast, several studies, particularly from India, Turkey, and Australia, report GN bacteria as the predominant pathogens. Sengar et al. [16] and Bajpai et al. (2023). [18] demonstrated GN dominance, with *E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* as leading pathogens. Notably, in some Indian cohorts, GN bacteria accounted for over 70% of BSI episodes [7,18].
- **Mixed Epidemiology:** Some centers, including South Africa [5] and Palestine [15], reported a balanced distribution of GP and GN pathogens, highlighting regional differences in microbial ecology.

Other Pathogens

Fungi, predominantly *Candida* spp., and viruses, including CMV and EBV, remain important opportunistic pathogens, especially in post-HSCT patients and those with prolonged neutropenia. Waker et al. (2020). [8] documented *Clostridium difficile* outbreaks in hematology wards, emphasizing the role of nosocomial pathogens in immunocompromised hosts.

Antimicrobial Resistance Patterns

Gram-Negative Bacteria (GNB)

MDRO prevalence among GNB is alarmingly high in hemato-oncology populations. Bajpai et al. (2023). [18] reported 78% MDR among GN isolates, with 38% carbapenem resistance, while Sengar et al. [16] observed 25% MDR and 41% ESBL prevalence. Common mechanisms include:

- **ESBL Production:** *E. coli* and *Klebsiella* spp. frequently produce extended-spectrum β -lactamases (ESBLs), limiting cephalosporin efficacy [2,10].
- **Carbapenem Resistance:** Increasing carbapenem resistance is documented across multiple centers. Bajpai et al. (2023). [18] highlighted high carbapenem resistance in *A. baumannii* and *P. aeruginosa*, whereas Gedik et al. (2014). [7] reported 12% resistance in Turkish cohorts. Fluoroquinolone resistance is also widespread, particularly in *P. aeruginosa* and *E. coli*, reducing the effectiveness of prophylactic regimens.

Gram-Positive Bacteria (GPB)

- **Methicillin Resistance:** Methicillin-resistant CoNS (MRCoNS) and MRSA remain highly prevalent. Dhingra et al. (2020). [4] and Bajpai et al. (2023). [18] reported MRSA rates up to 16%, while MRCoNS resistance can reach 50% in pediatric and adult populations.
- **Glycopeptide Resistance:** Vancomycin-resistant Enterococcus (VRE) is a major concern, particularly in *E. faecium*. Arman et al. (2022). [15] reported VRE rates exceeding 40%, whereas *E. faecalis* exhibited low or absent resistance.

Implications for Empiric Therapy

Resistance patterns significantly impact the appropriateness of initial empiric antibiotic therapy (EAT). Conn et al. (2017). [6] reported 11.6% of BSI isolates were resistant to empiric therapy, while Bajpai et al. (2023). [18] showed MDR GN BSIs were associated with higher mortality (42.5% vs. 11.2%). The choice of empiric therapy should thus be guided by local antibiograms and patient-specific risk factors, including post-HSCT status and degree of neutropenia [14].

Clinical Outcomes of Antimicrobial Resistance in Hemato-Oncology

The clinical impact of infections in hemato-oncology patients is profound, with antimicrobial resistance playing a pivotal role in determining patient prognosis and healthcare resource utilization.

- **Mortality:** Infection-related mortality is closely linked to both pathogen type and resistance profile. MDR Gram-negative bacteria (MDR GNB), especially carbapenem-resistant strains, are associated with significantly higher mortality rates. Bajpai et al. (2023). [18] reported an overall mortality of 32.6% among adults with hematolymphoid malignancies, rising to 42.5% in patients with MDR BSIs compared to 11.2% in non-MDR BSIs. Cornejo-Juárez et al. (2016) et al. [2] documented 30-day mortality of 39% in hematology and solid tumor patients with hospital-acquired MDR bacterial infections, underscoring the lethal potential of resistant pathogens.

- **Length of Hospitalization:** Culture-positive infections contribute to prolonged hospital stays, reflecting both the severity of illness and the additional management challenges posed by resistant organisms. In pediatric cohorts, Mattei et al. (2022). [17] observed that patients with MDR Gram-negative bacteremia required extended inpatient care, often exceeding standard treatment durations, increasing both clinical burden and healthcare costs.

- **ICU Admission and Disease Severity:** Resistance is also associated with more severe clinical courses necessitating intensive care. Castagnola et al. (2021). [10] demonstrated that pediatric patients with resistant BSIs were more likely to require ICU admission, and the presence of resistance correlated with higher rates of clinical deterioration. Waker et al. (2020). [8] similarly noted that nosocomial infections caused by genetically related, resistant strains (e.g., *Clostridium difficile*) resulted in increased ICU utilization in hematology wards, highlighting the compounding effects of both pathogen virulence and antimicrobial resistance.

These findings indicate that antimicrobial resistance in hemato-oncology significantly exacerbates morbidity, prolongs hospitalization, increases ICU requirements, and markedly elevates mortality risk. Early identification of high-risk patients, guided empiric therapy, and rigorous infection control measures are essential to mitigate these adverse outcomes.

Infection Control and Antimicrobial Stewardship Implications

The escalating prevalence of MDROs in hemato-oncology patients necessitates coordinated strategies encompassing antimicrobial stewardship, infection control, and targeted surveillance to mitigate morbidity and mortality.

1. Robust Antimicrobial Stewardship (AMS):

Effective AMS programs are critical to optimize antibiotic use and limit the emergence of resistance. Empiric therapy should be informed by institution-specific antibiograms, historical resistance patterns, and patient risk factors. De-escalation of broad-spectrum antibiotics based on culture results reduces selective pressure, while prophylactic regimens should be tailored to minimize unnecessary exposure, as emphasized by Bajpai et al. (2023). [18] and Castagnola et al. (2021). [10].

2. Rigorous Infection Control Protocols:

Strict adherence to hand hygiene, catheter care, environmental decontamination, and early patient isolation is essential to prevent nosocomial transmission of MDROs. Al-Mulla et al., (2014) et al. [1] and Arman et al. (2022). [15] highlighted that lapses in standard precautions contribute significantly to outbreaks of carbapenem-resistant Gram-negative bacteria (CR GNB) and vancomycin-resistant *Enterococcus* (VRE) in hematology wards.

3. Targeted Surveillance of High-Risk Pathogens:

Proactive surveillance, including rectal swabs for CR GNB and VRE screening, enables early identification of colonized or high-risk patients. This facilitates timely initiation of tailored infection control measures and empiric therapy, reducing the risk of overt infection and transmission. Studies by Gedik et al. (2014). [7] and Waker et al. (2020). [8] demonstrate that active surveillance can detect asymptomatic carriers, thereby preventing cluster outbreaks.

4. Tailored Empiric Therapy for High-Risk Populations:

High-risk cohorts, such as post-HSCT patients and those with prolonged neutropenia, require individualized empiric regimens informed by local resistance data. Leung et al. (2025). [14] reported that post-HSCT patients had a higher likelihood of antibiotic-resistant infections, underscoring the need for precision-guided empiric therapy rather than standard protocols.

Key Findings

Researchers indicate several additional findings beyond pathogen distribution and resistance patterns. Waker et al. (2020). [8] emphasize the genetic relatedness of *Clostridium difficile* strains, highlighting nosocomial transmission risks. Uemura et al. (2017). [11] report strain-specific outbreaks of ESBL-producing Enterobacteriaceae, stressing the importance of molecular surveillance. Rathod et al. [12] demonstrate that tailored antibiotic therapy based on local epidemiology improves clinical management of febrile neutropenia. Mattei et al. (2022). [17] observed that glycopeptide resistance in Gram-positive bacteria remains low, suggesting vancomycin retains effectiveness. Authors also note that antimicrobial resistance contributes not only to mortality but also to increased ICU utilization and prolonged hospital stay, even in non-MDR infections [6,10].

Study Limitations

Despite the comprehensive analysis of antimicrobial resistance and clinical outcomes in hemato-oncology patients, several limitations should be acknowledged. Many included studies were single-center and retrospective, potentially introducing selection and reporting biases [1,6,7]. Heterogeneity in patient

populations, including differences in age, underlying malignancy, and treatment regimens, limits generalizability. Resistance mechanisms were not uniformly characterized, and some studies lacked molecular confirmation of MDR pathogens [11,8]. Additionally, the impact of prophylactic antibiotic use and infection control interventions on outcomes was inconsistently reported. Prospective multicenter studies with standardized protocols are needed to validate these findings.

CONCLUSION

Antimicrobial resistance in hemato-oncology patients presents a critical challenge that directly impacts survival and treatment outcomes. The predominance of multidrug-resistant Gram-negative organisms, combined with increasing reports of MRSA, VRE, and antifungal resistance, has escalated infection-related mortality and complicated empiric therapy choices. Patients with resistant infections experience significantly higher mortality rates, prolonged hospitalization, and greater ICU utilization, collectively burdening healthcare systems. Evidence highlights the urgent need for region-specific stewardship programs guided by local resistance profiles and comprehensive surveillance to detect emerging pathogens. Infection control practices, including strict hand hygiene, catheter care, and isolation protocols, remain central to reducing transmission within oncology wards. Tailored empiric regimens, especially for high-risk groups such as post-transplant patients and those with prolonged neutropenia, are essential to improve clinical outcomes. Although numerous single-center studies provide valuable insights, multicenter prospective research is required to strengthen evidence and guide policy. Ultimately, addressing antimicrobial resistance in hemato-oncology necessitates a multifaceted strategy integrating stewardship, molecular diagnostics, and preventive care. This combined approach holds the potential to mitigate resistance-driven morbidity and mortality while safeguarding advances in cancer therapy.

Abbreviation	Full Form
AMR	Antimicrobial Resistance
MDRO	Multidrug-Resistant Organism
HSCT	Hematopoietic Stem Cell Transplantation
BSI	Bloodstream Infection
ICU	Intensive Care Unit
LMIC	Low- and Middle-Income Countries
ESBL	Extended-Spectrum β -Lactamase
MRSA	Methicillin-Resistant <i>Staphylococcus aureus</i>
VRE	Vancomycin-Resistant <i>Enterococcus</i>
CoNS	Coagulase-Negative <i>Staphylococcus</i>
GP	Gram-Positive
GN	Gram-Negative
GNB	Gram-Negative Bacteria
GPB	Gram-Positive Bacteria
CR GNB	Carbapenem-Resistant Gram-Negative Bacteria
AMS	Antimicrobial Stewardship
PEO	Population–Exposure–Outcome
NOS	Newcastle–Ottawa Scale
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
EAT	Empiric Antibiotic Therapy
CDI	<i>Clostridium difficile</i> Infection

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**Declaration Of Generative Ai
And Ai-Assisted Technologies**

In The Writing Process

The authors declare that they have not used generative AI (a type of artificial intelligence technology that can produce various types of content including text, imagery, audio and synthetic data. Examples include ChatGPT, NovelAI, Jasper AI, Rytr AI, DALL-E, etc) and AI-assisted technologies in the writing process before submission.

Competing Interests: The authors declare that they have no competing interests.

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