RESEARCH ARTICLE

Editorial Process: Submission:04/30/2025 Acceptance:11/12/2025 Published:11/21/2025

Post-Transplant Infections in Multiple Myeloma and Lymphoma: Early Vulnerabilities and Long-Term Risks in ASCT Recipients

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Abstract

Background: Patients with multiple myeloma (MM) and lymphoma undergoing autologous stem cell transplantation (ASCT) are at a higher risk of infection leading to increased morbidity and mortality. This study aims to analyze the infection patterns and outcomes in this population. **Methods:** A retrospective, descriptive study was conducted at Dr. Kariadi General Hospital, Semarang, Indonesia, involving 28 patients diagnosed with MM and lymphoma who underwent ASCT from January 2013 to May 2023. Data were collected from medical records and phone interviews. Infection patterns, bacterial pathogens, and outcomes were analyzed. **Results:** Of the 28 patients, 75% experienced post-ASCT infections. Infections occurred predominantly in the first 10 days post-transplant, with 85% of infections occurring during this period. Six patients experienced multiple infection episodes. Blood cultures revealed 52% Gram-positive and 29% Gram-negative bacterial infections. Three patients (14%) died within 28 days post-transplant, though these deaths were attributed to non-infectious causes, including pulmonary edema and hemorrhagic stroke. Two patients developed late-onset infections occuring more than 300 days post-transplant. **Conclusions:** Infections remain a significant complication following ASCT in MM and lymphoma patients, particularly within the early post-transplant period. Gram-positive bacteria, especially Staphylococcus species, were the predominant pathogens identified.

Keywords: Multiple myeloma- Lymphoma- Autologous stem cell transplantation- Infections

Asian Pac J Cancer Prev, **26 (11)**, 4103-4107

Introduction

Autologous stem cell transplantation (ASCT) is a well-established treatment modality for patients with haematological malignancies, particularly multiple myeloma (MM) and lymphoma [1, 2]. ASCT is frequently used following high-dose chemotherapy to restore bone marrow function and improve survival outcomes in these patient populations [3]. However, the immunosuppression induced by both the underlying malignancy and the transplantation process predisposes patients to a significantly increased risk of infections, which remain one of the major causes of morbidity and mortality post-transplantation [4].

Patients undergoing ASCT often experience prolonged periods of neutropenia and immune reconstitution, creating a vulnerable window for opportunistic infections .[4, 5] Bacterial, fungal, and viral pathogens are frequently implicated in post-transplant infections, with the type and timing of infections varying according to the patient's immune status and other clinical factors [6]. Identifying specific infection patterns and microbial pathogens is essential for improving patient management and guiding prophylactic and therapeutic interventions [7].

Despite advances in supportive care and infection control strategies, post-ASCT infections continue to pose challenges in clinical practice [8]. Bacterial infections are of particular concern, and blood culture results often reveal a spectrum of Gram-positive and Gram-negative organisms [9]. Understanding the prevalence, distribution, and outcomes of these infections in ASCT recipients is critical for optimizing post-transplant care and preventing

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adverse outcomes [7].

This study aims to analyze the infection patterns in patients with MM and lymphoma who have undergone ASCT. We present data on the incidence of infections, the microbial species identified through blood cultures, and patient outcomes during the post-transplant period We hope that our findings will contribute to the growing body of evidence on the importance of early detection and management of infections in this high-risk population.

Materials and Methods

Study Design and Setting

This study was a retrospective and descriptive analysis conducted at Dr. Kariadi General Hospital, Semarang, Indonesia. The study population consisted of patients diagnosed with multiple myeloma (MM) and lymphoma who underwent autologous stem cell transplantation (ASCT) between January 2013 and May 2023.

Study Population

The study included all patients with MM and lymphoma who had received ASCT within the specified period. Patients were identified through the hospital's medical record system. Inclusion criteria required a confirmed diagnosis of MM or lymphoma and completion of ASCT. All patients with insufficient data in their medical records were excluded from the study.

Data Collection

Data were obtained from both paper-based and electronic medical records (EMR). Information regarding patient demographics, underlying disease (MM or lymphoma), comorbidities, transplantation details, and infection-related outcomes post-ASCT was extracted. In cases where data was missing or unclear, follow-up phone calls were made to the contact numbers listed in the medical records to obtain additional information.

Study Variables

The primary outcome measured was the incidence and pattern of infections following ASCT. Secondary variables included patient demographics (age, gender), type of underlying malignancy, presence of comorbidities, and microbiological findings from blood cultures (Gram-positive, Gram-negative, or mixed bacterial infections).

Recurrent infection was defined as ≥2 distinct episodes of clinically and/or microbiologically confirmed infection occurring after ASCT, separated by a period of clinical improvement and/or completion of antimicrobial therapy, regardless of whether the pathogen was the same or different species.

Ethical Considerations

This study was conducted according to the ethical standards of the Declaration of Helsinki. Before data collection, ethical approval was obtained from the Ethics Committee of Dr. Kariadi General Hospital. Due to the retrospective nature of the study, informed consent was waived, but strict confidentiality and data privacy were maintained for all patients.

Statistical Analysis

Demographics, patterns of infection, and comorbidities were described descriptively using frequencies and percentages for categorical variables and median and interquartile ranges (IQRs) for continuous variables. Statistical analysis was performed by using the R software v.4.

Results

Subjects Characteristic

In this study, 28 patients were included, with 16 females and 12 males (57%, and 43% respectively). The median age of study subjects was 50, with a range of 33 to 57 years old. The study subjects were patients with multiple myeloma (MM) and lymphoma who had undergone autologous stem cell transplantation (ASCT), with 71% of them having lymphoma. Most subjects (57%) had no comorbidities before transplantation, although 11% had more than three comorbidities. We found that 75% of subjects experienced post-ASCT infections (Table 1).

Following ASCT, blood cultures were collected from all subjects. Seventy-five percent of subjects had positive blood cultures for bacterial infection. Among the infected subjects, 52% of cultures revealed Gram-positive species, 29% were Gram-negative, and the remaining subjects were infected by Gram-positive and Gram-negative bacteria. No fungal infections were detected. However, viral infection screening was not performed due to limited available modalities.

After determining that bacterium was the major cause of infection post ASCT in our center, we further investigated which specific bacterial species was involved. We identified various species of bacteria in the blood culture of our subjects. We elucidated that Staphylococcus sp. was most discovered, followed by Klebsiella sp., and Stenotrophomonas sp. Infections caused by other Gram-positive bacteria, include Aeromonas sp., Kytococcus sp., and Dermacoccus sp. Gram-negative bacterial infections

Table 1. Basic Characteristics of Subjects

Characteristic	Total(N=28) (%)
Recipient age, median (IQR)	50 (33-57)
Recipient Gender	
Female	16 (57)
Male	12 (43)
Type of Cancer	
Lymphoid	8 (29)
MM	20 (71)
Comorbidity	
None	16 (57)
1	7 (25)
2	2 (7)
>= 3	3 (11)
Status infection	
No	7 (25)
Yes	21 (75)

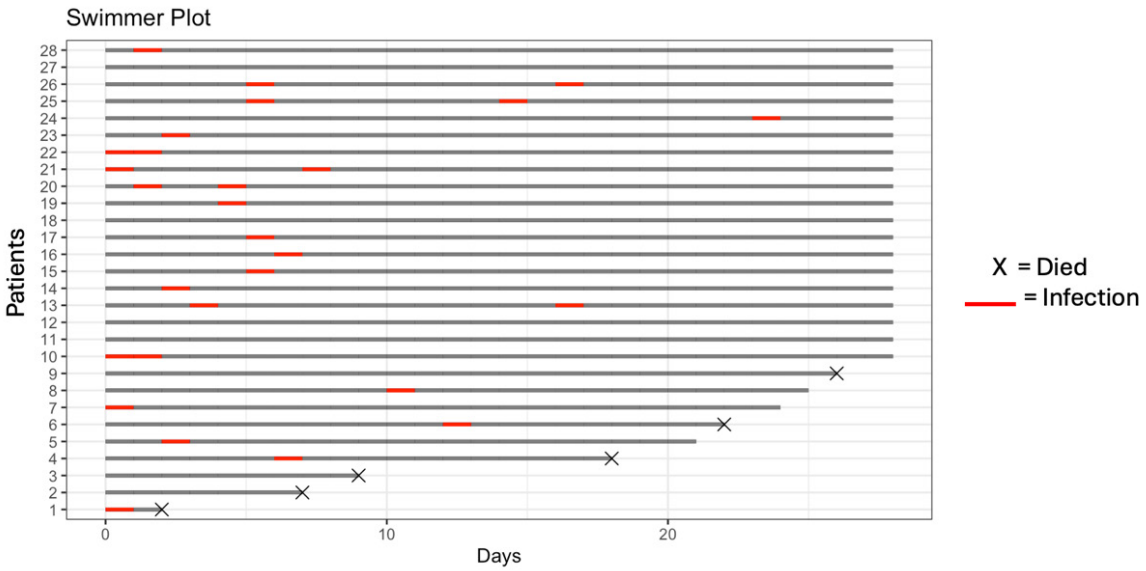

Figure 1. Infection Status Describe in 28 Days after day 0 of ASCT. Subjects were then observed for a period of 28 days after ASCT and displayed on a swimmer plot. Red bar indicates episodes of infection with X indicating death.

included Enterobacter cloacae, Escherecia coli, and Pseudomonas sp.

The 28 subjects were then followed up for a period of 28 days. The swimmer plot in Figure 1 demonstrates that 18 subjects experienced infection within the first 10 days post-transplant. Six subjects developed more than one episode of infection. Among 21 infected patients, 3 (14%) died within the 28-day observation period. Interestingly, these deaths were not attributed to the infections but were caused by pulmonary edema and hemorrhagic stroke. Additionally, infections were reported in two study subjects beyond 300 days post-transplantation, which could be attributed to various contributing factors (Figure 1). The median time to infection onset was 6 days post-ASCT (interquartile range [IQR] 4–9 days; range 2–320 days). Most early infections occurred during the neutropenic phase, with 85% of cases developing within the first 10 days after transplantation.

Discussion

In this study, the incidence of infections among patients with multiple myeloma (MM) and lymphoma following autologous stem cell transplantation (ASCT) was significantly high, with 75% of subjects developing post-transplant infections. This is consistent with previous studies, which have also reported a high prevalence of infections among ASCT recipients, primarily due to prolonged immunosuppression and neutropenia during the post-transplant recovery phase. The early occurrence of infections, with 85% of cases reported within the first 10 days, highlights the critical period of vulnerability following ASCT [10].

Interestingly, 52% of the bacterial infections identified were caused by Gram-positive organisms, including Staphylococcus species, while Gram-negative bacteria were responsible for 29% of infections. These findings align with those of other studies, Gram-positive bacteria have been the predominant cause of bloodstream infections in ASCT patients, likely due to the frequent use of central venous catheters and mucosal barrier injuries [7, 9]. However, unlike some reports that indicate fungal infections as a significant concern in ASCT patients, no fungal infections were identified in our cohort, possibly reflecting improved antifungal prophylaxis [6, 8].

Our study also observed that six subjects experienced recurrent infections, indicating the potential for chronic or relapsing infections in this population. Recurrent infections in ASCT recipients have been associated with delayed immune reconstitution and prolonged neutropenia, suggesting the need for vigilant monitoring and possibly more aggressive infection control strategies in high-risk patients [6].

In terms of mortality, while 14% of infected patients died within 28 days, it is noteworthy that none of these deaths were directly attributable to infection. Instead, causes of death included pulmonary edema and hemorrhagic stroke, conditions that have been previously recognized as complications in post-transplant patients due to underlying comorbidities or adverse effects of conditioning regimens [1, 4]. This finding underscores the complexity of managing ASCT recipients, where non-infectious complications can also significantly contribute to adverse outcomes [6].

Infections were also reported beyond 300 days post-transplantation in two subjects. Late-onset infections have been documented in several studies and are often attributed to chronic immunosuppression and long-term use of corticosteroids. Although our study did not identify the underlying cause of these late infections, they highlight the need for continued surveillance and possibly extended prophylactic measures in certain ASCT recipients [3, 11, 12].

This study has several limitations that should be acknowledged. First, the retrospective design inherently carries the risk of selection bias and reliance on the

accuracy of medical records, which may not capture all relevant clinical details, particularly for infections diagnosed outside of the hospital. Second, while the study focused on bacterial infections, the absence of routine viral and fungal screening limited the ability to assess the full spectrum of post-ASCT infections. Additionally, the follow-up period varied among patients, with some subjects followed for an extended period beyond the initial 28 days, while others were lost to follow-up, potentially underestimating the incidence of late-onset infections. Lastly, this study was conducted in a single center, which may limit the generalizability of the findings to other settings or populations with different clinical practices or infection control protocols.

In conclusion, our findings emphasize the high burden of bacterial infections, particularly Gram-positive infections, in MM and lymphoma patients post-ASCT. Early identification and management of infections remain critical for improving outcomes in these patients. Further studies focusing on long-term infection surveillance and the development of tailored prophylactic strategies are warranted to reduce infection-related morbidity and mortality in this high-risk population.

Author Contribution Statement

All authors contributed equally in this study.

Acknowledgements

We would like to express our deepest gratitude to the Director of Dr. Kariadi General Hospital, Semarang, for granting permission to conduct this study within the hospital's facilities. We also extend our sincere appreciation to the Medical Records Department of Dr. Kariadi General Hospital for their invaluable assistance in facilitating data collection and ensuring access to the required medical records. Their support has been instrumental in the successful completion of this research.

Funding disclosure

This study was financially supported by Indonesian Society of Hematology and Medical-Oncology (ISHMO) Semarang Chapter. The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethical Clearance

This study was conducted according to the ethical standards of the Declaration of Helsinki. Before data collection, ethical approval was obtained from the Ethics Committee of Dr. Kariadi General Hospital.

Availability Data

Data available upon request to the authors

Registration dataset

This study is not registered in registration dataset

Conflicts of interest

None Declare

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