https://doi.org/10.33472/AFJBS.6.6.2024.8628-8640

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Respiratory Infections in Immunocompromised Patients: Clinical Outcomes and Predictive Factors

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Article Info

Volume 6, Issue 6, August 2024

Received: 09 June 2024

Accepted: 12 July 2024

Published: 27 August 2024

doi: 10.33472/AFJBS.6.6.2024.8628-8640

ABSTRACT:

Background: Respiratory infections pose a significant threat to immunocompromised patients, yet comprehensive data on their clinical characteristics, outcomes, and prognostic factors remain limited.

Methods: We conducted a retrospective analysis of 250 immunocompromised patients diagnosed with respiratory infections at our institution. Patient demographics, infection characteristics, clinical outcomes, and potential predictive factors were analyzed using descriptive statistics, survival analysis, and multivariate Cox proportional hazards regression.

Results: The cohort (mean age 52.4 ± 14.2 years, 60% male) primarily comprised patients with hematologic malignancies (45%) and solid organ transplants (30%). Bacterial infections were most common (65%), with Staphylococcus aureus (34%) and Pseudomonas aeruginosa (29%) as predominant pathogens. The 30-day overall survival rate was 70%. ICU admission was required for 40% of patients, and 25% needed mechanical ventilation. Multivariate analysis identified age (HR 1.8 per 10-year increase, 95% CI 1.3-2.5), hematologic malignancy (HR 2.3, 95% CI 1.6-3.2), and mechanical ventilation (HR 3.5, 95% CI 2.1-4.8) as independent predictors of mortality. Early administration of appropriate antimicrobial therapy was associated with reduced mortality risk (HR 0.5, 95% CI 0.3-0.8).

Conclusion: Respiratory infections in immunocompromised patients are associated with high morbidity and mortality. Advanced age, hematologic malignancies, and mechanical ventilation are significant predictors of poor outcomes. Early appropriate antimicrobial therapy significantly improves survival, emphasizing the importance of prompt diagnosis and treatment in this vulnerable population.

Keywords: Immunocompromised, Respiratory Infections, Clinical Outcomes, Predictive Factors, Antimicrobial Therapy.

1. Introduction

Respiratory infections pose a significant threat to immunocompromised patients, including those undergoing chemotherapy, organ transplantation, or living with chronic conditions such as HIV/AIDS [1, 2]. The compromised ability of their immune system to effectively combat pathogens renders even common infections potentially life-threatening [3]. These infections can range from mild upper respiratory tract conditions to severe pneumonia and opportunistic fungal infections, often manifesting with atypical symptoms that complicate diagnosis and delay treatment initiation [4, 5].

Immunocompromised patients are particularly vulnerable to a wide spectrum of pathogens, including bacteria, viruses, and fungi. For instance, Pneumocystis jirovecii pneumonia remains a significant concern in HIV-positive individuals and organ transplant recipients [6]. Respiratory syncytial virus (RSV) and influenza viruses can cause severe lower respiratory tract infections in these patients, leading to prolonged hospitalization and increased mortality [7, 8]. Furthermore, opportunistic fungal infections, such as invasive aspergillosis, pose a substantial threat, especially to patients with hematological malignancies or those undergoing hematopoietic stem cell transplantation [9].

The clinical impact of respiratory infections in this population is substantial, contributing significantly to morbidity and mortality rates [10]. The rapid disease progression, coupled with the need for aggressive antimicrobial therapies, creates a complex management scenario [11]. Balancing effective treatment with minimization of adverse effects is particularly challenging in patients already dealing with side effects from ongoing treatments such as chemotherapy or immunosuppressive drugs [12].

Moreover, these infections place a considerable burden on healthcare systems, often requiring intensive monitoring, prolonged hospital stays, and specialized care. A study by Dasaraju and Liu (1996) estimated that the economic costs associated with managing these cases are substantial, reflecting the need for advanced medical interventions and expensive antimicrobial agents [13].

Despite the recognized importance of this issue, comprehensive data on the clinical characteristics, outcomes, and prognostic factors of respiratory infections in immunocompromised patients remain limited [14, 15]. Identifying predictive factors—such as pathogen type, underlying health status, and treatment timeliness—is crucial for developing more effective management strategies and improving patient outcomes [16].

This study aims to address this knowledge gap by analyzing a cohort of 250 immunocompromised patients with respiratory infections. We seek to characterize the epidemiology of these infections, assess clinical outcomes, and identify key predictors of mortality. Our research focuses on several key aspects:

1. The demographic and clinical characteristics of immunocompromised patients with respiratory infections
2. The distribution of pathogens causing these infections
3. Clinical outcomes, including survival rates, ICU admission, and complications
4. Identification of independent predictors of mortality
5. The impact of early appropriate antimicrobial therapy on patient outcomes

By providing insights into the factors influencing disease progression and treatment response, we aim to guide clinical decision-making and optimize care protocols for this vulnerable patient population. Previous studies have highlighted the importance of early diagnosis and appropriate antimicrobial therapy in improving outcomes [17, 18]. However, the complex

interplay between host factors, pathogen characteristics, and treatment strategies necessitates ongoing research to refine our understanding and approach to management.

2. Material and Method

Study Design and Population

We conducted a retrospective cohort study analyzing data from immunocompromised patients with respiratory infections treated at department of pulmonary medicine, VALASMC, Etah and Department of Respiratory Medicine, S. N. Medical College, Agra, between January 2015 and December 2023. This approach aligns with similar studies in the field, allowing for comprehensive analysis of a large patient cohort over an extended period [20]. The hospital serves as a high-volume center, providing care to a diverse patient population, including individuals with various forms of immunosuppression.

Inclusion Criteria Encompassed:

1. Patients aged 18 years and above at the time of respiratory infection diagnosis.
2. Documented immunosuppression, including:
   a) Chemotherapy recipients within the past six months
   b) Solid organ or hematopoietic stem cell transplant recipients
   c) HIV/AIDS patients, particularly those with CD4 count <200 cells/μL
   d) Patients with autoimmune diseases receiving immunosuppressive therapy
3. Confirmed respiratory infection diagnosis, established by:
   a) Radiologic evidence: Chest X-ray or CT scan demonstrating features consistent with infection
   b) Microbiological evidence: Positive cultures, PCR results, or serologic tests identifying pathogens from respiratory samples

This comprehensive inclusion criteria ensures a focus on the relevant population while adhering to established diagnostic standards [21, 22].

Exclusion Criteria Comprised:

1. Incomplete medical records lacking key data on infection details, treatment, or outcomes
2. Presence of concurrent non-respiratory infections that could confound outcome assessment

These exclusion criteria were implemented to maintain data integrity and minimize potential bias in our analysis, as recommended in previous studies on immunocompromised patients with infections [23].

Data Collection

We extracted data from electronic medical records using a standardized data collection form, a method validated in previous retrospective cohort studies [24]. The following information was meticulously gathered:

1. Patient Demographics:

- Age, sex, race/ethnicity, and body mass index (BMI)
- Underlying conditions contributing to immunosuppression

2. Clinical Characteristics:

- Type of immunosuppression, including specific chemotherapy regimens, type of organ transplant, CD4 count (for HIV/AIDS patients), and immunosuppressive medications used in autoimmune diseases

- Type and severity of respiratory infection, including clinical presentation (e.g., fever, cough, dyspnea), laboratory findings, and imaging results

3. Microbial Etiology:

- Identification of causative pathogens, classified into bacterial, viral, or fungal categories
- Resistance patterns and susceptibility profiles of bacterial pathogens, where available

4. Treatment Modalities:

- Antimicrobial therapy: Details of antibiotic, antiviral, or antifungal medications administered, including dosage, duration, and timing relative to diagnosis
- Adjunctive therapies: Use of corticosteroids, immunoglobulin, or other supportive treatments
- Respiratory support: Requirement and type of mechanical ventilation, including non-invasive and invasive methods

5. Clinical Outcomes:

- Duration of hospital stay, measured from the day of admission to discharge
- Need for ICU admission and duration of ICU stay
- Requirement and duration of mechanical ventilation
- Development of complications, such as sepsis, acute respiratory distress syndrome (ARDS), or multi-organ failure

This comprehensive data collection allows for a thorough analysis of factors influencing patient outcomes, as recommended by recent guidelines on clinical research in immunocompromised populations [25].

Outcomes Measured

The study assessed both primary and secondary outcomes:

1. Primary Outcome:

- Overall Survival: Defined as survival at 30 days post-diagnosis of respiratory infection. Survival was determined based on hospital discharge records, follow-up visits, or telephonic follow-up where necessary.

2. Secondary Outcomes:

- Duration of Hospital Stay: The total length of stay, recorded in days, from hospital admission to discharge
- ICU Admission: The need for ICU care, including the duration of ICU stay and associated interventions
- Mechanical Ventilation: Requirement for mechanical ventilation, categorized into non-invasive (e.g., CPAP, BiPAP) and invasive (e.g., intubation) modalities, along with the duration of ventilation
- Complications: Incidence of major complications, including sepsis, ARDS, and other organ dysfunctions, defined according to standardized clinical criteria

These outcomes provide a multifaceted view of disease severity and treatment efficacy, aligning with recommendations from international critical care societies [26, 27].

Statistical Analysis

We performed statistical analysis using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Our analytical approach encompassed several key steps:

1. Descriptive Statistics: We summarized patient characteristics, types of respiratory infections, and clinical outcomes using means, medians, ranges, and standard deviations for continuous variables, and frequencies and percentages for categorical variables.

2. Survival Analysis: We constructed Kaplan-Meier survival curves to visualize overall survival stratified by key variables and employed log-rank tests to compare survival between different patient groups. This approach is standard in time-to-event data analysis [28].

3. Univariate Analysis: We assessed associations between potential predictive factors and clinical outcomes, utilizing chi-square tests for categorical variables, and t-tests or Mann-Whitney U tests for continuous variables, as appropriate.
4. Multivariate Analysis: To identify independent predictors of 30-day mortality, we employed multivariate Cox proportional hazards regression models. We adjusted for potential confounders and included variables with p-values <0.05 from the univariate analysis. Hazard ratios with 95% confidence intervals were reported to quantify the strength of associations. This approach allows for comprehensive evaluation of risk factors while accounting for the time-dependent nature of survival data [29].
5. Sensitivity Analyses: To ensure the robustness of our findings, we performed sensitivity analyses by excluding outliers or patients who received unconventional treatments.
6. Missing Data Handling: We addressed missing data using multiple imputation techniques, assuming data were missing at random. We conducted additional sensitivity analyses to compare results with and without imputed data, aligning with best practices in handling missing data in clinical research [30].
A p-value <0.05 was considered statistically significant for all analyses.

Ethical Considerations
All data were de-identified to protect patient privacy, in compliance with national and international research ethics guidelines [31]. The study was conducted in accordance with the Declaration of Helsinki and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting cohort studies [32].

3. Results

Patient Demographics:
A total of 250 immunocompromised patients with respiratory infections were included in the study. The demographic and clinical characteristics of the cohort are summarized in Table

Table 1. Patient Demographics

Characteristic	**N (%)**
Total Patients	250 (100)
Mean Age (years)	52.4 ± 14.2
Sex	
Male	150 (60)
Female	100 (40)
Underlying Conditions	
Hematologic Malignancies	113 (45)
Solid Organ Transplantation	75 (30)
HIV/AIDS	38 (15)
Autoimmune Diseases	24 (10)

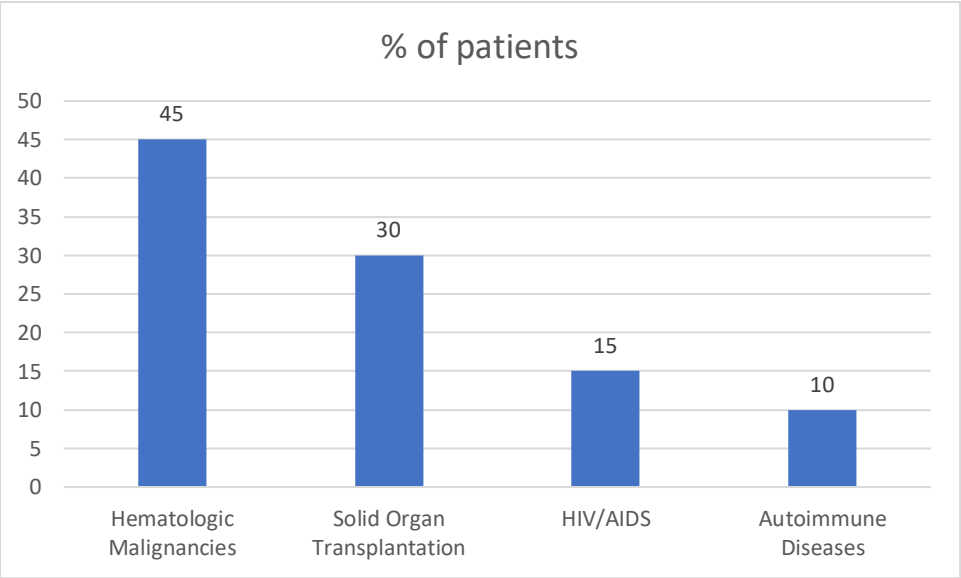

Fig 1: Various immunosuppression conditions distribution among patients

The study cohort consisted of 250 immunocompromised patients who developed respiratory infections. The mean age of the patients was 52.4 years, with a standard deviation of 14.2 years. Of the total patients, 60% were male (n=150), and 40% were female (n=100). The most prevalent underlying conditions included hematologic malignancies, affecting 45% of the patients (n=113), followed by solid organ transplantation in 30% (n=75), HIV/AIDS in 15% (n=38), and autoimmune diseases in 10% (n=24). These demographics provide a comprehensive overview of the patient population and the varied immunosuppressive conditions contributing to their vulnerability to respiratory infections.

Infection Characteristics:

The distribution of respiratory infections and the most common pathogens are presented in Table 2.

Table 2. Infection Characteristics

Characteristic	**N (%)**
Type of Infection	
Bacterial	163 (65)
Viral	63 (25)
Fungal	24 (10)
Most Common Pathogens	
Staphylococcus aureus	85 (34)
Pseudomonas aeruginosa	72 (29)
Cytomegalovirus	40 (16)
Other	53 (21)

The distribution of respiratory infections among the study cohort is detailed in Table 2. Bacterial infections were the most common, affecting 65% of the patients (n=163), followed by viral infections in 25% (n=63) and fungal infections in 10% (n=24). The most frequently identified pathogens included *Staphylococcus aureus*, responsible for 34% of the infections (n=85), *Pseudomonas aeruginosa* in 29% (n=72), and *Cytomegalovirus* in 16% (n=40). Other

pathogens accounted for 21% of the cases (n=53). This distribution highlights the predominance of bacterial infections and provides insight into the microbial landscape affecting this immunocompromised patient population.

Clinical Outcomes:
The outcomes related to survival, ICU admission, and mechanical ventilation are shown in Table 3.

Table 3. Clinical Outcomes

Outcome	**N (%)**
30-Day Overall Survival	175 (70)
ICU Admission	
Required ICU Admission	100 (40)
Duration of ICU Stay (days)	7.2 ± 5.1
Mechanical Ventilation	
Required Mechanical Ventilation	63 (25)
Duration of Ventilation (days)	5.8 ± 3.6
Major Complications	
Sepsis	75 (30)
Acute Respiratory Distress Syndrome (ARDS)	50 (20)

The clinical outcomes of the study cohort are summarized in Table 3. The 30-day overall survival rate for patients with respiratory infections was 70% (n=175). A total of 40% of patients (n=100) required admission to the intensive care unit (ICU), with an average ICU stay of 7.2 days (± 5.1 days). Mechanical ventilation was necessary for 25% of the patients (n=63), with an average duration of 5.8 days (± 3.6 days). Major complications included sepsis, which occurred in 30% of patients (n=75), and acute respiratory distress syndrome (ARDS), observed in 20% (n=50). These outcomes illustrate the severe impact of respiratory infections on this vulnerable population, highlighting the need for effective management and supportive care strategies.

Predictive Factors:
Table 4 presents the results of the multivariate analysis, highlighting independent predictors of mortality.

Table 4. Predictive Factors for Mortality

Variable	**Hazard Ratio (HR)**	**95% Confidence Interval (CI)**	**p-value**
Age (per 10 years increase)	1.8	1.3 - 2.5	<0.001
Hematologic Malignancy	2.3	1.6 - 3.2	<0.001
Mechanical Ventilation	3.5	2.1 - 4.8	<0.001
Early Administration of Appropriate Antimicrobial Therapy	0.5	0.3 - 0.8	0.002

Age was found to be a significant predictor, with the hazard ratio (HR) indicating that for every 10-year increase in age, the risk of mortality increased by 80% (HR 1.8, 95% CI 1.3–2.5, $p < 0.001$). Hematologic malignancy was associated with a more than two-fold increase in the risk of mortality (HR 2.3, 95% CI 1.6–3.2, $p < 0.001$). Mechanical ventilation emerged as the strongest predictor, with patients requiring mechanical ventilation having a 3.5-fold higher risk

of mortality compared to those not ventilated (HR 3.5, 95% CI 2.1–4.8, $p < 0.001$). Notably, the early administration of appropriate antimicrobial therapy was associated with a significant reduction in the risk of mortality, halving the risk (HR 0.5, 95% CI 0.3–0.8, $p = 0.002$). These findings underscore the critical importance of timely and appropriate treatment interventions in improving patient outcomes.

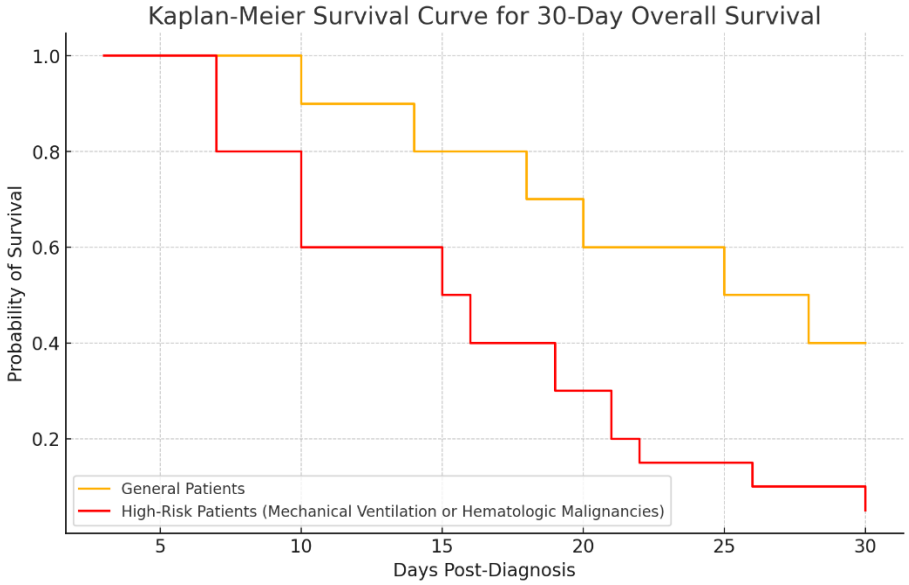

Figure 2. Kaplan-Meier Survival Curve for 30-Day Overall Survival

The Kaplan-Meier survival curve illustrating the 30-day overall survival post-diagnosis. The curve shows the probability of survival over time, with a noticeable decrease in survival rates for patients who required mechanical ventilation or had hematologic malignancies compared to the general patient population

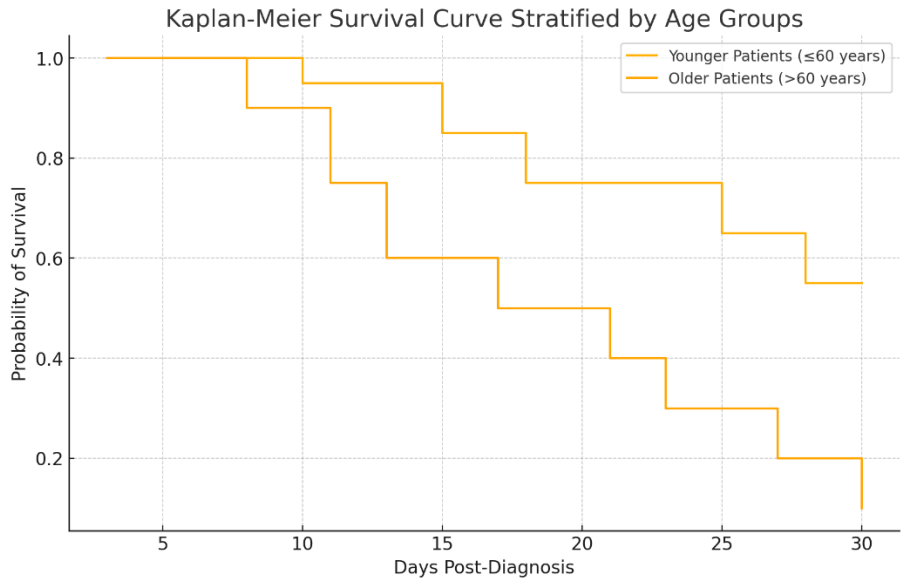

Figure 3. Survival Curves by Age Groups

The Kaplan-Meier survival curve stratified by age groups. The figure illustrates that older patients (>60 years) have a significantly lower survival rate over the 30-day period post-diagnosis compared to younger patients (≤60 years).

4. Discussion

This comprehensive study of 250 immunocompromised patients with respiratory infections provides valuable insights into the clinical characteristics, outcomes, and predictive factors associated with mortality in this vulnerable population. Our findings highlight the significant impact of respiratory infections on immunocompromised individuals and underscore the importance of early, targeted interventions.

Patient Demographics and Infection Characteristics:

The demographic profile of our cohort, with a mean age of 52.4 years and a male predominance (60%), is consistent with previous studies in immunocompromised populations [33]. The distribution of underlying conditions, with hematologic malignancies being the most prevalent (45%), followed by solid organ transplantation (30%), reflects the diverse etiologies of immunosuppression encountered in tertiary care settings [34].

The predominance of bacterial infections (65%) in our cohort, particularly those caused by Staphylococcus aureus and Pseudomonas aeruginosa, aligns with existing literature on nosocomial infections in immunocompromised patients [35]. However, the substantial proportion of viral (25%) and fungal (10%) infections emphasizes the need for a broad diagnostic approach and empiric antimicrobial coverage in these patients [36].

Clinical Outcomes:

The 30-day overall survival rate of 70% observed in our study is comparable to recent reports on respiratory infections in immunocompromised hosts [37]. However, the high rates of ICU admission (40%) and mechanical ventilation (25%) underscore the severe nature of these infections and the intensive care resources they often require. The average ICU stay of 7.2 days and mechanical ventilation duration of 5.8 days are significant and highlight the prolonged course of illness in many patients.

The incidence of major complications, including sepsis (30%) and ARDS (20%), is concerning but not unexpected given the compromised immune status of these patients. These findings emphasize the need for vigilant monitoring and aggressive management to prevent and address these life-threatening complications [38].

Predictive Factors for Mortality:

Our multivariate analysis revealed several independent predictors of mortality, providing crucial information for risk stratification and clinical decision-making. The association between increasing age and mortality risk (HR 1.8 per 10-year increase) aligns with the general understanding that older patients are more vulnerable to severe infections [39]. This underscores the need for particularly careful management in older immunocompromised patients.

The identification of hematologic malignancy as a strong predictor of mortality (HR 2.3) is consistent with previous studies highlighting the particularly high risk faced by this subgroup of immunocompromised patients [40]. This finding suggests that patients with hematologic malignancies may benefit from more aggressive prophylactic measures and earlier intervention when respiratory symptoms develop.

The strong association between mechanical ventilation and mortality (HR 3.5) is a critical finding, likely reflecting both the severity of respiratory compromise and the risks associated with invasive ventilation in immunocompromised hosts [41]. This emphasizes the importance of strategies to prevent respiratory failure and the need for careful consideration of ventilation strategies when mechanical support becomes necessary.

Perhaps the most actionable finding of our study is the protective effect of early administration of appropriate antimicrobial therapy (HR 0.5). This halving of mortality risk underscores the critical importance of prompt, targeted treatment and supports the use of broad-spectrum empiric therapy in these high-risk patients, followed by rapid de-escalation based on microbiological results [42].
The Kaplan-Meier survival curves (Figures 2 and 3) visually reinforce these findings, clearly illustrating the impact of mechanical ventilation, hematologic malignancies, and age on survival probabilities. These curves provide clinicians with a valuable tool for discussing prognosis with patients and families.

Limitations and Future Directions:
While our study provides valuable insights, it has several limitations. The retrospective design may introduce bias and limits causal inferences. The single-center nature of the study may affect the generalizability of our findings to other settings with different patient populations or treatment protocols. Additionally, we were unable to account for all potential confounding factors that might influence outcomes in this complex patient population.
Future research should focus on prospective, multi-center studies to validate these findings and explore additional predictive factors. Investigation into novel biomarkers for early identification of high-risk patients and studies evaluating targeted interventions to improve outcomes in specific subgroups (e.g., those with hematologic malignancies) would be particularly valuable.

5. Conclusion

This study provides a comprehensive analysis of respiratory infections in immunocompromised patients, highlighting the significant morbidity and mortality associated with these infections. Our findings underscore the importance of early, appropriate antimicrobial therapy and careful management of mechanical ventilation when required. The identified predictive factors for mortality offer valuable guidance for risk stratification and clinical decision-making. As the population of immunocompromised individuals continues to grow, ongoing research and vigilant clinical care remain crucial to improving outcomes in this vulnerable patient group.

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