Clinical Characteristics, Outcomes, and Antimicrobial Resistance of Non-*aeruginosa Pseudomonas* Infection in Adult Cancer Patients

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Background: *Non-aeruginosa Pseudomonas (NAP)* species, historically considered environmental contaminants, are increasingly recognized as clinically significant pathogens, particularly in immunocompromised patients. While *Pseudomonas aeruginosa* is well-studied, less is known about the epidemiology and resistance patterns of NAP species.

Methods: We conducted a retrospective review of culture-confirmed NAP infections in adult inpatients at a cancer center from 2012 to 2022. Data on demographics, infection sites, malignancy types, and antimicrobial susceptibilities were extracted from electronic medical records.

Results: Among 104 infections, the most common species were *Pseudomonas putida* (63.5%), *P. fluorescens* (25%), *P. stutzeri* (7%), and *P. mendocina* (4%). Urinary and respiratory infections predominated, frequently linked to indwelling devices. *P. fluorescens* infections had the highest 30-day mortality (19%) versus *P. putida* (7%). Polymicrobial infections were common. Fluoroquinolone susceptibility was high across all species (85%–100%).

Discussion: NAP species are emerging as relevant pathogens in oncology patients, especially those with hematologic malignancies. Species-level differences in clinical impact and resistance underscore the need for targeted diagnostics and stewardship strategies.

Key Words: non-*aeruginosa Pseudomonas*, immunocompromised patients, cancer infections, antimicrobial resistance, fluoroquinolone susceptibility, hospital-acquired infections, oncology infectious diseases, *Pseudomonas putida*, *Pseudomonas fluorescens*, species-specific outcomes

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BACKGROUND

The genus *Pseudomonas* comprises gram-negative, aerobic bacilli commonly found in soil, water, and vegetation, as well as in the normal human flora. To date, over 270 species have been identified across various hosts, including animals, plants, fungi, and algae.[1] Among them, *P. aeruginosa* is the most well-recognized species due to its high virulence and association with severe opportunistic infections, particularly in patients with bronchiectasis and cystic fibrosis.[2–4] However, in recent years, increasing attention has been directed toward non-*aeruginosa Pseudomonas* (NAP) species, which were historically considered environmental contaminants or of limited pathogenicity.[5]

Emerging evidence suggests that NAP species have become significant pathogens, particularly in immunocompromised patients.[6] Although they account for approximately 1% of all *Pseudomonas* isolates, their pathogenicity varies widely, with many strains remaining susceptible to broad-spectrum antibiotics.[7] Clinical presentations range from skin and soft tissue infections to bloodstream infections, and while overall mortality rates are generally lower than those observed with *P. aeruginosa*, certain species, such as *P. fluorescens*, have been implicated in outbreaks and severe infections.[8,9]

One notable outbreak occurred between 2005 and 2006 in Michigan and South Dakota, where *P. fluorescens* bloodstream infections were linked to contaminated heparin flush solutions, underscoring the importance of vigilance in healthcare settings.[10] Similar concerns have been raised regarding contamination in intravenous solutions and even drinking water, particularly in oncology and bone marrow transplant units.[11] Additionally, recent reports suggest increasing antimicrobial resistance in some species, such as *P. putida*, highlighting the need for continuous surveillance and cautious antibiotic use.[12] Conversely, species like *P. mendocina* have demonstrated good antibiotic susceptibility and low associated mortality, indicating variability in clinical significance among NAP species.[13]

Despite the growing recognition of NAP as potential pathogens, limited data exist regarding their clinical characteristics, antimicrobial resistance patterns, and outcomes, particularly in cancer patients. This study aims to address this gap by analyzing cases of NAP infections in adult cancer patients over a 10-year period at an academic cancer center. The primary objective is to delineate the clinical presentation, antimicrobial susceptibility patterns, and patient outcomes, while also assessing potential risk factors associated with these infections. Importantly, our study did not identify any outbreaks related to contaminated solutions, further emphasizing the sporadic yet clinically significant nature of these infections in immunocompromised populations.

METHODS

This retrospective study examined culture-confirmed NAP infections in adult inpatients at the H. Lee Moffitt Cancer Center and Research Institute over a 10-year period from 2012 to 2022. Following institutional review board approval, we identified 104 cancer patients with positive cultures for NAP species.

Data were extracted from electronic medical records, including infection sites, microbiological species isolated, antibiotic susceptibility profiles to a standard panel (including fluoroquinolones, beta-lactams, aminoglycosides, and carbapenems when available), recent surgical procedures or chemotherapy, and the presence of polymicrobial infections. While fluoroquinolone susceptibility was consistently available, other antimicrobial susceptibilities were

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variably reported; carbapenem susceptibility data were collected when available but were incomplete and thus not analyzed in aggregate. Thirty-day mortality was also recorded.

Bacterial species identification and antibiotic susceptibility testing were performed using standard microbiological protocols. Patients were categorized based on underlying malignancy type, distinguishing between those with solid tumors and those with hematologic malignancies. Statistical analyses were conducted to evaluate species distribution, infection characteristics, and clinical outcomes, with a focus on identifying trends in disease severity and antibiotic resistance.

RESULTS

Patient Demographics and Clinical Characteristics

Over the 10-year study period, 104 cases of NAP infections were identified. The mean patient age was approximately 60 years, with a relatively even gender distribution across species (Table 1). Among the total cases, 66 (63.5%) involved *P. putida*, 26 (25%) involved *P. fluorescens*, 8 (7%) involved *P. stutzeri*, and 4 (3%) involved *P. mendocina*. Most infections occurred in patients with underlying malignancies, with solid tumors being more prevalent than hematologic malignancies.

Infection Sites and Cancer Subtypes

The urinary tract and respiratory tract were the most frequently identified infection sites, reflecting the high prevalence of genitourinary and gynecological cancers in this cohort (Fig. 1). Urinary tract infections accounted for 44% (n = 29) of *P. putida* cases. All patients with hematologic malignancies had central venous catheters, and many patients with solid tumors likely had indwelling devices as well, although we were unable to systematically determine this. These likely contributed to increased infection risk.

Although solid tumors were more common overall, hematologic malignancies were more frequently associated with *P. fluorescens* infections. Among *P. fluorescens* cases, 10 (38%) occurred in patients with leukemia or lymphoma, compared to 19 (29%) of *P. putida* cases (Table 1). These findings suggest that host factors, including the degree of immunosuppression, may influence species distribution.

Species Distribution and Clinical Outcomes

P. putida was the most frequently isolated species, accounting for 66 (63.5%) cases, followed by *P. fluorescens* in 26 (25%), *P. stutzeri* in 8 (7%), and *P. mendocina* in 4 (3%) (Table 1). Despite the immunocompromised status of the patient population, most infections were associated with relatively low mortality rates. However, *P. fluorescens* demonstrated a notably higher 30-day mortality rate of 19% (n = 5), in contrast to 7% (n = 5) for *P. putida* and 0% for both *P. stutzeri* and *P. mendocina*.

The increased mortality associated with *P. fluorescens* infections may be attributed to the fact that affected patients were more likely to have hematologic malignancies, which inherently carry a poorer short-term prognosis compared to solid tumors. These findings suggest that while NAP species are generally less virulent than *P. aeruginosa*, certain species such as *P. fluorescens* may have a more significant clinical impact in specific patient populations.

Polymicrobial Infections and Antibiotic Resistance

Polymicrobial infections were frequently observed, occurring in 68% (n = 45) of *P. putida* cases, 73% (n = 19) of *P. fluorescens* cases, 63% (n = 5) of *P. stutzeri* cases, and 50% (n = 2) of *P. mendocina* cases (Table 1). This high prevalence underscores the complexity of infections in cancer patients, where multiple pathogens may contribute to disease severity.

Despite the frequent presence of polymicrobial infections, antibiotic resistance remained relatively low. Fluoroquinolone susceptibility was retained in 86% (n = 57) of *P. putida* isolates, 85% (n = 22) of *P. fluorescens* isolates, 88% (n = 7) of *P. stutzeri* isolates, and 100% (n = 4) of *P. mendocina* isolates. These findings indicate that while NAP infections are increasingly recognized in immunocompromised patients, they have not yet developed widespread resistance patterns seen in *P. aeruginosa*.

P. putida has been associated with high rates of carbapenem resistance in prior studies. In a cohort of 18 patients with *P. putida* bacteremia, Kim et al (2012) reported imipenem and meropenem resistance rates of 22% and 28%, respectively, along with a 39% 30-day mortality rate.[7] Similarly, Bashar et al (2017) documented the emergence of a blaVIM-2-producing *Pseudomonas stutzeri* strain carrying an integron-mediated carbapenemase gene cassette, highlighting resistance potential among non-*aeruginosa* species.[14] However, our study did not collect data on carbapenem susceptibility, as these results were not available in the electronic

TABLE 1. Characteristics and Outcomes of NAP

Characteristics and Outcomes	Putida, n = 66	Fluorescens, n = 26	Stutzeri, n = 8	Mendocina, n = 4
Mean age (year)	58.93	62.81	62.125	60.5
Leukemia/lymphoma	19 (29%)	10 (38%)	1 (12%)	0 (0%)
Solid malignancy	47 (71%)	16 (62%)	7 (88%)	4 (100%)
Female	27 (41%)	13 (50%)	4 (50%)	2 (50%)
Male	39 (59%)	13 (50%)	4 (50%)	2 (50%)
Fever > 100.4	11 (17%)	8 (31%)	0 (0%)	1 (25%)
SIRS present	14 (21%)	7 (27%)	1 (13%)	0 (0%)
WBC > 12	15 (23%)	4 (15%)	3 (38%)	1 (25%)
Surgical procedures in the past 30 days	21 (32%)	5 (19%)	1 (13%)	3 (75%)
ID consult	25 (43%)	11 (42%)	4 (50%)	1 (25%)
Fluoroquinolone susceptibility	57 (86%)	22 (85%)	7 (88%)	4 (100%)
Polymicrobial infection	45 (68%)	19 (73%)	5 (63%)	2 (50%)
Mortality at 30 days	5 (7%)	5 (19%)	0 (0%)	0 (0%)
Prevalence	66 (63%)	26 (25%)	8 (7%)	4 (3%)

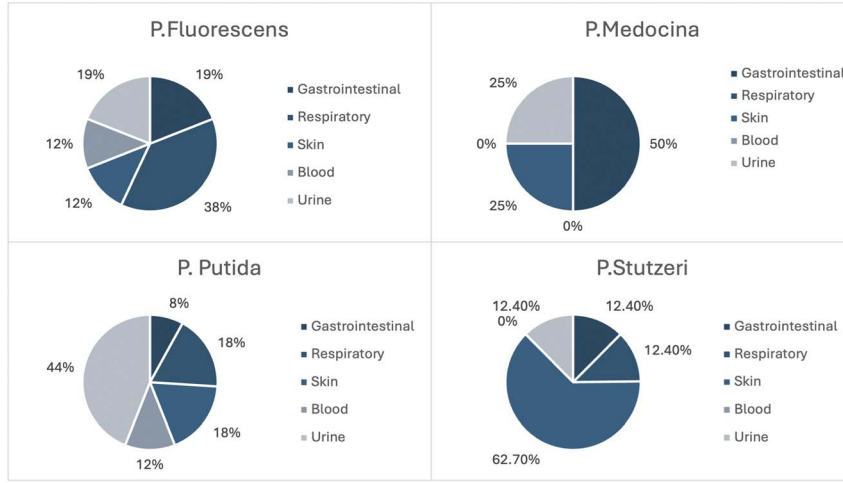

FIGURE 1. Types of infection sources.

medical record and would have required manual retrieval from the microbiology department.

Survival and Mortality Outcomes

Despite the immunosuppressed state of the patient population, overall survival rates were high. However, *P. fluorescens* infections were associated with an increased 30-day mortality rate compared to other NAP species (Table 1). Five (19%) patients with *P. fluorescens* infections died within 30 days, compared to five (7%) with *P. putida* infections, while no deaths were reported in *P. stutzeri* or *P. mendocina* infections. This observation suggests that while these infections are generally less severe than those caused by *P. aeruginosa*, certain species within this group may pose a greater risk in vulnerable patients, particularly those with hematologic malignancies. These findings highlight the need for continued surveillance, targeted antimicrobial stewardship, and careful management of medical devices in patients at risk for NAP infections.

DISCUSSION

This study highlights the clinical and microbiological characteristics of NAP infections in immunocompromised patients, particularly those with malignancies. The predominance of *P. putida* and *P. fluorescens* in our cohort underscores the need for greater awareness of these emerging pathogens, which have been increasingly implicated in nosocomial infections.

Species Distribution and Clinical Outcomes

P. putida was the most frequently isolated species, aligning with previous reports that demonstrate its adaptability and prevalence in hospital environments.[6,7,12,15] This species has been associated with high rates of carbapenem resistance, as observed in our study, posing significant challenges for treatment.[7,12] Additionally, *P. fluorescens* exhibited a concerning 30-day mortality rate, which may be attributed to its association with hematologic malignancies, as previously suggested.[9,16,17] Notably, an outbreak of *P. fluorescens* in a bone marrow transplant unit due to contaminated drinking water has been documented, emphasizing the role of environmental reservoirs in hospital-acquired infections.[11] This finding reinforces the importance of early identification and targeted therapy in high-risk populations.

Antimicrobial Resistance Patterns

Antibiotic resistance remains a major concern in the management of NAP infections. Although we did not collect data on carbapenem resistance, prior studies have suggested that *P. putida* may exhibit notable resistance to this class of antibiotics, posing significant challenges for treatment.[7,12] In contrast, *P. mendocina* displayed susceptibility to most tested antibiotics except for ampicillin, supporting its classification as a less virulent pathogen.[5,13,18,19] These variations in resistance profiles underscore the necessity for tailored antimicrobial stewardship strategies to mitigate the spread of resistant strains.[12] Furthermore, recent studies indicate that *P. putida* actively forms biofilms as a protective mechanism under antibiotic stress, which may contribute to its persistence in nosocomial environments.[20] Whole-genome analyses have also revealed that *P. putida* possesses extensive metabolic capabilities that allow it to withstand harsh environmental conditions and antibiotic exposure.[15]

Genotypic and Phenotypic Variability

Comparative genomic analyses have revealed substantial diversity within the *P. stutzeri* complex, including extensive horizontal gene transfer and genomic plasticity.[21] This genetic variability likely contributes to the differential pathogenicity and resistance patterns observed among NAP species. Additionally, *P. putida* has been shown to mediate bacterial killing and biofilm invasion using a type IVB secretion system, which may play a role in its environmental adaptability and competitive advantage.[22] Furthermore, whole-genome analyses of *P. mendocina* strains have identified virulence mechanisms such as leukotoxin and secretion systems, which could enhance pathogenic potential in clinical settings.[5]

Implications for Clinical Management

The high prevalence of urinary and respiratory tract infections in our cohort underscores the importance of stringent infection control measures, particularly in patients with medical devices such as catheters and tracheostomy tubes. Given the observed differences in virulence and resistance patterns, species-level identification should be prioritized in clinical microbiology laboratories to guide appropriate treatment decisions. The generally favorable outcomes in our study, despite the immunocompromised status of the patients, suggest that NAP species may be less virulent than *P. aeruginosa*;

however, their ability to cause severe infections in vulnerable hosts should not be underestimated.

CONCLUSIONS

This study contributes to the growing body of evidence regarding the clinical significance of NAP infections, particularly in immunocompromised populations. The findings highlight the necessity for continued surveillance, antimicrobial stewardship, and species-specific diagnostic approaches to improve patient outcomes. Future research should focus on elucidating the mechanisms underlying the observed differences in virulence and resistance, which could inform novel therapeutic strategies.

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