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Piperacillin/Tazobactam Resistance in Clinical Isolates of *Pseudomonas* and *Klebsiella* Species at a University Hospital in North Cyprus: A Retrospective Study

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Abstract

BACKGROUND/AIMS: Antibiotic resistance has become a significant problem for healthcare systems, with the *Pseudomonas aeruginosa* and *Klebsiella* species being of particular concern due to their high resistance rates. These resistant strains are making healthcare-associated infections increasingly difficult to treat, leading to a pressing public health crisis. This retrospective study aimed to evaluate the incidence of piperacillin/tazobactam (PTZ) resistance in clinical isolates of the *Pseudomonas* and *Klebsiella* species.

MATERIALS AND METHODS: Patient demographics and antimicrobial susceptibility outcomes were examined from the medical records at a university hospital in North Cyprus, between January, 2016 and March, 2022 in order to determine the extent of resistance to PTZ in these strains. A total of 812 *Pseudomonas* and 865 *Klebsiella* isolates from various hospital departments were assessed for PTZ resistance using the Vitek 2-Compact System (BioMérieux) and SPSS.

RESULTS: According to our findings, the resistance rates for PTZ were 22.9% and 26.6% for the *Pseudomonas* and *Klebsiella* species, respectively. Interestingly, the demographic distributions of resistance rates displayed a difference between genders and age groups. The elderly group had the highest resistance rates. Female patients exhibited lower resistance rates than male patients. In terms of hospital departments, the intensive care unit had the highest resistance rates (37.3% and 42.6% for *Pseudomonas* and *Klebsiella* isolates, respectively), followed by cardiology (27.9% and 33.3%) and chest disease and allergy (27.6% and 30.8%).

CONCLUSION: Given the high rates of PTZ resistance observed in this study, it is imperative to manage PTZ with caution and implement comprehensive infection prevention and control measures in healthcare facilities in order to address this public health concern.

Keywords: Piperacillin/tazobactam, resistance, *Pseudomonas*, *Klebsiella*, North Cyprus

INTRODUCTION

The escalation of antimicrobial resistance poses a significant threat to humanity. Multidrug-resistant bacteria which cause diseases have emerged and spread globally, creating a challenge for public health.[1] Misuse and overuse of antimicrobial agents have increased bacterial resistance to the available drugs, rendering antimicrobial treatments less effective.[2,3] *Enterobacteriaceae* are considered the most significant bacteria which result in diseases in humans. Among them, *Escherichia coli* is the species with the highest clinical relevance, while *Pseudomonas aeruginosa* (*P. aeruginosa*) is accountable for the highest rate of failure in antibacterial therapy.[4,5]

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The *P. aeruginosa* and *Klebsiella* species cause nosocomial infections such as urinary tract infections, surgical site infections, pneumonia, and bloodstream infections. Unfortunately, these bacteria are becoming increasingly resistant to various antibiotics, including piperacillin/tazobactam (PTZ).[6,7] PTZ is commonly used to cover Gram-negative bacteria empirically and remains active against a significant proportion of Extended Spectrum Beta Lactam-Gram-negative resistant strains.[8] Researchers have also reported PTZ resistance,[9,10] but few studies have evaluated PTZ in a clinical setting regarding the isolates of the *Pseudomonas* and *Klebsiella* species. Long-term antibiotic use, infection management practices, underlying health status, patient age, and local transmission are the risk factors which make bacterial pathogens susceptible to PTZ resistance.[11-14] This retrospective study aimed to evaluate PTZ resistance rates in *Pseudomonas* and *Klebsiella* isolates to provide surveillance data for the rational use of this antibiotic and effective infection control measures in a secondary care hospital in Nicosia, Turkish Republic of North Cyprus.

MATERIALS AND METHODS

Sample Collection

This study was conducted at a university hospital, located in North Cyprus. Diverse clinical samples, including abscess/wound material, aspirate fluid, blood, bronchial lavage, catheter tip, cerebrospinal fluid, pleural fluid, semen, sputum, urethral discharge, urine, and vaginal discharge, were collected from patients in various hospital departments. All reports of *Pseudomonas* pathogens from January 2016 to March 2023, and *Klebsiella* pathogens from January 2017 to March 2023 were included in this study. The specific inclusion/exclusion criteria applied were as follows: *Pseudomonas* isolates between January 1, 2016, and March 30, 2022, and all *Klebsiella* isolates from January 1, 2017, to March 30, 2022. All *Pseudomonas* and *Klebsiella* isolates from the same patient isolated in different years were included. Repeated tests of patients documenting the same species of *Pseudomonas* or *Klebsiella* isolates in the same month were excluded unless it was a different species of *Pseudomonas* or *Klebsiella*. The bacterial species were identified, and their resistance to PTZ was evaluated using the automated VITEK 2 system (BioMérieux). The results were interpreted using the Clinical and Laboratory Standards Institute guidelines for determining PZT resistance. The MIC breakpoint for PZT susceptibility/resistance was ≤4 µg/mL. The Near East University Scientific Research Ethics Committee approval was obtained for this study (approval number: NEU/2023/115-1742, date: 21.06.2023). However, informed consent was not required because this was a retrospective research study. The data used for analysis were taken from pre-existing sources and de-identified to ensure participant anonymity.

Statistical Analysis

We carried out separate assessments for children (0-17 years old), adults (18-64 years old), and older individuals (≥65 years old). Qualitative data values are represented using frequency and percentages. In order to investigate the relationship between two or more demographic variables in the population, we utilized the chi-square test. The level of significance was set at a 95% confidence interval (CI) with a p-value of 0.05. The main findings of our research are presented in tables, and all statistical analyses were performed using IBM SPSS version 22 (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 812 *Pseudomonas* and 865 *Klebsiella* isolates were retrospectively reviewed and screened for PTZ resistance. These isolates were collected from various units of the university hospital between January 1, 2016 and March 31, 2022. The demographics of the study population are given in Table 1 while Table 2 summarizes the demographic representation of the patient's population from whom PTZ-resistant *Pseudomonas* or *Klebsiella* species were isolated. For *Pseudomonas* isolates, females accounted for 46.7% (n=379) of the study population, while males accounted for 53.3% (n=433). The age groups for *Pseudomonas* isolates included 370 adults (37.8%), 401 elderly (49.4%), and 104 children (12.8%). Similarly, for *Klebsiella* isolates, females accounted for 56.1% (n=485) of the study population, while males accounted for 43.9% (n=380). The *Klebsiella* isolate age groups consisted of 292 adults (33.8%), 439 elderly (50.8%), and 134 children (15.5%). For simplification and statistical analysis, the ages of the patients were divided into three groups: pediatrics (0-17 years), adults (18-64 years), and the elderly (65 years or older). The age of patients from whom clinical samples were obtained ranged in age from 0 to 96 years. Table 3 displays the susceptibility rates of *Pseudomonas* and *Klebsiella* isolates to PTZ. The overall resistance rates among *Pseudomonas* isolates, including *P. aeruginosa, Pseudomonas luteola, Pseudomonas putida,* and *Pseudomonas fluorescens*, was 22.9% (n=186). Notably, *P. aeruginosa*

Table 1. Demographics of the patient's population

Characteristic	*Pseudomonas* isolates, n (%)	*Klebsiella* isolates, n (%)
Gender		
Female	379 (46.7)	485 (56.1)
Male	433 (53.3)	380 (43.9)
Total	812 (100)	865 (100)
Age group		
Adult[a]	307 (37.8)	292 (33.8)
Elderly[b]	401 (49.4)	439 (50.8)
Pediatric[c]	104 (12.8)	134 (15.5)
Total	812 (100)	865 (100)

[a]Represents patients within the age range of 18-64 years, [b]Represents patients within the age range of 65 years and above, [c]Represents patients within the age range of 0-17 years and above.

Table 2. Demographic representation of the patient's population from whom PTZ-resistant *Pseudomonas* and *Klebsiella* species were isolated

Characteristics	*Pseudomonas* isolates, n (%)		*Klebsiella* isolates, n (%)	
Gender	**Resistant**	**Sensitive**	**Resistant**	**Sensitive**
Female	60 (15.8)	319 (84.2)	127 (26.2)	358 (73.8)
Male	126 (29.1)	307 (70.9)	103 (27.1)	277 (72.9)
Total	186 (22.9)	626 (77.1)	230 (26.6)	635 (73.4)
Age group				
Adult[a]	70 (22.8)	237 (77.2)	70 (24.0)	222 (76.0)
Elderly[b]	96 (23.9)	305 (76.1)	140 (31.9)	299 (68.1)
Pediatric[c]	20 (19.2)	84 (80.8)	20 (14.9)	114 (85.1)
Total	186 (22.9)	626 (77.1)	230 (26.6)	635 (73.4)

[a]Represents patients within the age range of 18-64 years, [b]Represents patients within the age range of 65 years and above, [c]Represents patients within the age range of 0-17 years and above.

exhibited the highest resistance rate of 22.9% (n=181), surpassing the other *Pseudomonas* species. Among the other species, resistance was observed in *Pseudomonas fluorescens* (n=1), *Pseudomonas luteola* (n=2), and *Pseudomonas putida* (n=2). Conversely, *Pseudomonas stutzeri, Pseudomonas mendocina,* and *Pseudomonas pseudoalcaligenes* did not demonstrate any resistance. Subsequently, the susceptibility rates of individual *Pseudomonas* species were determined, with *P. aeruginosa* having the highest susceptibility rate of 77.1% (n=609/790). The rest had the following susceptibilities: *Pseudomonas fluorescens* (n=2), *Pseudomonas luteola* (n=2), *Pseudomonas putida* (n=9), *Pseudomonas stutzeri* (n=2), *Pseudomonas mendocina* (n=1), and *Pseudomonas pseudoalcaligenes* (n=1).

In contrast to *Klebsiella pneumoniae (K. pneumoniae)*, which exhibited the highest resistance rate of 26.9% (n=217), *Klebsiella oxytoca* and *Klebsiella ozaenae* displayed lower resistance profiles, with 21.2% (n=11) and (n=2), respectively. PTZ susceptibility mirrored these resistance trends, with 73.1% (n=591) of *K. pneumoniae* isolates, 78.8% (n=41) of *Klebsiella oxytoca* isolates, and all *Klebsiella ozaenae* (n=2) and *Klebsiella rhinoscleromatis* isolates (n=1) demonstrating susceptibility to the antibiotic.

Table 3. Percentage susceptibility of *Pseudomonas* and *Klebsiella* isolates to piperacillin/tazobactam

Isolate	**Resistant, n (%)**	**Sensitive, n (%)**
Pseudomonas aeruginosa	181 (22.9)	609 (77.1)
Pseudomonas fluorescens	1	2
Pseudomonas luteola	2	2
Pseudomonas mendocina	0	1
Pseudomonas pseudoalcaligenes	0	1
Pseudomonas putida	2	9
Pseudomonas stutzeri	0	2
Total	186 (22.9)	626 (77.1)
***Klebsiella* species**		
Isolate	**Resistant, n (%)**	**Sensitive, n (%)**
Klebsiella oxytoca	11 (21.2)	41 (78.8)
Klebsiella ozaenae	2	2
Klebsiella pneumoniae	217 (26.9)	591 (73.1)
Klebsiella rhinoscleromatis	0	1
Total	230 (26.6)	635 (73.4)

Table 3 summarizes the demographic data of the patients from whom resistant *Pseudomonas* and *Klebsiella* species were isolated. The resistance rate was 15.8% among females and 29.6% among males. PTZ sensitivity was observed in 84.2% of the female population, compared to 70.9% of the male population. Furthermore, PTZ-resistant *Pseudomonas* isolates were identified in 22.8% of adults, 23.9% of the elderly, and 19.2% of children. Similarly, PTZ-susceptible *Pseudomonas* isolates were distributed across the age groups in the following proportions: 77.2% for adults, 76.1% for the elderly, and 80.8% for children.

Similarly, the resistance rate for *Klebsiella* isolates was 26.2% among females and 27.1% among males. PTZ susceptibility was found in 73.8% of female isolates and 72.9% of male isolates. Furthermore, PTZ-resistant *Klebsiella* were identified in 24.0% of adults, 31.9% of the elderly, and 14.9% of children. Correspondingly, PTZ-susceptible *Klebsiella* isolates were distributed across the age groups in the following proportions: 76.0% for adults, 68.1% for the elderly, and 85.1% for children.

Table 4 summarizes the results of the chi-square tests conducted to assess the associations between PTZ resistance and gender and age groups in *Pseudomonas* and *Klebsiella* isolates. In *Pseudomonas* isolates, a significant association between PTZ resistance and gender was observed ($p<0.001$), while no such association was evident in *Klebsiella* isolates ($p=0.761$). Conversely, our study identified a significant association between PTZ resistance and age for *Klebsiella* isolates ($p<0.001$), but no association was found in *Pseudomonas* isolates ($p=0.585$).

Table 5 presents the percentage distribution of PTZ resistance among *Pseudomonas* isolates collected from January 1, 2016, to March 30, 2022, and *Klebsiella* isolates collected from January 1, 2017, to March 30, 2022. Among *Pseudomonas* isolates, the highest resistance rate occurred in 2021, with 46 isolates (28.4%), followed by 2017 (29 isolates, 19.2%), 2020 (23 isolates, 19.7%), 2019 (19 isolates, 19.8%), 2016 (13 isolates, 14.8%), and 2022 (10 isolates, 27.8%). Similarly, for *Klebsiella* isolates, the peak resistance rate was observed in 2021, involving 73 isolates (36.3%), followed by 2020 (46 isolates, 27.2%), 2019 (33 isolates, 21.3%), 2017 (31 isolates, 21.2%), and 2022 (22 isolates, 39.3%).

The analysis of PTZ resistance in different sample types revealed that for *Pseudomonas* species, aspiration fluid had the highest value of 48.4% (n=75), followed by urine, sputum, abscess/wound, catheter tip, and blood with values of 11.4% (n=35), 23.9% (n=34), 16.7% (n=20), 27.8% (n=10), and 17.8% (n=8), respectively. In contrast, *Klebsiella* bacteria

Table 4. The result of the chi-square test conducted to determine the association between PTZ resistance and gender and age groups in both *Pseudomonas* and *Klebsiella* isolates

Characteristics	***Pseudomonas* isolates, n (%)**					***Klebsiella* isolates, n (%)**				
Gender	**Resistant, n (%)**	**Sensitive, n (%)**	**X^2**	**p**	**df**	**Resistant, n (%)**	**Sensitive, n (%)**	**X^2**	**p**	**df**
Female	60 (15.8)	319 (84.2)	20,147	<0.001	1	127 (26.2)	358 (73.8)	0.092	0.761	1
Male	126 (29.1)	307 (70.9)				103 (27.1)	277 (72.9)			
Total	186 (22.9)	626 (77.1)				230 (26.6)	635 (73.4)			
Age group										
Adult[a]	70 (22.8)	237 (77.2)	1.040	0.585	2	70 (24.0)	222 (76.0)	16,685	<0.001	2
Elderly[b]	96 (23.9)	305 (76.1)				140 (31.9)	299 (68.1)			
Pediatric[c]	20 (19.2)	84 (80.8)				20 (14.9)	114 (85.1)			
Total	186 (22.9)	626 (77.1)				230 (26.6)	635 (73.4)			

[a]Represents patients within the age range of 18-64 years, [b]Represents patients within the age range of 65 years and above, [c]Represents patients within the age range of 0-17 years and above.

Table 5. Percentage distribution of PTZ susceptibility within the years 2016 to 2022 in *Pseudomonas* and *Klebsiella* isolates

Year	*Pseudomonas* species		*Klebsiella* species	
	Resistant, n (%)	Sensitive, n (%)	Resistant, n (%)	Sensitive, n (%)
2016	13 (14.8)	75 (85.2)	**	**
2017	29 (19.2)	122 (80.8)	31 (21.2)	115 (78.8)
2018	46 (28.4)	116 (71.6)	25 (18.1)	113 (81.9)
2019	19 (19.8)	77 (80.2)	33 (21.3)	122 (78.7)
2020	23 (19.7)	94 (80.3)	46 (27.2)	123 (72.8)
2021	46 (28.4)	116 (71.6)	73 (36.3)	128 (63.7)
2022	10 (27.8)	26 (72.2)	22 (39.3)	34 (60.7)
Total	186 (22.9)	626 (77.1)	230 (22.6)	635 (73.4)

**Data for *Klebsiella* isolates began in the year 2017 to March 2022.

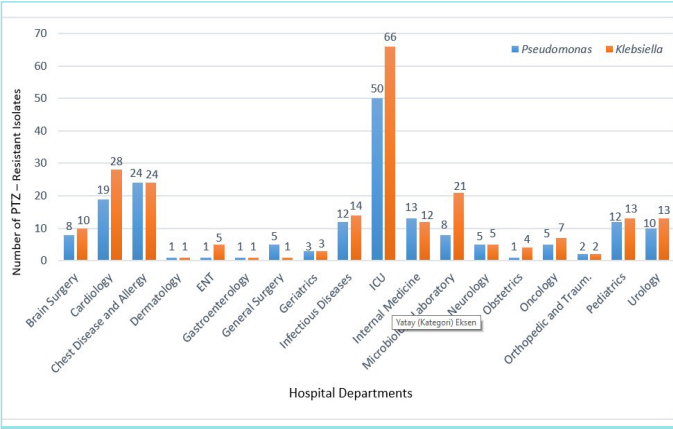

Figure 1. The distribution of resistant *Pseudomonas* and *Klebsiella* isolates according to the different hospital departments from which they were isolated.

PTZ: Piperacillin/tazobactam, ENT: Ear, nose, and throat surgery, ICU: Intensive care unit.

showed the highest resistance rates in urine (19.4%, n=96), followed by aspirate fluid, sputum, blood, and abscess/wound with resistance rates of (39.3%, n=44), (36.1%, n=41), (35.6%, n=21), and (27.1%, n=13), respectively.

Figure 1 shows the distribution of resistant *Pseudomonas* and *Klebsiella* isolates according to the different hospital departments from which they were isolated. A comprehensive examination of PTZ resistance across various hospital wards revealed that the intensive care unit (ICU) exhibited the highest resistance rates for both *Pseudomonas* and *Klebsiella* isolates. Specifically, the resistance rates for *Pseudomonas* species were distributed as follows: ICU (50 isolates, 37.3%), chest disease and allergies (n=24, 27.6%), cardiology (n=19, 23.3%), internal medicine (n=13, 23.6%), infectious diseases (n=12, 28.6%), pediatric health (n=12, 16.9%), brain surgery (n=10, 20%), urology (n=10, 18.2%), microbiology laboratory (n=8, 14.5%), general surgery (n=5), neurology (n=5), oncology (n=5, 18.5%), ear, nose, and throat surgery (ENT) (n=1), geriatrics (n=3), dermatology (n=1), and gastroenterology (n=1), respectively.

The resistance patterns of PTZ in *Klebsiella* isolates mirrored those observed in *Pseudomonas* isolates, with the ICU displaying the highest resistance rate (66 isolates, 42.6%) among the hospital departments. Following closely were cardiology (28 isolates, 33.3%), chest diseases and allergies (24 isolates, 30.8%), microbiology laboratory (21 isolates, 38.9%), infectious diseases (13 isolates, 30.2%), internal medicine (12 isolates, 18.2%), urology (13 isolates, 17.8%), pediatric health (9 isolates, 7.8%), brain surgery (8 isolates, 25%), and oncology (7 isolates, 20%). The resistance rates for the other departments were as follows: dermatology (1 isolate), ENT (5 isolates), neurology (4 isolates), obstetrics (4 isolates), geriatrics (3 isolates), pediatric surgery (3 isolates), orthopedics and traumatology (2 isolates), gastroenterology (1 isolate), general surgery (1 isolate), hematology (1 isolate), nephrology (1 isolate), and plastic surgery (1 isolate).

DISCUSSION

Assessing the incidence and antibacterial susceptibility patterns of bacterial isolates is necessary in order to determine the optimal empirical treatment for infections caused by nosocomial pathogens.[15,16] Likewise, analyzing patient data epidemiologically can help manage patients appropriately in healthcare facilities. This study aimed to determine the resistance of *Pseudomonas* and *Klebsiella* isolates to the antibiotic PTZ. This study found that the resistance rates for PTZ were 22.9% for the *Pseudomonas* and 26.6% for the *Klebsiella* species, which were significantly different from the report of the National Healthcare Safety Network.[6,14] This increase in resistance rates may be attributed to Harris et al.'s[17], identification of PTZ as a risk factor for resistance in *P. aeruginosa*, as well as Oliver et al.'s[18] observation that antibiotic use frequently leads to resistance against the antibiotic.

PTZ resistance in *P. aeruginosa* has emerged as a concerning public health issue, with *P. aeruginosa* isolates exhibiting the highest resistance rate (22.9%) among the *Pseudomonas* species. The other *Pseudomonas* species, including *Pseudomonas stutzeri, Pseudomonas mendocina,* and *Pseudomonas pseudoalcaligenes*, displayed minimal resistance, with no resistance observed for the latter two species. *Pseudomonas luteola, Pseudomonas mendocina, Pseudomonas pseudoalcaligenes,* and *Pseudomonas stutzeri* had the lowest PTZ sensitivity rates, while *P. aeruginosa* had the highest sensitivity rate (77.1%). *K. pneumoniae* isolates showed a similar pattern of resistance, with the highest resistance rate (26.9%) observed for *K. pneumoniae*, followed by *Klebsiella oxytoca* (21.2%). The least resistance was observed in *Klebsiella ozaenae* (n=2). *Klebsiella rhinoscleromatis* was completely sensitive to PTZ, and the remaining *Klebsiella* species exhibited moderate sensitivity, with *K. pneumoniae* demonstrating the highest sensitivity (68.3%).

In our investigation, a noteworthy pattern emerged in the demographic distribution of PTZ resistance among *Pseudomonas* and *Klebsiella* isolates, revealing intriguing differences between the male and female gender groups. Our study revealed a consistent pattern of higher PTZ resistance in males compared to females, with an overall resistance rate of 22.9% for *Pseudomonas* and 26.6% for *Klebsiella*. The male gender exhibited resistance rates of 29.1% for *Pseudomonas* and 27.1% for *Klebsiella*, while the female gender had resistance rates of 15.8% for *Pseudomonas* and 26.2% for *Klebsiella*. The association between gender and PTZ resistance was statistically significant for *Pseudomonas* species at a 95% CI ($p<0.001$), but not for *Klebsiella* species ($p=0.761$). This study's findings concerning gender disparity to antibiotic resistance differ from those reported by Lee et al.[19], which observed higher susceptibility rates of Gram-negative bacteria to cefotaxime and cefoxitin in females (85%) compared to males (below 75%). This contrast underscores the complexity of antibiotic resistance patterns and prompts consideration of factors contributing to gender-specific variations, including differences in bacterial species or study populations. Additionally, our results align with the report by Ruiz-Garbajosa and Cantón[20] which investigated PTZ resistance rates in *P. aeruginosa* across EU hospitals (36.1%), Spanish hospitals (29.7%), and U.S. hospitals (27.1%). This broader comparison situates our findings within a global context, emphasizing the importance of understanding regional and international trends in antibiotic resistance. The underlying reasons for these gender-based differences in PTZ resistance are still unclear, and further investigation is needed to explore potential factors such as hormonal influences, genetic predispositions, or healthcare-seeking behaviors. The high rates of PTZ resistance in both males and females highlight the need to investigate the mechanisms driving these disparities. The higher resistance rates in males may be presumed to be related to their occupation, antibiotic use, and higher risk factors for resistance. The factors which make the female gender more susceptible to antimicrobial resistance could include employment types, excessive domestic care work, and limited access to healthcare.[21]

Furthermore, the elderly age group exhibited the highest rates of PTZ resistance, reaching 23.9% and 31.9% for *P. aeruginosa* and *Klebsiella* species, respectively. This finding underscores the need for further investigation to identify the factors contributing to the elevated resistance levels among the elderly population, which could potentially be linked to decreased immunity, prolonged antibiotic use, or increased exposure to environmental pathogens. The adult age group exhibited resistance rates of 22.8% and 24% for *Pseudomonas* and *Klebsiella* species, respectively, while the pediatric age group demonstrated the lowest resistance rates at 12.2% and 14.9% for *Pseudomonas* and *Klebsiella* species, respectively. The association between age groups and PTZ resistance was statistically significant for *Klebsiella* species at a 95% CI ($p<0.001$), but not for *Pseudomonas* species ($p=0.585$). These findings suggest that the factors influencing PTZ resistance differ between *Pseudomonas* and *Klebsiella* species, with gender playing a role in *Pseudomonas* isolates and age playing a role in *Klebsiella* isolates.

A comprehensive analysis of PTZ resistance patterns across various hospital wards revealed a consistent trend of higher resistance rates in ICUs compared to other departments. For both *Pseudomonas* and *Klebsiella* isolates, the ICU exhibited the highest resistance rates, with 50 (37.3%) and 66 (42.6%) isolates exhibiting resistance, respectively. This finding is consistent with previous studies which have linked ICU environments with increased antibiotic resistance due to the prolonged use of antibiotics in critically ill patients.[22,23]

The high incidence of PTZ resistance in both *Pseudomonas* and *Klebsiella* strains in the ICU may be attributed to several factors, including a vulnerability of the critically ill patient population, a high use of invasive procedures, and the ICU serving as a focal point for infections, as well as various factors which promote the rapid transmission of multidrug-resistant pathogens in the ICU, such as new mutations, the selection of resistant strains, and inadequate infection surveillance and treatment.[24] The high resistance rates observed in ICUs underscore the need for stringent antibiotic stewardship programs in these settings. A targeted antibiotic use and the timely discontinuation of unnecessary antibiotics can help to curb the spread of resistant bacteria and protect vulnerable patients from healthcare-associated infections.

In Table 5, the resistance rates of *Pseudomonas* and *Klebsiella* species exhibited notable variations over the period 2016-2022. For *Pseudomonas* species, the resistance rate demonstrated a fluctuating trend, rising from 14.8% in 2016 to 28.4% in 2018, dipping in 2019, and subsequently oscillating between 19.7% and 28.4% in the subsequent years. A slight increase to 27.8% was observed in 2022. The overall resistance rate for *Pseudomonas* species across the study period was 22.9%.

In contrast, the resistance rates for *Klebsiella* species followed a distinct pattern. The resistance rate increased from 2017 to 2018, reaching 27.2%. A notable surge to 36.3% occurred in 2021, followed by a decline to 31.9% in 2022. The overall resistance rate for *Klebsiella* species across the study period was 22.6%. A comparison of the resistance rates of *Pseudomonas* and *Klebsiella* species shows that they exhibited a relative similarity over the years, with some fluctuations in specific years. Generally, both species displayed an upward trend in resistance rates, with *Klebsiella* species presenting a slightly higher overall rate of 26.6% compared to *Pseudomonas* species at 22.9%.

These findings underscore the dynamic and multifaceted nature of the antibiotic resistance patterns for *Pseudomonas* and *Klebsiella* species over the study period. The observed fluctuations may be influenced by various factors, such as changes in antibiotic prescribing practices, patient demographics, or the emergence of resistant strains. Further investigation into the underlying causes of these trends could contribute to a deeper understanding of antibiotic resistance dynamics in this healthcare facility.

The findings of this study are consistent with those of De et al.[25], who observed that susceptibility patterns in regional hospitals reflect their antibiotic policies. These results suggest that the use of PTZ to manage infections caused by *Pseudomonas* and *Klebsiella* strains at this tertiary healthcare facility could potentially have contributed to the high rates of PTZ resistance reported in this study.

Study Limitations

Since this was a single-center retrospective study, it is difficult to extrapolate the results to other healthcare facilities. The study's findings may not be generalizable across hospitals due to variations in patient population characteristics, antimicrobial usage, and regional patterns of resistance. For its data, this study used retrospective information from medical records. Limitations in terms of data accuracy, completeness, and potential bias may exist, as with any retrospective study. Moreover,

this study examined PTZ resistance in *Klebsiella* and *Pseudomonas* species. The use of alternative antibiotics or the existence of additional resistance mechanisms were not examined in this study as additional causes of antibiotic resistance. As a result, it is possible that the findings did not fully explain the patterns of overall antibiotic resistance present in these bacterial strains.

CONCLUSION

This study investigated the frequency of PTZ resistance among clinical isolates of *Pseudomonas* and *Klebsiella* species. The results showed that approximately 23% of *Pseudomonas* strains and 27% of *Klebsiella* strains were resistant to PTZ. Socio-demographic analysis revealed that both the male and female gender groups exhibited PTZ resistance in both species, with higher resistance rates observed in males for both *Pseudomonas* and *Klebsiella* isolates. Resistance rates were also evaluated by age groups, with the elderly age group showing the highest resistance rates in both species, followed by adults and then pediatric patients.

Patients in the ICU, chest disease, and cardiology departments had the highest rates of PTZ resistance in *Pseudomonas* species, while patients in the ICU, cardiology, chest disease and allergy, and microbiology laboratory departments had the highest rates in *Klebsiella* isolates. These findings revealed a high rate of PTZ resistance in *Pseudomonas* and *Klebsiella* bacteria in this institution, which necessitates careful antimicrobial use and periodic antibacterial sensitivity evaluations in the ICUs. Addressing this issue is crucial in order to reduce the development and transmission of antimicrobial-resistant diseases.

MAIN POINTS

- This retrospective study aimed to evaluate piperacillin/tazobactam (PTZ) resistance rates in *Pseudomonas* and *Klebsiella* isolates in North Cyprus.
- This study found that the overall resistance rates for PTZ were 22.9% for the *Pseudomonas* and 26.6% for *Klebsiella* species, significantly higher than the rates reported by the National Healthcare Safety Network.
- In both *Pseudomonas* and *Klebsiella* isolates, the intensive care unit exhibited the highest resistance rates, with 50 (37.3%) and 66 (42.6%) of isolates showing resistance, respectively.
- The resistance rates for both the *Pseudomonas* and *Klebsiella* species displayed notable fluctuations over the period 2016 to 2022.

ETHICS

Ethics Committee Approval: The Near East University Scientific Research Ethics Committee approval was obtained for this study (approval number: NEU/2023/115-1742, date: 21.06.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Concept: C.E.N., G.E.D., N.Ç., Design: C.E.N., Data Collection and/or Processing: C.E.N., N.Ç.; Analysis and/or Interpretation: C.E.N., G.E.D., Literature Search: C.E.N., Writing: C.E.N., G.E.D.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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