

Association Between Antibiotic Consumption and *Pseudomonas aeruginosa* Non-Susceptibility: A Five-Year Ecological Study at Bali Regional General Hospital

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Abstract

Background: *Pseudomonas aeruginosa* is a major cause of healthcare-associated infections (HAIs), which are difficult to eradicate because of the bacterium's intrinsic and acquired resistance mechanisms. However, evidence regarding the association between hospital antibiotic consumption and antimicrobial resistance remains inconsistent.

Objective: This study determines the association between systemic antibiotic consumption and *P. aeruginosa* non-susceptibility using five years of hospital surveillance data.

Methods: A retrospective ecological study was conducted using surveillance data from Bali Regional General Hospital between January 2019 and December 2023. The relationship between antibiotic consumption [defined as daily doses (DDD) per 100 patient-days] and resistance was analyzed by a generalized linear model in which the number of non-susceptible isolates was used as the dependent variable. Moreover, antibiotic consumption, the bed occupancy rate (BOR), the calendar year, and the antibiotic agent (with meropenem taken as the reference category) were used as independent variables.

Results: The study included 77 *P. aeruginosa* isolates and 35 antibiotic-year observations. No statistically significant association was found between antibiotic consumption and non-susceptibility (OR 1.049, 95% CI 0.980–1.122; $p = 0.168$) or between BOR and non-susceptibility (OR 1.024, 95% CI 0.992–1.057; $p = 0.152$). Calendar year was inversely associated with the modeled non-susceptibility outcome (OR 0.716, 95% CI 0.592–0.866; $p < 0.001$). Ceftazidime and cefepime had higher odds of non-susceptibility than meropenem.

Conclusion: Antibiotic consumption does not fully explain *P. aeruginosa* non-susceptibility. Factors such as antibiotic-specific resistance mechanisms and infection prevention and control practices might also have a role in the differences in non-susceptibility.

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INTRODUCTION

Pseudomonas aeruginosa is a Gram-negative opportunistic pathogen and the major cause of healthcare-associated infections (HAIs). It can cause four common types of nosocomial infections, is widely prevalent in hospital settings, and its intrinsic antibiotic resistance limits available clinical treatment regimens.^{1–3} The Global Burden of Disease (GBD) reported that infections caused by drug-resistant *P. aeruginosa* lead to approximately 84,600 deaths worldwide. As a high-fatality Gram-negative bacterium, its drug resistance disrupts empirical treatment, prolongs hospital stays, drives up medical costs, and raises patient mortality rates.⁴

Antibiotic resistance of *P. aeruginosa* has emerged as a major global public health threat. The recent update of the 2024 WHO Bacterial Priority Pathogens List (BPPL) continues to rank carbapenem-resistant *P. aeruginosa* (CRPA) as the most critical priority pathogen, showing that this clinically relevant bacterium remains an important target for both novel antibiotic infections and resistance management programs. The WHO explained that although the disease's importance shifted from critical on the first list to high priority in 2024, this does not mean there has been a reduction in burden but rather an evolution of global epidemiology and necessity for regional control strategies.⁵

An important feature that distinguishes *P. aeruginosa* from other Gram-negative pathogens is its ability to acquire resistance using several mechanisms simultaneously. Low outer membrane permeability, production of AmpC β -lactamase, biofilm formation, and overexpression of efflux pumps confer intrinsic resistance to this bacterium. In addition, *P. aeruginosa* can also acquire resistance genes by horizontal gene transfer, such as extended-spectrum β -lactamases (ESBLs) and carbapenemase-producing genes, which will hasten the emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and difficult-to-treat resistant strains (DTR).¹

Several studies have demonstrated antibiotic consumption to be a major driver of *P. aeruginosa* resistance emergence. This relationship is not robust in other countries and hospitals. For example, several studies have found a positive correlation between the use of antipseudomonal antibiotics and non-susceptibility rates. However, some studies have found no significant association after accounting for local epidemiology, infection control practices, clonal spread, and Antimicrobial Stewardship Program (ASP) implementation. In addition, some hospital characteristics might also affect antibiotic resistance. High occupancy ratio is associated with crowding, increased workload of healthcare workers, and opportunities for cross-transmission of multidrug-resistant organisms (MDRO). At the same time, hospital bed capacity indicates use in the healthcare system as well as healthcare consumption and may impact antibiotic use and resistance patterns. The variability in these results suggests that there is a complex and locally dependent relationship between antibiotic consumption and resistance.^{3,6,7}

Therefore, this study aimed to determine the relationship between systemic antibiotic consumption and antibiotic non-susceptibility in *P. aeruginosa* using 5 years of hospital surveillance data. This study aims to identify the factors associated with *P. aeruginosa* resistance by incorporating antibiotic consumption data, bed occupancy rate (BOR), and resistance surveillance data. The results of this study will provide evidence to strengthen AMS programs, assist policymakers in implementing policies that encourage rational antibiotic prescribing, and support the development of a more robust AMR surveillance system for hospitals.

METHODS

This retrospective ecological study used hospital surveillance data from January 2019 through December 2023. The analysis period was restricted to these five consecutive years because complete, matched annual antibiotic-consumption and antibiogram data were available for this period in the supplied study dataset; 2024–2025 hospital-level data were not available and were not extrapolated. Annual operational bed counts recorded in hospital statistical reports were 266, 166, 244, 230, and 254 beds, respectively, with BOR values of 59%, 72%, 44%, 53%, and 59%. The changes in bed numbers reflect annual operational bed availability as recorded by the hospital; the reasons for individual changes were not separately evaluated. Ethical approval was obtained in June 2026 (approval number 070/25813/RSUD). Informed consent was not required because the study used secondary aggregate data and involved no direct participant contact.

Data on antibiotic consumption (expressed as Defined Daily Dose (DDD) per 100 patient-days) and Bed Occupancy Rate (BOR), used as independent variables, were obtained from the Hospital Pharmacy Unit, and antibiograms were obtained from the Clinical Microbiology Laboratory. Antibiogram data were used to calculate the percentage of *P. aeruginosa* resistance as a dependent variable.

Study Population and Eligibility

All *P. aeruginosa* isolates recovered from hospitalized patients between January 2019 and December 2023, as recorded in the hospital's annual antibiogram reports, were included. For each study year, all *P. aeruginosa* isolates included in the annual antibiogram were tested against all seven antipseudomonal antibiotics evaluated in this study. Therefore, the number of isolates tested was identical across the seven antibiotics within each year, although the number of isolates varied between years. The study used aggregated annual antibiogram data, and patient-level identifiers were not available to independently assess duplicate isolates. The available dataset also did not contain specimen-specific or ward-specific information; therefore, these characteristics could not be separately analyzed. Systemic antibiotics (ATC group J01) were eligible when both annual consumption data and susceptibility results were available for every year of the study period. The analysis of antibiotic consumption included seven systemic antibiotics with antipseudomonal activity: amikacin, cefepime, ceftazidime, ciprofloxacin, gentamicin, levofloxacin, and meropenem.

***P. aeruginosa* Non-Susceptibility**

Annual antibiogram reports provided the total number of isolates recovered each year and the percentage susceptible to each antibiotic. Because the available antibiogram data did not provide separate intermediate and resistant categories, the percentage of non-susceptible isolates was calculated as 100% minus the reported susceptibility percentage for each antibiotic and each year. Therefore, the resulting outcome represents non-susceptibility and may include both intermediate and non-susceptible isolates. The term “non-susceptibility” was consequently used throughout the manuscript rather than “resistance”. For each study year, the number of *P. aeruginosa* isolates tested was the same across the seven antipseudomonal antibiotics evaluated in this study. For the Generalized Linear Model (GLM), the number of non-susceptible isolates was derived by applying the annual non-susceptibility percentage to the number of *P. aeruginosa* isolates tested in that year and rounding to the nearest whole isolate.

Antimicrobial susceptibility testing was performed by the hospital’s clinical microbiology laboratory as part of routine microbiological testing. The available annual antibiogram reports did not provide information on the specific AST method or instrument, susceptibility testing standard and version (CLSI or EUCAST), or interpretive breakpoints used during the 2019–2023 study period. Therefore, these parameters could not be independently verified, and potential changes in interpretive criteria during the study period could not be assessed.

Antibiotic Consumption

The analysis of antibiotic consumption included seven systemic antibiotics with antipseudomonal activity: amikacin, cefepime, ceftazidime, ciprofloxacin, gentamicin, levofloxacin, and meropenem. Antibiotics were classified according to the World Health Organization (WHO) Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) classification system. Antibiotic consumption was calculated using the Defined Daily Dose (DDD) methodology recommended by the WHO Collaborating Centre for Drug Statistics Methodology and expressed as DDD per 100 patient-days. Annual antibiotic consumption was standardized to the total number of inpatient days recorded in the hospital statistical reports using the following equation (1).^{8,9}

$$\text{DDD per 100 patient-days} = \frac{\{\text{total amount of antibiotic used (g)}/\text{DDD WHO (g)}\} \times 100}{\text{total patient days}} \dots\dots\dots (1)$$

Antibiotic consumption data were obtained from hospital pharmacy sales records for hospitalized patients and therefore represented dispensing data rather than individual-level administration data. Only antibiotics supplied for inpatient use were included. Oral and parenteral formulations were quantified separately and converted to their corresponding WHO-assigned DDDs before being combined. The total amount of antibiotic used refers to the cumulative quantity of each antibiotic dispensed for one year. Patient-days were defined as the total number of inpatient days recorded during the same year. Antibiotic consumption was calculated annually for each of the seven study antibiotics and expressed as DDD per 100 patient-days from 2019 to 2023. The WHO ATC/DDD Index 2026, last updated on 20 January 2026, was used for ATC classification and DDD assignment.^{8,9}

Data Analysis

Annual antibiotic consumption, bed occupancy rate (BOR), the number of isolates tested, the number of non-susceptible isolates, and non-susceptibility rates were summarized using descriptive statistics. The statistical unit of analysis was the antibiotic-year observation, resulting in 35 observations from seven antibiotics across five study years. The association between antibiotic consumption and antibiotic non-susceptibility was assessed using a generalized linear model (GLM). The number of non-susceptible isolates was used as the dependent variable, with the number of isolates tested as the binomial denominator. Annual antibiotic consumption (DDD per 100 patient-days), BOR (%), calendar year, and antibiotic agent were included as independent variables, with meropenem as the reference category. Calendar year was treated as a continuous variable. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Because only aggregated annual antibiogram data were available, it was not possible to determine whether isolates tested against different antibiotics within the same year were the same isolates. Therefore, potential correlation between antibiotic-specific observations within the same year could not be directly assessed or modeled. Statistical significance was defined as a p-value of <0.05. All analyses were conducted using IBM SPSS Statistics version 26.0.

RESULT AND DISCUSSION

This study analyzed the consumption of seven systemic antibiotics and the non-susceptibility profiles of *P. aeruginosa* over a five-year surveillance period (2019–2023). Antibiotic consumption varied substantially across agents, with a median of 0.80 DDD per 100 patient-days (IQR 0.45–10.40) and a range of 0.05 to 39.75 DDD per 100 patient-days, reflecting markedly heterogeneous utilization of antibiotics in routine clinical practice. Bed occupancy rate (BOR) also fluctuated considerably, with a median of 59.0% (IQR 53.0–59.0) and a range of 44.4% to 72.0%. The annual number of isolates tested varied from 3 to 27 (median 21), while the number of non-susceptible isolates ranged from 0 to 9 per antibiotic–year, giving a median resistance of 23.81% (IQR 10.32–33.33) (Table 1).

Table 1. Characteristics of Study Variables

Variable	Median (IQR)	Minimum	Maximum
Antibiotic consumption (DDD/100 patient-days)	0.80 (0.45–10.40)	0.05	39.75
Bed occupancy rate (%)	59.00 (53.00–59.00)	44.42	72.00
Isolates tested (n)	21.00 (5.00–21.00)	3.00	27.00
Non-susceptible isolates (n)	3.00 (1.00–4.50)	0.00	9.00
Antibiotic non-susceptibility (%)	23.81 (10.32–33.33)	0.00	100.00

Information:

DDD : defined daily dose

IQR : interquartile range

Antibiotic consumption varies widely across antibiotics, ranging from 0.05 to 39.75 DDD per 100 patient days. This level of variation is common in hospitals rather than unusual. National surveillance of German acute care hospitals found that some antibiotics were used more than ten times more frequently than others in the same institution, and that the use of different antibiotics rose and fell in opposite directions over the same period. Therefore, a single figure for total antibiotic consumption masks large differences between individual agents.¹⁰ Examining each agent separately, as in this study, reveals more clearly which antibiotics exert the greatest selective pressure.

Antibiotic Consumption

The consumption of antibiotics at a Bali Regional General Hospital was dominated by fluoroquinolones. Levofloxacin averaged 27.91 DDD per 100 patient-days and ciprofloxacin 11.77, whereas every remaining agent averaged below 1.05 DDD per 100 patient-days (Table 2).

A similar study at a hospital in Bandung in 2020 stated that the highest-consumed antibiotic was levofloxacin.¹¹ The high consumption of fluoroquinolones rather than the broadest-spectrum agents nonetheless diverges from prescribing patterns observed where stewardship programs are mature. In a Japanese hospital applying prospective audit and feedback, fluoroquinolones represented only 8.9% of broad-spectrum days of therapy, with carbapenems and piperacillin–tazobactam accounting for the majority.¹² Fluoroquinolones are a group of antibiotics that are included in the WHO WATCH category. Globally, hospitals in low- and middle-income countries contribute disproportionately to the use of WHO “Watch” category antibiotics, of which fluoroquinolones form a substantial part.¹³

Differences in antibiotic use should therefore be interpreted in the context of local prescribing practices and the implementation of antimicrobial stewardship programs, rather than being viewed as indicators of prescribing quality alone. A nationwide study in Indonesia reported that although most hospitals had established antimicrobial stewardship programs, their overall level of implementation remained moderate, with a median development score of 48.4%. Restrictive prescribing policies were among the least developed components of these programmes.¹⁴ The high use of fluoroquinolones observed in the present study is in line with these findings and suggests that optimizing fluoroquinolone prescribing should be considered a priority for local antimicrobial stewardship efforts.

Table 2. Annual Systemic Antibiotic Consumption at a General Regional Hospital in Indonesia from 2019 to 2023

ATC Code	Antibiotic	Antibiotic consumption (DDD/100 patient-days)					Mean
		2019	2020	2021	2022	2023	
J01MA12	Levofloxacin	24.32	31.42	39.75	21.94	22.12	27.91
J01MA02	Ciprofloxacin	11.11	9.70	12.56	13.12	12.34	11.77
J01DH02	Meropenem	0.37	0.80	1.92	1.29	0.80	1.04
J01DE01	Cefepime	1.16	2.25	0.45	0.44	0.76	1.01
J01GB03	Gentamicin	0.78	0.55	1.23	0.72	0.81	0.82
J01DD02	Ceftazidime	0.50	0.09	0.45	1.25	0.72	0.60
J01GB06	Amikacin	0.05	0.10	0.14	0.31	0.28	0.18

***P. aeruginosa* Non-Susceptibility Patterns**

As shown in **Table 3**, pooled non-susceptibility over the study period was highest for ciprofloxacin (31.17%), followed by ceftazidime (29.87%) and levofloxacin (25.97%). Lower pooled non-susceptibility was observed for cefepime (22.08%), gentamicin (14.29%), meropenem (10.39%), and amikacin (6.49%). Annual non-susceptibility estimates and their 95% confidence intervals are presented in **Table 3**. Given the small number of isolates in some study years and the resulting wide confidence intervals, these differences should be interpreted cautiously.

Table 3. *P. aeruginosa* Non-Susceptibility Patterns at a General Regional Hospital in Indonesia from 2019 to 2023

ATC code	Antibiotic	Non-susceptible isolates, n (%)										Pooled Resistance	
		2019 (N = 5)	95% CI	2020 (N = 3)	95% CI	2021 (N = 21)	95% CI	2022 (N = 27)	95% CI	2023 (N = 21)	95% CI	n/N	%
J01MA02	Ciprofloxacin	3 (60.0)	14.7–94.7	1 (33.3)	0.8–90.6	9 (42.9)	21.8–66.0	8 (29.6)	13.8–50.2	3 (14.3)	3.0–36.3	24/77	31.17
J01DD02	Ceftazidime	2 (40.0)	5.3–85.3	1 (33.3)	0.8–90.6	5 (23.8)	8.2–47.2	8 (29.6)	13.8–50.2	7 (33.3)	14.6–57.0	23/77	29.87
J01MA12	Levofloxacin	2 (40.0)	5.3–85.3	1 (33.3)	0.8–90.6	8 (38.1)	18.1–61.6	6 (22.2)	8.6–42.3	3 (14.3)	3.0–36.3	20/77	25.97
J01DE01	Cefepime	5 (100.0)	47.8–100.0	1 (33.3)	0.8–90.6	3 (14.3)	3.0–36.3	2 (7.4)	0.9–24.3	6 (28.6)	11.3–52.2	17/77	22.08
J01GB03	Gentamicin	3 (60.0)	14.7–94.7	1 (33.3)	0.8–90.6	4 (19.0)	5.4–41.9	3 (11.1)	2.4–29.2	0 (0.0)	3.0–36.3	11/77	14.29
J01DH02	Meropenem	2 (40.0)	5.3–85.3	0 (0.0)	0.0–70.8	1 (4.8)	0.1–23.8	3 (11.1)	2.4–29.2	2 (9.5)	1.2–30.4	8/77	10.39
J01GB06	Amikacin	0 (0.0)	0.0–52.2	0 (0.0)	0.0–70.8	0 (0.0)	0.0–16.1	1 (3.7)	0.1–19.0	4 (19.0)	5.4–41.9	5/77	6.49

Information:

N : total number of *P. aeruginosa* isolates recovered in that year.

n/N : non-susceptible isolates over isolates recovered across the study period.

Meropenem non-susceptibility of 10.39% is substantially lower than contemporary Indonesian estimates. A 2024 systematic review of Indonesian surveillance data reported carbapenem resistance of 35.8% among hospital *P. aeruginosa* isolates, while national surveillance reported carbapenem resistance of approximately 25%.^{15,16} The low level of meropenem resistance observed in this study can be explained by several factors. Meropenem consumption at this hospital was low throughout the study period, which may have reduced the selective pressure for the emergence of resistant *P. aeruginosa* strains. The study was conducted in a regional general hospital rather than a tertiary referral centre. Patients treated in tertiary hospitals are generally more severely ill, require more invasive procedures, and are exposed to broad-spectrum antibiotics for longer periods, all of which increase the risk of carbapenem-resistant *P. aeruginosa*. Therefore, low carbapenem resistance in non-tertiary Indonesian hospitals is likely to reflect the local epidemiological situation.^{15,16}

Amikacin showed the lowest non-susceptibility rate among the antibiotics evaluated, despite having the lowest level of consumption (mean 0.18 DDD per 100 patient-days). This finding may be related to its limited use in the hospital, resulting in lower selective pressure for resistant *P. aeruginosa* strains. In addition, resistance to aminoglycosides is mainly mediated by overexpression of the MexXY-OprM efflux pump and the production of aminoglycoside-modifying enzymes, mechanisms that differ from those responsible for resistance to many other antipseudomonal agents. Because these resistance mechanisms are not consistently selected by exposure to other antibiotic classes, the relatively low use of amikacin may have contributed to preserving its antibiotic activity.^{17,18} Taken together, amikacin showed the highest in-vitro susceptibility among the antibiotics evaluated in this hospital dataset.

Association Between Antibiotic Consumption and *P. aeruginosa* Resistance

As shown in **Table 4**, antibiotic consumption was not significantly associated with non-susceptibility (OR 1.049 per 1 DDD per 100 patient-days; 95% CI 0.980–1.122; $p = 0.168$). There was no statistically significant association detected for bed occupancy rate (OR 1.024 per percentage point; 95% CI 0.992–1.057; $p = 0.152$). Calendar year was inversely associated with non-susceptibility (OR 0.716; 95% CI 0.592–0.866; $p < 0.001$).

Table 4. Multivariable Generalized Linear Model of Factors Associated with *P. aeruginosa* Resistance

Variable	B	SE	Wald χ^2	OR (95% CI)	P value
Antibiotic consumption, per 1 DDD/100 patient-days	0.048	0.034	1.905	1.049 (0.980–1.122)	0.168
Bed occupancy rate, per 1 percentage point	0.023	0.016	2.057	1.024 (0.992–1.057)	0.152
Calendar year, per 1 year	–0.333	0.097	11.826	0.716 (0.592–0.866)	<0.001

Information: B is regression coefficient on the logit scale; SE is standard error; OR is odds ratio; and CI is confidence interval.

The absence of an association between consumption and resistance is not unusual in ecological analyses. In the Japanese study at the Hyogo Medical University Hospital, no correlation was found between total broad-spectrum antibiotic use and the resistance rate for any Gram-negative organism examined. Instead, resistance in *P. aeruginosa* correlated inversely with the diversity of antibiotic consumption.¹² A fourteen-year longitudinal study encompassing 14,852 *P. aeruginosa* isolates similarly found that resistance to ceftazidime, gentamicin, amikacin, ciprofloxacin, and levofloxacin declined. At the same time, consumption of several agents rose, with stewardship measures rather than consumption volume appearing to drive the observed changes.³

The nature of both the exposure measure and the biology of *P. aeruginosa* may explain the absence of a significant association. DDD per 100 patient-days reflects overall antibiotic consumption at the hospital level but does not represent antibiotic exposure at the individual patient level. Since broad-spectrum antibiotics are often concentrated among a relatively small number of critically ill patients, hospital-wide consumption may not correspond directly to the patients at greatest risk of developing resistant infections. In addition, resistance in *P. aeruginosa* is caused through several intrinsic and acquired mechanisms, including AmpC derepression, reduced OprD expression, efflux pump overexpression, and the dissemination of high-risk epidemic clones. These mechanisms can contribute to resistance independently of changes in antibiotic consumption.^{1,17,18}

Bed occupancy varied considerably over the five-year study period, allowing evaluation of whether changes in hospital occupancy were associated with antibiotic resistance. Previous studies have suggested that high bed occupancy may increase opportunities for the transmission of multidrug-resistant organisms. A meta-analysis conducted in intensive care units found that patients admitted to beds previously occupied by individuals colonized or infected with multidrug-resistant organisms had a higher risk of acquiring these pathogens.¹⁹ However, in this study, BOR was not significantly associated with *P. aeruginosa* resistance after adjustment for other variables. This result suggests that patient occupancy alone was not the main factor that caused resistance in the hospital. Other factors, such as the effectiveness of antimicrobial stewardship programs, infection prevention and control measures, and the intrinsic resistance mechanisms of *P. aeruginosa*, may have had a greater influence on the resistance patterns observed.^{1,14,18,20} A meta-analysis of 32 studies found that stewardship programs reduced the incidence of multidrug-resistant Gram-negative infection by 51%, and that the effect was greater when stewardship was implemented together with infection control measures, particularly hand hygiene.²¹ A six-year prospective study of 2,241 *P. aeruginosa* isolates likewise achieved control of resistance through combined stewardship and infection control programmes.²²

Calendar year was the only variable independently associated with *P. aeruginosa* resistance, with the adjusted odds of non-susceptibility decreasing over the study period (**Table 4**). However, this temporal trend should be interpreted cautiously because the number of isolates was small, particularly in 2019 and 2020, when only 5 and 3 isolates were tested, respectively. A change in only one isolate could therefore substantially affect the annual non-susceptibility percentage and the estimated year effect. Similar temporal patterns have been reported by the Indonesian national antimicrobial resistance surveillance programme.¹⁶ Several factors may potentially contribute to this observed temporal pattern. These include improvements in antimicrobial resistance control and management programs, strengthened infection prevention and control practices during the COVID-19 pandemic, and continued implementation of measures such as hand hygiene and personal protective equipment use.^{14,23,24} However, these factors were not measured in the present study and therefore cannot be established as explanations or causes of the observed decline. Increased use of broad-spectrum antibiotics during the pandemic may also have influenced non-susceptibility patterns, but its relationship with the observed temporal trend could not be directly assessed using the available data.

Nevertheless, the observed decline in resistance should be interpreted with caution. Only five *P. aeruginosa* isolates were identified in 2019 and three in 2020 (**Table 3**). With such small numbers, a single isolate could substantially alter the annual resistance rate, resulting in changes of approximately 20–33 percentage points. The low number of isolates in 2020 is consistent with reports describing disruption of microbiological surveillance during the COVID-19 pandemic. An international survey involving laboratories from 73 countries found reductions in clinical and screening cultures, accompanied by shortages of laboratory reagents and personnel.²⁵ National surveillance data from Japan, involving more than 1,300 hospitals, showed that fewer patients had microbiologically confirmed pathogens in 2020 than in the previous year.²⁶ In this study, however, bed occupancy reached its highest level in 2020, indicating that the reduced number of isolates was unlikely to be explained by lower hospital utilization. Because the earliest years of observation also recorded the highest non-susceptibility rates, part of the downward trend may reflect random variation

or regression to the mean rather than a true reduction in resistance. Continued surveillance with a larger number of isolates will be necessary to determine whether this pattern is sustained over time.

Antimicrobial resistance is expected to remain a major global health challenge over the coming decades, with low- and middle-income countries predicted to experience the greatest burden.²⁷ The findings of this study reinforce the importance of using local resistance data when selecting empirical treatment for suspected *P. aeruginosa* infections. Although monitoring antibiotic consumption remains an essential component of antimicrobial stewardship, it should be complemented by regular surveillance of resistance patterns and periodic evaluation of the hospital antibiogram. Together, these measures can support more appropriate empirical antibiotic selection and help preserve the effectiveness of currently available antipseudomonal agents.

Table 5 showed the association between antibiotic agent and *P. aeruginosa* non-susceptibility. Using meropenem as the reference category, the odds of non-susceptibility were significantly higher for ceftazidime (OR 3.901, 95% CI 1.598–9.522; $p = 0.003$) and cefepime (OR 2.569, 95% CI 1.022–6.459; $p = 0.045$), whereas no statistically significant differences were detected for the other antibiotics. These ORs represent comparisons of the non-susceptibility profiles of the respective antibiotic agents with meropenem and should not be interpreted as causal effects of antibiotic consumption. Although ceftazidime and cefepime showed higher non-susceptibility despite relatively low use, with annual consumption below 1.1 DDD per 100 patient-days (**Table 2**), this finding does not establish a causal relationship between antibiotic consumption and non-susceptibility.

Table 5. Association Between Antibiotic Agent and *P. aeruginosa* Non-Susceptibility

ATC code	Antibiotic	B	SE	Wald χ^2	OR (95% CI)	P value
J01DD02	Ceftazidime	1.361	0.455	8.938	3.901 (1.598–9.522)	0.003
J01DE01	Cefepime	0.944	0.470	4.025	2.569 (1.022–6.459)	0.045
J01MA02	Ciprofloxacin	0.869	0.597	2.120	2.384 (0.740–7.677)	0.145
J01GB03	Gentamicin	0.388	0.502	0.598	1.474 (0.552–3.939)	0.439
J01MA12	Levofloxacin	−0.155	1.062	0.021	0.856 (0.107–6.868)	0.884
J01GB06	Amikacin	−0.475	0.601	0.624	0.622 (0.192–2.019)	0.429
J01DH02	Meropenem	—	—	—	Reference	—

Information: B is regression coefficient on the logit scale; SE is standard error; OR is odds ratio; and CI is confidence interval.

Several biological mechanisms can explain the increased resistance to these two antipseudomonal cephalosporins. In *P. aeruginosa*, resistance to ceftazidime and cefepime commonly results from overproduction of chromosomal AmpC β -lactamase, reduced outer membrane permeability, overexpression of multidrug efflux pumps, or the accumulation of multiple resistance mechanisms within the same isolate. These mechanisms may develop under selective pressures other than the direct consumption of a particular antibiotic and can reduce susceptibility to several β -lactam agents simultaneously. Therefore, differences in resistance between antibiotic agents are likely to reflect the underlying resistance mechanisms circulating in the hospital rather than differences in antibiotic consumption alone.^{1,18,28}

The result of this study highlights the importance of considering local resistance profiles when selecting empirical therapy for suspected *P. aeruginosa* infections. While monitoring antibiotic consumption is a critical aspect of antimicrobial stewardship, surveillance of resistance mechanisms and periodic review of the hospital antibiogram are equally important to guide appropriate antibiotic selection and preserve the effectiveness of available antipseudomonal agents.

Limitation

Several limitations should be considered when interpreting these findings. First, the number of *P. aeruginosa* isolates was small, ranging from 3 to 27 per antibiotic-year observation, which was below the 30-isolate recommendation in CLSI M39.²⁹ The small sample size resulted in wide confidence intervals and may have limited the statistical power of the analysis. Therefore, differences in non-susceptibility between years should be interpreted with caution.

Second, the annual antibiograms provided only the number of isolates tested and the percentage susceptible. Therefore, the number of non-susceptible isolates was estimated by subtracting the percentage susceptible from 100% and rounding the resulting count to the nearest whole isolate. Separate intermediate and resistant categories were not available. The estimated values may therefore differ slightly from those obtained from individual isolate-level data.

Third, the unit of analysis was the antibiotic-year observation, giving 35 observations across the five-year study period. Although the number of isolates tested was the same for each antibiotic within a given year, the available aggregated data did not indicate whether the same isolates were tested against different antibiotics. Thus, potential dependence between antibiotic-specific observations within the same year could not be assessed or accounted for directly.

Finally, only five annual time points were available. Information on the AST method or instrument, testing standard and version, and interpretive breakpoints was also unavailable, so possible changes in susceptibility interpretation during the study period could not be assessed. Antibiotic consumption data were based on hospital pharmacy dispensing records rather than individual administration records. Data beyond 2023 were not available from the hospital.

CONCLUSION

This ecological study from 2019 to 2023 found no statistically significant hospital-level association between systemic antipseudomonal antibiotic consumption and *P. aeruginosa* non-susceptibility. Non-susceptibility varied across antibiotic agents and showed a decreasing pattern over the study period. These findings should be interpreted cautiously because of the small annual number of isolates and the use of aggregated outcome data. Further studies using larger datasets, longer surveillance periods, and individual isolate-level susceptibility data are needed to better understand the relationship between antibiotic consumption and *P. aeruginosa* non-susceptibility.

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GENERATIVE AI DISCLOSURE STATEMENT

Grammarly was used solely to improve the language quality of selected sections of the manuscript, including grammar, spelling, punctuation, and readability. No generative artificial intelligence tools contributed to the study design, data collection, data analysis, interpretation of the findings, or writing of the scientific content. All content was reviewed by the authors, who take full responsibility for the accuracy, originality, and final version of the manuscript.

AUTHOR CONTRIBUTION STATEMENT

Dwi Arymbhi Sanjaya: Conceptualization, Formal analysis, Writing – original draft; **Herleeyana Meriyani:** Formal analysis, Writing – review and editing; **Rr Asih Juanita:** Data curation; **Nyoman Budiarta Siada:** Data curation; **I Putu Yudistira Mahaputra:** Investigation. All contributing authors have examined and consented to the final published manuscript.

CONFLICT OF INTEREST DECLARATION

The authors declare no conflict of interest.

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