ISSN: 2643-461X

Vo et al. Int J Trop Dis 2022, 5:058
DOI: 10.23937/2643-461X/1710058
Volume 5 | Issue 1
Open Access

International Journal of Tropical Diseases

ORIGINAL ARTICLE

Antimicrobial Resistance Patterns of *Pseudomonas aeruginosa* in a Vietnamese Tertiary Care Hospital

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Abstract

Background: Vietnam is one of the countries at high alert of antibiotic resistance. This study aimed to evaluate the antimicrobial susceptibility of *P. aeruginosa* isolates collected from a Vietnamese hospital in 2019.

Methods: A retrospective review was conducted of all reports of *P. aeruginosa* isolates from the records of the laboratory of Nhan Dan Gia Dinh Hospital between January 01 2019 to December 31 2019.

Results: Of 224 samples, the most common infection from which *P. aeruginosa* was isolated was pneumonia in hospitalized patients (49.1%) followed by skin and skin-structure infections (19,6%), and intra-abdominal infections (18.8%). The rates of isolates with MDR, XDR, and PDX were 7.1%, 20.5%, and 0.0%. Colistin was the most active agent overall (100.0%). Amikacin was the second most active agent, inhibiting 78.9% of all isolates. Other commonly used antipseudomonal β-lactams (cefepime, ceftazidime, imipenem, meropenem, and piperacillin-tazobactam) had susceptibilities for all isolates ranging from 68.0% to 70.9%. Ciprofloxacin and levofloxacin had overall 64.0%S and 61.8%S, respectively. Ticarcillin/Clavulanic acid was the least active antimicrobial tested with overall susceptibility of 38.1%.

Conclusions: The results of this investigation highlight the high rates of antibiotic resistance in *P. aeruginosa* in the hospital which will challenge optimizing empirical antimicrobial therapy for *P. aeruginosa* infections and require urgent antibiotic stewardship programs effectively.

Keywords

Antimicrobial, Multidrug resistance, *Pseudomonas aeruginosa*, Surveillance, Susceptibility

Abbreviations

ABR: Antibiotic Resistance; ASP: Antibiotic Stewardship Programs; VNMOH: Vietnam Ministry of Health; NDGDH: Nhan Dan Gia Dinh Hospital; CLSI: Clinical Laboratory Standards Institute; SSSI: Skin-Soft Tissue Infection; MDR: Multiple Drug Resistance; XDR: Extensively Drug-Resistant; PDR: Pan Drug-Resistant; NS: Non Sensible

Introduction

Antibiotic resistance (ABR) has been recognized as a global health issue. P*seudomonas aeruginosa* is one of the most challenging organisms involved in a variety of infections. The World Health Organization (WHO) published a list of highly antibiotic resistant bacteria that are in need of priority for the research and development of new antibiotics. The list was divided into 3 levels, in which the most critical is the carbapenem-resistant *Pseudomonas aeruginosa* [1].

A geographic and temporal trend in resistant phenotypes of *P. aeruginosa* from ≥ 400 medical centers worldwide over the 20 years of the SENTRY Antimicrobial Surveillance Program during the period from 1997 to 2016 found that the most common

Citation: Vo TH, Bui QH, Nguyen HH, Pham HT (2022) Antimicrobial Resistance Patterns of *Pseudomonas aeruginosa* in a Vietnamese Tertiary Care Hospital. Int J Trop Dis 5:058. doi.org/10.23937/2643-461X/1710058

Accepted: March 15, 2022; **Published:** March 17, 2022

infection from which *P. aeruginosa* was isolated was pneumonia in hospitalized patients (44.6%) followed by bloodstream infection (27.9%), with a high rate of multiple drug resistance (MDR) (27.7% vs. 23.7, respectively) [2]. Regional variations in antibiotic resistance patterns for different organisms including *P. aeruginosa* also occur [2], which could be due to differences in antibiotic prescribing practices. Better understanding of global trends in antibiotic resistance for the organism is obtained through local and regional surveillance studies [3].

In Vietnam, *P. aeruginosa* has appeared as the most commonly isolated organisms in hospitals, causing 20-30% of all nosocomial infections [4]. In 2016, the Vietnam Ministry of Health (VNMOH) approved a national program in the effort of preventing the spread of ABR and a guideline on the implementation of "Antibiotic stewardship programs (ASP) in hospitals" [5]. ASP is a multifaceted, multidisciplinary team approach to combat antibiotic misuse. Of which periodic testing and evaluation of antibiotic resistance of bacterial agents is useful for physicians to detect resistance pattern and assist in the selection of an appropriate antibiotic for empiric treatment in a particular setting.

Therefore, this study aimed to determine the status of antimicrobial resistance to anti-pseudomonal agents and the magnitude of the multi-drug resistance to *P. aeruginosa* in one hospital.

Material and Methods

Study design and setting

A retrospective review was conducted of all reports of *P. aeruginosa* isolates from the records of the laboratory of Nhan Dan Gia Dinh Hospital (NDGDH) between January 01, 2019 to December 31, 2019. NDGDH is a 1500-bed tertiary care referral hospital in Ho Chi Minh City, Vietnam. In cases where more than one *P. aeruginosa* was isolated from a single patient, the sample that is considered to be the primary source of infection is included (i.e. pulmonary excretions rather than blood in cases of pneumonia).

Isolation and identification

Submitted samples were analyzed using the traditional culture methods. Urine samples were inoculated onto blood agar and MacConkey agar. Sputum and tracheal aspirates were inoculated onto blood agar, MacConkey agar and chocolate agar. Blood samples were inoculated onto BACTEC Aerobic Plus vial, while cerebrospinal fluid and other body fluids were inoculated onto blood agar, MacConkey agar, trypticase soy broth and chocolate agar.

Identification of *P. aeruginosa* was based on routine biochemical methods that included the following reactions: Gram-negative bacilli, oxidase positive, unable to ferment sugars on triple sugar iron, motile, do not produce sulfide and indole, citrate positive, urease negative, lysine decarboxylase positive, lysine deaminase negative, able to grow at 42 °C, and pigmented.

Antibiotic susceptibility test

The investigated antibiotics were ticarcillin, ticarcillin/acid clavulanic, piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, tobramycin, amikacin, ciprofloxacin, levofloxacin, and colistin. The *in vitro* susceptibility of these antibiotics was tested using the Kirby-Bauer disk diffusion method under the M02-A11 guidelines of the Clinical Laboratory Standards Institute (CLSI) and were confirmed by the automated VITEK 2 system (bioMérieux Inc., France). The subsequent results of the tests were then interpreted in accordance with the M100-S25 document.

Resistant phenotypes

Resistant phenotypes analysed using EUCAST criteria were as follows: MDR (NS to at least 1 antimicrobial in ≥ 3 drug classes), extensively drug-resistant ([XDR] NS to at least 1 agent in all but ≤ 2 drug classes), and pan drug-resistant (PDR), according to Magiorakos, et al. [6]. Ceftazidime-non sensible (NS) and meropenem-NS were determined according to EUCAST interpretive criteria.

Quality control

P. aeruginosa, with American type culture collection (ATCC) number 27853, was used as the reference strain for quality control of culture media, biochemical tests and susceptibility testing.

Ethical consideration

The study was approved by the Nhan Dan Gia Dinh Hospital's ethical review board with approval number 15/HĐĐĐ, on 06 January 2020. The study was conducted in a spirit of respecting the private information related to patients and health care providers. Information which was collected from routine data of drug charts was anonymized.

Statistical analysis

All data was analysed by using SPSS software version 20.0. The proportion of susceptible isolates was calculated as the sum of susceptible organisms (neither intermediately susceptible nor resistant) relative to the total number of organisms tested. The drug resistance pattern of *P. aeruginosa* with site of infection, specific antibiotics, and resistance phenotypes was summarized in terms of frequencies and percentages.

Results

Sample and infection type

Of 224 samples, the most common infection from which *P. aeruginosa* was isolated was pneumonia in

hospitalized patients (49.1%) followed by skin-soft tissue infection (SSSI) (19.6%), and intra-abdominal infection (18.8%) as shown in Table 1.

The rates of isolates with MDR and XDR were 7.1% and 20.5%. Pneumonia had a higher rate of isolates with MDR and XDR (11.8% and 21.8%, respectively) than BSIs (0.0% and 20.0%, respectively) as shown in Table 2. There was no PDR isolate. The frequency of XDR, ceftazidime-NS, and meropenem-NS isolates were highest in the urinary tract infection (61.1%, 76.0%, and 72.0%).

Activities of specific antimicrobials are shown in Figure 1 for all isolates and in Figure 2 for infection type. Colistin was the most active agent overall (100.0%). Amikacin was the second most active agent, inhibiting 78.9% of all isolates. Tobramycin and gentamicin were slightly less active than amikacin and inhibited 74.1% and 71.9% of all isolates, respectively. Other commonly used antipseudomonal β-lactams (cefepime, ceftazidime, imipenem, meropenem, and piperacillin-tazobactam) had susceptibilities for all isolates ranging from 68.0% to 70.9%. Ciprofloxacin and levofloxacin had overall 64.0%S and 61.8%S, respectively. Ticarcillin/Acid clavulanic was the least active antimicrobial tested with overall susceptibility of 38.1%.

The resistance patterns of *P. aeruginosa* to the antibiotics are almost identical among infection types (Figure 2). Colistin and aminoglycosides are still the most effective as compared to other antibiotics, and ticarcillin/acid clavulanic was still noted to have the highest resistance. However, resistance of *P. aeruginosa* is highest in urinary tract infection, followed by BSIs.

Table 1: Distribution of *Pseudomonas aeruginosa* isolated by infection and sample type antimicrobial susceptibility.

Infection type/Sample	Frequency	Ratio
Pneumonia	110	49.1
Sputum	103	46.0
Blood	6	2.7
Bronchoalveolar lavage	2	0.9
Pleural fluid	1	0.4
Skin - soft tissue infection (SSTI)	44	19.6
Pus	26	11.6
Skin/soft tissue drainage	18	8.0
Intra-abdominal infection	42	18.8
Abdominal fluid and pus	42	18.8
Urinary tract infection	18	8.0
Urine	18	8.0
Bloodstream infection (BSI)	10	4.4
Blood	9	4.0
Vessel catheter	1	0.4
Total	224	100.0

Discussion

Antimicrobial susceptibility

Resistance profile of *P. aeruginosa* in some studies in the literature is summarized in Table 3. Over the 20 years of SENTRY Program surveillance [2], the rates of resistant phenotypes for *P. aeruginosa* were highest in 2005-2008 and decreased in 2009-2016. The Asia-Pacific region had an overall lower frequency of MDR *P. aeruginosa* than Latin America and Europe. The region saw an increase in MDR *P. aeruginosa*, from 15.6% in 1997-2000 to 24.7% in 2005-2008 and decreased to 15.0% in 2013-2016. MDR *P. aeruginosa* in our study was lower (7.1%). XDR *P. aeruginosa* in 2013-2016 of SENTRY Program surveillance was 15.2% which was lower than one in our study (20.5%).

The frequency of Ceftazidime-NS, and meropenem-NS isolates were one third and were highest in the urinary tract infection. A study by Biedenbach, et al. [7] found that frequency of ceftazidime-NS, and meropenem-NS *P. aeruginosa* from 5 medical centers in Vietnam provided 529 *P. aeruginosa* isolates from patients with hospital-acquired or ventilator-associated pneumonia from 2012 to 2014 was 57,7% and 43.5%, respectively.

The resistance patterns of *P. aeruginosa* to the antibiotics are almost identical in many studies. Colistin and aminoglycosides are still the most

Table 2: *Pseudomonas aeruginosa* isolates 2019 stratified by infection type and percentage of isolates with resistant phenotypes.

Infection type/Resistant Phenotype	MDR	XDR	PDR	Ceftazidime -NS	Meropenem -NS
Pneumonia (n = 110)	11.8%	21.8%	0.0%	29.6%	35.5%
Skin-soft tissue (n = 44)	2.3%	13.6%	0.0%	20.8%	16.0%
Intra-abdomen (n = 42)	2.4%	7.1%	0.0%	18.8%	16.1%
Urinary tract (n = 18)	5.6%	61.1%	0.0%	76.0%	72.0%
Bloodstream (n = 10)	0.0%	20.0%	0.0%	22.2%	22.2%
Total (n = 224)	**7.1%**	**20.5%**	**0.0%**	**30.8%**	**32.0%**

MDR: Multidrug Resistant; EDR: Extensively Drug Resistant; PDR: Pan Drug Resistant; NS: Non-Sensible. Criteria as published by European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2018.

DOI: 10.23937/2643-461X/1710058

Table 3: Non-susceptibilities of *Pseudomonas aeruginosa* of different studies.

Authors	Period	Samples	Population	Settings	MDR	XDR	PDR	Colistin NS	Amikacin NS	Ceftazidime NS	Cefepime NS	Mero-penem NS	Piper/ Tazo NS	Cipro-floxacin NS
Shortridge D, et al. [2]	1997-2016	52022	All	≥ 400 medical centers representing the Asia-Pacific, European, Latin American, and North American regions	24.9	17.6	0.1	0.6%	7.0%	22.5	20.7	23.9	26.9	27.1
	2013-2016	16461			21.8	15.2	0.1			19.2		22.6		
Biedenbach-DJ, et al. [7]	2012-2014	529	hospital-acquired or ventilator-associated pneumonia	5 medical centers in Vietnam	-	-	-	-	18.4	57.7	39.9	43.5	43.9	45.0
Phu VD, et al. [8]	2012-2013	100	Hospital-acquired infections	15 ICU in 14 hospital in Vietnam	-	-	-	-	-	-	-	55.7%*	-	-
Pfaller MA, et al. [9]	2013-2015	489	All hospitalized patients	14 medical centers located in 7 countries in the APAC region (minus China, Australia and New Zealand)	27.4	-	-	1.6%	7.8%	25.8%	20.9%	28.3%	27.9%	26.0%#
		108		Korean						38.9%		46.3%	42.6%	
		37		India						32.4%		33.3%	40.5%	
		138		Thailand						27.5%		33.3%	29.0%	
		63		Singapore						20.6		17.5	19.0%	
		21		Taiwan						19.0%		19.0	25.0%	
		90		Malaysia						14.4		11.1	14.4	
		32		Hong Kong						12.5		15.6	15.6	
Sader HS, et al. [10]	2012-2015	7452	All	79 U.S. medical centers	15.5	9.4	-	0.7	3.0	15.7	14.6	18.0	19.4	22.5
Our study	2019	244	All	A hospital in Vietnam	7.1	20.5	0.0	0.0	21.1	30.8	30.9	32.0	29.1	36.0

*Carbapenem resistance; #Levofloxaci

ISSN: 2643-461X

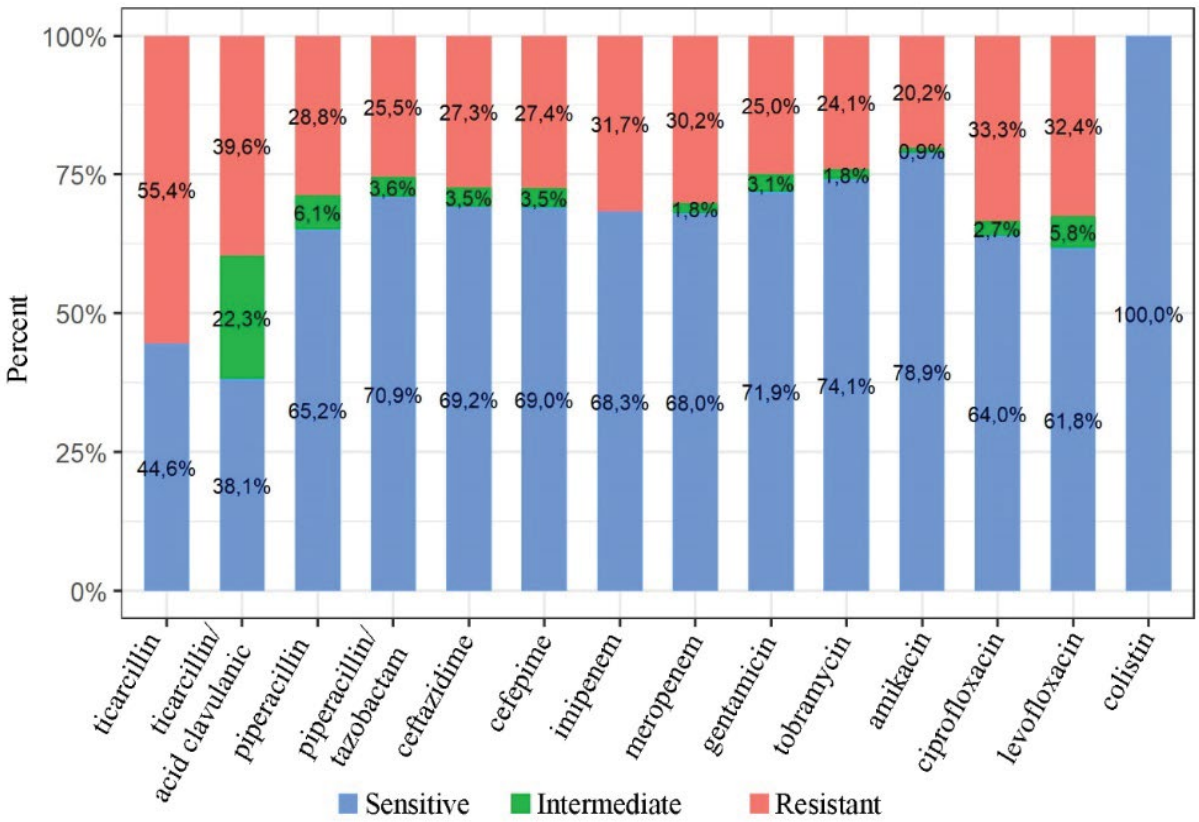

Figure 1: Susceptibilities of *Pseudomonas aeruginosa* (n = 224).

effective as compared to other antibiotics, followed by antipseudomonal β-lactams (cefepime, ceftazidime, imipenem, meropenem, and piperacillin-tazobactam), then quinolones. However, the rates of antibiotic -NS *P. aeruginosa* in our study are higher in ones in SENTRY Program surveillance.

Pneumonia had a higher rate of isolates with MDR and XDR than BSIs while the frequency of XDR, ceftazidime-NS, and meropenem-NS isolates were highest in the urinary tract infection. A study by Biedenbach, et al. [7] found that the rates of isolates NS antipseudomonal β-lactams and quinolones of Vietnamese patients with hospital-acquired or ventilator-associated pneumonia was very high and in range of 40.0%-60.0%. Similarly, carbapenem resistance was most common in *Pseudomonas aeruginosa* (55.7%) in Vietnamese patients in Intensive Care Units with hospital-acquired infections [8].

Compared to the results of a study by Pfaller, et al. in the period 2013-2015 [9] and Sader, et al. in the period 2012-2015 [10], our frequency of antibiotic-resistant *P. aeruginosa* were lower than Korea and India; and similar to Thailand; and higher than Singapore, Taiwan, Malaysia, Hong Kong, and United States.

Limitations

Studies in the Asia-Pacific region have shown an increasing prevalence of metallo-β-lactamases and carbapenemases in *P. aeruginosa*, particularly the ST235 clone, which may explain the increase in MDR [11]. However, strain typing was not performed in this study, it is unknown whether the decrease in resistance is due to the prevalence of ST235 or other causes.

Conclusion

The results of this investigation highlight the high rates of antibiotic resistance in *P. aeruginosa* in our hospital which will challenge optimizing empirical antimicrobial therapy for *P. aeruginosa* infections and require urgent ASP effectively.

Acknowledgements

No.

Sources of Support

There is no funding available for this study.

Conflicts of Interest

All authors don't have any conflicts of interest to declare.

Statement of Equal Authors' Contribution

Pham HT: Conceptualization, Methodology, Writing- Reviewing and Editing, Supervision; Bui QH: Data curation, Formal analysis Writing- Original draft preparation; Nguyen HH: Conceptualization, Writing-Reviewing and Editing; VoTH: Conceptualization, Methodology, Writing- Reviewing and Editing, Supervision.

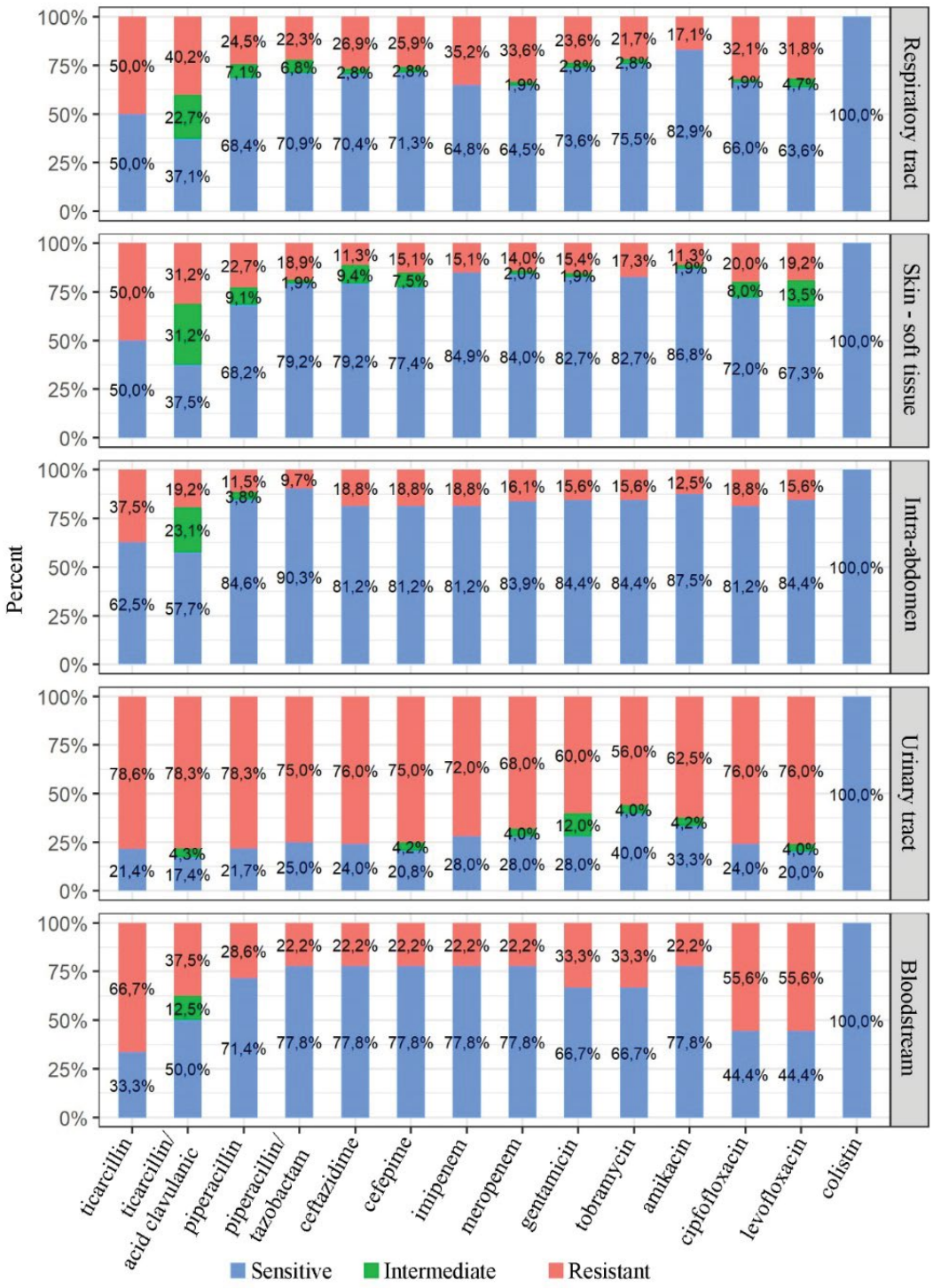

Figure 2: Susceptibilities of *Pseudomonas aeruginosa* for infection type (n = 224).

References

1. World Health Organization (2017) Global priority list od antibiotic resistant bacteria to guide research, discovery and development od new antibiotics.
2. Shortridge D, Gales AC, Streit JM, Huband MD, Tsakris A, et al. (2019) Geographic and temporal patterns of antimicrobial resistance in Pseudomonas aeruginosa over 20 years from the SENTRY antimicrobial surveillance program, 1997-2016. Open Forum Infect Dis 6: S63-S68.
3. Khan MA, Faiz A (2016) Antimicrobial resistance patterns of Pseudomonas aeruginosa in tertiary care hospitals of Makkah and Jeddah. Ann Saudi Med 36: 23-28.
4. Vietnam Ministry of Health (2012) Training materials for infection prevention and control 2012 [Tài liệu đào tạo dự phòng và kiểm soát nhiễm khuẩn].
5. Vietnam Ministry of Health (2020) The guideline on the implementation of “Antibiotic stewardship programs (ASP) in hospitals [Hướng dẫn quản lý kháng sinh trong bệnh viện].
6. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, et al. (2012) Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 18: 268-281.
7. Biedenbach DJ, Giao PT, Hung Van P, Minh Tuyet NS, Thanh Nga TT, et al. (2016) Antimicrobial-resistant

Pseudomonas aeruginosa and Acinetobacter baumannii from patients with hospital-acquired or ventilator-associated pneumonia in Vietnam. Clin Ther 38: 2098-2105.

8. Phu VD, Wertheim HFL, Larsson M, Nadjm B, Dinh QD, et al. (2016) Burden of hospital acquired infections and antimicrobial use in Vietnamese adult intensive care units. PLoS One 11: e0147544.

9. Pfaller MA, Shortridge D, Sader HS, Castanheira M, Flamm RK (2018) Ceftolozane/tazobactam activity against drug-resistant Enterobacteriaceae and Pseudomonas aeruginosa causing healthcare-associated infections in the Asia-Pacific region (minus China, Australia and New Zealand): Report from an Antimicrobial Surveillance Programme (2013-2015). Int J Antimicrob Agents 51: 181-189.

10. Sader HS, Huband MD, Castanheira M, Flamm RK (2017) Pseudomonas aeruginosa antimicrobial susceptibility results from four years (2012 to 2015) of the International Network for optimal resistance monitoring program in the United States. Antimicrob Agents Chemother 61: e02252-16.

11. Kim MJ, Bae IK, Jeong SH, Kim SH, Song JH, et al. (2013) Dissemination of metallo-β-lactamase-producing Pseudomonas aeruginosa of sequence type 235 in Asian countries. J Antimicrob Chemother 68: 2820-2824.