Antibiotic susceptibility of *Pseudomonas aeruginosa* isolated at 108 Military Central Hospital from 01/2020 to 06/2022

Do Thu Trang*, Nguyen Dang Minh Chau, Vu Thi Nguyet*, Nguyen Van Nguyen*, Nguyen Thi La*, Nguyen Dang Manh*, Bui Thanh Thuyet*, Bui Tien Sy***

*108 Military Central Hospital, **University of Science and Technology of Hanoi

Summary

Objective: To determine antibiotic susceptibility patterns of *Pseudomonas aeruginosa* isolated at the 108 Military Central Hospital from January 2020 to June 2022. *Subject and method:* A total of 784 *Pseudomonas aeruginosa* strains were isolated from patient specimens from different departments. Bacteria identification and antibiotic susceptibility test were performed using the Vitek MS system and the Vitek-2 Compact system, respectively. Multidrug-resistant and/or carbapenem-resistant *Pseudomonas aeruginosa* (MDR/CPR *P. aeruginosa*) strains were determined. Colistin susceptibility test was done using cation-modified Muller-Hinton broth diffusion method (CBDE, colistin broth disk elution). *Result: Pseudomonas aeruginosa* was highly resisting to fluoroquinolones (62.8%), and aminoglycosides (53.4%). The proportion of MDR/CPR *P. aeruginosa* was 54.3% (426/784), of which the highest proportion was found in the Department of Infectious Diseases (65.52%), ICU (64.39%) and the Internal Respiratory Department (45.69%). Carbapenem-resistant *Pseudomonas aeruginosa* was highly prevalent in urine specimens (65.38%) and respiratory specimens (56.76%). Of 258 MDR/CPR *P. aeruginosa* isolates, 11.2% isolates were resistant to colistin, 26.6% and 33.3% of these remained susceptible to amikacin and piperacillin/tazobactam, respectively. *Conclusion:* The prevalence of antibiotic resistante *Pseudomonas aeruginosa* remains high, including resistance to carbapenem and colistin. Antibiotic regimen should include amikacin or piperacillin/tazobactam in combination with other antibiotics. The study suggested the routine application of diagnostic tools for the rapid detection of resistant strains.

Keywords: Carbapenem, colistin, antibiotic resistance, multidrug-resistant *Pseudomonas aeruginosa.*

1. Background

Pseudomonas aeruginosa is a gram-negative, rod-shaped, strictly aerobic and opportunistic pathogenic bacterium that often causes severe acute and persistent infections. The latest CDC report estimated that in the United States, more than 2.8 million people get sick each year with antibiotic-resistant infections, at least 35,000 deaths and there are about 29% infections linked to *P. aeruginosa*. Of those, more than 32,600 were multidrug-resistant, with approximately 2,700 deaths due to infection [7]. Thus, MDR/CPR *P. aeruginosa* is becoming a burden for the global healthcare system. Polymyxins (colistin and polymyxin B) are as the last choice of antibiotic use to treat infections caused by MDR/CPR *P. aeruginosa*. Recently, the use of polymyxins (colistin) in clinical practice has increased due to the increasing prevalence of MDR/CPR *P. aeruginosa* infection and has led the emergence of colistin-resistant bacterial strains. Therefore, determining colistin susceptibility of MDR/CPR *Pseudomonas aeruginosa* strains plays a

***Received**: 24 October 2022, **Accepted**: 1 January 2023*

***Correspondence to:** Do Thu Trang, Department of Microbiology, 108 Military Central Hospital*

***Email:** dr.thutrang.1709@gmail.com*

very important role in treatment. This study aims to determine the antibiotic resistance characteristics of *Pseudomonas aeruginosa* isolated at the 108 Military Central Hospital from January 2020 to June 2022.

2. Subject and method

2.1. Study subjects

Pseudomonas aeruginosa strains were isolated from patient samples at 108 Military Central Hospital from 01/2020 to 06/2022.

Pseudomonas aeruginosa isolates with Vitek-2 compact antibiogram results were enrolled the present study.

MDR *Pseudomonas aeruginosa* was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories.

2.2. Method

A descriptive cross-sectional study.

Bacteria were identified using the Vitek MS automated system and AST were performed using the Vitek-2-compact system.

Colistin susceptibility test was implemented for MDR/CPR *P. aeruginosa* using colistin broth disk elution assay following the guidlines of CLSI 2021.

3. Result

3.1. Distribution of P. aeruginosa strains and MDR/CPR P. aeruginosa strains

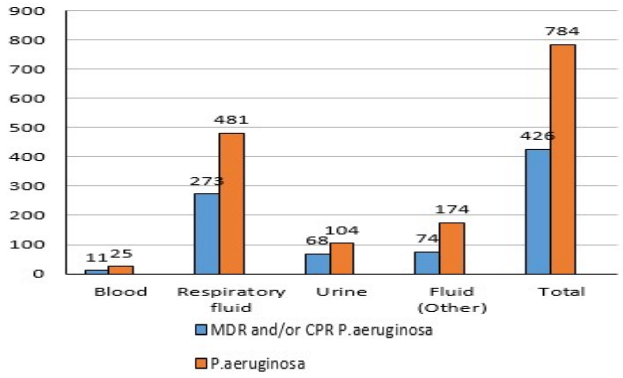

Figure 1. Distribution of *P. aeruginosa* strains and MDR/CPR *P. aeruginosa* strains by specimen types

MDR/CPR *P. aeruginosa* was isolated in almost all types of specimens. Specifically, the highest proportion was found in urine specimens with 65.38% (68/104), followed by respiratory specimens with 56.76% (273/481) and blood specimens with 44.0% (11/25) and the lowest incidence was recorded in the aerobic fluids specimens with 42.53% (74/174) (Figure 1).

Table 1. Distribution of *P. aeruginosa* and MDR/CPR *P. aeruginosa* by departments

Department	*P. aeruginosa*	MDR/CPR *P.aeruginosa*
Intensive Care Center	132	85 (64.39%)
Institute of Infectious Diseases	116	76 (65.52%)
Department of Internal Respiratory Medicine	116	53 (45.69%)
Other departments	420	212 (50.48%)
Total	***784***	***426(54.59%)***

MDR/CPR *Pseudomonas aeruginosa* was also detected in all departments of the hospital. The highest proportion was recorded in the Institute of Infectious Diseases (65.52%), followed by the ICU (64.39%), the Department of Internal Respiratory Medicine (45.69%), and other departments with 50.48% (Table 1).

3.2. Antibiotic resistance characteristics of 784 strains of Pseudomonas aeruginosa isolated

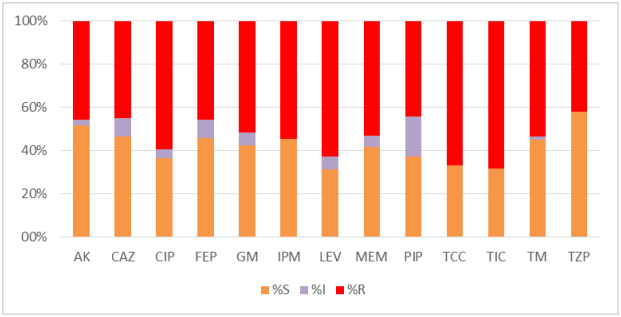

Figure 2. Antibiotic susceptibility of *Pseudomonas aeruginosa*

Pseudomonas aeruginosa had a high resistance rate to the fluoroquinolone group (59.4-62.8%), ticarcillin/ ticarcillin-clavulanic acid (66.6-68.4%), aminoglycoside group excluding amikacin (51.7-53.4%). The proportion of *Pseudomonas aeruginosa* MDR/CPR was high from 52.9% to 54.3%. However, *Pseudomonas aeruginosa* remained susceptible to the following antibiotics: amikacin (45.8%) and piperacillin/tazobactam (42.0%) (Figure 2).

3.3. Antibiotic resistance characteristics of 258 MDR/CPR Pseudomonas aeruginosa strains

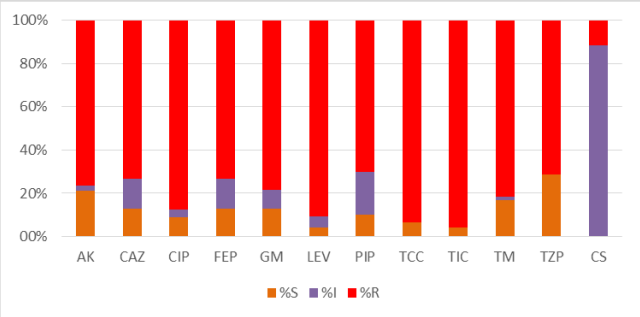

Figure 3. Antibiotic susceptibility of MDR/CPR *P. aeruginosa* strains

For MDR/CPR *P. aeruginosa* strains, the rate of resistance was highest to ticarcillin and ticarcillin/clavulanic acid (93.4-95.7%), followed by the fluoroquinolones (87.6-90.7%), other antibiotic groups accounting for over 70%. However, the MDR/CPR *P. aeruginosa* strains remained 21.3% and 28.7% susceptible to amikacin and piperacillin/tazobactam, respectively (Figure 3).

Of these 258 strains of MDR/CPR *P. aeruginosa*, the colistin resistance rate was 11.2% (Figure 3).

Table 1. Characteristics of resistance to amikacin and piperacillin/tazobactam of colistin-resistant *P. aeruginosa*

Antibiotic \ Susceptibility		Piperacillin/Tazobactam	
		S	**R**
Amikacin	*S*	2	7
	R	8	13

Despite resistance to colistin, the proportion of *Pseudomonas aeruginosa* strains susceptible to amikacin and piperacillin/tazobactam were 26.6% (9/30) and 33.33% (10/30), respectively (Table 2).

4. Discussion

According to WHO, antibiotic resistance is one of the global medical threats. In 2017, the World Health Organization (WHO) published a list of the 12 most dangerous groups of super drug-resistant bacteria in the world, which are the biggest threat to human health, including *Pseudomonas aeruginosa* at the top of the table, priority should be given to the development of new antibiotics. The World Health Organization ranks Vietnam among the countries with the highest rates of antibiotic resistance in the world. Therefore, investigating drug resistance, and providing regular and timely information on the status of bacterial resistance, especially for the last choice drugs in each clinical area, is essential to effectively manage the spread of drug-resistant strains in hospitals and communities on a national scale.

Pseudomonas aeruginosa is a common cause of nosocomial infections worldwide. The rapid emergence of MDR *Pseudomonas aeruginosa* strains (resistant to at least one or more antibiotic groups) or *Pseudomonas aeruginosa* strains resistant to most β-lactams, including carbapenems pose great challenges to treatment and endanger the global health system.

We also found the high rates of MDR/CPR *P. aeruginosa* in the Institute of Infectious Diseases (65.52%) and the Intensive Care Unit (64.39%). This is also completely consistent with the actual treatment because these are the 2 departments with the largest carbapenem consumption in the hospital [3]. According to the study of Tran Van Ngoc et al, surveying the antibiotic resistance characteristics of *P. aeruginosa* at Cho Ray Hospital in 2013-2014, similar results were recorded with the high rate of carbapenem-resistant *P. aeruginosa* in ICU and Tropical Diseases departments of 42% and 22% [4]. According to the study in 2016 by Phu et al that collected data on 3287 patients received in 15 intensive care units of hospitals nationwide, the

proportion of *P. aeruginosa* resistant to carbapenem was 55.7% [2]. Thus, the rate of *P. aeruginosa* resistant to carbapenems recorded at the Institute of Infectious Diseases and Intensive Care Unit of 108 Military Central Hospital is higher than that of the ICU units at other hospitals in the country, indicating a high rate of MDR/CPR of *P. aeruginosa* has increased year by year, and because 108 Military Central Hospital is a last-line hospital, the number of severe patients from the lower glands has increased with severe infections, especially hospital infections and patients have been given strong and prolonged antibiotics, so drug resistance increased.

P. aeruginosa is capable to progress into multidrug-resistant bacterium that could make infections difficult to treat and lead to increased mortality rates ranging from 18% to 61% [6]. Our study found that the proportion of carbapenem-resistant *P. aeruginosa* associated with urinary tract infections was highest (65.38%), followed by respiratory infections (56.76%) and septicemia (44%), and infections from other body fluid specimens (42.53%). According to the study of Adrian J Brink, most infections caused by *P. aeruginosa* belonged to respiratory specimens, accounting for 44.6%, similar to our study, followed by blood samples accounting for 27.9%, lower than our study [5].

Previous studies have shown that Vietnam has a high prevalence of carbapenem-resistant *Pseudomonas aeruginosa*. A study on antibiotic resistance of *P. aeruginosa* isolated on specimens of the Pasteur Institute of Ho Chi Minh City in 2014 showed that *P. aeruginosa* is resistant to the most commonly used antibiotics: Ciprofloxacin (48.2%), cefepime (45.8%), gentamycin (55.6%), imipenem (42.6%), ticarcillin/clavulanic acid (54.2%), amikacin (42.9%) [1]. According to the study of Kuan-Yin et al., the proportions of antibiotic-resistant *P. aeruginosa* were: ceftazidime (52.24%), ticarcillin/clavulanic acid (35.82%), ciprofloxacin (56.72%), amikacin (5.97%) piperacillin/tazobactam (40.3%) [8]. In this study, *P. aeruginosa* had a high rate of antibiotic resistance compared to what was described in the above studies, specifically: Fluoroquinolone group (59.4-62.8%), ticarcillin and ticarcillin/clavulanic acid (66.6-68.4%), aminoglycoside group (51.7-53.4%), but still susceptible to amikacin antibiotics (45.8%) and piperacillin/tazobactam (42%), similar to the susceptibility rate of these two antibiotics in the above studies.

The proportion of MDR/CPR *Pseudomonas aeruginosa* in our study was at a high level: meropenem 52.9% and imipenem 54.3%. This ratio is similar to the meropenem resistance rate in Kuan-Yin et al.'s study was 53.73% [8]. Thus, the ratio of MDR/CPR *P. aeruginosa* has increased rapidly. This was possibly because in recent years, the proportion of carbapenem antibiotics use for the treatment of patients has increased, thus creating selective pressure for bacteria resistant to this antibiotic group.

Colistin is a prophylactic drug used to treat MDR/CPR *P. aeruginosa* infections. However, the prevalence of colistin resistance was rarely reported. In our study, the colistin resistant proportion of MDR/CPR *P. aeruginosa* was 11.2%. This rate is equivalent to the colistin resistance rate of *P. aeruginosa* of 10.6% in the study of Pham Thi Hoai An et al (2014) [1] but lower than the study of Mumina Javed et al. in 2018, on 131 strains of *P. aeruginosa* isolated in Sandiago, USA, there were 31 strains (23.6%) resistant to colistin [9]. This may indicate that in 108 Military Central Hospital, the management of the use of colistin antibiotics is being ensured, limiting the increase in antibiotic resistance.

According to present study, of 30 MDR/CPRMDR/CPR and colistin-resistant *P. aeruginosa* isolates, 26.6% and 33.3% isolates remained susceptible to amikacin and piperacillin/tazobactam, respectively. Thus, for colistin-resistant *strains of P. aeruginosa*, amikacin or piperacillin may be selected in combination treatment.

5. Conclusion

Multidrug-resistant and/or carbapenem-resistant *Pseudomonas aeruginosa* has emerged in the 108 Military Central Hospital. *Pseudomonas*

aeruginosa is highly resistante to carbapenems (54.3%), and the fluoroquinolones (62.8%) and tends to increase year by year. Multidrug-resistant and/or carbapenem-resistant *Pseudomonas aeruginosa* strains are resistant to colistin at a rate of 11.2% but these are still susceptible to amikacin and piperacillin/tazobactam. Therefore, it is necessary to have instructions for the use of antibiotics to treat *P. aeruginosa* infection including the combination therapy of amikacin or piperacillin/tazobactam with other antibiotics, as well as the application of diagnostic tools for the rapid detection of resistant strains.

References

1. Brink AJ (2019) *Epidemiology of carbapenem-resistant Gram-negative infections globally*. Curr Opin Infect Dis 32(6): 609-616. doi: 10.1097/QCO.0000000000000608.
2. Phạm Thị Hoài An, Vũ Lê Ngọc Lan, Uông Nguyễn Đức Ninh, Phan Ngọc Thảo, Cao Hữu Nghĩa (2014) Khảo *sát sự kháng kháng sinh của Klebsiella pneumoniae trên bệnh phẩm phân lập được tại Viện Pasteur, TP Hồ Chí Minh*. Tạp chí KHOA HỌC ĐHSP TP. HCM, Số 61, tr. 146-155.
3. Kang CI, Kim SH, Kim HB, Park SW, Choe YJ, Oh MD, et al (2003) *Pseudomonas aeruginosa bacteremia: risk factors for mortality and influence of delayed receipt of effective antimicrobial therapy on clinical outcome*. Clin Infect Dis 37: 745-751.
4. CDC's Antibiotic Resistance Threats in the United States, 2019.
5. Lin KY, Lauderdale TL, Wang JT, Chang SC (2016) *Carbapenem-resistant Pseudomonas aeruginosa in Taiwan: Prevalence, risk factors, and impact on outcome of infections*. Journal of Microbiology, Immunology and Infection 49(1): 52-59.
6. Le NK, Hf W, Vu PD, Khu DTK, Le HT, Hoang BTN, Vo VT, Lam YM, Vu DTV, Nguyen TH, Thai TQ, Nilsson LE, Rydell U, Nguyen KV, Nadjm B, Clarkson L, Hanberger H, Larsson M (2016) *High prevalence of hospital-acquired infections caused by gram-negative carbapenem resistant strains in Vietnamese pediatric ICUs: A multi-centre point prevalence survey*. Medicine (Baltimore) 95(27): e4099. doi: 10.1097/MD.0000000000004099.
7. Javed M, Ueltzhoeffer V, Heinrich M, Siegrist HJ, Wildermuth R, Lorenz FR, Neher RA, Willmann M (2018) *Colistin susceptibility test evaluation of multiple-resistance-level* Pseudomonas aeruginosa *isolates generated in a morbidostat device*. Ournal of Antimicrobial Chemotherapy 73(12): 3368-3374.
8. Nam NS and & Eight ND (2018) *Analysis of carbapenem antibiotic consumption at the 108th Army Central Hospital from 2015 to 2017*. Journal of 108 - Clinical Medicine and Phamarcy13(8): 78-84.
9. Trần Văn Ngọc, Phạm Thị Ngọc Thảo, Trần Thị Thanh Nga (2017) *Khảo sát đặc điểm kháng thuốc của Pseudomonas aeruginosa và Acinetobacter baumannii gây viêm phổi bệnh viện*. Thời sự Y học, tr. 64-69.