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Research Article

# Prevalence and pattern sensitivity multidrug antibiotics resistant *pseudomonas aeruginosa* in the high care unit at Dr. Soetomo General Academic Hospital Period 2022-2023

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## ABSTRACT

The prevalence of Multidrug antibiotic-resistant *Pseudomonas aeruginosa* (MDRPA) has been increasing during the decade And has become attention in hospital patients. This retrospective descriptive descriptive aimed to determine the prevalence of MDRPA and its sensitivity patterns. Data were taken from the results of bacterial culture and antibiotic resistance tests from various clinical specimens from patients at Dr. Soetomo General Academic Hospital throughout 2022-2023. The resistance test was carried out using a Vitek 2 compact and Phoenix BD instrument. MDRPA is defined as *Pseudomonas aeruginosa* that is not sensitive to three or more of the following classes of antipseudomonal antibiotics: aminoglycoside, fluoroquinolone, carbapenem, penicillin/cefalosporin. The prevalence of MDRPA was 42.86%. MDRPA isolates were also the most common origin from the burn unit and HCU A (high care unit A), mostly from pus specimens and sputum. *Pseudomonas aeruginosa* sensitivity was best with piperacillin/tazobactam (55.5%), meropenem (54.8%), amikacin (47.5%), gentamicin (46.5%), cefepime (46.3%), ceftazidime (45.0%), ciprofloxacin (44.7%) and aztreonam (43.2%). The sensitivity of MDRPA to antibiotics is much lower than that of *Pseudomonas aeruginosa*. This study showed a high number of MDRPA specifically in Surabaya and the pattern sensitivity of *Pseudomonas aeruginosa* can become guidelines in Dr. Soetomo General Academic Hospital choosing antibiotics treatment for patients.

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## INTRODUCTION

*Pseudomonas aeruginosa* is an important opportunistic pathogen that causes nosocomial infection, especially on immuno-compromised patients (Wu et al., 2011). Nosocomial infection can happen because of medical device instrumentation or long treatment at the hospital, for example, installation of intravenous catheters (El Zowalaty et al., 2015). Nosocomial infection caused by *Pseudomonas aeruginosa* is generally difficult to overcome because of the possibility of intrinsic resistance and its ability to obtain many antimicrobial resistances (Lister et al., 2009).

The incidence of nosocomial infections caused by *Pseudomonas aeruginosa* bacteria occurs around 10-15% in the world and around 10-20% in intensive care units (ICU), usually occurs in patients with septicemia, cystic fibrosis, burns, and wound infections (Arora, 2014). According to the results of a study conducted in West European ICUs, *Pseudomonas aeruginosa* is one of the most common organisms; almost one-third (29%) of all gram-negative isolates (Nathwani et al., 2014). The Infectious Disease Society of America added *Pseudomonas aeruginosa* is on the "ESKAPE" list of pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter*). These pathogens are the largest health threats due to the increasing in prevalence and antimicrobial resistance (Nathwani, et al., 2014).

Multi-Drug Resistant *Pseudomonas aeruginosa* (MDRPA) is a condition where the bacteria are resistant to three or more classes of antibiotics such as penicillins, cephalosporins, monobactams, carbapenems, aminoglycosides, and fluoroquinolones (Ullah et al., 2016). Inadequate antibiotic therapy continuously causes *Pseudomonas aeruginosa* to become resistant to several classes of antibiotics. The prevalence of MDRPA increased during the last decade and has become a major concern among patients in hospital (Katvoravutthichai et al., 2016). Therefore, this study aimed to determine the prevalence of MDRPA and its sensitivity patterns in Dr. Soetomo General Academic Hospital during 2022 – 2023.

## METHODS

This is a retrospective descriptive study and used a total sampling method. All *Pseudomonas aeruginosa* culture results and antibiotic resistance tests from various clinical specimens of patients at Dr. Soetomo General Academic Hospital from 1 November 2022 – 1 December 2023 were included. These data were taken from the Clinical Microbiology laboratory at Dr. Soetomo General Academic Hospital medical records. All data has been collected using Microsoft Excel and has been statistically analysis using Chi-Square test by SPSS. P-value < 0.05 was considered significant. This study was approved by Dr. Soetomo General Academic Hospital ethics committee with certificate number 0853/KEPK/XII/2023.

## RESULTS

Throughout 2022-2023, 1,320 bacteria were isolated from patient's specimens. The number of *Pseudomonas aeruginosa* isolates were 140, and it ranks as the third most frequently isolated organism. MDRPA was found in 60 of 140 (42.86 %) *Pseudomonas aeruginosa* isolates. In this study, it was also found that *Pseudomonas aeruginosa* which was resistant to all antibiotics was 11 of 140 isolates (7.86 %).

The distribution of MDRPA and *Pseudomonas aeruginosa* origin room can be seen in Table 1. Most MDRPA isolates came from Burn

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Unit (48.98%), followed by High Care Unit A (40%). Based on the statistical tests, there was no significant difference in the proportion of MDRPA and *Pseudomonas aeruginosa* based on room origin (p>0.05).

The distribution of MDRPA and *Pseudomonas aeruginosa* based on the specimen's origin can be seen in Table 2. MDRPA was mostly found in pus (48.89%) and sputum (33.96%) specimens. Based on statistical tests, there was no significant difference in the proportion of MDRPA and *Pseudomonas aeruginosa* based on the origin of the specimen (p>0.05).

Antimicrobial sensitivity patterns of *Pseudomonas aeruginosa* and MDRPA can be seen in Table 3. *Pseudomonas aeruginosa* sensitivity was best with piperacillin/ tazobactam (55.5%), meropenem (54.8%), amikacin (47.5%), gentamicin (46.5%), cefepime (46.3%), ceftazidime (45.0%), ciprofloxacin (44.7%) and aztreonam (43.2%). The sensitivity of MDRPA to antibiotics is much lower than that of *Pseudomonas aeruginosa*. This study showed a high number of MDRPA specifically in Surabaya and the pattern sensitivity of *Pseudomonas aeruginosa* can become guidelines in Dr. Soetomo General Academic Hospital choosing antibiotics treatment for patients. The sensitivity of *Pseudomonas aeruginosa* to other antibiotics was very low, less than 10%.

**Table 1.** Distribution MDRPA and *Pseudomonas aeruginosa* based on Origin Room

| Room | MDRPA | *Pseudomonas aeruginosa* | Total |
|---|---|---|---|
| Burn Unit | 24 | 25 | 49 |
| High care unit A | 12 | 18 | 30 |
| Surgical wards | 10 | 15 | 25 |
| Pediatric intensive care | 8 | 13 | 21 |
| Medical wards | 6 | 9 | 15 |
| Total | 60 | 80 | 140 |

p= 0.1 20

**Table 2.** Distribution MDRPA and *Pseudomonas aeruginosa* based on Specimen

| Specimen | MDRPA | *Pseudomonas aeruginosa* | Total |
|---|---|---|---|
| Pus | 22 | 23 | 45 |
| Sputum | 18 | 22 | 40 |
| Blood and LCS | 10 | 15 | 25 |
| Urine | 6 | 14 | 20 |
| Jaringan | 4 | 6 | 10 |
| Total | 60 | 80 | 140 |

p = 0.245

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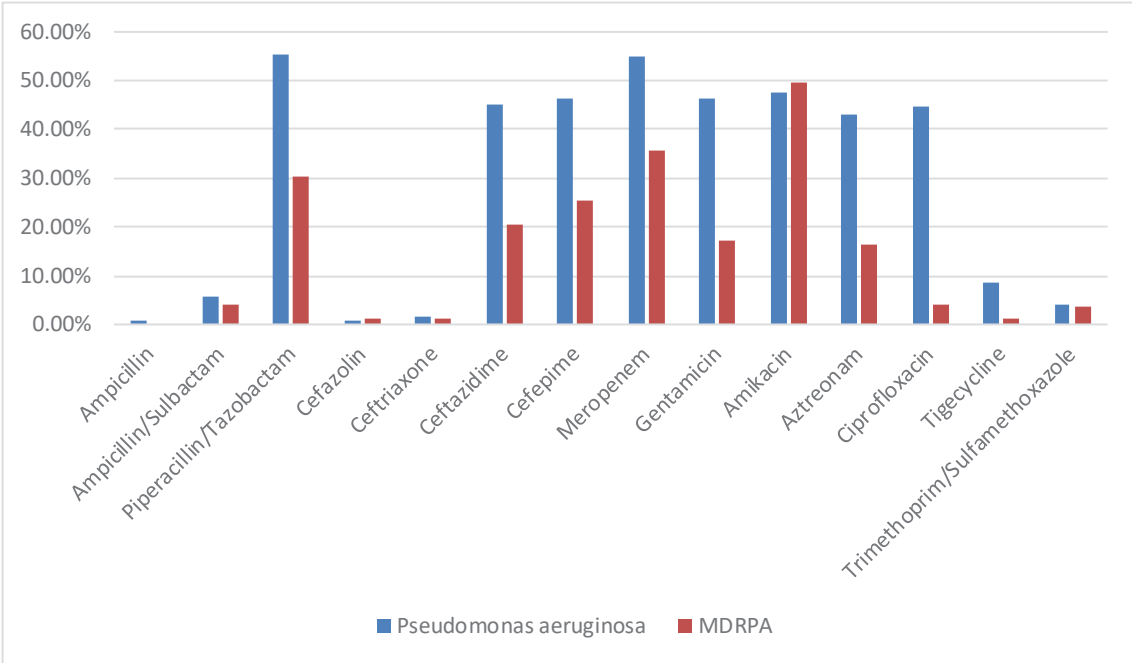
**Diagram** Pattern Sensitivity Antimicrobial *P. aeruginosa*




## DISCUSSION

*Pseudomonas aeruginosa* has intrinsic resistance to many antibiotics, this bacterium can also acquire resistance to other antibiotics during therapy. These characteristics make the choice of antibiotics for *Pseudomonas aeruginosa* limited (Kanj & Kanafani, 2011). In this study, the prevalence of MDRPA was 42.86%. The prevalence of MDRPA varies depending on geographic location and the type of surveillance research, with rates ranging from 0.6–32%. Other reviews have reported MDRPA rates varying from low values of 1–6%, up to 70% (Nathwani et al., 2014).

National surveillance in Thailand in 2000–2005 found MDRPA rates ranging from 20–30%, whereas in a tertiary hospital in Bangkok it was 43.22% (Dejsirilert et al., 2009)(Katvoravutthichai et al., 2016). The results of a meta-analysis in China, up to 2014, found that the MDRPA rate in hospital infections was 29.0% and this figure increased significantly from year to year (Peng et al., 2015). The carbapenem-resistant *Pseudomonas aeruginosa* rate in Taiwan in 2000–2005 was relatively low; 10.2% (Peng et al., 2015). In addition, the study in Fukuoko, Japan found the MDRPA rate was 3.3% in 2006–2008 (Lin et al., 2016) (Yoshimura et al., 2009).

Research in ten countries on the European continent in 1997–2000, reported the MDRPA rate was 12.2%, this figure varied from 50% in Turkey, 25% in Italy, and 14% in Belgium to 3% in Spain, England, Germany, Bulgaria, and Malta. The prevalence of MDRPA in the United States in 2000–2009 in pediatric patients admitted with sepsis and pneumonia ranged from 10.7–13.5% and 19.2–21.7%, respectively (Logan et al., 2017). The prevalence of MDRPA in Brazil in 2010–2012 was 37% (Matos et al., 2016).

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In this study, there was no significant difference in the proportion of MDRPA and *Pseudomonas aeruginosa* based on room origin. The most common MDRPA comes from the Burn Unit and High Care Unit A. Risk factors associated with the incidence of MDRPA are intensive care unit (ICU) patients, undergoing surgery and using invasive medical devices. Several studies report that the prevalence of MDRPA is significantly higher in ICU patients compared to non-ICU patients, other reports also show extraordinary occurrences of MDRPA in the ICU (Kanj & Kanafani, 2011)(Matos et al., 2016).

There was no significant difference in the proportion of MDRPA and *Pseudomonas aeruginosa* based on the origin of the specimens in this study. Most MDRPA isolates came from pus and sputum specimens. National Antimicrobial Resistance Surveillance, Thailand (NARST) has found that *Pseudomonas aeruginosa* was most often found in sputum, pus and urine (Dejsirilert et al., 2009). Research in Pakistan also get MDRPA is most often found in pus, wounds, urine, blood, and sputum (Ullah et al., 2016). P. aeruginosa is the most common cause of hospital pneumonia, the third most common cause of urinary tract infections, the fourth most common cause of surgical site infections and the seventh most common pathogen. most frequently isolated from blood (Nathwani et al., 2014). *Pseudomonas aeruginosa* has various antibiotic resistance mechanisms, such as production of the beta-lactamase enzyme AmpC, production of the extended-spectrum beta-lactamase enzyme, modification of porins specific for carbapenems, multi-drug efflux pump, and biofilm formation (El Zowalaty et al., 2015).

The sensitivity of *Pseudomonas aeruginosa* in this study was best with amikacin. Amikacin is an aminoglycoside class of antibiotics. Antipseudomonal aminoglycosides are important components of antipseudomonal chemotherapy. This class of antibiotics is bactericidal and also shows synergy with other antipseudomonals, especially the beta-lactams class. Resistance to aminoglycosides varies widely throughout the world, varying from less than 25% to more than 50%. Resistance rates to tobramycin and amikacin have been reported in several studies to range from 2–50% (El Zowalaty et al., 2015). A similar result was also found in Brazil, the sensitivity *Pseudomonas aeruginosa* obtained from the ICU against amikacin was also the best (85.2%), while with gentamicin it was 53.7% (Matos et al., 2016). The sensitivity of *Pseudomonas aeruginosa* in Pakistan to amikacin was 46.1%, slightly lower than imipenem (56.9%) (Ullah et al., 2016).The fairly good sensitivity to amikacin indicates that amikacin should not be used too often, due to the risk of ototoxicity and nephrotoxicity and its high price (El Zowalaty et al., 2015).

In this study, the sensitivity of *Pseudomonas aeruginosa* to the beta-lactam group was around 50%. The best sensitivity was with the antibiotic piperacillin/tazobactam (55.5%) and was also followed by meropenem (54.8%), and fourth-generation cephalosporins, namely cefepime (46.3%), and ceftazidime (45.0%). The sensitivity with the monobactam aztreonam group is only 43.2%. Beta-lactam antibiotics which have antipseudomonal properties are the main component of treating infections by *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* obtained from the ICU in Brazil had lower sensitivity to beta-lactamase group, namely piperacillin/tazobactanm (53.7 %), ticarcillin (70.89%), imipenem and meropenem respectively 35.2%, cefepime 51.9% and ceftazidime (37.0%). The sensitivity of *Pseudomonas aeruginosa* in Pakistan to imipenem is 43.1% and cefoperazone/ sulbactam 50.98%(Matos et al., 2016). The

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piperacillin/tazobactam resistance rate is reported differently in different parts of the world varying from 9% to 29% (El Zowalaty et al., 2015). This difference is caused by differences in usage levels. in various regions. The limited use of piperacillin/tazobactam is related to its high price (El Zowalaty et al., 2015).

Carbapenem resistance in clinical isolates of *Pseudomonas aeruginosa* is increasing due to the very widespread use of carbapenems. This is a very difficult challenge because carbapenems are the last choice of antibiotic therapy for *Pseudomonas aeruginosa*. Reports from various countries show that resistance to meropenem is increasing, varying from less than 10% to 46% (El Zowalaty et al., 2015). Resistance rates to ceftazidime are also increasing, varying in various countries between 10 and 50%.

The sensitivity of MDRPA in this study was much lower when compared with *Pseudomonas aeruginosa*. The sensitivity of MDRPA was best with amikacin, but the percentage was only 49.6%. Other antibiotics that are therapeutic options for *Pseudomonas aeruginosa* have sensitivity below 30%. Strategies for treating MDRPA include the use of alternative antibiotics, giving alternative doses, and combinations of antibiotics and inhaled antibiotics for pneumonia. Colistin has become the standard therapy for MDRPA infections. The use of this antibiotic in various countries is limited due to its nephrotoxicity effects (Álvarez-Lerma & Grau, 2012)(Cerceo et al., 2016), but Colistin is not available in Indonesia. Alternative antibiotics for infections by MDRPA include ceftazidime/avibactam and also ceftolozan/tazobactam (Álvarez-Lerma & Grau, 2012). However, these two antibiotics are not yet available in Indonesia. The combination of fosfomycin with other antibiotics such as carbapenems could be an alternative regimen (Cerceo et al., 2016). Intravenous fosfomycin is an old antibiotic that has excellent in vitro bactericidal activity against many organisms, including *Pseudomonas aeruginosa*, especially multiresistant ones (Falagas et al., 2009). Several clinical trials have reported clinical and microbiological improvements. administering a combination of fosfomycin with other antibiotics in infections by *Pseudomonas aeruginosa* (Samonis et al., 2012).

## CONCLUSION

This study revealed the number of MDRPA specifically in the high-care unit of Dr. Soetomo General Academic Hospital, and the pattern sensitivity of Pseudomonas aeruginosa can serve as guidelines for choosing antibiotic treatment for patients.

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