Research Article

Jurnal Teknologi Kesehatan Borneo, Vol. 4, No.1 (2023) 22-28
Available online at: *http://jtk.poltekkes-pontianak.ac.id/index.php/JTKB/*
p-ISSN: 2723-3790 e-ISSN 2723-3782
Doi: https://doi.org/10.30602/jtkb.v4i1.253

Profile of Carbapenem Resistant Gram Negative Bacilli in Grha Kedoya Hospital Jakarta

Venny Patricia, Ahmad Yani, Etik Sutarti

Department of Medical Laboratory Technology, Poltekkes Kemenkes Banten, Serang, Indonesia

* Correspondence: venny840621@gmail.com

Abstract. Carbapenems are beta-lactam antibiotics included in the 3rd line of antibiotics, which are the last choice in therapy to overcome various bacterial infections. The more use of antibiotics that are not in accordance with the clinical situation, the more cases of carbapenem resistance found in the hospital. This study aims to analyze gram-negative bacteria, which are resistant to carbapenem antibiotics, in Grha Kedoya Hospital from January to March 2022 using an observational analytical research design for bacterial identification and antibiotic sensitivity testing using colorimetric and turbidimetric methods with a cross-sectional research design. The examination material was all samples infected with Gram-negative bacteria, as many as 174 samples. The data analysis used in this study was descriptive crosstabs. The results stated that there were carbapenem-resistant bacteria in as many as 32 samples (18.4%); the most carbapenem-resistant bacteria were Acinetobacter baumannii bacteria in as many as 16 patients (50%); Pseudomonas aeruginosa and Klebsiella pneumoniae in as many as 8 patients (25%); and the resistance test showed 100% resistance to the antibiotics Doripenem, Imipenem, Meropenem, and Ertapenem.

Keywords: Carbapenems, Resistant, Gram-Negative Bacilli

1. Introduction

Carbapenems are beta-lactam antibiotics. Carbapenems have a broad antimicrobial spectrum and have effective antibacterial activity. Carbapenems are generally used as a last resort in gram-negative bacterial infections with multiple drug resistance (MDR). But looking at the conditions of the last few years, the development of antibiotic use has increased, which has led to an increasing rate of resistance of Gram-negative bacteria to carbapenems(Kumala 2017). In recent decades, carbapenem-resistant Gram-negative bacilli have been on the rise, especially from Enterobacteriaceae species. Carbapenem-resistant Gram-negative bacilli infections are strongly associated with a high risk of inappropriate antibiotic use(Zilberberg et al. 2017).

In the last decade, an increasing number of gram-negative bacteria have shown resistance to most antibiotics. The emergence of carbapenem-resistant enterobacteriaceae (CRE) is a global threat because carbapenems are antibiotics of last resort in therapy to manage various bacterial infections. The logical consequences of the emergence of this phenomenon are increased patient mortality, increased hospitalization, and increased treatment costs. The Carbapenem-Resistant Enterobacteriaceae (CRE) phenomenon is certainly a threat that occurs throughout the world(Kastawa, Ramona, and Fatmawati. 2020).

The overuse of carbapenem antibiotics in Extended Spectrum Beta Lactamases (ESBL) bacterial infections in the Southeast Asian region shows an increase in the prevalence of Gram-negative Multiple Drug Resistance (MDR) bacteria. The high prevalence of Extended Spectrum Beta Lactamases (ESBL) enzyme-producing bacterial infections has been a major problem since 2005. Although Southeast Asia is not an endemic area for Carbapenem-resistant Enterobacteriaceae (CRE), there is currently an increase in reported cases of Carbapenem-resistant Enterobacteriaceae (CRE) bacterial infections. Based on the Comparative Activity of Carbapenem Testing (COMPACT) II study during April–July 2010, Carbapenem Resistant Acinetobacter Baumannii (CRAB) was the most common pathogen associated with nosocomial infections in this region, accounting for 73% of clinical isolates, followed by Carbapenem Resistant Pseudomonas Aeruginosa (CRPA) at 29.8%, and Carbapenem Resistant Enterobacteriaceae (CRE) at 2.8%(Kumala 2017). Antibiotic options for therapy of CRE infections are fosfomycin, aminoglycosides, and colistin; combination antibiotics are Avibactam in combination with carbapenem antibiotics such as Ceftazidime-Avibactam, Meropenem-Vaborbactam, imipenem-Relebactam, Plazomicin, Cefiderocol, Eryacycline, and aztreonam-avibactam(Tilahun et al. 2021).

Age, gender, length of hospitalization, treatment in the Intensive Care Unit (ICU), comorbid diseases, immunocompromised conditions, use of invasive tools and procedures, and previous antibiotic use are some of the risk factors that play a role in the occurrence of carbapenem-resistant Gram-negative bacterial infections. Understanding the characteristics of risk factors for patients with carbapenem-resistant Gram-negative bacteria can help clinicians make early patient management decisions, which have a direct effect on patient outcomes, as well as design prevention strategies in an effort to reduce the incidence of infection and the problems caused by it(Kumala 2017).

Risk factors for antibiotic resistance include irrational use of antibiotics, massive use of antibiotics in endemic or pandemic cases, use of antibiotics with unclear indications, and a lack of public knowledge so that people buy antibiotics without a prescription from a doctor(Kumala 2017). There is no data related to carbapenemase in the Grha Kedoya Hospital Laboratory, so researchers tried to conduct research related to the prevalence of carbapenemase in gram-negative bacteria.

2. Metode

2.1 Research Design

This study used a cross-sectional research design and observational analysis to look at how well colorimetric and turbidimetric methods identified bacteria and how well antibiotics worked on them. Observations were made at the same time.

2.2 Population and Sample

The population in this study were all patients who performed aerobic culture tests in the period January to March 2022 at the Grha Kedoya Hospital Laboratory. Samples are the research subjects studied, namely samples with antibiotic-resistant test results that indicated carbapenem resistance with colorimetric and turbidimetric methods in the Grha Kedoya Hospital laboratory. Samples in this study used inclusion criteria for samples of examination of patient culture results that indicated carbapenem antibiotic resistance and exclusion criteria for samples of examination of culture results that did not indicate carbapenem antibiotic resistance. The sampling technique used in this study was purposive sampling. Purposive sampling is a data sampling technique based on certain considerations, where the data taken is patient data identified as resistant to carbapenem antibiotics. The time span of data collection was carried out from January to March 2022.

2.3 Sample Preparation

Before the research, BAP and MCA bacterial culture media were made. Then plant the sample using an ose, plant it on BAP media and MCA media by strik, then incubate at 37 oC and observe the growth of bacteria after 24 hours. Gram preparations were made on colonies that grew on the media, then Gram staining was done. After that, check the identification and resistance tests of bacteria using the Automatic Microbiology Analyzer (Vitek 2 Compact) colorimetry and turbidimetry methods.

2.4 Data Analysis

The data analysis used in this study was descriptive crosstabs. All data obtained in this study were processed with Microsoft Excel and presented in tabular form.

3. Results

The results of the carbapenem-resistant study at Grha Kedoya Hospital, which was conducted for three months from January to March 2022, involved a population of 239 samples, and 174 samples were studied for Gram-negative Bacilli bacterial growth. The examination was carried out colorimetrically and turbidimetrically using an automatic microbiology analyzer (Vitek 2 Compact).

3.1 The results of the identification examination of Gram-negative bacilli

Scientists looked at 174 samples to see what kinds of Gram-negative bacteria were present and found that many different types of these bacteria grew.Some species of bacteria that grew were Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, and other species of bacteria. The data obtained are as in Table 1.

Table 1. Results of identification examination with the growth of Gram-negative bacilli at Grha Kedoya Hospital from January to March 2022.

Bacteria	Total sample	Percentage
Escherichia coli	50	28.7%
Klebsiella pneumoniae	46	26.4%
Pseudomonas aeruginosa	25	14.4%
Acinetobacter baumannii	24	13.8%
Bakteri spesies lain	29	16.7%
Total	174	100%

Based on Table 1, the frequency of the number of Gram-negative bacilli bacteria that grew was Escherichia coli as many as 50 samples (28.7%), then Klebsiella pneumoniae as many as 46 samples (26.4%), Pseudomonas aeruginosa as many as 25 samples (14.4%), Acinetobacter baumannii as many as 24 samples (13.8%), and other species of bacteria as many as 29 samples (16.7%).

3.2 Prevalence of sensitive carbapenem and resistant carbapenem resistance results

The frequency distribution of sensitive carbapenem and resistant carbapenem resistance results is as follows: Based on Table 2, the results of the antibiotic sensitivity test for sensitive carbapenems were 142 samples (81.6%) and resistant carbapenems were 32 samples (18.4%).

Table 2. Results of sensitive carbapenem resistance and resistant carbapenem in Grha Kedoya Hospital from January to March 2022.

Bacteria	Carbapenem sensitive	Carbapenem resistant
Escherichia coli	50	0
Klebsiella pneumoniae	38	8
Pseudomonas aeruginosa	17	8
Acinetobacter baumannii	8	16
Bakteri spesies lain	29	0
Total	142	32
Percentage	81.6%	18.4%

3.3 Classification of carbapenem-resistant bacteria

The results of the identification examination of gram-negative bacilli with carbapenem-resistant results were carried out on 32 samples. Data obtained from three bacteria in carbapenem-resistant cases The bacteria that grew were Acinetobacter baumannii, Klebsiella pneumoniae, and Pseudomonas aeruginosa.

Table 3. Classification of carbapenem-resistant bacteria in Grha Kedoya Hospital from January to March 2022.

No.	Bacteria	Bacteria count	Percentage
1	*Acinetobacter baumannii*	16	50%
2	*Klebsiella pneumoniae*	8	25%
3	*Pseudomonas aeruginosa*	8	25%
	Total	32	100%

Based on the results of the study, Table 3 shows the number and percentage of the three bacterial species. The number of bacteria that grew was Acinetobacter baumannii in 16 patients (50%), Pseudomonas aeruginosa, and Klebsiella pneumoniae in 8 patients (25%) each. The bacteria that caused the most carbapenem-resistant bacteria to grow were Acinetobacter baumannii.

Table 4. Frequency distribution of carbapenem antibiotics resistant to gram-negative bacteria in Grha Kedoya Hospital January - March 2022

Bacteria	Carbapenem antibiotics	Bacteria count	MIC Value (µg/mL)	Percentage
Acinetobacter baumannii	Doripenem	16	R (≥ 16)	100%
	Imipenem	16	R (≥ 16)	100%
	Meropenem	16	R (≥ 16)	100%
Klebsiella pneumoniae	Doripenem	8	R (≥ 16)	100%
	Ertapenem	8	R (≥ 8)	100%
	Imipenem	8	R (≥ 8)	100%
	Meropenem	8	R (≥ 16)	100%
Pseudomonas aeruginosa	Doripenem	7	R (≥ 16)	100%
		1	R (≥32)	
	Imipenem	8	R (≥ 16)	100%
	Meropenem	8	R (≥ 16)	100%

The results showed that Acinetobacter baumannii bacteria were resistant to doripenem, imipenem, and meropenem antibiotics. A total of 16 samples tested were found to be 100% resistant to carbapenems with resistant MIC values (≥ 16 µg/mL). In Klebsiella pneumoniae bacteria, 8 samples (100%) showed carbapenem-resistant results with resistant MIC values (≥ 16 µg/mL) on Doripenem and Meropenem antibiotics; on Ertapenem and Imipenem antibiotics, results with resistant MIC values (≥ 8 µg/mL) were obtained. In Pseudomonas aeruginosa bacteria, 8 samples (100%) showed carbapenem results; imipenem and meropenem antibiotics obtained results with resistant MIC values (≥ 16 µg/mL) as many as 8 samples; doripenem antibiotics obtained results with resistant MIC values (≥ 16 µg/mL) as many as 7 samples; and resistant MIC values (≥ 32 µg/mL) as many as 1 sample.

4. Discussion

This study was conducted using colorimetric and turbidimetric methods using a microbiology analyzer (Vitek 2 Compact). Because the Vitek 2 microbiology analyzer is a Highly Automatic System tool for antimicrobial identification and sensitivity tests, it allows the results of antimicrobial identification and sensitivity to be completed within 5-8 hours. The results of antibiotic identification and sensitivity have been validated and interpreted in accordance with international standards This study was conducted using colorimetric and turbidimetric methods using a microbiology analyzer

(Vitek 2 Compact). Because the Vitek 2 microbiology analyzer is a highly automatic system tool for antimicrobial identification and sensitivity tests, it allows the results of antimicrobial identification and sensitivity to be completed within 5-8 hours. The results of antibiotic identification and sensitivity have been validated and interpreted in accordance with international standards (CLSI) Clinical and Laboratory Standards International (CLSI) Clinical and Laboratory Standards International (CLSI)(Mukherjee, Mandal, and Kumar 2021).

The examination was carried out on gram-negative bacilli in as many as 174 samples. The use of antibiotics in infectious diseases is expected to have a positive impact, but the irrational use of antibiotics will have a negative impact, including the emergence and development of bacteria resistant to antibiotics and the occurrence of the toxicity of drug side effects, so that the care and treatment of patients become more expensive (Huda 2014). Mono-cyclic beta-lactam antibiotics with an antibacterial spectrum are limited to Gram-negative bacteria and should not be given alone for therapy without a diagnostic basis because these drugs are not effective for Gram-positive germs(BPOM 2021).

According to the research that has been done, it is known that the prevalence of gram-negative bacteria that are resistant to carbapenem antibiotics at Grha Kedoya Hospital, which was carried out for three months from January to March 2022, was 18.4% (32 samples). In line with research conducted by(Lestari, Andrajati, and Nusatia 2020) in patients at St. Carolus Hospital was 53% (79 samples), and research (Ajwad, 2021) Antibiotic sensitivity tests using the Vitek 2 compact method on 23 clinical samples tested against carbapenem antibiotics (Imipenem, Meropenem, and Doripenem) showed 100% (23 isolates) were resistant. The reading of the antibiotic sensitivity test is based on the Minimum Inhibitory Concentration (MIC) value that appears. The MIC of an antibiotic against microbes is used to determine the sensitivity of microbes to antibiotics. The MIC value is opposite to the sensitivity of the tested microbe. The lower the MIC value of an antibiotic, the greater the sensitivity of the bacteria. The MIC of an antibiotic against a microbial species is the average MIC against all strains of that species. Strains of some microbial species are very different in terms of their sensitivity(Kowalska-Krochmal and Dudek-Wicher 2021).

The results of the examination of 32 samples that are resistant to carbapenem antibiotics show that the most species are Acinetobacter baumannii bacteria, with as many as 16 samples (50%). The results of this study are in accordance with Jamhal (2017), where the most species were also found in Acinetobacter baumannii, namely 5 samples (55.5%) in patients at RSUP. Dr. Wahidin Sudirohusodo from January to September 2017(*Jamhal, 2017*). This is because Acinetobacter baumannii is one of the low-level pathogens that has virulence factors, so its toxicity and pathogenicity can increase. Acinetobacter baumannii can become endemic in hospitals due to its good genetic ability and ability to survive in unfavorable environments. Some strains of Acinetobacter baumannii are known to survive exposure to commonly used disinfectants such as chlorhexidine, gluconate, and phenol, especially if not used in appropriate concentrations(Lestari, Andrajati, and Nusatia 2020). Acinetobacter baumannii is one of the major pathogenic bacteria found worldwide. Acinetobacter baumannii is commonly found as a bacterium that causes nosocomial infections. This bacterium is the pathogen responsible for opportunistic infections(Rosalino et al. 2020). A. baumannii has been widely reported to have XDR resistance for nosocomial bacteremia and VAP (ventilator-associated pneumonia)(Zaidan, Hornak, and Reynoso 2021).

The nature of resistance to carbapenem antibiotics occurs in doripenem, imipenem, and meropenem antibiotics in this study, experienced by A. baumannii bacteria as many as 16 (50%) isolates, K. pneumoniae, and P. aeruginosa as many as 8 (25%) isolates. This study is in line with research conducted at RSMH Palembang on 35 bacterial isolates obtained: 17 (48.6%) isolates of K. pneumoniae, 8 (22.9%) isolates of E. coli, 7 (20%) isolates of E. cloacae, and 3 (8.7%) isolates of S. marcescens bacteria that are resistant to carbapenemase and contain blaIMP gene mutations(Sabrina et al. 2019). Another study stated that of the 88 isolates examined, 73 (83%) were resistant to Ertapenem and Meropenem(Amalia et al. 2019). A study in China that examined 935 samples from adult and pediatric patients found that the dominant bacteria were K. pneumoniae isolates (64.6%, 457/709) in adult patients and E. coli isolates (96.0%, 143/149) in children(Han et al. 2020). A Carbapenemase beta lactamase phenotype confirmation test can be done with CDST (Combined Disk Synergy Test), which was reported in 88 isolates and confirmed positive by as many as 87 (98.8%), with the most bacteria resistant to meropenem and ertapenem antibiotics, namely K. pneumoniae, namely 10 (22.2%) and 8 (17.7%)(Patricia V, 2023).

5. Conclusion

Based on the results of the research and discussion above, it can be concluded that in the study conducted on 174 samples with Gram-negative bacillus growth, the results of carbapenem resistance were 32 samples (18.4%), and the bacteria that caused many cases of carbapenem resistance were Acinetobacter baumannii in as many as 16 patients (50%). Resistance tests showed 100% resistance to doripenem, imipenem, meropenem, and ertapenem antibiotics.

References

Ajwad, M. 2021. "Gambaran Kejadian Resistensi Acinetobacter Baumannii Terhadap Antibiotik Golongan Karbapenem di RSUP Dr. Wahidin Sudirohusodo Makassar." : 1–189.

Amalia, Ella et al. 2019. "Identification of Carbapenemases Enterobacteriaceae Producing Gene BlaVIM in Clinical Isolates." *Journal of Physics: Conference Series* 1246: 012004.

BPOM. 2021. "Bab-5-Infeksi/51-Antibakteri/512-Sefalosporin-Dan-Antibiotik-Beta-Laktam - Lainnya."

Han, Renru et al. 2020. "Dissemination of Carbapenemases (KPC, NDM, OXA-48, IMP, and VIM) Among Carbapenem-Resistant Enterobacteriaceae Isolated From Adult and Children Patients in China." *Frontiers in Cellular and Infection Microbiology* 10(July).

Huda, Misbahul. 2014. "Resistensi Bakteri Gram Positif Terhadap Antibiotik Di UPTD Balai Laboratorium Kesehatan Lampung Tahun 2012-2014 Resistance Gram Positive Bacteria Against Antibiotics In UPTD Health Laboratory Lampung Year 2012-2014." *Jurnal Analisis Kesehatan* 5(1): 467–74.

Jamhal, Farnida. 2017. *Prevalensi Mdro (Multidrug Resistant Organism) Pada Pasien Non Bedah Di Icu Rsup Dr Wahidin Sudirohusodo Dari Januari-September 2017*. Makasar.

Kastawa, Ni Wayan Eka Putri Gayatri, Yan Ramona, and N.N. Dwi Fatmawati. 2020. "Metode Deteksi Carbapenem Resistant Enterobacteriaceae." *Metamorfosa: Journal of Biological Sciences* 7(1): 48.

Kowalska-Krochmal, Beata, and Ruth Dudek-Wicher. 2021. "The Minimum Inhibitory Concentration of Antibiotics: Methods, Interpretation, Clinical Relevance." *Pathogens* 10(2): 1–21.

Kumala, Swiandini. 2017. "Multidrug Resistant: Faktor Risiko Infeksi Bakteri Gram Negatif Resisten Karbapenem Pada Pasien Rawat Inap Di Rsud Dr. Soetomo Surabaya, Jawa Timur'." : 1–5.

Lestari, Yovita E., Retnosari Andrajati, and Angela C. M. Nusatia. 2020. "Hubungan Kejadian Infeksi Carbapenem Resistant Acinetobacter Baumannii Dengan Penggunaan Antibiotika Golongan Karbapenem Pada Pasien Di Rumah Sakit St. Carolus." *Indonesian Journal of Clinical Pharmacy* 9(3): 189.

Mukherjee, Purba, Kajari Mandal, and Atindra Kumar. 2021. "International Journal of Scientific Research in Dental and Medical Sciences The Titbits of Multi-Drug Resistant Organisms Reigning in the Diabetic Foot Ulcers : Regional Epidemiology From a Tertiary Care Hospital of Eastern India." 3: 6–11.

Patricia V, Yani A. 2023. "Gram Negatif Di Rsup Moh . Hoesin Palembang Identification Of Metallo-B -Lactamase (MBL) In Gram Negative Bacteria Isolates In Hospital of Moh . Hoesin Palembang. *Jurnal Kesehatan Poltekkes Palembang* 18(1): 65–72.

Rosalino, V et al. 2020. "Acinetobacter Baumannii Resistance : A Real Challenge for Clinicians." *Antibiotics* 9(205): 1–22.

Sabrina, T. et al. 2019. "Identification of Bla<inf>IMP</Inf> Gene Carbapenem-Resistant Enterobacteriaceae (CRE) Isolated from Patient Infection." In *Journal of Physics: Conference Series*,.

Tilahun, Mihret, Yeshimebet Kassa, Alemu Gedefie, and Melaku Ashagire. 2021. "Emerging Carbapenem-Resistant Enterobacteriaceae Infection, Its Epidemiology and Novel Treatment Options: A Review." *Infection and Drug Resistance* 14: 4363–74.

Zaidan, Noor, J Patrik Hornak, and David Reynoso. 2021. "Extensively Drug-Resistant Acinetobacter Baumannii Nosocomial." *Antimicrobial Agents and Chemotherapy* 65(11): e00924-21.

Zilberberg, Marya D. et al. 2017. "Carbapenem Resistance, Inappropriate Empiric Treatment and Outcomes among Patients Hospitalized with Enterobacteriaceae Urinary Tract Infection, Pneumonia and Sepsis." *BMC Infectious Diseases* 17(1): 1–13.