Original Research Report

BACTERIAL PROFILE AND ANTIBIOTIC USE IN CATHETER-ASSOCIATED URINARY TRACT INFECTION PATIENTS AT A TERTIARY REFERRAL HOSPITAL IN SURABAYA, INDONESIA

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ABSTRACT

Catheter-associated urinary tract infection (CAUTI) is the most typical type of infection associated with healthcare. This infection constitutes a significant health problem due to its complications and frequent recurrence. The high annual incidence of CAUTI leads to infectious complications and a high cost of treatment. Antibiotic-resistant bacteria further complicate the problem because multiresistant pathogenic bacteria are often responsible for these infections. Moreover, the lack of a comprehensive case reporting system in Indonesia hinders the determination of CAUTI incidence. This study aimed to determine the bacterial profile and antibiotic use in CAUTI patients (n=22) at the Internal Medicine Inpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. This retrospective descriptive study collected data from patient medical records to describe the incidence, type of bacteria, sensitivity patterns, and antibiotic use in CAUTI patients. The data collection process included collecting medical records, recording information on data collection sheets, and recapitulating and analyzing the data. The criteria for CAUTI diagnosis were a bacterial count of ≥105 CFU/mL and a catheterization that lasted more than 48 hours. Samples were selected using non-probability sampling, also known as saturation sampling. Meanwhile, variables analyzed in this study were the type of pathogenic bacteria, antibiotics used, age, and sex. Descriptive analysis was employed to analyze the data. The findings suggested that the most common bacteria were Escherichia coli, with eight of nine bacteria showing extended-spectrum beta-lactamase (ESBL) production. Female patients aged 35-65 years were the majority of the CAUTI patients. Amikacin was the antibiotic with the highest sensitivity (90.9%), while ceftriaxone was the most common type of antibiotic administered to the patients. In addition, intravenous (IV) administration was the most common route of antibiotic administration, with an average therapy duration of seven days. In conclusion, identifying the type of pathogenic bacteria and performing antibiotic susceptibility testing can help minimize antibiotic resistance and prevent more severe complications in CAUTI patients.

Keywords: Catheter-associated urinary tract infection; healthcare-associated infections; *Escherichia coli*; infectious disease

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Highlights:

1. This study examined patients with catheter-associated urinary tract infections (CAUTI) to find the prevalent bacteria and the frequency of antibiotic use.

2. Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* sensitive to amikacin was found to be the most common pathogen in CAUTI, while ceftriaxone was the most commonly used antibiotic.

3. The findings of this study encompass patients profiles, which may help in understanding patient needs and determining more effective CAUTI treatments.

INTRODUCTION

Catheter-associated urinary tract infection (CAUTI)

is an infection of the urinary tract brought on by a tube that has been implanted to drain urine from the bladder. Patients having indwelling catheters at the time of the infection or within 48 hours of it occurring are considered to have CAUTI (Press & Metlay 2013, Chuang & Tambyah 2021). CAUTI is the most common healthcare-associated infection. accounting for approximately 1 million cases per year in the United States. It is the most common cause of secondary bloodstream infections. The risk factors for CAUTI include age, female gender, diabetes mellitus, and a long duration of catheter insertion. The duration of catheter insertion is the most important factor in the development of bacteriuria (Werneburg 2022). In 2011, there were an estimated 93,000 CAUTI cases. It accounted for more than 13,000 deaths from all healthcare-related urinary tract infections in the United States (Letica-Kriegel et al. 2019). The prevalence of CAUTI ranges from 2.7% to 16% in Medan. Indonesia. However, the total incidence of CAUTI in Indonesia is still unclear due to a flawed case-reporting system (Anggi et al. 2019, Sitepu & Putra 2019). This study is required to establish the precise incidence of CAUTI in Indonesia and at local area levels. Therefore, it is anticipated that CAUTI guidelines can be established to prevent complications from this infection and lower the level of antibiotic resistance in Indonesia. The incidence rate is still unknown in Indonesia as there are only a few CAUTI studies in the country, despite the world's and Indonesia's increasing levels of antibiotic resistance.

Gram-negative bacterial species, including Escherichia coli and Enterococcus spp., are the most common organisms that cause CAUTI. In addition to pathogenic bacteria, CAUTI can be caused by fungi, one of which is Trichosporon asahii, which has been recorded in India (Urs et al. 2018, Werneburg 2022). Fungal organisms other than Trichosporon asahii and Candida spp. are reported to cause CAUTI. Although CAUTI morbidity and mortality rates are relatively low compared to other healthcare-associated infections, the high annual incidence and overuse of antibiotics can lead to many complications and high costs of care (Rishpana 2015, Werneburg 2022).

Increased resistance of pathogenic bacteria to antibiotics is a common problem because multiresistant pathogenic bacteria often cause this infection. Inappropriate use of antibiotics for patients with urinary catheters is a significant factor in the increase in bacterial resistance (Köves et al. 2017). In Pakistan, resistance to ceftazidime and cefotaxime antibiotics against pathogenic bacteria that cause CAUTI occurred. By knowing the pattern of resistance of pathogenic bacteria, it is hoped that if there are CAUTI patients, they can find out the possible type of bacteria causing it and use empirical antibiotic therapy to prevent further resistance and more severe complications (Sayeed et al. 2019). This present study was conducted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, which is a referral hospital and the largest in eastern Indonesia with diverse patient characteristics. Therefore, we chose the hospital as the research location and expected the research questions to be answered correctly. This study aimed to investigate the bacterial profile and antibiotic use by examining urine specimens taken from patients diagnosed with CAUTI.

MATERIALS AND METHODS

This study was a retrospective descriptive study of 22 hospitalized patients diagnosed with CAUTI. The patients were over the age of 18. Data were obtained sequentially from urine culture. bacterial identification, and antibiotic susceptibility tests carried out at the Clinical Microbiology Laboratory, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, for one year between May 2020 and May 2021. Medical records were used to extract additional information about patient profiles. The data were collected and analyzed retrospectively. IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) was used to descriptively evaluate the data (Utami et al. 2022).

Patients with urinary indwelling catheters provided urine samples at the beginning of the study. When the bacterial count was greater than or equivalent to 105 CFU/mL and the catheterization lasted more than 48 hours, the CAUTI diagnosis was determined. Any urine samples that had two or more distinct bacterial colonies were not taken into consideration for further investigation (Utami et al. 2022). This study was ethically approved by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, with reference No. 0616/LOE/301.4.2/IX/2021 dated 27/9/2021.

RESULTS

Patient characteristics

A total of 18 (81.82%) of the 22 patients were women. Most patients were in the age groups of 36– 45 years and 56–65 years. A summary of the patients' age and sex distribution is provided in Table 1.

Bacteriological investigations

Most of the bacteria that caused CAUTI are Gramnegative bacteria (n=10). *Escherichia coli* was the most common bacterium in this study, with a total of nine cases (56%). Eight of nine *Escherichia coli* isolates were extended-spectrum beta-lactamase (ESBL)-producing strains. The distribution of bacteria is provided in Table 1.

Category		Total (n, %)
Sex	Male	4 (18.18%)
	Female	18 (81.82%)
Age	36–45 years	7 (31.82%)
	46-55 years	5 (22.73%)
	56–65 years	7 (31.82%)
	>65 years	3 (13.63%)
Bacteria	Escherichia coli	9 (56%)
	Staphylococcus haemolyticus	1 (6%)
	Moraxella species	1 (6%)
	Enterococcus faecalis	2 (13%)
	Candida species	3 (19%)
Administrati	Oral	(21.05%)
on route	Intravenous	(78.95%)
Treatment	Seven days	21 (95.45%)
duration	Three days	1 (4.55%)
Antibiotics	Ceftriaxone	17 (45.94%)
	Moxifloxacin	4 (10.81%)
	Cefixime	4 (10.81%)
	Cefoperazone- sulbactam	3 (8.1%)
	Ciprofloxacin	3 (8.1%)
	Meropenem	2 (5.4%)
	Ampicillin- sulbactam	1 (2.7%)
	Cotrimoxazole	1 (2.7%)
	Cefotaxime	1 (2.7%)
	Levofloxacin	1 (2.7%)

 Table 1. Patient demographics, pathogenic bacteria, and antibiotics used in CAUTI.

Patterns of antibiotic use

The most common route of antibiotic administration in CAUTI patients was intravenous (78.95%). The average duration of antibiotic therapy in CAUTI patients was seven days (n=21, 95.45%). The most common antibiotic for CAUTI patients was ceftriaxone (n=17). Table 1 presents the complete data on patterns of antibiotic use.

Antibiotics susceptibility

Antibiotics that had a high susceptibility to Escherichia were amikacin coli (90.9%), imipenem meropenem (86.4%), (77.3%). piperacillin-tazobactam (63.6%), and cephalexin (59.1%). However, several antibiotics showed lower susceptibility to Escherichia coli or even no susceptibility at all, i.e., cefazolin and ciprofloxacin. Table 2 shows the complete data on antibiotic susceptibility.

	Escherichia
Antibiotics	coli
Amikacin	90.9 %
Meropenem	86.4 %
Imipenem	77.3 %
Piperacillin-tazobactam	63.6 %
Cephalexin	59.1 %
Cefoperazone-sulbactam	36.4 %
Tigecycline	27.3 %
Amoxicillin-clavulanic acid	22.7 %
Cefepime	22.7 %
Fosfomycin	22.7 %
Trimethoprim-	22.7 %
sulfamethoxazole	22.1 %
Ceftazidime	18.2 %
Ceftriaxone	18.2 %
Gentamicin	18.2 %
Cefotaxime	13.6 %
Ampicillin-sulbactam	13.6 %
Aztreonam	13.6 %
Moxifloxacin	13.6 %
Tetracycline	13.6 %
Piperacillin	9.1 %
Chloramphenicol	4.5 %
Levofloxacin	4.5 %
Cefazolin	0
Ciprofloxacin	0

Table 2. The susceptibility rate of antibiotics to Escherichia coli.

DISCUSSION

Patient characteristics

The shorter urethra in women than in men makes the female urinary tract more vulnerable, increasing the incidence of CAUTI. The current findings indicated that CAUTI was more prevalent in women. These findings are corroborated by another study, which stated that 59% of their patients with CAUTI were women (Smith et al. 2019). The incidence of CAUTI is determined by age and gender. In this study, patients in the age groups of 36-45 years and 56-65 years were the largest populations who experienced CAUTI, or about 31.82% of the entire population. This is consistent with an earlier study by Hariati et al. (2019) who found that CAUTI was more prevalent in people over 60 years old. Older age and immobility were two additional significant risk variables, although they could be influenced by other factors (Setyorini et al. 2019). Patients with diabetes mellitus have a significant risk of developing urinary tract infections since their urine is a source of microbial growth, and they typically have immunocompromised states. As a result, they require careful blood glucose management to stop the development and spread of CAUTI (Li et al. 2019).

Bacteriological investigations

The majority of bacteria that cause CAUTI come from the perineum's endogenous microbiota, which ascends the urethra to the bladder along the catheter's outer surface. A smaller percentage of microorganisms (34%) were added by intraluminal contamination of the collecting system from exogenous sources, typically as a result of organisms being transferred from the hands of healthcare workers. In a study at a hospital, patientto-patient transmission accounted for 15% of instances of bacteriuria connected with health care (Clarke 2014).

The typical test for identifying the bacteria responsible for CAUTI is a urine culture. There are numerous methods for collecting urine cultures, including the straight catheter technique, the midstream technique with or without purging, and suprapubic aspiration. In pediatric patients, the technique of collecting diapers and sterile bags is the most common collection technique. The best way to prevent microorganisms from contaminating a specimen is through suprapubic collection, especially in the distal urethra. This approach is rarely used since it is invasive, uncomfortable for patients, lacks an indication, and wastes resources. The next best method is to collect urine using just one catheter (straight catheter approach) (Karah et al. 2020). However, this treatment is only applied when necessary because it is labor-intensive and has the risk of introducing germs into the bladder, which can lead to a UTI. In a comparison between suprapubic aspiration and the single catheter method, the colony counts from the obtained samples match rather well. Whereas in adult patients, the mid-stream technique is the most commonly used because it is non-invasive (Sinawe & Casadesus 2023).

The patient's history, clinical signs and symptoms, and other laboratory tests should all be taken into consideration when interpreting the results of a urine culture. Nonetheless, many patients are diagnosed with CAUTI with negative urine cultures because the clinical signs and symptoms suggest a urinary tract infection. Negative urine culture results in patients with CAUTI are influenced by the number of days of urinary catheter insertion and the patient's maximum temperature (Podkovik et al. 2019, Karah et al. 2020).

Patterns of antibiotic use

Treatment with antibiotics for CAUTI aims to eliminate bacteria and bacterial colonies, relieve symptoms, treat sepsis, and prevent sequelae. Musinguzi et al. (2019) stated that the pathogenic bacteria of CAUTI showed resistance to commonly prescribed antibiotics. *Escherichia coli* has the highest antibiotic resistance to all antibiotics. All Gram-negative bacteria were sensitive to imipenem (100%) and gentamicin (83%), but the high cost of these antibiotics and the nephrotoxic effect of gentamicin continue to limit their use (Musinguzi et al. 2019).

The current research suggests that CAUTI is the only case where systemic antibiotic treatment is necessary. When a CAUTI is identified, a new catheter should be used, and treatment should begin initially with broad-spectrum antibiotics by considering the local susceptibility patterns and later modifying the treatment according to the results of urine or blood culture tests (Karah et al. 2020). Analysis of prognostic factors for CAUTI caused by bacteremia catheters revealed a poor prognosis and higher mortality linked to incorrect empirical treatment. The likelihood that the bacteremia was brought on by antibiotic-resistant uropathogens was much higher, and the likelihood that such pathogens had previously been exposed to antibiotic therapy and associated with bacteremia in a medical setting was a predictive factor (Tenke et al. 2014).

The most typical method of administering antibiotics to CAUTI patients is intravenous, particularly for those with significant systemic symptoms such as high fever, hemodynamic instability, poor oral tolerability, and reduced absorption. At 48 to 72 hours, the clinical response can be assessed. Parenteral antibiotic therapy can be reviewed after culture results are available. For many patients, oral therapy can also be selected after reviewing the results of the urine culture or after 72 hours of intravenous antibiotics (Spoorenberg et al. 2014).

If there is an indication, antibiotics should be chosen according to the urine culture results. It is also advised to initiate empirical antibiotic therapy while awaiting the findings of the culture if the patient exhibits moderate to severe symptoms. Ampicillin and gentamicin are still suitable as initial empiric therapy alternatives for parenteral antibiotic therapy. Broad-spectrum beta-lactam antibiotics (such as cefotaxime, ceftriaxone, and piperacillin or tazobactam) and other cell wall-active drugs are an option for empirical parenteral therapy. Antifungal medications should be taken for 14 days to treat symptomatic CAUTI brought on by *Candida* spp. (Clarke 2014).

The majority of CAUTI patients receive antibiotic treatment for seven days. Furthermore, according to a study by Clarke Clarke (2014) seven days of antibiotic therapy can be sufficient in cases when there is a rapid clinical worsening, such as a drop in temperature within 72 hours. For those who have a

delayed reaction, a small amount of antibiotics is administered for 10–14 days. The most common type of antibiotic given to CAUTI patients is ceftriaxone. This medication is often administered to patients with CAUTI caused by *Enterococcus* spp., elderly patients, and those who experience urinary tract infections due to catheterization. These results are supported by previous study by Karlović et al. (2018).

Antibiotic susceptibility

Some antibiotics are resistant to both Gram-negative and positive bacteria. The rise of ESBL uropathogenic strains can result in the development of beta-lactam antibiotic resistance, particularly for Gram-negative bacteria. In this study, ESBLproducing *Escherichia coli* were resistant to ciprofloxacin and cefazolin. This resistance occurred because ESBL is an enzyme capable of hydrolyzing the beta-lactam ring, which caused a loss of beta-lactam antibiotic activity (Bush 2018).

Escherichia coli has a varying sensitivity to several antibiotics. In this study, the sensitivity levels of Escherichia coli to amikacin (90.9%), meropenem (77.3%), (86.4%), imipenem piperacillintazobactam (63.6%), and cephalexin (59.1%) were found. However, some antibiotics were not sensitive to Escherichia coli, i.e., cefazolin and ciprofloxacin, with a sensitivity level of 0%. These results are consistent with previous studies, which revealed that Escherichia coli was sensitive to amikacin (82.6%), piperacillin-tazobactam (78.2%), nitrofurantoin (82.1%), and imipenem (98.9%) (Niranjan & Malini 2014). The sensivity of Escherichia coli to ampicillin, cefuroxime, ceftriaxone, norfloxacin, and ciprofloxacin varied between 11% and 25%. In another study, Escherichia coli was sensitive to ampicillin (39.1%), amoxicillin-clavulanic acid (64.9%), cefotaxime (94.9%), gentamicin (93.9%), and amikacin (98.6%) (Daoud et al. 2020).

Strength and limitations

The limitation of this study is that it is a retrospective study using patient medical records carried out in one center, so a small number of samples were obtained. The data only represent that specific center and may not be representative or cannot be used in other centers or hospitals. The impact of this research on clinical practice is that it can be used as a reference for intervention or management of CAUTI patients at the center or in the local area. It is expected to help reduce the level of antibiotic resistance, which has been increasing recently. For further research, prospective research can be carried out in several areas or centers so that a large number of samples can be obtained and comparisons can be made with other centers to find out the shift in pathogenic bacteria.

CONCLUSION

Escherichia coli was the most common bacterial pathogen associated with CAUTI, with the majority of cases attributed to gram-negative bacteria. Sensitivity testing showed that amikacin was effective against Escherichia coli, while cefazolin and ciprofloxacin were resistant to Escherichia coli. Intravenous administration was the preferred route for antibiotic administration, with an average therapy duration of seven days, and the most frequently prescribed antibiotic was ceftriaxone. Further research is recommended to be conducted in at least two different hospitals to represent a larger population and to compare the causative bacteria. In addition, the research can be carried out periodically to investigate any shifts in the pattern of pathogenic bacteria.

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Conflict of interest

None.

Ethical consideration

This study was conducted with the approval from the Health Research Ethics Committee, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, with reference No. 0616/LOE/301.4.2/IX/2021 dated 27/9/2021.

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Author contribution

EAV contributed to the conceptualization and design as well as the data collection, analysis, and interpretation. TPA participated in the drafting, design, critical revision, and final approval of the article for publication. ADWW made crucial revisions to the article and approved the final draft before it was published. BER made crucial revisions to the article and approved the final draft before it was published.

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