East Asian Journal of Multidisciplinary Research (EAJMR)
Vol. 3, No.5 2024: 1795-1812

Bacterial Uropathogens and Antibiotic Susceptibility Patterns in Urinary Tract Infections: Cross-sectional Study at a Secondary Hospital in Southeast Bali

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A R T I C L E I N F O

Keywords: Antibiotic, Resistance, Susceptibility, Uropathogens, UTI

Received : 18, March
Revised : 20, April
Accepted: 22, May

A B S T R A C T

Urinary tract infections (UTIs) are the most common infection in outpatient settings. Although antibiotics are the primary UTIs treatment, the antibiotic resistance threatens its effectiveness, posing a significant risk to public health. This study aims to explore the common bacterial uropathogens in UTIs patients and to plot the antibiotic susceptibility patterns through a cross-sectional retrospective study. Patients provided aseptic urine samples after consenting, which included clean-catch midstream urine and specimens obtained via straight or indwelling catheters, all stored in sterile containers. Escherichia coli was the most prevalent UTI-causing bacteria (29.2%), followed by Klebsiella pneumoniae (20.8%) and Pseudomonas aeruginosa (10%). Among all pathogens, 34.6% were Extended Spectrum β-lactamase (ESBL), including some of Escherichia coli and Klebsiella Pneumoniae. Escherichia coli was the most prevalent UTI-causing bacteria (29.2%), followed by Klebsiella pneumoniae (20.8%) and Pseudomonas aeruginosa (10%).

DOI prefix: https://doi.org/10.55927/eajmr.v3i5.9250
ISSN-E: 2828-1519 (Online)
https://journal.formosapublisher.org/index.php/eajmr

INTRODUCTION

Urinary tract infections (UTIs) are among the most frequently encountered infections in clinical settings worldwide. They represent the predominant type of infection observed in healthcare facilities . In 2019, the global incidence of urinary tract infections (UTIs) was approximately 4,046.12 × 105 cases, marking a 60.4% increase from 1990. UTI was common in two age groups, 25-34 and 0-14 years old. In Indonesia, UTIs estimated 90-100 cases per 100,000 patient and 180,000 new cases per year. UTIs affect the quality of life (QoL) of individuals and contributes to elevated clinical and economic burdens around the world. According to the European Association of Urology (EAU) Urological Infection Guideline, UTIs is classified into uncomplicated UTIs, complicated UTIs, recurrent UTIs, catheter-associated UTIs, and urosepsis. The gold standard for diagnosing UTIs involves identifying the pathogen in conjunction with clinical symptoms. This detection and identification process is carried out through urine culture. A significant urine bacterial level is characterized by the presence of a bacterial count of 105 Colony-forming Unit per milliliter (CFU/ml) of clean-catch midstream urine in two consecutive cultures.

Antibiotics stand as the primary treatment for UTIs, targeting the underlying bacterial infection to alleviate symptoms and promote recovery. To prescribe the right antibiotics, performing a urine culture is necessary. However, it is time-consuming and expensive. Majority of patients with suspected uncomplicated UTIs do not undergo urine culture and are instead treated with empiric antibiotics. This widespread use of empiric antibiotics contributes to the escalation of antimicrobial resistance, making pathogens more resilient against these drugs. Such antibiotic resistance poses a significant threat to public health, undermining the effectiveness of therapy and complicating management strategies. This study aims to explore the bacterial uropathogens in UTIs patients and to plot the antibiotic susceptibility patterns in Klungkung General Hospital through a cross-sectional study.

THEORETICAL REVIEW

Urinary tract infections (UTIs) are among the most frequently encountered infections in clinical settings worldwide. They represent the predominant type of infection observed in healthcare facilities. In 2019, the global incidence of urinary tract infections (UTIs) was approximately 4,046.12 × 105 cases, marking a 60.4% increase from 1990. UTI was common in two age groups, 25-34 and 0-14 years old

Antibiotics stand as the primary treatment for UTIs, targeting the underlying bacterial infection to alleviate symptoms and promote recovery. To prescribe the right antibiotics, performing a urine culture is necessary. However, it is time-consuming and expensive

METHODOLOGY

This study adopts a descriptive research design with a cross-sectional retrospective approach utilizing secondary data extracted from electronic medical records in Klungkung General Hospital. A total of 130 samples were collected between February 2021 and December 2023. Data extracted from the medical records includes patients' name, gender, age, patients' room, date of sample taken, pathogen's name, antibiogram, and type of resistance (sensitive, resistant, or not tested). The inclusion criteria of this study were the patients who underwent antibiotic therapy and possessed antibiotic sensitivity test results as part of its criteria. The exclusion criteria were the samples with negative or no growth, colonization, and contamination culture results, or those with positive culture results that were not subjected to antibiotic sensitivity testing.

Patients were advised to collect the urine sample aseptically to prevent contamination. Patients' consent was taken first before collecting the specimen. The samples were obtained from clean-catch midstream urine as well as urine obtained through both straight and indwelling catheters, then stored in sterile containers later. Subsequently, sterile urine samples were inoculated onto sheep blood agar (SBA) and MacConkey agar (MA) for uropathogen isolation, followed by incubation at 35±1°C for 18-24 hours. The culture will then undergo identification and antimicrobial susceptibility testing (AST) using VITEK2 and Microscan/Autoscan in accordance to Clinical and Laboratory Standards Institute (CLSI) M100. Furthermore, additional AST were conducted on the Kirby-Bauer disk diffusion on Mueller-Hinton agar, then the results were interpreted according to the CLSI M100 guidelines. This study has passed ethical clearance in Klungkung General Hospital with the registration number 000.9.2/1021/RSUD/2024. The data was analyzed using IBM SPSS Statistics 26 for Windows.

RESULTS

Between February 2021 and December 2023, the Clinical Microbiology Laboratory at Klungkung General Hospital received a total of 130 positive culture isolates from urine samples. Most of the patients were male (72.3%), with the majority of them (30.9%) aged 70-79 years old. Among female patients, the highest proportion (25%) fell within the 60-69 age range (Figure 1). Out of all the samples, 80.8% were obtained from in-patients, 13.8% were from out-patients, 4.6% were from the Intensive Care Unit (ICU), and 0.8% were from the Emergency Room (ER) (Figure 2). Of these, 7.7% isolates were from 2021, 30% from 2022, and 62.3% from 2023. Notably, there was a progressive increase in sample submissions over the study period, with a substantial proportion received in 2023, constituting 62.3% of the total samples (Figure 3).

The analysis revealed *Escherichia coli* as the predominant uropathogen, accounting for 29.2% of isolates, followed by *Klebsiella pneumoniae* (20.8%) and *Pseudomonas aeruginosa* (10%) (Table 1). Among all pathogens in this study, 34.6% were Extended Spectrum β-lactamase (ESBL) bacteria, 5.4% showed resistance to the Carbapenem, and 0.8% were Multi-Drug Resistant Organisms (MDRO) (Figure 4). Specifically, 22 out of 38 *Escherichia coli* isolates and 19 out of 27 *Klebsiella pneumoniae* isolates were ESBL bacteria. Among *Pseudomonas aeruginosa*, 6 of them were Carbapenem resistant and 1 of them were MDRO (Table 3).

Additionally, *Enterococcus faecalis* (8.5%), *Enterobacter cloacae* (3.8%), *Acinetobacter baumannii* and *Staphylococcus saprophyticus* (both 3.1%), *Proteus mirabilis* and *Candida spp.* (both 2.3%) were also identified. The remaining uropathogens, including *Burkholderia cepacia complex, Citrobacter koseri, Streptococcus mitis,* and *Staphylococcus epidermidis*, accounted for 1.5% each. Furthermore, several pathogens such as *Enterococcus gallinarum, Enterobacter aerogenes, Enterococcus faecium, Streptococcus agalactiae, Archromobacter denitrificans, Chryseobacterium indologenes, Citrobacter amalonaticus, Morganella morganii, Providencia rustigianii, Pseudomonas luteola, Staphylococcus cohnii, Staphylococcus haemolyticus, Streptococcus anginosus group,* and *Streptococcus pneumoniae* were also present at a prevalence rate of 0.8% each (Table 1).

Penicillin group showed no sensitivity towards three most common bacteria. Piperacillin-Tazobactam demonstrated the best sensitivity among the β-lactamase inhibitors, with 73.7% sensitivity towards *Escherichia coli*, 51.9% to *Klebsiella pneumoniae*, and 23.1% to *Pseudomonas aeruginosa* (Table 2). This drug also had high sensitivity towards ESBL-*Escherichia coli* (72.7%), ESBL-*Klebsiella pneumoniae* (42.1%) (Table 3). In contrast, Amoxicillin-Clavulanic acid had no sensitivity towards these bacteria. Meanwhile in the Cephalosporins group, Cefepime was the most sensitive antibiotics against *Escherichia coli* (52.6%) and *Klebsiella pneumoniae* (44.4%), while Ceftazidime was the most sensitive against *Pseudomonas aeruginosa* (30.8%) (Table 2). Cefepime also displayed 27.3% sensitivity against ESBL-*Escherichia coli* and 31.6% against ESBL-*Klebsiella pneumoniae* (Table 3).

In contrast, Fluoroquinolones showed minimal sensitivity against the identified uropathogens. Ciprofloxacin had 5.3% sensitivity against *Escherichia coli*, 11.1% against *Klebsiella pneumoniae*, and 7.7% against *Pseudomonas aeruginosa*. Levofloxacin had 7.9% sensitivity against *Escherichia coli*, 14.8% against *Klebsiella pneumoniae*, and 7.7% against *Pseudomonas aeruginosa*. In the Aminoglycoside group, Amikacin displayed high sensitivity towards *Escherichia coli* (100%) and *Klebsiella pneumoniae* (92.6%), but relatively low sensitivity towards *Pseudomonas aeruginosa* (30.8%) (Table 2). Amikacin was also highly sensitive against ESBL-*Escherichia coli* (100%) and MDRO-*Pseudomonas aeruginosa* (100%) (Table 3).

Similarly, Meropenem demonstrated high sensitivity towards *Escherichia coli* (97.4%) and *Klebsiella pneumoniae* (96.3%), but lower sensitivity towards *Pseudomonas aeruginosa* (23.1%) (Table 2). In the contrary, Meropenem had very low sensitivity against ESBL-*Klebsiella pneumoniae* (Table 3). Aztreonam from the Monobactam group showed limited sensitivity to *Escherichia coli* (23.7%), *Klebsiella pneumoniae* (14.8%), and *Pseudomonas aeruginosa* (15.4%). Trimethoprim-Sulfamethoxazole had 26.3% sensitivity to *Escherichia coli*, 25.9% to *Klebsiella pneumoniae*, and 0% sensitivity against *Pseudomonas aeruginosa*. Nitrofurantoin exhibited high resistance to the identified pathogens, only 7.9% effective against *Escherichia coli* and totally resistant against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (Table 2).

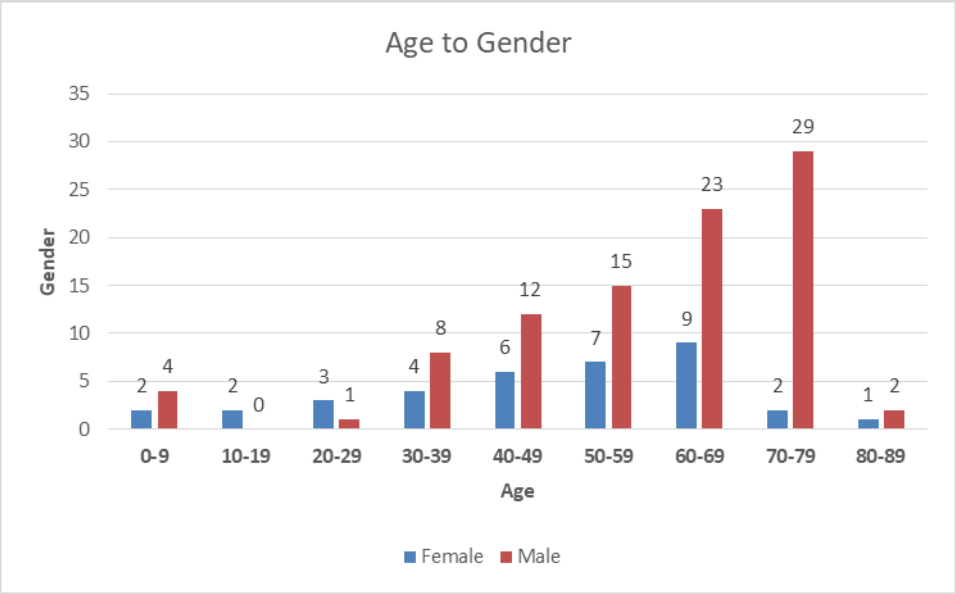

Figure 1. Age to Gender

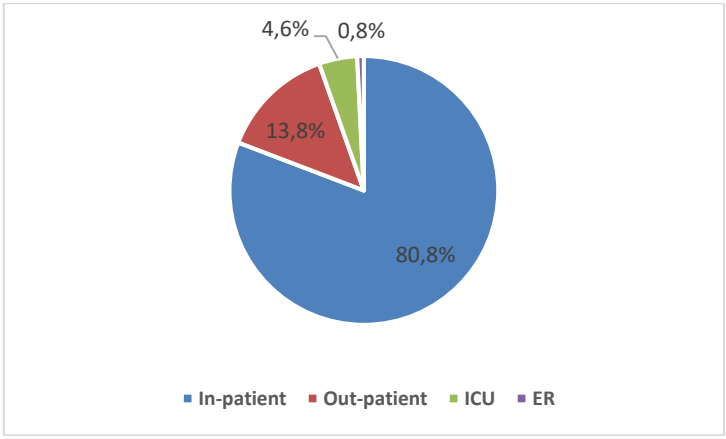

Figure 2. Patient's Room

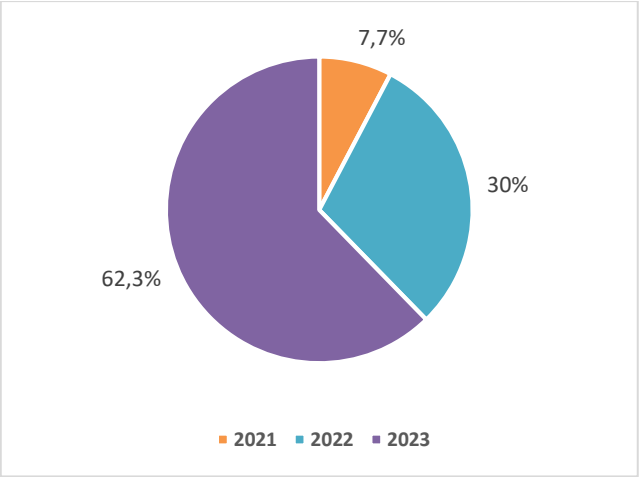

Figure 3. Year of the Samples Taken

Table 1. List of All Uropathogens

Uropathogen's Name	Frequency	Percentage (%)
Escherichia coli	38	29.2
Klebsiella pneumoniae	27	20.8
Pseudomonas aeruginosa	13	10
Enterococcus faecalis	11	8.5
Enterobacter cloacae	5	3.8
Acinetobacter baumannii	4	3.1
Proteus mirabilis	3	2.3
Candida spp.	3	2.3
Burkholderia cepacia complex	2	1.5
Citrobacter koseri	2	1.5
Staphylococcus epidermidis	2	1.5
Staphylococcus saprophyticus	4	3.1
Streptococcus mitis	2	1.5
Enterococcus gallinarum	1	0.8
Enterobacter aerogenes	1	0.8
Enterococcus faecium	1	0.8
Streptococcus agalactiae	1	0.8

Archromobacter denitrificans	1	0.8
Chryseobacterium indologenes	1	0.8
Citrobacter amalonaticus	1	0.8
Morganella morganii	1	0.8
Providencia rustigianii	1	0.8
Pseudomonas luteola	1	0.8
Staphylococcus cohnii	1	0.8
Staphylococcus haemolyticus	1	0.8
Streptococcus anginosus group	1	0.8
Streptococcus pneumoniae	1	0.8
Total	130	100

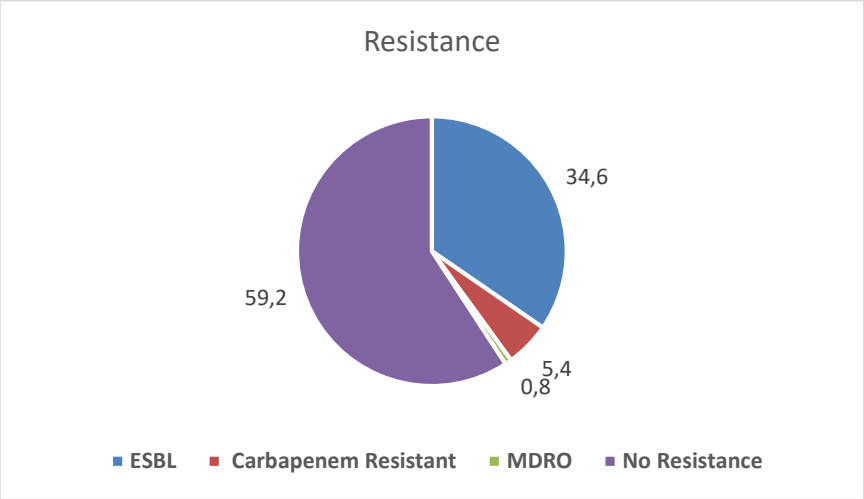

Figure 4. Resistance Pattern of All Uropathogens

Table 2. Antibiogram of the Most Common Uropathogens

	Escherichia coli	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*
Number of isolates	**38**	**27**	**13**
Amoxicillin/Clavulanic Acid (AMC)	0.0%	0.0%	0.0%
Amoxicillin	0.0%	0.0%	0.0%
Amikacin	100.0%	92.6%	30.8%
Aztreonam	23.7%	14.8%	15.4%
Ceftazidime	36.8%	37.0%	30.8%
Cefuroxime	2.6%	3.7%	0.0%
Ciprofloxacin	5.3%	14.8%	7.7%
Ceftriaxone	36.8%	25.9%	0.0%
Cefotaxime	28.9%	14.8%	0.0%
Cefoperazone	2.6%	3.7%	0.0%
Cefazolin	28.9%	14.8%	0.0%
Cefepime	52.6%	44.4%	15.4%
Nitrofurantoin	7.9%	0.0%	0.0%
Gentamicin	21.1%	25.9%	7.7%
Levofloxacin	7.9%	11.1%	7.7%
Meropenem	97.4%	96.3%	23.1%
Benzylpenicillin	0.0%	0.0%	0.0%
Piperacillin	0.0%	0.0%	0.0%
Ampicillin/Sulbactam (SAM)	15.8%	18.5%	0.0%
Trimethoprim/Sulfamethoxazole (SXT)	26.3%	25.9%	0.0%
Tetracycline	13.2%	14.8%	0.0%
Piperacillin/Tazobactam (TZP)	73.7%	51.9%	23.1%

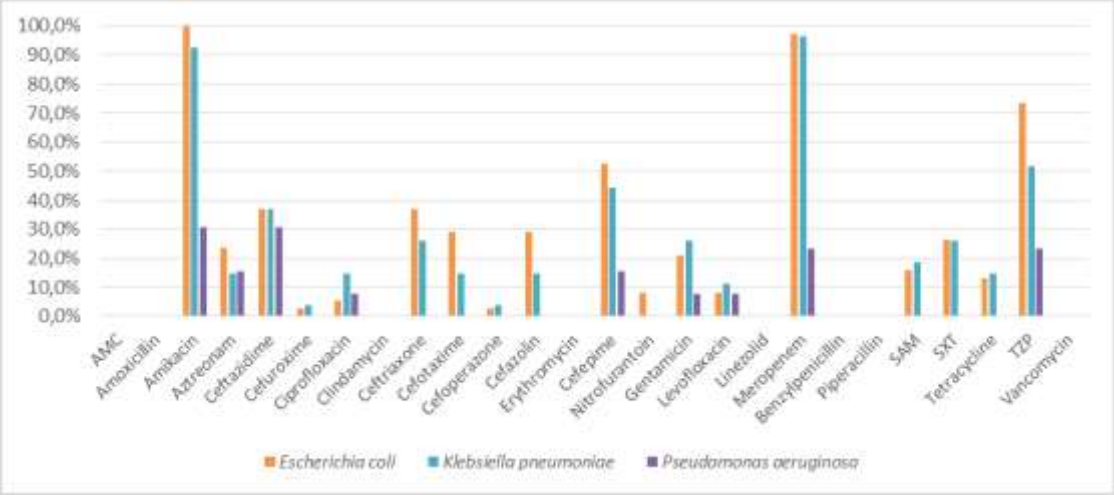

Figure 5. Antibiogram of the Most Common Uropathogens

Table 3. Antibiogram and Resistance Pattern of The Most Common Uropathogens

	Escherichia coli	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	
Resistance pattern	**ESBL**	**ESBL**	**Carbapenem resistant**	**MDRO**
Number of isolates	**22**	**19**	**6**	**1**
Amoxicillin/Clavulanic Acid (AMC)	0.0%	0.0%	0.0%	0.0%
Amoxicillin	0.0%	0.0%	0.0%	0.0%
Amikacin	100.0%	5.3%	0.0%	100.0%
Aztreonam	0.0%	0.0%	16.7%	0.0%
Ceftazidime	9.1%	15.8%	0.0%	0.0%
Cefuroxime	0.0%	0.0%	0.0%	0.0%
Ciprofloxacin	0.0%	0.0%	0.0%	0.0%
Ceftriaxone	0.0%	0.0%	0.0%	0.0%
Cefotaxime	0.0%	5.3%	0.0%	0.0%
Cefoperazone	0.0%	0.0%	0.0%	0.0%
Cefazolin	0.0%	0.0%	0.0%	0.0%

Cefepime	27.3%	31.6%	0.0%	0.0%
Nitrofurantoin	13.6%	0.0%	0.0%	0.0%
Gentamicin	13.6%	15.8%	0.0%	0.0%
Levofloxacin	0.0%	0.0%	0.0%	0.0%
Meropenem	0.0%	5.3%	0.0%	0.0%
Benzylpenicillin	0.0%	0.0%	0.0%	0.0%
Piperacillin	0.0%	0.0%	0.0%	0.0%
Ampicillin/Sulbactam (SAM)	13.6%	0.0%	0.0%	0.0%
Trimethoprim/Sulfamethoxazole (SXT)	18.2%	5.3%	0.0%	0.0%
Tetracycline	13.6%	5.3%	0.0%	0.0%
Piperacillin/Tazobactam (TZP)	72.7%	42.1%	0.0%	0.0%

DISCUSSION

In this research, the demographic distribution of UTI patients was the highest among males aged 70-79 years. This finding contrasts with a 2019 study on the disease burden of UTI, revealing the Age-Standardized Incidence Rate (ASIR) among females was 3.6 times greater than that among males, with rates of 79.64 cases per 1,000 for females compared to 22.12 cases per 1,000 for males. Another study indicated that UTI incidence was prevalent among individuals aged 25-34 and 0-14 years old, with the highest in the 30-34 age group. This highlights the importance of age and gender considerations in UTI risk assessment and management protocols. The predominance of Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa reflects their substantial role in UTIs. These findings align with the current studies where Escherichia coli remains as the most common causative agent of UTIs. In recent researches, the prevalence of other common uropathogens varied. Klebsiella pneumoniae and Pseudomonas aeruginosa were recognized as the subsequent most common bacteria causing UTIs other than Escherichia coli.

Extended Spectrum β-lactamase (ESBL) bacteria accounted for 34.6% of all pathogens in this study, with Escherichia coli and Klebsiella pneumoniae being the predominant contributors. A case series in Qatar and a cross-sectional study in Nepal support this finding, where they similarly identified Escherichia coli and Klebsiella pneumoniae as the primary ESBL-producing bacteria. A multicenter study in Sweden also noted Escherichia coli and Klebsiella pneumoniae as the ESBL-producing pathogens. Additionally, Carbapenem resistance was observed in 5.4% of the bacteria, primarily represented by Pseudomonas aeruginosa. In a study by Shields et al. in 2021, it was observed that 4.4% of the specimens from UTI patients contained Carbapenem-resistant bacteria, with Pseudomonas aeruginosa being the most prevalent. The study also stated that pathogen's resistance to Carbapenem poses heavy burden on healthcare systems. Meanwhile, Multi-Drug Resistant Organisms (MDRO) were identified in 0.8% of the cases, with Pseudomonas aeruginosa being the sole uropathogen in this category. Coyne et al. stated that Pseudomonas aeruginosa had unique ability contributing to its resistance, adapting to evade host defenses and rapidly developing resistance to multiple antibiotics. Consequently, it underscores the importance of choosing proper antibiotics to treat this kind of bacteria.

It is evident in this study that some proportion of the identified uropathogens exhibited resistance to key antibiotics. Penicillin group exhibited no efficacy against the identified bacteria. Among the β-lactamase inhibitors, Piperacillin-Tazobactam demonstrated the highest sensitivity towards Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Piperacillin-Tazobactam was found to be effective on patients with febrile UTI. A study by Al-Shahrani stated that Piperacillin-Tazobactam was sensitive against those pathogens. Piperacillin-Tazobactam was also found to be highly sensitive to Cephalosporin-resistant pathogens . Meanwhile, Amoxicillin-Clavulanic acid was not effective against any of the bacteria mentioned. This is also mentioned in studies by Mareş et al. (14) and Reda et al., which stated that Escherichia coli had high resistance to Amoxicillin-Clavulanic acid.

Within the category of Cephalosporins, Cefepime exhibited the highest sensitivity against Escherichia coli (52.6%) and Klebsiella pneumoniae (44.4%), whereas Ceftazidime demonstrated the greatest sensitivity against Pseudomonas aeruginosa (30.8%). A study by Tarek et al. in Egypt stated that Escherichia coli and Klebsiella pneumoniae had an increasing resistance to different generation of Cephalosporins, potentially due to high rates of its prescription. According to Kang et al. (26), there were emerging cases of Third Generation Cephalosporin Resistant (3GCR) UTI pathogens. Study by Dustin et al. found that Ceftazidime, Cefepime, and Ceftriaxone all had 100% sensitivity against Non-3GCR pathogens, but only 38%, 14%, and 1% respectively against 3GCR pathogens. This should raise awareness in prescripting antibiotics for UTI patients.

Antibiotics in the Fluoroquinolones group, Ciprofloxacin and Levofloxacin, both displayed minimal sensitivities. These antibiotics have traditionally been crucial in UTI treatment, but their increasing resistance demands greater concern (28). In Asia, there was a significant rise in Ciprofloxacin resistance from 25% to over 40% between 2008 and 2014 . A study by Critchley et al. found that Escherichia coli was resistant to Ciprofloxacin and Levofloxacin in 24.3% and 25.8% of the cases, respectively. Similarly, Faine et al. (31) reported that Escherichia coli had a resistance rate of 22.1% to Fluoroquinolones. Amikacin demonstrated high sensitivity to Escherichia coli and Klebsiella pneumoniae but limited efficacy against Pseudomonas aeruginosa. Critchley et al. revealed that Amikacin displayed high sensitivity against Escherichia coli, with a resistance rate as low as 0.1%. Carlotta et al. mentioned that Amikacin was the most susceptible antibiotics (2.3%) against Gram-negative UTI pathogens. Study by Perdana et al. found that Amikacin had 75% sensitivity against Klebsiella pneumoniae. Additionally, Altamimi et al. highlighted the high susceptibility of Escherichia coli and Klebsiella pneumoniae to Amikacin, with sensitivity rates of 99% and 97.1%, respectively. In the settings of limited resources, parenterally-administered Amikacin could also be effective to treat UTI caused by ESBL bacteria.

Meropenem exhibited notable sensitivity to Escherichia coli (97.4%) and Klebsiella pneumoniae (96.3%), although its efficacy against Pseudomonas aeruginosa (23.1%) was comparatively lower. A study by Perdana et al. also had similar result, stating that Meropenem was highly sensitive to Escherichia coli (92.3%) and Klebsiella pneumoniae (84.6%). This was also supported in a study by Altamimi et al., stated that Meropenem was highly susceptible to Escherichia coli (99.2%) and Klebsiella pneumoniae (92.2%) Aztreonam from the Monobactam group showed limited sensitivity to Escherichia coli (23.7%), Klebsiella pneumoniae (14.8%), and Pseudomonas aeruginosa (15.4%). This was similar to a study by Ariana et al. which stated that Escherichia coli was highly resistant to Aztreonam (99.7%). Meanwhile, Trimethoprim-Sulfamethoxazole had 26.3% sensitivity to Escherichia coli, 25.9% to Klebsiella pneumoniae, and 0% sensitivity against Pseudomonas aeruginosa. According to Raz et al., Escherichia coli was the primary resistant pathogen to Trimethoprim-Sulfamethoxazole, comprising 81% of all isolates. The study also stated that 8% of Klebsiella sp. And 3% of Pseudomonas aeruginosa was also resistant to Trimethoprim-Sulfamethoxazole.

In this study, Nitrofurantoin displayed low susceptibility to Escherichia coli (7.9%) and no sensitivity against Klebsiella pneumoniae and Pseudomonas aeruginosa. This is supported by a study by Montelin et al. in 2024, which demonstrated significant resistance of Escherichia coli to Nitrofurantoin. Meanwhile, study by Perdana et al. stated that Nitrofurantoin had a low sensitivity to Klebsiella pneumoniae (7.1%), but was highly effective against Escherichia coli (80.8%). Similarly, Altamimi et al. also found that Nitrofurantoin was highly effective against Escherichia coli (96.8%) and mildly effective against Klebsiella pneumoniae (59.4%). The study encountered various limitations. First, the retrospective nature of the study limited our ability to control for confounding variables and biases. Then, the relatively small sample size may not fully represent the true prevalence and diversity of uropathogens in the population. While the

study identified a wide range of uropathogens and their resistance patterns, the results may not be generalizable to other healthcare settings or geographical regions. Variations in patient populations, healthcare practices, and antimicrobial stewardship programs could influence the prevalence and resistance profiles of uropathogens. Despite these limitations, this study provides valuable insights into the epidemiology and antimicrobial resistance patterns of UTIs in the local patient population. Future research with larger sample sizes and more comprehensive clinical data is warranted to further elaborate the factors contributing to antibiotic resistance and guide evidence-based management strategies. Careful consideration when choosing antibiotics needs to be taken.

CONCLUSIONS AND RECOMMENDATIONS

The study identified Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa as the primary pathogens. Escherichia coli and Klebsiella pneumoniae were the predominant Extended Spectrum β-lactamase (ESBL) bacteria, while Pseudomonas aeruginosa had significant resistant to Carbapenem and was the sole multi-drug resistant organism (MDRO). Amikacin and Meropenem had the highest sensitivity against these prevalent bacteria, while the others antibiotics had low sensitivity against them. The findings underscore the need for continued surveillance and antimicrobial stewardship efforts to mitigate the impact of UTIs on patient outcomes and healthcare resources. Careful consideration when choosing antibiotics needs to be taken.

FURTHER STUDY

Still doing further research to find out more about Bacterial Uropathogens and Antibiotic Susceptibility Patterns in Urinary Tract Infections: Cross-sectional Study at a Secondary Hospital in Southeast Bali

ACKNOWLEDGMENT

Thank you to all the staff in Klungkung General Hospital for helping this research.

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