

Bacteria Resistant Pattern Causing Urinary Tract Infections (UTI) Against Antibacterial in Poly Surgical Hospital Dr. Achmad Mochtar Bukittinggi

Tika Afriani^{1*}, Rizky Yulion², Deby Vista Lestari³

^{1,2,3}Faculty of Health Sciences, Universitas Mohammad Natsir Bukittinggi, Bukittinggi

*email: tika.afriani91@gmail.com

Abstract

Urinary tract infections (UTIs) are one of the diseases in the urinary tract caused by various microorganisms such as bacteria, viruses, and fungi, but the disease most commonly caused by bacteria. The pattern and test of germ sensitivity to antibiotics are crucial, intended for identification and governance. The purpose of this research is to investigate the bacteria associated with UTI cases and their antibiotic susceptibility pattern in HOSPITAL Dr. Achmad Mochtar Bukittinggi, Indonesia. This method of research uses a retrospective design that is presented in a descriptive with laboratory data that meets 13-person inclusion criteria. The results showed that female-sex UTIs patients (53.85%) Unknown to the most bacteria cause UTIs is the bacteria Escherichia coli (30.76%). The result of the resistance test showed E. coli resistant to antibiotics Amphotericin B, Cefuroxime, Ciprofloxacin, Levofloxacin, Norfloxacin, and Tetracycline. It can be concluded women more often experience UTIs than in males with the cause of E. coli bacteria and are resistant to antibiotics penicillin, cephalosporin, and Fluoroquinolone.

Kata Kunci: Antibacterial; Bacteria; UTI; Pattern of Resistance

INTRODUCTION

Urinary tract infections (UTIs) are one of the diseases in the urinary tract caused by various microorganisms such as bacteria, viruses, and fungi, but the disease most commonly caused by bacteria. In the normal state, urine does not contain bacteria, viruses or other microorganisms. According to WHO the main bacteria related to UTIs in children in developing countries are gram-negative organisms, such as *Escherichia coli* (Haris, Sarindah, Yusni, & Raihan, 2012)

In Indonesia, women are at greater risk of developing UTIs than are men due to anatomical differences with a general population number of 5-15% (Pranoto, Kusumawati, & Hapsari, 2012). Microorganisms can reach the urinary tract by hematogenous or lymphatic dispersion, but there are many clinical and experimental evidence indicating that the rise of microorganisms from the urethra is the most common pathway that leads to UTI, especially organisms derived from

enteric (*E. coli* and *Enterobacteriaceae*) (Ikatan Ahli Urologi Indonesia, 2015)

Antibacterial therapy is the main therapy for urinary tract infections. The choice of the right antibacterial depends on the type of microorganism, the location of the infection, acute or chronic infection, initial or recurrent infection, side effects of the drug, and the results of the test for bacterial sensitivity to antibacterial (Dewi, Arimbawa, & Abdul Khodir Jaelani, 2018; Mailani, 2017). UTI is treated by broad-spectrum antibiotics and usually started empirically without performing antimicrobial susceptibility testing (Hammad, Sulaiman, Aziz, & Noor, 2017). This therapy can lead to antibiotic resistance and treatment failure because of unreasonable antibiotics prescriptions. According to the World Health Organization in 2014, antimicrobial resistance is increasingly a global threat for public health (World Health Organization, 2014)

UTI can be treated easily if the identification of bacteria which causes UTIs and antibiotic susceptibility analysis patterns was done (Farrell, Morrissey, de Rubeis, Robbins, & Felmingham, 2003). The aim of this study was to investigate the bacteria associated with UTI cases and their antibiotic susceptibility pattern in HOSPITAL Dr. Achmad Mochtar Bukittinggi, Indonesia.

METHOD

A retrospective study was performed at the urology department of Dr. Achmad Mochtar Bukittinggi Hospital during period from January 2016 to December 2018. Samples were selected using total sampling method. To be eligible for participants, samples must be a patient undergoing treatment of UTI at the urology department of Dr. Achmad Mochtar Bukittinggi Hospital. From the criteria, about 13 samples were obtained for this study. Antimicrobial susceptibility testing was performed with a standard procedure in the hospital. Secondary data was obtained from the result of data laboratory of patients that include gender and drugs that sensitive and resistant for patients. The result of this study the compared with literature and the guidelines of diagnosis and therapy of Dr. Achmad Mochtar Bukittinggi Hospital.

RESULT

Urine culture had been done for all patients who include in this study. Prevalence of UTI had higher in females (53.85%) than males (46.15%). Frequency of gender distribution of UTI in HOSPITAL Dr. Achmad Mochtar Bukittinggi period January 2016 to December 2018 was shown in Table 1. The most common organism was *E. coli* which was isolated from 13 patients with percentage 30.76% (4). *E. coli* was the predominant followed by *Hemoly* 15.38% (2), *E. Intermedium* 15.38% (2), *Pseudomonas* 7.69% (1), *E. Aeruginosa* 7.69% (1), *Staphylococcus aureus* 7.69% (1), *Staphylococcus epidermidis* 7.69% (1),

and *S. Sapro* 7.69% (1). The frequency distribution of isolated bacteria from urine culture of UTI patients was shown in Table 2. These data show that Gram-negative bacteria is the highest cause of UTI than Gram-positive bacteria.

Table 1. Frequency of gender distribution of UTI in HOSPITAL Dr. Achmad Mochtar Bukittinggi period January 2016 to December 2018

Gender	Frequency (%)
Male	6 (46.15)
Female	7 (53.85)
Total	13 (100)

Table 2. Frequency distribution of isolated bacteria from urine culture of UTI patients in HOSPITAL Dr. Achmad Mochtar, Bukittinggi period January 2016 – December 2018

Types of Bacteria	Frequency (%)	Total
Gram-positive bacteria		
<i>Staphylococcus aureus</i>	1 (7.69)	3
<i>Staphylococcus epidermidis</i>	1 (7.69)	
<i>S. sapro</i>	1 (7.69)	
Gram-negative bacteria		
<i>Escherichia coli</i>	4 (30.76)	10
<i>Pseudomonas sp</i>	1 (7.69)	
<i>Hemoly</i>	2 (15.38)	
<i>E. aeruginosa</i>	1 (7.69)	
<i>E. intermedium</i>	2 (15.38)	
Total	13 (100)	13

The antimicrobial susceptibility testing was carried out with a standard procedure in the hospital for all the bacterial isolates to the most common antibiotic agents used in the treatment of UTI as shown in Table 3. The common urinary pathogens such as *E. coli* showed resistance almost to all antibiotics

tested. *E. coli* showed an 50% resistance rate to cefuroxime and ciprofloxacin and 37.5% resistance rate to amoxcillin, ampicillin, levofloxacin, norfloxacin, and tetracyclin. *Pseudomonas* showed an 37.5% resistance rate to levofloxacin, norfloxacin, and tetracyclin, while *hemolysis*, *E. aeruginosa*, *E. intermedium*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *S. sapro* had 12.5% resistance rates, respectively.

Table 3. Antimicrobial resistance pattern of Gram-negative and Gram-positive bacteria from UTI patients in HOSPITAL Dr. Achmad Mochtar, Bukittinggi period January 2016 – December 2018

Antibacteri al		<i>E. coli</i>	<i>Pseudomonas</i>	<i>Haemolysis</i>	<i>E. aeruginosa</i>	<i>E. intermedium</i>	<i>S. aureus</i>	<i>S. epidermidis</i>	<i>S. sapro</i>
Amoxicillin *	A M L	3 7. 5 %	0%	0%	0%	0%	0 %	12. 5 %	0 %
Amikacin	A N	0 %	0%	0%	0%	0 %	12. 5 %	1 2. 5 %	0 %
Ampicillin	A M P	3 7. 5 %	0%	12. 5 %	12. 5 %	0 %	0 %	0 %	0 %
Aztreonam	A T M	1 2. 5 %	0%	0%	0%	12.5 %	0 %	0 %	0 %
Azithromycin	A Z M	0 %	0%	12. 5 %	0%	0%	0 %	1 2. 5 %	0 %
Cefazolin*	C Z	1 2. 5 %	0%	0%	0%	0 %	0 %	0 %	0 %
Cefepime	F E B	1 2. 5 %	0%	12. 5 %	0%	12.5 %	1 2. 5 %	12. 5 %	0 %
Cefuroxime *	C X M	5 0 %	0%	12. 5 %	12. 5 %	12.5 %	0 %	12. 5 %	0 %
Cefotaxime	C T X	1 2. 5 %	0%	12. 5 %	0%	12.5 %	1 2. 5 %	12. 5 %	0 %
Ceftazidime	C A Z	1 2. 5 %	0%	12. 5 %	0%	12.5 %	0 %	12. 5 %	0 %
Ceftri	C	2	0%	12.	0%	0%	1	0%	0

axone	R O	5 %		5%			2. 5 %		%
Cefoperazone	C F P	2 5 %	0%	0%	0%	0%	0 %	0%	0 %
Chloramphenicol	C	0 %	0%	12. 5 %	12. 5 %	0%	0 %	0%	1 2. 5 %
Ciprofloxacin*	C I P	5 0 %	12.5 %	12. 5 %	0%	0%	0 %	12. 5 %	1 2. 5 %
Clavulanic acid	A M C	1 2. 5 %	0%	0%	0%	0%	0 %	0%	0 %
Erythromycin	E	1 2. 5 %	12.5 %	0%	0%	0%	0 %	0%	1 2. 5 %
Gentamicin	G M	1 2. 5 %	12.5 %	12. 5 %	0%	12.5 %	0 %	12. 5 %	1 2. 5 %
Levofloxacin	L V X	3 7. 5 %	37.5 %	0%	0%	0%	0 %	12. 5 %	1 2. 5 %
Meropenem	M E M	0 %	0%	0%	0%	0%	0 %	12. 5 %	0 %
Nalidixic acid	N A	0 %	0%	0%	0%	0%	0 %	12. 5 %	0 %
Neomycin	N	0 %	0%	0%	0%	12.5 %	0 %	12. 5 %	0 %
Norfloxacin*	N O R	3 7. 5 %	37.5 %	12. 5 %	0%	25 %	1 2. 5 %	12. 5 %	1 2. 5 %
Sulfamethoxazole	S X T	1 2. 5 %	12. %	12. 5 %	12. %	0%	0 %	12. 5 %	1 2. 5 %
Tetracycline*	T E	3 7. 5 %	37.5 %	25 %	12. 5 %	12.5 %	0 %	0%	1 2. 5 %
Trimethoprim*	T M P	1 2. 5 %	12.5 %	0%	0%	12.5 %	0 %	12. 5 %	0 %

Note: * → Most resistant

DISCUSSION

Our study was conducted in case UTI with complications (53.8%) and without complication (46.2%) in Dr. Achmad Muchtar Hospital, Bukittinggi. From the result, UTI reported mostly infected women than men. Women have a greater risk of being infected with UTI than men (OR: 3.755, CI:95%; 1.714-8.227). UTI's occur in women significantly more than men - in

fact, 40% of women will get a UTI in their lifetimes while only about 12% of men will get the same condition (Al-Badr & Al-Shaikh, 2013). The primary reason for this is because of female anatomy. Urinary tract in women shorter than men, it means that bacteria do not have to travel as far from the urethral opening outside of the body to get to the bladder or other parts of the urinary tract. woman's urethra opening is located close to the anus, so it is easier to bring bacteria from the anus into the urethra. This is often done when wiping after urinating or passing a bowel movement, but it's also easy to do during sexual activity. While it is possible for a man to inadvertently transfer the bacteria as well, it is less likely since a male's urethra is further away.

UTI is listed among one of the most common infections caused by various Gram-positive and Gram-negative bacteria (Foxman, 2010). To successfully treat the patients who are suffering from UTI, it is crucial to accurately identify the causative pathogen. In this study, Gram-Negative bacteria (*Escherichia coli*) are the most common cause of UTI disease (30.76%) following by *Hemolysis* and *E. intermedium* (15.38%), *Pseudomonas* sp. and *E. aeruginosa* (7.69%). This result relates with other studies that state *Escherichia coli* was the common cause of UTI (Alanazi, Alqahtani, & Aleanizy, 2018)

Escherichia coli known as the most germ as a cause of UTI, these germs are flora normal in the colon and harmless, but on certain conditions of this germ can cause infection opportunistic if found in other organs, for example, lower UTI to pyelonephritis, meningitis in neonates, to sepsis. This *Escherichia coli* can spread through contaminated water, especially in individuals experiencing decreased conditions immune system (Mahon, Lehman, & George, 2017)

Escherichia coli uropatogen causes UTI can be explained through the mechanism of attachment of pili or colonized *Escherichia coli* in vagina and urinary tract in mucosal epithelium releasing adhesin compounds to adhere to bladder

mucosa, besides that there are other factors which accounts for the virulence of these germs are cytolysin and aerobactin, cytolysin kills effector cells and inhibits phagocytosis and chemotaxis of leukocyte cells. Aerobactin helps germs digest iron which is then used for cell metabolism germs, so *Escherichia coli* can easily replicate and penetrate the defense mechanism from host body, this process can take place faster in individuals who are immunocompromised (Mahon et al., 2017)

Antibiotic resistance is a specific type of drug resistance when a microorganism has the ability of withstanding the effects of antibiotics. Antibiotic resistance evolves via natural selection acting upon random mutation, but it can also be engineered by applying an evolutionary stress on a population. As bacterial resistance increased in recent decades, the isolates of the present study recovered from UTIs showed high resistance. Hence, Gram negative and Gram positive bacterial demonstrated resistance to at least one antibiotic. The result of this study shows that Bacteri Gram Negative (*E coli*) has resistance in 19 test antibacterial (76%). The most resistance of the bacterial isolates was against Cefuroxime and Ciprofolaxin (50%), in penicillin group 37.5%, fluoroquinolon group 37.5% and in tetracyclin group has resistance about 37.5%.

Cefuroxime is a second generation cephalosporin which has a broader spectrum than the first generation and is active against *Enterobacter* sp, indole-positive and *Klebsiella* sp. The resistance mechanism is the inability of antibiotics to reach their workplace or changes in PBP that are the target (Gilman and Goodman 2012). The inability of antibiotics to reach the target because bacteria produce beta-lactamase enzymes, both gram-positive and gram-negative bacteria. Gram-positive bacteria secrete beta-lactamase enzymes out of cells in relatively large amounts so that drugs that will penetrate the cell wall become inactive. Gram-negative bacteria secrete beta-lactamase enzymes in small amounts, but its strategic location is to the periplasma chamber. The drug that is able to

penetrate the outer membrane cannot reach its target, namely PBP (Goodman, 2008)

Ciprofloxacin is a quinolone group that works by inhibiting nucleic acid synthesis. Its antimicrobial activity is broad-spectrum bactericide. Resistance can arise during therapy through mutations in bacterial chromosome genes that encode DNA-gyrase or topoisomerase IV or through active transport of drugs out of bacteria (Goodman, 2008). The plasmid-mediated quinolone resistance (PMQR) gene *qnrA1* causes only a modest decrease in ciprofloxacin susceptibility but facilitates the selection of mutants with higher levels of ciprofloxacin resistance (1). In *Escherichia coli*, ciprofloxacin resistance results from mutations in the quinolone resistance-determining region (QRDR) of the GyrA subunit of DNA gyrase and mutations altering the regulation of efflux pumps, especially AcrAB (2, 3). Gyrase mutations are frequent in ciprofloxacin-resistant mutants of *E. coli* J53 without *qnr* but are surprisingly rare in its presence (Apsari, Dwicandra, & Abdul Khodir Jaelani, 2017; Hooper & George A. Jacoby, 2015). *Pseudomonas* bacteria shows the most resistance was against fluoroquinolone group (37.5%) and in tetracycline group (37.5%). Hemolysis, *E. aeruginosa*, *E. intermedium*, *Staphylococcus aureus*, *S. Epidermidis* and *S. sapro* has resistance level about 12.5% against test antibacterial.

The result shows that Gram Negative bacteria has resistance generally. It can be caused because of the Gram Negative Bacteria are able to make a self-defense mechanism against antibiotics with extrinsic and intrinsic factors. The intrinsic factors such as excessive use of antibiotics, irregular time taking medication, mis-use of antibiotics, inappropriate administration of antibiotics. Factor intrinsic included mediated plasmid. The ability of bacteria to make metabolites such as occurs in resistance to chloramphenicol, trimethoprim is caused by plasmid mediated. The formation of resistance can be reduced by: preventing the use of

antibiotics without difference in cases that do not require antibiotics, stopping the use of antibiotics in common infections, using the right antibiotics with the right dose also so that the infection will heal quickly, using antibiotics others if there are signs that an organism will become resistant to the antibiotics used previously (Pranoto et al., 2012; Triono & Purwoko, 2012)

Resistance can appear in a bacterium and spread to other bacteria. Bacteria develop resistance in various ways, including: (1) producing enzymes to destroy antibiotic molecules, (2) making "efflux pumps", which are special pumps that function to remove antibiotics out of their cells, (3) changing certain parts in bacterial cells who are usually targeted by antibiotics, so that they cannot be attacked again by antibiotics, and (4) develop alternative pathways that can no longer be attacked by antibiotics. Of course, these various resistance mechanisms will not work without a control or control system. The system is coordinated by resistance genes, which are contained in the plasmid and bacterial chromosomes (Kementriam Kesehatan Republik Indonesia, 2011; Sumolang, Porotu'o, & Standy Soeliongan, 2013).

CONCLUSION

Based on the results of the research conducted at Dr. HOSPITAL. Achmad Mochtar Bukittinggi period January 2016 – December 2018 women more often experience UTI than men. The most bacteria types found in UTIS are *Escherichia coli* bacteria, a Gram-negative colony resistant to quinolone antibacterials such as amoxicillin (25%), Cefepime (25%), Cefuroxime (50%), Ciprofloxacin (50%), Norfloxacin (37.5%), Sulfametaxazole (12.5%), and Tetracycline (37.5%).

ADVICE

Further examination of the pattern of resistance of bacteria to antibacterial, especially in diseases of urinary tract infections (UTI) periodically considering the

occurrence of germ pattern shifts and body resistance to antimicrobial and special attention in the use of antibiotics to be reduced and the inevitable recitency in the use of antibiotics. For the energy in the field of health services to be able to engage the community on how to prevent UTI disease especially in vulnerable groups of women, pregnant women, and parents

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