RESISTANCE PATTERN OF *Escherichia Coli* AGAINTS ANTIBIOTICS IN URINARY TRACT INFECTION PATIENTS IN RSUD DR. SOETOMO SURABAYA

Novi Ariana*[1], Pestariati[1], Retno Sasongkowati[1], Debby Kusumaningrum[2]

[1]Department of Health Analyst, Politeknik Kesehatan Kemenkes Surabaya, Indonesia [2]SMF Mikrobiologi, Dr. Soetomo General Academic Hospital, Indonesia

ABSTRACT

Pathogenic bacteria cause Urinary Infection imore or lessi about 85 - 95% are bacteria Escherichia coli. The treatment of Urinary Tract Infection (UTI) requires adequate supportive therapy and antibiotics, but antibiotic resistance is an obstacle in UTI treatment. This study aims to determine the types of antibiotics that are resistant to Escherichia coli in patients with UTI. This is an observational study with a descriptive method to determine the type of antibiotic-resistant to Escherichia coli in patients with UTI in the Laboratory of Clinical Microbiology RSUD Dr. Soetomo. Antibiotics that were resistant to Escherichia coli in UTI patients were cefazolin (80.49%), Amoxicillin Clavulanic Acid (73.17%), Ampicillin (73.17%), Tetracycline (68.29%), while antibiotics that were resistant to Escherichia coli ESBL was Amoxicillin Clavulanic Acid (100%), Ampicillin (100%), Cefazolin (99.7%), Aztreonam (99.7%), Ceftazidime (99.7%). The prevalence of Escherichia coli in UTI patients was 27.5%, while Escherichia coli ESBL was 72.5%. Based on the results of the research that has been obtained, it is better to do research on antibiotic resistance patterns periodically

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CORRESPONDING AUTHOR

Novi Ariana
✉novi.mikrobiologi@gmail.com
Clinical Microbiology. Jl. Mayjen Prof. Dr. Moestopo 6-8 GDC lt.5 Mikrobiologi Klinik, Surabaya, Indonesia

INTRODUCTION

Urinary Tract Infection (UTI) is an inflammatory response of the urothelial cells that line the urinary tract due to a bacterial infection characterized by bacteriuria and pyuria.[1] UTI is a common bacterial infection with an estimated 150 million patients every year worldwide. Surveillance studies in the United States reported 10.8 million patients attending UTI/year and 1.8 million patients (16.7%) hospitalized. Surveillance data with PPRA, Balitbangkes, WHO, in 2013 showed the prevalence of ESBL enzyme-producing bacteria in 6 Teaching Hospitals in Indonesia for *Escherichia coli* was 27-57% while *Klebsiella pneumoniae* was 32-56%.[2]

The pathogenic bacteria that cause UTI are approximately 85-95% are *Escherichia coli*, and 5-20 % *Enterobacteriaceae, Enterococcus and Staphylococcus.*[3]

The germ map of Dr. Soetomo Surabaya showed that the most common germs found in urine isolates were *Eschericia coli* (32.2%), *Klebsiella pneumoniae* (8.4%), *Pseudomonas aeruginosa* (4.8%), *Enterococcus faecalis* (8.0%), *Acinetobacter baumannii* (2.8%), *Enterobacter cloacae* (1.8%), *Proteus mirabilis* (1.2%).[4]

Besides UTIs it is the number one infection that leads to prescription of antibiotics after doctor visits. UTI symptoms are generally mild, and improper use of antibiotics can lead to antibiotic resistance, therefore it is important to establish appropriate criteria for treatment using narrow spectrum antibiotics for the optimal duration.[5]

Based on Silvia Sutandhio's research in 2015 at Dr. Soetomo, the most effective antimicrobials in inhibiting the growth of *Escherichia coli* from the isolates collected were meropenem (97.5%), amikacin (94.1%) and fosfomycin (85.5%). Meanwhile, the worst antimicrobial effectiveness against Eschericia coli were ampicillin (4.4%), tetracycline (16.7%), and nalidixic acid (18.3%). The diagnosis of Urinary Tract Infection is based on the urine culture method by counting the amount of bacterial colony from the urine specimen. It is said that bacteriuria is significant if bacteria are found in the urine = 103 CFU / ml, while it is said that the middle portion of the urine is 105 CFU / ml.[6]

Escherichia coli is a gram-negative rod bacteria which is the normal flora in the intestine. *Escherichia coli* can be opportunistic, produce endotoxins, have capsules and pili that allow it to attach to the patient's urinary tract mucosa when the body's weakened defense system colonizes and causes inflammation. The attachment of bacteria to epithelial cells is the initial stage and then the bacteria will colonize which in turn will cause UTIs.[7]

Escherichia coli can mutate, and become an organism that produces Extended-Spectrum Beta Lactamase (ESBL), an enzyme that can hydrolyze most beta-lactam antimicrobials. ESBL-producing genes can be passed from one bacterium to its offspring or transferred from one bacterium to another, the process of this resistance is called acquired resistance. The mechanism of bacterial resistance to antimicrobials can also occur intrinsically, for example by limiting cell wall permeability and efflux to prevent antimicrobials from reaching their target of action.[8]

Antimicrobial resistance is the ability of microbes to survive against the antimicrobial action. One of the management of infectious diseases is the administration of antimicrobials to kill or inhibit microbial growth, which will be destroyed by the human body's defense system, if the microbes that cause infection are resistant to the antimicrobials used, the microbes will survive and reproduce so that the infection process continues and becomes more severe.[9]

The irrational use of antibiotics in the treatment of UTIs can lead to the emergence of resistant bacteria as a result, the bacteria will be difficult to treat, the choice of antibiotics is limited, prolonging the length of hospital stay, the hospital burden increases. Antibiotic administration must be considered based on isolated bacteria with the patient's clinical condition and otherinvestigations. Therapy with rational antibiotic administration should be adjusted according to the sensitivity of the culture results.

MATERIALS AND METHODS

This is an observational study with a descriptive method to determine the type of antibiotic-resistant *Escherichia coli* bacteria in Urinary Tract Infection (UTI) patient in Laboratory Installation , Clinical Microbiology, RSUD Dr. Soetomo. This research was conducted period 1 July to 31 December 2018, population of research were all bacterial isolates Urinary Tract Infection (UTI) patients were examined in Microbiology Laboratory Installation, RSUD Dr. Soetomo, Surabaya.

RESULT

Table 1. Research data was based on the resistance pattern of *Escherichia coli* to antibiotics in urinary tract infections.

Sample code	Antibiotics	Culture results	Sensitive	Intermediate	Resistant
1	Amikasin (AK)	*Eschericia coli*	40	1	0
		Eschericia coli ESBL	107	1	0
2	Gentamicin (CN)	*Eschericia coli*	74	33	1
		Eschericia coli ESBL	74	33	1
3	Astreonam (ATM)	*Eschericia coli*	37	0	4
		Eschericia coli ESBL	1	107	108
4	Clavulanic Amoxicillin (AMC)	*Eschericia coli*	28	6	7
		Eschericia coli ESBL	0	107	1
5	Ampicillin (AMP)	*Eschericia coli*	10	30	1
		Eschericia coli ESBL	0	108	0
6	Ampicillin Sulbactam (SAM)	*Eschericia coli*	20	14	7
		Eschericia coli ESBL	3	105	0
7	Piperacillin Tazobactam (TZP)	*Eschericia coli*	35	3	3
		Eschericia coli ESBL	57	42	9
8	Cephazolin (KZ)	*Eschericia coli*	8	0	33
		Eschericia coli ESBL	1	0	107
9	Ceftacidine (CAZ)	*Eschericia coli*	37	0	4
		Eschericia coli ESBL	1	0	107
10	Sefotaxim (CTX)	*Eschericia coli*	37	0	4
		Eschericia coli ESBL	2	0	106
11	Seftriaksone (CRO)	*Eschericia coli*	37	0	4
		Eschericia coli ESBL	3	0	105
12	Sefepim (FEB)	*Eschericia coli*	35	0	6
		Eschericia coli ESBL	9	0	99
13	Cotrimosasol (CTX)	*Eschericia coli*	24	0	17
		Eschericia coli ESBL	25	0	83
14	Tetracyclines (TE)	*Eschericia coli*	13	0	28
		Eschericia coli ESBL	18	0	90
15	Ciprofloxacin (CIP)	*Eschericia coli*	24	0	17
		Eschericia coli ESBL	19	0	89
16	Lefofloxacin (LEV)	*Eschericia coli*	24	0	17
		Eschericia coli ESBL	20	1	87
17	Imipenem (IPM)	*Eschericia coli*	34	1	6
		Eschericia coli ESBL	84	12	12
18	Meropenem (MEM)	*Eschericia coli*	39	0	2
		Eschericia coli ESBL	9	13	4
Total *Eschericia coli* isolate				149	

From table 1, the results of the highest antibiotic resistance against Escherichia coli in a row from the highest are as follows: Cephazolin (80.49%), Amoxicillin Clavulanic Acid (73.17%), Ampicillin (73.17%), Tetracycline (68 , 29%). From table 1 also obtained the results of the highest antiobiotic resistance against

Escherichia coli ESBL in a row from the highest are as follows: Amoxicillin Clavulanic Acid (100%), Ampicillin (100%), Cefasolin (99%), Astreonam (99%), Ceftacidin (99%) (Figure 1).

From Table 2 obtained the results of the growth of Escherichia coli cultures were 41 (27.5%), while Escherichia coli ESBL were 108 (72.5%).

Table 2. Culture of Clinical Isolates for UTI Patients from July to December 2018

Culture results	Total	
	n	(%)
Escherichia coli	41	27.5
Escherichia coli ESBL	108	72.5
Total	149	100

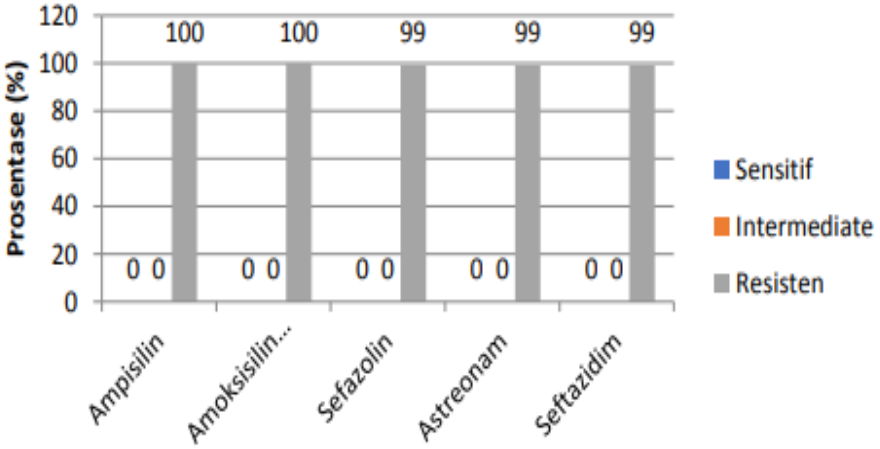

Figure 1. Distribution of ESBL *Escherichia coli* for the July - Dec 2018 period.

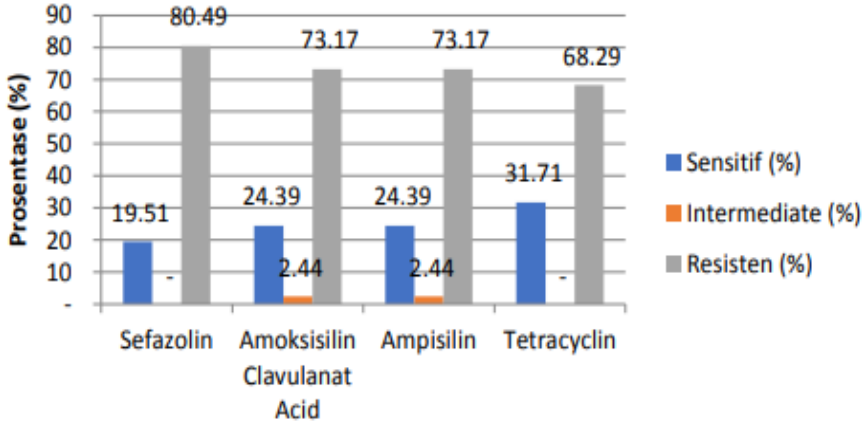

Figure 2. Distribution of *Escherichia coli* for the July-Dec 2018 period.
Description: Cephazolin (KZ), Amoxicillin Clavulanic Acid (AMC), Ampicillin (AMP), Tetracycline (TE), Astreonam (ATM), Ceftazidim (CAZ).

DISCUSSION

The results of this study found that the highest distribution of resistance to Escherichia coli was cefazoline, Amoxicillin Clavulanic Acid, Ampicillin, Tetracycline, while the highest ESBL *Escherichia coli* was

Amoxicillin Clavulanic Acid, Ampicillin, Cefazolin, Astreonam, Ceftazidime.

The provision of broad spectrum antibiotics and their combination which routinely is the management of infectious diseases by clinicians is one of the factors supporting changes in the pattern of bacteria that cause infection and the pattern of resistance to various antibiotics. The resistance of Escherichia coli to Sephalotin, Sephazolin, Ampicillin is due to the ability of bacteria to produce beta lactamase enzymes. Beta lactamase enzymes work on the synthesis of bacterial cell walls by inhibiting polymeration and adhesion of peptidoglycan to the cell walls. This resistance is because ESBL-producing bacteria have the ability to hydrolyze the beta-lactam membrane ring, which is played by the mutated beta-lactamase enzyme which is coded through plasmids. This causes an increase in beta lactamase enzyme activity. This enzyme will cause the bacterial cell wall to become resistant to antibiotics.[10]

Resistance can occur in several ways, such as damaging antibiotics with the enzymes produced, changing the antibiotic catch-point receptors, changing the physico-chemical target of antibiotics on bacterial cells, antibiotics cannot penetrate the cell walls, due to changes in cell wall properties. bacteria, antibiotics enter the bacterial cell, but are immediately removed from the bacterial cell, but are immediately removed from the cell by an active transport mechanism outside the cell. Studies have found that about 40 - 62% of antibiotics are used inappropriately, among other things, for diseases that do not require antibiotics. In the study the quality of antibiotic use in various parts of the hospital was found to be 30% to 80% not based on indications. The relatively high intensity of antibiotic use causes various problems and is a global threat to health, especially bacterial resistance to antibiotics. In addition to having an impact on morbidity and mortality, it also has a very high negative economic and social impact.[11]

Based on the results of the research that has been obtained, it is advisable to conduct research on antibiotic resistance patterns periodically so that it can be considered by clinicians in the first treatment of Urinary Tract Infections (UTIs) before obtaining urine culture results. Antibiotic administration should be considered based on isolated bacteria with the patient's clinical condition and other investigations. Need to do educating the clinician, the public in the administration of antibiotics must be adapted to h a sil culture so appropriate antibiotics wisely.

CONCLUSION

Based on the results of research on the resistance pattern of Escherichia coli to antibiotics in urinary tract infection patients conducted at Dr. Soetomo obtained several conclusions: 1) The types of antibiotics that are resistant to Escherichia coli in Urinary Tract Infection patients are cefazolin (80.49%), Amoxicillin Clavulanic Acid (73,17), Ampicillin (73,17), Tetracyclines (68,29). 2) The types of antibiotics that are resistant to Escherichia coli ESBL are Amoxicillin Clavulanic Acid (100%), Ampicillin (100%), Cefasolin (99%), Astreonam (99%), Ceftacidin (99%). 3) The prevalence of Escherichia coli in Urinary Tract Infection (UTI) patients was 27.5%, whereas *Escherichia coli* ESBL was 72.5%.

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