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ORIGINAL ARTICLE

The Bacterial Profile and Antibiotic Resistance Among Patients with Urinary Tract Infection in Surabaya, Indonesia

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ABSTRACT

Introduction: Urinary tract infections (UTIs) are mainly caused by microorganisms and occur in the urinary tract to the kidneys. Management of UTI related to antibiotic therapy, rational use of antibiotics is needed to prevent bacterial resistance. This objective of this study is to determine the pattern of bacteria, resistance and sensitivity to antibiotics in patients with UTI at Islamic Hospital Surabaya, Indonesia, in January 2019 - March 2020. **Methods:** This was an observational analytical study using a cross-sectional approach. Data were obtained from UTI patients' urine culture results and medical records. **Results:** There were 33 UTI patients, but only 22 patients (66,7%) showed positive to urine cultures with several types of bacteria. This study obtained *Escherichia coli* (24,0%) and *Enterococcus sp.* (24,0%) as the most bacteria causing UTI. These microorganisms showed resistance to Trimethoprim-sulfamethoxazole but sensitive against the antibiotics Fosfomycin, Nitrofurantoin, Ciprofloxacin, Levofloxacin, beta-lactam antibiotics (eg. Piperacillin-tazobactam, Amoxicillin-clavulanate). **Conclusion:** Our results showed that *Escherichia coli* and *Enterococcus sp.* as frequent bacterial found among UTI patients. Our results urged that initial screening for resistance/sensitivity pattern for antibiotics could help to choose suitable treatment for UTI patients.

Keywords: Antibiotics resistance, Antibiotic sensitivity, *Escherichia coli*, *Enterococcus sp.*, Urinary tract infections

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INTRODUCTION

Urinary tract infection (UTI) is marked by pathogenic microorganisms found in the urinary tract. It can be classified as common infections and it can lead to morbidity and mortality (1). The incidence of UTIs in Indonesia is relatively high and its prevalence is correlated with age. The prevalence of UTI among individual at the age of 40-60 years is 3.2% and it increases to 20% at the age of 65 or older. Men and women of all ages can suffer urinary tract infections. In case of women, 15% of them can experience one attack of acute UTI in their lifetime. The majority cases of UTI are asymptomatic. Pregnant women are among those who are prone to UTI infection with prevalence of 5-6% and increased to 10% for high risk individuals (2).

For better management of UTI, it is necessary to discriminate between uncomplicated and complicated UTI. Uncomplicated UTI imply to healthy individuals without abnormality in structural or neurological urinary tract. Inflammation of the bladder or known as cystitis as part of uncomplicated UTI. Other uncomplicated UTI, if it is involving waist pain and fever, this indicates infection of the kidneys (pyelonephritis). While complicated UTI imply to condition with urinary obstruction or retention caused by several condition such as immunosuppression, neurological disease, pregnancy, renal transplantation, renal failure, indwelling catheters and the existence of foreign bodies (eg. calculi) (3–5).

The typical cystitis symptoms are dysuria (pain on passing urine), frequency and urgency of urination and suprapubic pain. A diagnosis of UTI requires over 10^5 CFU/mL from a midstream urine specimen. In the majority of UTIs, the infecting organism comes from the patient's fecal flora (6). Biochemical tests help to investigate UTI, but the gold standard for UTI detection is using urine culture (7,8).

Numerous bacteria natively can develop resistance to specific classes of antibiotics. The first-line antibiotic choice will either be expansive (but microorganisms identified is susceptible to this antibiotic) or non-

adequate effectivity (since infected microorganisms intrinsic or acquired/developed resistance). Thus, it is important to identify the causative microorganisms and its resistance/susceptibility pattern to help in appropriate decision for starting antibiotic therapy (1).

MATERIALS AND METHODS

Samples

A retrospective study was conducted at Islamic Hospital Surabaya, Indonesia, between January 2019 to March 2020. The inclusion criteria were patients with all gender and age, and patients diagnosed UTI with urine cultures. The information about gender, age, antimicrobial susceptibility and resistance among antibiotics were collected from the medical records provided by hospital.

Antimicrobial Susceptibility Testing

All observed bacteria were tested for antibiotic resistance and susceptibility against various antibiotics using Kirby Bauer`s disc diffusion method. Antimicrobial discs (Oxoid, Ltd, UK) used in this study are ampicillin (10 µg), ceftriaxone (30 µg), amoxicillin-clavulanic acid (30 µg), ciprofloxacin (30 µg), gentamycin (10 µg), nitrofurantoin (50 µg), norfloxacin (10 µg), tetracycline (25 µg) were put onto inoculated Muller-Hinton agar plate. Incubation at 37˚C, then the inhibition zone was calculated with a caliper. For resistant and sensitivity confirmation, diameters of zone inhibition were then compared to the Clinical and Laboratory Standards Institute (CLSI) guidelines (9).

Statistical Analysis

Data analysis was performed descriptively, which included the distribution of UTI patients based on sex, age, bacterial patterns, and antibiotic susceptibility patterns. All data were showed as n (%).

RESULTS

Patient Characteristics

Our results showed 23 patients were positive UTI based on urine culture (69.70%). Based on the gender of UTI patients, it showed the highest incidence in female patients with 19 patients (57.58%) compared to male patients who only reached 4 patients (12.12%). There are no significantly different between gender and prevalence of UTI (Table I, $\chi 2 = 3.74$ and p=0.05).

While based on Ministry of Health Republic of Indonesia, we categorize group of age to child (0-11 years old), teenager (12-25 years old), adult (26-45 years old), elderly (45-65 years old) and seniors (above 65 years old). We found that in children, adult and elderly have high prevalence of UTI with 21.21%, 18.19% respectively (Table II). But again, the difference among range group of age does not correlate with the difference prevalence of UTI ($\chi^2 = 2.16$ and p=0.71).

Tabel I : Distribution of Urinary Tract Infection based on Gender and Age

Characteristics	Urinary Tract Infection (UTI)		Chi Square	#p
	Positive	Negative		
	n (%)	n (%)		
Gender				
Female	19 (57,58)	5 (15.15)	3.74	0.05
Male	4 (12.12)	5 (15.15)		
Total	23 (69.70	10 (30.30)		
Age				
0-11 years	7 (21.21)	2 (6.06)	2.16	0.71
12-25 years	1 (3.03)	1 (3.03)		
26-45 years	6 (18.19)	4 (12.12)		
46-65 years	6 (18.19)	1 (3.03)		
>65 years	3 (9.10)	2 (6.06)		
Total	23 (69.70)	10 (30.30)		

Tabel II : Distribution of Microorganisms found in Urinary Tract Infection

Microorganisms	Total n (%)
Escherichia coli	6 (24)
Enterococcus sp.	6 (24)
Pseudomonas aeruginosa	3 (12)
Klebsiella pneumoniae	2 (8)
Staphylococcus haemolyticus	2 (8)
Staphylococcus non-haemolyticus	2 (8)
Proteus mirabilis	1 (4)
Acinetobacter sp.	1 (4)
Staphylococcus saprophyticus	1 (4)
Staphylococcus epidermidis	1 (4)
Total	**25 (100)**

In this outpatient setting, we found all cases of uncomplicated UTI. There were four patients (17.39%, all female) with recurrent UTI cases among four patients there was one patient with complicated UTI (catheter usage) but in found negative from urine culture. Mainly symptoms observed in these patients were dysuria (14 patients, 60.87%), suprapubic pain (9 patients, 39.13%).

Escherichia coli and *Enterococcus sp.* were dominantly found in UTI patients

Our result showed that *E. coli* and *Enterococcus sp* were dominantly found in UTI (24% Table 2). There are three out of 22 patients with positive urine culture has two different types of bacteria in one patient. Other bacteria, such as *Pseudomonas aeruginosa* (12.0%), *Klebsiella pneumoniae* (8.0%), *Staphylococcus haemolyticus* (8.0%), *Staphylococcus non-haemolyticus* (8.0%), *Proteus mirabilis* (4.0%), *Acinetobacter sp.*

Tabel III : Antibiotic Resistance among Microoganism found in Urinary Tract Infection

Microoganisms	Antibiotic Resistance (%)									
	Ciprofloxacin	Levofloxacin	Cefepime	Ceftriaxone	Piperacillin tazobactam	Cefazolin	Amoxicillin clavulanate	Fosfomycin	Nitrofurantoin	Trimethoprime-sulfamethoxazole
Escherichia coli	40,0	66,7	40,0	40,0	0,0	0,0	33,3	0,0	0,0	66,7
Enterococcus sp.	20,0	33,3	100,0	100,0	0,0	0,0	0,0	25,0	0,0	100,0
Pseudomonas aeruginosa	0,0	0,0	0,0	100,0	0,0	100,0	100,0	0,0	0,0	100,0
Klebsiella pneumoniae	0,0	0,0	100,0	50,0	0,0	0,0	0,0	0,0	0,0	0,0
Staphylococcus haemolyticus	0,0	0,0	100,0	100,0	0,0	100,0	100,0	0,0	0,0	100,0
Staphylococcus non-haemolyticus	0,0	50,0	0,0	100,0	100,0	0,0	0,0	50,0	0,0	50,0
Proteus mirabilis	100,0	0,0	0,0	100,0	0,0	100,0	0,0	0,0	100,0	0,0
Acinetobacter sp.	0,0	0,0	0,0	100,0	0,0	0,0	0,0	0,0	0,0	100,0
Staphylococcus saprophyticus	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	100,0
Staphylococcus epidermidis	0,0	0,0	100,0	0,0	100,0	0,0	100,0	0,0	0,0	0,0

Tabel IV : Antibiotic Sensitivity among Microoganism found in Urinary Tract Infection

Microoganisms	Antibiotic Sensitivity (%)									
	Ciprofloxacin	Levofloxacin	Cefepime	Ceftriaxone	Piperacillin tazobactam	Cefazolin	Amoxicillin clavulanate	Fosfomycin	Nitrofurantoin	Trimethoprime-sulfamethoxazole
Escherichia coli	60,0	33,3	60,0	60,0	100,0	0,0	66,7	75,0	100,0	33,3
Enterococcus sp.	60,0	66,7	0,0	0,0	100,0	0,0	100,0	75,0	100,0	0,0
Pseudomonas aeruginosa	100,0	100,0	100,0	0,0	100,0	0,0	0,0	100,0	0,0	0,0
Klebsiella pneumoniae	100,0	100,0	0,0	0,0	0,0	0,0	100,0	100,0	0,0	100,0
Staphylococcus haemolyticus	100,0	100,0	0,0	0,0	0,0	0,0	0,0	0,0	100,0	0,0
Staphylococcus non-haemolyticus	0,0	50,0	100,0	0,0	100,0	0,0	100,0	50,0	0,0	50,0
Proteus mirabilis	0,0	0,0	100,0	0,0	100,0	0,0	0,0	0,0	0,0	100,0
Acinetobacter sp.	100,0	100,0	0,0	0,0	100,0	0,0	0,0	100,0	0,0	0,0
Staphylococcus saprophyticus	100,0	100,0	0,0	0,0	0,0	0,0	0,0	0,0	100,0	0,0
Staphylococcus epidermidis	100,0	100,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0

(4.0%), *Staphylococcus saprophyticus* (4.0%), and *Staphylococcus epidermidis* (4.0%) were also found in the urine culture of UTI patients.

Antimicrobial Resistance and Susceptibility Pattern

Most of the bacteria that cause UTIs experienced >60% resistance to several antibiotics. including *Escherichia coli* and *Enterococcus sp. Escherichia coli* showed resistant to Levofloxacin and Trimethoprim-sulfamethoxazole. *Enterococcus sp.* showed resistant to Cefepime, Ceftriaxone, and Trimethoprim-Sulfamethoxazole. Among several tested antibiotics Trimethoprim-sulfamethoxazole and Ceftriaxone showed high resistance in seven type of microorganisms found in UTI patients (Table III).

In addition to antibiotic resistance, most bacteria still showed sensitivity >60% of several antibiotics such as quinolone antibiotic (ciprofloxacin and levofloxacin). piperacillin tazobactam. *Escherichia coli* showed sensitive to Ciprofloxacin, Cefepime, Ceftriaxone, Piperacillin-tazobactam, Amoxicillin-clavulanate, Fosfomycin, and Nitrofurantoin. *Enterococcus sp.* showed sensitive to Ciprofloxacin, Levofloxacin, Piperacillin-tazobactam, Amoxicillin-clavulanate, Fosfomycin, and Nitrofurantoin (Table IV).

DISCUSSION

Urinary tract infection is included in the most common infection experienced by human in wide range of age, both male and female. Though our result showed female preference, which is prone to UTI, but this difference was not statistically significant. One possible answer could be due to anatomical difference, in which female has a shorter urethra than their counterpart. With shorter urethra, it is easy for pathogens to travel inside to reach the bladder (10). Another risk it will be high exposure to anal pathogens which can double its chance to UTI (11). Our result also showed that there were 4 female patients with recurrent UTI. The risk factor for recurrent UTI in female with normal urinary tract anatomy, is the frequency of sexual intercourse (12).

Based on age, individual in the range of 26-45 and 46-65 years old were susceptible to UTI. The increase in age can increase the chances of UTI (13). But in this study, we didn`t find the significant in age could lead to difference prevalence of UTI. Among those infected in pre-menopausal age, the risk factors for UTI are the age of the first UTI, the onset of symptoms right after sexual intercourse, maternal history of UTI and voiding dysfunction, the use of contraception(14–16). While in children, UTI symptoms can be distinguish by the urgency to void, daytime incontinence, and increase or decrease in the frequency of urination without any neurological disease or abnormality in the lower urinary tract (17). Elderly patients also have a risk of UTI infection. The study results showed that beyond 65 years old patients (9.10%) also suffer UTI. In the elderly, the whole system in the body will degenerate. One of them is the degeneration of the bladder so that its capacity to resettle urine is reduced. Decreased bladder capacity and frequent bladder contractions can cause urgency and frequency (18).

Most patients with positive urine cultures are diagnosed with cystitis. Cystitis is the most frequently seen type of lower UTI. Clinical symptom of cystitis is acute dysuria (19). With an increased in age, the recurrence rate may increase (16). The determinant factor for recurrence rate is frequent sexual intercourse (12).

Most uncomplicated UTI cases are caused by gram negative bacteria such as *E. coli*, *Enterococcus* species, *Klebsiella* species, *Proteus* species, *Staphylococcus epidermidis* (19). *Uropathogenic Escherichia* coli (UPEC) is an agent often found as a cause of UTI, including cystitis and pyelonephritis. P fimbriae is an adherence factor possessed by UPEC strains, which serves to bridge the attachment of Escherichia coli bacteria to uroepithelial cells. Therefore, the digestive tract of patients with *Escherichia coli* who have P fimbriae is more at risk for UTI than the general population (20).

Antimicrobial therapy is necessary for UTI treatment. As for lower UTI, recommended first regimen are trimethoprim-sulfamethoxazole (TMP-SMX) for three days, nitrofurantoin for 5 days or fosfomycin. While for alternative it is also recommended to treated with ciprofloxacin for three days, levofloxacin for three days or beta-lactam antibiotics such as amoxicillin-clavulanate (21). Our study showed that several bacteria showed resistance to TMP-SMX, so this antibiotic is not recommended for treated UTI patient in this study. Other study showed that there is an increase in TMP-SMX resistance thus, it is advisable to use fluoroquinolones and nitrofurantoin (22). As for alternative treatment, our study showed that all bacteria found were still sensitive to ciprofloxacin, levofloxacin and beta-lactam antibiotics (eg., amoxicillin-clavulanate). We can conclude that in our study it is still safe to use first line regimen such as nitrofurantoin and Fosfomycin (except TMP-SMX) to treat lower UTI or acute uncomplicated cystitis as it is observed in this study.

CONCLUSION

This study showed that Escherichia coli and Enterococcus sp. were the most common cause of UTI with the same percentage of 24.0%. Antibiotic sensitivity pattern showed that microorganisms found in this study still sensitive to first line regimen such as nitrofurantoin and Fosfomycin also several alternative antibiotics such as ciprofloxacin, levofloxacin, and amoxicillin-clavulanate, Piperacillin tazobactam.

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REFERENCES

REFERENCES

1. Dasgupta R, Rane A, Chiu C, Cohen D, Grabe M, King D, Lee HA, Mufti UB, Shaikh TSA. Urinary Tract Infection. 1st ed. Rane A, Dasgupta R, editors. London: Springer-Verlag; 2013.
2. Sasongkowati R, Chitraningtyas D, Suliati, Christyaningsih J. The study on the susceptibility of Enterococcus faecalis and Klebsiella ozaenae cause UTI to antibiotics in East Java, Indonesia. Res J Pharm Biol Chem Sci. 2015;6:1539–44.
3. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13(5):269–84. Available from: https://pubmed.ncbi.nlm.nih.gov/25853778
4. Foxman B. Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am. 2014;28(1):1-13. Available from: https://doi.org/10.1016/j.idc.2013.09.003
5. Hannan TJ, Totsika M, Mansfield KJ, Moore KH, Schembri MA, Hultgren SJ. Host-pathogen checkpoints and population bottlenecks in persistent and intracellular uropathogenic Escherichia coli bladder infection. FEMS Microbiol Rev. 2012;36(3):616–48.
6. Jones T. Crash Course Renal and Urinary System. 4th ed. Horton-Szar D, editor. St. Louis Missouri: Mosby Ltd; 2015.
7. Cheesbrough M. District Laboratory Practice in Tropical Countries Part 2. 2nd ed. Cambridge, New York: Cambridge University Press; 2006.
8. Chu CM, Lowder JL. Diagnosis and treatment of urinary tract infections across age groups. Am J Obstet Gynecol. 2018;219(1):40–51.
9. CLSI. M100S Performance Standards for Antimicrobial. 26th ed. Wayne P., editor. Clinical and Laboratory Standards Institute; 2016.
10. Finer G, Landau D. Pathogenesis of urinary tract infections with normal female anatomy. Lancet Infect Dis. 2004;4(10):631–5.
11. McLellan LK, Hunstad DA. Urinary Tract Infection: Pathogenesis and Outlook. Trends Mol Med. 2016;22(11):946–57. Available from: https://pubmed.ncbi.nlm.nih.gov/27692880
12. Kodner CM, Gupton EKT. Recurrent urinary tract infections in women: Diagnosis and management. Am Fam Physician. 2010;82(6):638–43.
13. Schmiemann G, Kniehl E, Gebhardt K, Matejczyk MM, Hummers-pradier E. The Diagnosis of Urinary Tract Infection. 2010;107(21):361–8.
14. Mohsin R, Siddiqui KM. Recurrent urinary tract infections in females. J Pak Med Assoc. 2010;60(1):55–9.
15. Foster RTS. Uncomplicated urinary tract infections in women. Obstet Gynecol Clin North Am. 2008;35(2):235–48.
16. Scholes D, Hooton TM, Roberts PL, Stapleton AE, Gupta K, Stamm WE. Risk factors for recurrent urinary tract infection in young women. J Infect Dis. 2000;182(4):1177–82.
17. Hellström AL, Hanson E, Hansson S, Hjälmås K, Jodal U. Micturition habits and incontinence in 7-year-old Swedish school entrants. Eur J Pediatr. 1990;149(6):434–7.
18. Meiner SE, Yeager JJ. Gerontologic Nursing. 7th ed. St. Louis, Missouri: Elsevier; 2018.
19. Colgan R, Williams M. Diagnosis and treatment of acute uncomplicated cystitis. Am Fam Physician. 2011;84(7):771–6.
20. Bien J, Sokolova O, Bozko P. Role of uropathogenic escherichia coli virulence factors in development of urinary tract infection and kidney damage. Int J Nephrol. 2012;2012:1-15.
21. Still KL, Norwood DK. Uncomplicated Urinary Tract Infections: A Focus on Women's Health. US Pharm. 2012;37(9):56–60.
22. Drekonja DM, Johnson JR. Urinary tract infections. Prim Care. 2008;35(2):345–67.

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PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5