**Quantitative Study of Antibiotic Use in Urinary Tract Infection Patients at RSU X in East Jakarta 2019**

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| ***Keywords***:  Antibiotics, urinary tract infections, ATC/DDD, DU 90% | **ABSTRACT**  Urinary tract infection is a health problem that can increase morbidity and even increase the death rate both in Indonesia and in the world. Urinary tract infection is the second most common infectious disease after upper respiratory tract infection which in its treatment must use antibiotic therapy, so the treatment must be appropriate and rational. The purpose of this study was to determine the use of antibiotics quantitatively using the ATC/DDD and 90% DU methods in patients with urinary tract infections at RSU X in East Jakarta. Methods, This research is a descriptive study using a cross-sectional design. Data collection was carried out retrospectively through the medical records of urinary tract infection patients at RSU X in East Jakarta in 2019, data analysis was carried out using the ATC/DDD method and DU 90%, sample size was 115 urinary tract infection patients who met the inclusion and exclusion criteria. The results showed that the total DDD/100 patient-days in this study was 96.65% with the highest type of antibiotic, namely levofloxacin, 44.07% DDD/100 patient-days. Drugs included in the DU segment 90% were levofloxacin (45.60%), ceftriaxone (21.54%), cefoperazone (11.33%), and amoxicillin clavulanate (9.00%). Keywords: Antibiotics, urinary tract infection, ATC/DDD, 90% DU |

**INTRODUCTION**

Infectious diseases are one of the main health problems that cause morbidity and even mortality of millions of people in various developed and developing countries including Indonesia (Hikmawati and Setiyabudi, 2021). The World Health Organization (WHO) states that as many as more than 16 million deaths in the world in 2016 were caused by infectious diseases, one of which is urinary tract infections (Talebi Bezmin Abadi *et al.*, 2019).

Urinary tract infection (UTI) is an infectious disease that occurs due to the presence of bacteria in the urine with very large numbers (Beadini *et al.*, 2023). Urinary tract infections are the second most common infectious disease after upper respiratory tract infections (Noori *et al.*, 2023). The incidence of urinary tract infections in the world is quite high, the results of research by the American Urological Association in 2016, stated that around 150 million people in the world experience urinary tract infections with 1.8 million inpatient visits per year. According to the Centers for Disease Control and Prevention (CDC) in 2007, about 8.6 million people in America suffer from urinary tract infections of which 84% occur in women5. According to the Ministry of Health of the Republic of Indonesia in 2014 quoted by Irawan E, Mulyana (2018) stated that the number of patients with urinary tract infections in Indonesia is estimated to reach 90-100 cases per 100,000 population per year or around 180,000 cases per year, where the treatment must use antibiotics7.

Antibiotics used for the treatment of urinary tract infections are generally trimethoprim-sulfamethoxazole, phosphomycin, nitrofurantoin, ciprofloxacin, levofloxacin, and amoxicillin clavulanate4. Based on a preliminary survey of antibiotic use at RSU X January-December 2019, it shows that antibiotics used to treat urinary tract infections include cefixime, ceftriaxone, meropenem, ciprofloxacin, levofloxacin, cefoperazon, claneksi (amoxicillin + clavulanate), cefoperazon + sulbactam, phosphomycin, cefepim, cefotaxime, and ampicillin sulbactam.

According to WHO, antibiotics are the most widely used drug class in the world related to the number of infectious events caused by bacteria, so their use must be appropriate and rational. The purpose of this study was to determine the quantitative use of antibiotics with the ATC / DDD and DU methods 90% in urinary tract infection patients at RSU X in JakaTimur in 2019 (Yulia, Mariza and Herawati, 2020). To achieve this goal, it is necessary to conduct a study on the use of antibiotics in UTI patients at RSU X in East Jakarta (Karuniawati, van Doorn and Hamers, 2022). The study used quantitative analysis with the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) method (Apriyanti, 2023). This method is a classification and measurement system for drug use recommended by WHO to determine the accuracy of the average dose per day of antibiotic use in adult patients and DU 90% (Morris, 2014).

The results of research conducted at one of the hospitals in Yogyakarta area in 2004, 2006, and 2008 on the comparison of the use of antibiotics in urinary tract infections with the ATC / DDD method, showed a total DDD value in 2004 of 105 (Karuniawati, van Doorn and Hamers, 2022).

DDD/100 patient-days, with a DU of 90% namely amoxicillin (41.81%) and ciprofloxacin (47.5%). In 2006 showed a total DDD value of 107.3 DDD/100 patient-days with a DU of 90%, namely amoxicillin (40.34%), ciprofloxacin (44.89%), and ceftriaxone (9.37%)11.

Research conducted at General Hospitals in India in 2011 with the same method showed a total DDD value of 2.82 DDD/1000 inhabitants-day, with 90% DU namely norfloxacin (24.46%), cefixime (22.34%), amoxicillin (17.02%), metronidazole (15.95%), and ciprofloxacin (14.18%)12.

The results of a similar study with the ATC / DDD method in hospitals in Jepara in 2012 showed a total DDD value of 100.61 DDD / 100 patient-days, with 90% DU namely ciprofloxacin (31.74%), amoxicillin (25.72%), ceftriaxone (13.73%), cefotaxime (12.93%), metronidazole (4.48%), and cefixime (2.92%)13.

The results of another study with a similar method at Khrisna hospital in Karad in 2015 showed a total DDD value of 39.60 DDD / 1000 inhabitants-day, with antibiotics that DU 90% namely ceftriaxone (32.60%), azithromycin (14.34%), ciprofloxacin (10.81%), nitrofurantoin (5.85%), amoxicillin (5.29%), cefixime (4.25%), amikacin (3.76%), levofloxacin (2.98%), amoxicillin + clavulanate (2.81%), cefepim (2.43%), cefodocsim (2.21%) and norfloxacin (1.87%)14.

Another study in tertiary hospitals in South India in 2015 showed DDD values of 47.38 DDD/1000 inhabitants-day, with antibiotics that were 90% DU namely cefoperazon + sulbactam (37.53%), nitrofurantoin (15.32%), ofloxacin (10.09%), ciprofloxacin (8.08%), amikacin (5.42%), norfloxacin (4.69%), doxycycline (4.60%), and levofloxacin (3.65%)15.

The results of other studies at Azeezia, Kollam, and Kerala hospitals in India in 2018 showed a total DDD value of 21.79 DDD/1000 inhabitants-day, with antibiotics that were 90% DU namely ceftriaxone (35.52%), ciprofloxacin (20, 47%), cefotaxime (16.98%), ofloxacin (6.56%) norfloxacin (6.06%), and amikacin (5.14%)16.

Another study at Dr. Moewardi Hospital in 2018 showed a total DDD value of 11.45 DDD / 100 patient-days, with antibiotics that DU 90%, namely ceftriaxone (63.97%), levofloxacin (24.42%), ciprofloxacin (4.34%), meropenem (3.49%), cefoperazon + sulbactam (2.76%), cephalozolin (0.58%), and ceftazidim (0.44%)17.

Based on the background description above, it shows that urinary tract infection is an infectious disease caused by bacteria, dangerous and can cause morbidity and even mortality, therefore it is necessary to study the use of antibiotics in patients suffering from urinary tract infections. The study was conducted using the ATC / DDD and DU 90% methods, the aim was to determine the number and type of antibiotics used by urinary tract infection patients hospitalized at RSU X in East Jakarta in 2019.

**RESEARCH METHODS**

**Research Design**

This study used a cross-sectional research design with retrospective data collection, namely by tracing medical record documents of urinary tract infection patients hospitalized at RSU X in East Jakarta in January-December 2019.

**Research Population**

The population in this study was all adult patients from the age of 18 years suffering from urinary tract infections who were hospitalized at RSU X from January - December 2019. The sample size in this study was 115 UTI patients who met the inclusion and exclusion criteria, data collected in addition to patient characteristics. The use of drugs, as well as laboratory data as support (urinalysis tests: leukocytes, leukocytes esterase, and bacteria), patients with medical records and patient status contain complete information.

**Data Analysis**

**Univariat Analysis**

Data processed using univariate analysis are patient characteristics which include:

a. Age

b. Gender

c. Comorbidities

d. Length of treatment days.

**Data Analysis with ATC/DDD Method and DU 90%**

Data analysis was carried out by calculating the quantity of antibiotic use in urinary tract infection patients in the inpatient installation of RSU X with the ATC / DDD method processed with a combination of Microsoft Excel 2007 programs.

Formula:

DDD/100 *patient days* =

**RESULTS AND DISCUSSION**

**Research Results**

**Patient Characteristics Data**

**Table 1. Frequency Distribution of Urinary Tract Infection Patient Characteristics at RSU X in East Jakarta in 2019**

|  |  |  |  |
| --- | --- | --- | --- |
| **No.** | **Characteristics** | **Frequency (n = 115)** | **(%)** |
| 1. | **Gender:**  1. Man  2. Woman | 43  72 | 37,4  62,6 |
| 2. | **Age:**  1. 18-30  2. 31-40  3. 41-50  4. 51-60  3. 61-70  6. >70 | 19  8  19  23  30  16 | 16,5  7  16,5  20  26,1  13,9 |
| 3. | **Comorbidities:**  1. There are comorbidities  2. No Comorbidities | 112  3 | 97,4  2,6 |
| 4. | **Length of Day care (days):**  1. 1-3  2. 4-7  3. >7 | 21  75  19 | 18,3  65,2  16,5 |

The table above shows the characteristics of urinary tract infection patients hospitalized at RSU X, the sex of the most subjects is female (62.6%), the age of the subjects ranges from 18-70 years, the most ranges from 51-70 years (about 60%), subjects who have comorbidities (97.4%), and the length of hospitalization days ranges the most from 4-7 days (65.2%).

**Overview of the types of comorbidities**

**Table 2. Distribution of Comorbidities for Urinary Tract Infection Patients in the Inpatient Installation of RSU X in 2019**

|  |  |  |  |
| --- | --- | --- | --- |
| **No.** | **Comorbidities** | **Frequency (n= 301)** | **(%)** |
| 1 | Hypokaleemia | 31 | 10,3 |
| 2 | Dyspepsia | 26 | 8,7 |
| 3 | Diabetes mellitus | 23 | 7,6 |
| 4 | Hypertensive | 20 | 6,6 |
| 5 | Anemia | 20 | 6,6 |
| 6 | Hematuria | 15 | 5,0 |

Table 3.2 shows that the most common types of comorbidities in urinary tract infection patients in the inpatient installation of RSU X in 2019 were hypokalemia (10.3%), followed by dyspepsia (8.7%), diabetes mellitus (7.6%), hypertension (6.6%), anemia (6.6%), hematuria (5%)

**Distribution of Antibiotic Therapy Use Profile**

**Table 3. Profile Distribution of Antibiotic Therapy Use in UTI Patients in RSU X Inpatient Installation in 2019**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No.** | **Types of therapy** | **Drug Name** | **Frequency (n=115)** | **(%)** |
| 1. | Monotherapy | **Fluorokuinolon**  Levofloksasin | 34 | 29,6 |
| **Sefalosporin**  Sefoperazon  Seftriakson  Sefoperazon + Sulbaktam  Sefiksim  Sefepim  Sefotaksim | 27  24  6  2  1  1 | 23,5  20,9  5,2  1,7  0,9  0,9 |
| **Penisilin**  Amoksisilin + klavulanat  Ampisilin + Sulbaktam | 10  1 | 8,7  0,9 |
| **Karbapenem**  Meropenem | 3 | 2,6 |
| **Golongan Lain**  Fosfomisin | 2 | 1,7 |
| **Total** | | | **111** | **96,6** |
| 2. | Combination | **Penisilin +Fluorokuinolon**  (Amoksisilin + klavulanat) + Levofloksasin | 2 | 1,7 |
| **Fluorokuinolon + Sefalosporin**  Levofloksasin + Seftriakson | 2 | 1,7 |
| **Total** | | | **4** | **3,4** |

Table 3.3 shows that antibiotic use is grouped based on the type of therapy received by patients, where as many as 96.6% of urinary tract infection patients received monotherapy and 3.4% of patients received combination therapy. The most widely prescribed antibiotic as monotherapy was levofloxacin (29.6%), followed by cefoperazon (23.5%), ceftriaxone (20.9%), and amoxicillin + clavulanate (8.7%). As for the combination therapy of antibiotics prescribed are (amoxicillin, clavulanate) with levofloxacin (1.7%) and levofloxacin with ceftriaxone (1.7%).

**Table 4. Number of Days to Treat Urinary Tract Infection Patients at RSU X Years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No.** | **Moon** | **n (115)** | **LOS (hari)** | **Rata-rata hari** |
| 1 | January | 5 | 26 | 5,20 |
| 2 | February | 6 | 29 | 4,83 |
| 3 | March | 2 | 14 | 7,00 |
| 4 | April | 7 | 36 | 5,14 |
| 5 | May | 8 | 43 | 5,38 |
| 6 | June | 4 | 22 | 5,50 |
| 7 | July | 11 | 70 | 6,36 |
| 8 | August | 14 | 60 | 4,29 |
| 9 | September | 29 | 129 | 4,45 |
| 10 | October | 13 | 51 | 3,92 |
| 11 | November | 12 | 61 | 5,08 |
| 12 | Desember | 4 | 11 | 2,75 |
| **Total** | | **115** | **552** | **59,9** |
| **Average** | | **9,58** | **46** | **4,99** |

LOS (length of stay) is the length of the patient's stay starting from the first day the patient enters the hospital until the patient is discharged from the hospital. LOS was obtained from medical records of 115 research samples. Table 3.4 shows that the average LOS of urinary tract infection patients with or without comorbidities in the inpatient installation of Budhi Asih Hospital in 2018 was 5 days. This means that in 2018 out of 115 study subjects, the average hospitalization for 5 days for the total number of patient inpatient days was 552 days

**Quantity of Antibiotic Use for Urinary Tract Infection Patients at RSU X in East Jakarta in 2019**

**Table 5. Distribution of Antibiotic Use and Calculation of DDD/100 patient-days values at Budhi Asih Hospital for the 2019 Period**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Golongan** | **Medicine**  **Antibiotik** | **Preparatory Forms** | **DDD Standard Values from WHO (g)** | **Preparatory Strength (g)** | **Usage Count (g)** | **DDD/100 *patien-days*** |
| Fluorokuinolon | **Levofloksasin** | Tablet | 0,5 | 0,5 | 2,5 | **44,07** |
| Injection | 0,75 | 119,25 |
| Sefalosporin | **Seftriakson** | Injection | 2 | 1 | 230 | **20,82** |
| **Sefoperazon** | Injection | 4 | 1 | 242 | **10,95** |
| Sefiksim | Capsule | 0,4 | 0,2 | 6,48 | **2,93** |
| Sefepim | Injection | 4 | 1 | 6 | **0,27** |
| Sefoperazon + Sulbaktam | Injection | 4 | 1 | 40 | **1,81** |
| Sefotaksim | Injection | 4 | 1 | 27 | **1,22** |
| Penisilin + Inhibitor Beta Laktamase | **Amoksisilin + Klavulanat** | Injection | 3 | 1 | 144 | **8,69** |
| Ampisilin + Sulbaktam | Injection | 6 | 1 | 48 | **1,45** |
| Karbapenem | **Meropenem** | Injection | 3 | 1 | 57 | **3,44** |
| Other Groups | Fosfomisin | Injection | 8 | 2 | 44 | **1,00** |

Table 5 above shows that there are 5 classes of antibiotics used as therapy in urinary tract infection patients. After analysis with the DDD method, there were 4 major antibiotics used, namely levofloxacin 44.07 DDD / 100 patient-days, followed by ceftriaxone 20.82 DDD / 100 patient-days, cefoperazon 10.95 DDD / 100 patient-days, and amoxicillin clavulanate 8.69 DDD / 100 patient-days.

**Table 6. Du Profile of 90% Antibiotic Use in Urinary Tract Infection Patients at RSU X East Jakarta 2019**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **ATC code** | **Antibiotics** | **DDD/100 *Patient-days*** | **Use (%)** | **Segment DU** |
| 1 | J01MA12 | Levofloksasin | 44,07 | 45,60 | **90%** |
| 2 | J01DD04 | Seftriakson | 20,82 | 21,54 |
| 3 | J01DD12 | Sefoperazon | 10,95 | 11,33 |
| 4 | J01CR02 | Amoksisilin + klavulanat | 8,69 | 9,00 |
| 5 | J01DH02 | Meropenem | 3,44 | 3,56 | **10%** |
| 6 | J01DD08 | Sefiksim | 2,93 | 3,03 |
| 7 | J01DD62 | Sefoperazon + Sulbaktam | 1,81 | 1,87 |
| 8 | J01CR01 | Ampisilin + Sulbaktam | 1,45 | 1,50 |
| 9 | J01DD01 | Sefotaksim | 1,22 | 1,26 |
| 10 | J01XX01 | Fosfomisin | 1,00 | 1,03 |
| 11 | J01DE01 | Sefepim | 0,27 | 0,28 |
| **Sum** | | | **96,65** | **100,00** |  |

Table 6 shows that drugs that enter the DU segment 90% after cumulative are levofloxacin (45.60%), followed by cetriaxone (21.54%), cefoperazon (11.33%), and amoxicillin + clavulanate (9.00%). Drugs that fall into the DU segment are 90% of the most widely used drugs in RSU X in 2019.

**Gender**

The table above shows the characteristics of urinary tract infection patients hospitalized at Budhi Hospital, where the sex of the study subjects was mostly female (62.6%). The results of this study are in accordance with previous research conducted by (Mantu, 2015), (Insani and Wunaini, 2018), and (Tanwar *et al.*, 2018) which stated that many urinary tract infection patients were female. The results of this study are also in accordance with the results of a Centers for Disease Control (CDC) study in 2007 which showed that about 8.6 million people in America suffer from urinary tract infections, 84% of which occur in women. In addition, data from the World Health Organization (WHO) in 2011 also states that as many as 50% of women have experienced a urinary tract infection in their lives (Öztürk and Murt, 2020). According to the theory, this happens because of anatomical differences between men and women (Homey, 2018). Anatomically the length of the female urethra is shorter than that of men, so bacteria from the outside more easily reach the bladder located close to the anus (Sykes and Westropp, 2014). While in men urinary tract infections rarely occur, this is because men have prostate fluid whose antibacterial properties can inhibit the growth and entry of bacteria into the urinary tract (Walsh and Collyns, 2017).

**Age**

Based on age, it was found that the most research subjects of urinary tract infection patients at RSU X were the age group of 61-70 years, followed by the age group of 51-60 years, and the age of 41-50 years (Ramaraj, 2014). Based on the research conducted, the results showed that the incidence of urinary tract infections increased at the age of 40 years and over, this is in line with previous research conducted at RSPAD Gatot Subroto Jakarta on the pattern of antibiotic prescribing in urinary tract infection patients in 2018 which stated that urinary tract infections mostly occur at the age of 40 years and over. This is due to a decrease in body resistance in elderly patients, in addition to changes in the urinary system that can reduce the ability to empty the bladder so that urine in the bladder can cause infection23. While urinary tract infections that occur at a young age are generally caused by factors such as lack of maintaining intimate organ hygiene, sexual activity, and the use of contraceptives or spermicidal gels. This is because sexual activity can cause bacteria to enter the female bladder. while the use of spermicide can increase vaginal colonization with Eschericia coli bacteria to vaginal epithelial cells24.

Generally, risk factors for urinary tract infections can increase in postmenopausal women (women who have passed menopause for one year), because in postmenopausal women there is a decrease in estrogen hormone production which results in increased pH in vaginal fluids thereby increasing the development of microorganisms in the vagina. While in men, the increased incidence of urinary tract infections is caused by anatomical abnormalities such as prostatic hypertrophy, fecal incontinence, and catheterization21.

**Comorbidities**

The results showed that more urinary tract infection patients hospitalized at RSU X were accompanied by comorbidities compared to patients without comorbidities. One factor that influences the variety of comorbidities in urinary tract infection patients is the age of patients who are mostly elderly20.

The results of this study are in accordance with previous research conducted at RSUD Undata Palu on the rationality of using antibiotics in urinary tract infection patients in the inpatient installation of RSUD Undata Palu in 2012 which stated that patients with urinary tract infections accompanied by comorbidities were more than without comorbidities25.

Based on the data obtained, it shows that the most common types of comorbidities experienced by urinary tract infection patients at RSU X East Jakarta in 2019 are hypokalemia, followed by dyspepsia, diabetes mellitus, hypertension, chronic kidney disease and other diseases. The results of this study are in accordance with research conducted at RSUP DR. Wahidin Sudirohusodo on the analysis of the effectiveness and side effects of antibiotics in urinary tract infection patients in 2018 which stated that the comorbidities that occur in many urinary tract infection patients are diabetes mellitus, hypertension, and chronic kidney disease. This is because diabetes can increase blood sugar and blood sugar levels in the urine, causing bacteria to multiply more easily. In addition to diabetes mellitus, hypertension is also a comorbidity that is a risk factor for urinary tract infections, this is because hypertension is one of the causes of chronic kidney disease, where one of the complications of chronic kidney disease is immunological disorders that often cause infections, one of which is urinary tract infections23.

But in this study the most comorbidities in patients with urinary tract infections were hypokalemia. According to research conducted by (Nathania, 2018) hypokalemia can be caused by several conditions such as diabetes, kidney disease, chronic diarrhea, alcohol withdrawal, hyperthyroidism, acute myocard infarction, severe head injury, and the use of certain drugs26, where in this study there are several comorbidities that are at risk of causing hypokalemia in patients with urinary tract infections, namely diabetes mellitus, chronic kidney disease, acute kidney disease, diabetic ketoacidosis, kidney stones, renal colic, bilateral nephroxisk, renal cyst, renal abscess, contracted kidney, and nephritis for a total amount of 20.1%.

**Length of day Rawat**

Based on the length of hospitalization days, the results showed that the percentage of urinary tract infection patients who underwent hospitalization at RSU X was at most around 4-7 days. The results of this study are almost the same as research conducted at Undata Hospital Palu in 2012 on urinary tract infection (UTI) patients, the results showed the length of the most days of hospitalization more than 3 days25. According to the general theory, the condition of urinary tract infection patients without comorbidities will improve after the use of 3-day antibiotic therapy. The length of hospitalization days that are more than 3 days is caused because most patients are accompanied by other diseases that can aggravate infectious conditions, thus prolonging the healing process 20.

**Distribution of Antibiotic Therapy Use Profile**

The distribution of antibiotic therapy use profiles aims to determine what antibiotics are used by urinary tract infection patients in the inpatient installation of RSU X 2019.

The results in this study showed that patients received more single therapy than combination therapy, where the most antibiotic used as monotherapy was levofloxacin. As for combination therapy, the antibiotics used are amoxicillin, clavulanate plus levofloxacin and levofloxacin plus ceftriaxone. This is similar to research conducted at Roemani Hospital Semarang in 2015, giving antibiotic monotherapy to urinary tract infection patients is more widely used than combination therapy27.

According to guidelines for the management of urinary tract infections and male genitalia, monotherapy is generally given to urinary tract infection patients who do not experience anatomical structural abnormalities3. While combination therapy is usually used to achieve effective drug action, because the right combination will provide better clinical benefits. In addition, combination therapy can also provide a synergistic effect and inhibit the emergence of bacterial resistance to the antibiotics used28.

In choosing antibiotics as therapy in urinary tract infection patients, there are generally several things that are taken into consideration in order to achieve optimal therapy, including antibiotic sensitivity, the risk of side effects, and the risk of bacterial resistance to antibiotics. Therefore, to achieve this, it can be done the selection of treatment with monotherapy or combination therapy4.

**Evaluation of the use of antibiotics in quantity in DDD units**

In this study, the dosage form of antibiotics with peroral and parenteral routes had the same Defined Daily Dose value. During 2019, there are 11 types of antibiotics from 5 classes of antibiotics used in urinary tract infection patients, namely penicillin antibiotics, cephalosporins, fluoroquinolones, carbapenems, and other groups.

During the year 2019 from January to December, the total number of inpatient days (Length of Stay) of 115 patients was 552 days shown in table 4. The total LOS used in this study is for the calculation of DDD as a divisor with the DDD standard value from WHO.

The quantity of antibiotic use at RSU X East Jakarta in units of DDD/100 patient-days is shown in table 4. The quantity of antibiotic use that had the highest amount in 2019 was levofloxacin. DDD calculation for levofloxacin in 2019 reached 44.07 DDD/100 patient-days. This showed that there were 44 patients from all study subjects who consumed 1 DDD levofloxacin of 0.5 grams daily.

Levofloxacin is a third-generation fluoroquinolone broad-spectrum antibiotic with better activity against gram-positive bacteria and has a lower level of bacterial resistance to antibiotics than other fluoroquinolones, this is because many studies show that as many as 20-30% of bacteria that cause urinary tract infections are resistant to fluoroquinolone antibiotics, especially ciprofloxacin29,30.

Levofloxacin is an antibiotic recommended as empirical therapy in urinary tract infection patients, because levofloxacin can reach expected levels both in serum and in urine, besides levofloxacin is also included in the list of national formularies in 2018 as a therapy for urinary tract infections28,31.

The mechanism of action of levofloxacin as an antibiotic is by inhibiting the formation of bacterial DNA by inhibiting topoisomerase II (DNA gyrase which functions to maintain superhelical bacterial DNA needed for DNA replication and transcription, DNA repair, recombination, and transition) and bacterial topoisomerase IV so as to prevent relaxation of DNA chains needed for transcription and replication.

Levofloxacin has a peak action of 1-2 hours, excreted through the kidneys, and has a relatively long half-life of 6-8 hours, so it can be given at a dose once a day32,33.

Levofloxacin is a third-generation fluoroquinolone group broad-spectrum antibiotic with better activity against gram-positive bacteria and has a lower level of bacterial resistance to antibiotics than fluoroquinolone and others.

The results of other studies showed that about 20-30% of bacteria that cause urinary tract infections are resistant to fluoroquinolone antibiotics, especially ciprofloxacin 29.30.

**Antibiotic Use Profile Based on DU 90%**

Drug Utilization (DU) 90% is obtained by dividing the number of DDD/100 patient-days, based on the type of antibiotic used at RSU X in East Jakarta by the total DDD/100 patient-days of all antibiotics used then at 100% times. The percentage of antibiotic use is further cumulative and sorted from the highest percentage to the lowest percentage.

Drugs that enter the DU segment 90% are drugs that enter the accumulation of 90% on use. The DU profile of 90% of antibiotic use based on antibiotic type in RSU X 2019 can be seen in table 6.

Table 6 shows that antibiotics that fall into the segment of 90% use (DU 90%) consist of levofloxacin (45.60%), ceftriaxone (21.54%), cefoperazon (11.33%), amoxicillin clavulanate (9.00%). While antibiotics included in the 10% DU segment are meropenem (3.56%), cefixime (3.03%), cefoperazon sulbactam (1.87%), ampicillin sulbactam (1.50%), cefotaxime (1.26%), phosphomycin (1.03%), and cefepim (0.28%). The results of this study are different from the research conducted at Dr. Moewardi hospital which showed that antibiotics with 90% DU in the hospital were ceftriaxone (63.97%), levofloxacin (24.42%), ciprofloxacin (4.34%), meropenem (3.49%), cefoperazon + sulbactam (2.76%), cephaloline (0.58%), and ceftazidim (0.44%)17. This difference can occur because, among others, there are differences in the number of samples in the study.

This study has obtained Ethical Approval from the RS X Ethics Committee Team in East Jakarta in 2019.Table 6 shows that drugs that enter the DU segment 90% after being cumulative are levofloxacin (45.60%), followed by cetriaxone (21.54%), cefoperazon (11.33%), and amoxicillin + clavulanate (9.00%). Drugs that fall into the DU segment are 90% of the most widely used drugs in RSU X in 2019.

**Jenis Kelamin**

The table above shows the characteristics of urinary tract infection patients hospitalized at Budhi Hospital, where the sex of the study subjects was mostly female (62.6%). The results of this study are in accordance with previous research conducted by Mantu, et al (2015), Insani (2018), and Sharma and Shweta (2018) which stated that many urinary tract infection patients were female15,17,18. The results of this study are also in accordance with the results of a Centers for Disease Control (CDC) study in 2007 which showed that about 8.6 million people in America suffer from urinary tract infections, 84% of which occur in women5. In addition, data from the World Health Organization (WHO) in 2011 also states that as many as 50% of women have experienced a urinary tract infection in their lives19. According to the theory, this happens because of anatomical differences between men and women. Anatomically the length of the female urethra is shorter than that of men, so bacteria from the outside more easily reach the bladder located close to the anus20. While in men urinary tract infections rarely occur, this is because men have prostate fluid whose antibacterial properties can inhibit the growth and entry of bacteria into the urinary tract21.

**Age**

Based on age, it was found that the most research subjects of urinary tract infection patients at RSU X were the age group of 61-70 years, followed by the age group of 51-60 years, and the age of 41-50 years. Based on the research conducted, the results showed that the incidence of urinary tract infections increased at the age of 40 years and over, this is in line with previous research conducted at RSPAD Gatot Subroto Jakarta on the pattern of antibiotic prescribing in urinary tract infection patients in 2018 which stated that urinary tract infections mostly occur at the age of 40 years and over22. This is due to a decrease in body resistance in elderly patients, in addition to changes in the urinary system that can reduce the ability to empty the bladder so that urine in the bladder can cause infection23. While urinary tract infections that occur at a young age are generally caused by factors such as lack of maintaining intimate organ hygiene, sexual activity, and the use of contraceptives or spermicidal gels. This is because sexual activity can cause bacteria to enter the female bladder. while the use of spermicide can increase vaginal colonization with Eschericia coli bacteria to vaginal epithelial cells24.

Generally, risk factors for urinary tract infections can increase in postmenopausal women (women who have passed menopause for one year), because in postmenopausal women there is a decrease in estrogen hormone production which results in increased pH in vaginal fluids thereby increasing the development of microorganisms in the vagina. While in men, the increased incidence of urinary tract infections is caused by anatomical abnormalities such as prostatic hypertrophy, fecal incontinence, and catheterization21.

**Comorbidities**

The results showed that more urinary tract infection patients hospitalized at RSU X were accompanied by comorbidities compared to patients without comorbidities. One factor that influences the variety of comorbidities in urinary tract infection patients is the age of patients who are mostly elderly20.

Hasil penelitian ini sesuai dengan penelitian sebelumnya yang dilakukan di RSUD Undata Palu tentang rasionalitas penggunaan antibiotik pada pasien infeksi saluran kemih di instalasi rawat inap RSUD Undata Palu tahun 2012 yang menyatakan bahwa pasien infeksi saluran kemih yang disertai dengan penyakit penyerta lebih banyak dibandingkan tanpa penyakit penyerta25.

The results of this study are in accordance with previous research conducted at Undata Hospital Palu on the rationality of using antibiotics in urinary tract infection patients in the inpatient installation of Undata Hospital Palu in 2012 which stated that urinary tract infection patients accompanied by comorbidities were more than without comorbidities25.

Based on the data obtained, it shows that the most common types of comorbidities experienced by urinary tract infection patients at RSU X East Jakarta in 2019 are hypokalemia, followed by dyspepsia, diabetes mellitus, hypertension, chronic kidney disease and other diseases. The results of this study are in accordance with research conducted at RSUP DR. Wahidin Sudirohusodo on the analysis of the effectiveness and side effects of antibiotics in urinary tract infection patients in 2018 which stated that the comorbidities that occur in many urinary tract infection patients are diabetes mellitus, hypertension, and chronic kidney disease. This is because diabetes can increase blood sugar and blood sugar levels in the urine, causing bacteria to multiply more easily. In addition to diabetes mellitus, hypertension is also a comorbidity that is a risk factor for urinary tract infections, this is because hypertension is one of the causes of chronic kidney disease, where one of the complications of chronic kidney disease is immunological disorders that often cause infections, one of which is urinary tract infections23.

But in this study the most comorbidities in patients with urinary tract infections were hypokalemia. According to research conducted by (Nathania, 2018) hypokalemia can be caused by several conditions such as diabetes, kidney disease, chronic diarrhea, alcohol withdrawal, hyperthyroidism, acute myocard infarction, severe head injury, and the use of certain drugs26, where in this study there are several comorbidities that are at risk of causing hypokalemia in patients with urinary tract infections, namely diabetes mellitus, chronic kidney disease, acute kidney disease, diabetic ketoacidosis, kidney stones, renal colic, bilateral nephroxisk, renal cyst, renal abscess, contracted kidney, and nephritis for a total amount of 20.1%.

**Length of day Rawat**

Based on the length of hospitalization days, the results showed that the percentage of urinary tract infection patients who underwent hospitalization at RSU X was at most around 4-7 days. The results of this study are almost the same as research conducted at Undata Hospital Palu in 2012 on urinary tract infection (UTI) patients, the results showed the length of the most days of hospitalization more than 3 days25. According to the general theory, the condition of urinary tract infection patients without comorbidities will improve after the use of 3-day antibiotic therapy. The length of hospitalization days that are more than 3 days is caused because most patients are accompanied by other diseases that can aggravate infectious conditions, thus prolonging the healing process 20.

**Distribution of Antibiotic Therapy Use Profile**

The distribution of antibiotic therapy use profiles aims to determine what antibiotics are used by urinary tract infection patients in the inpatient installation of RSU X 2019.

The results in this study showed that patients received more single therapy than combination therapy, where the most antibiotic used as monotherapy was levofloxacin. As for combination therapy, the antibiotics used are amoxicillin, clavulanate plus levofloxacin and levofloxacin plus ceftriaxone. This is similar to research conducted at Roemani Hospital Semarang in 2015, giving antibiotic monotherapy to urinary tract infection patients is more widely used than combination therapy27.

According to guidelines for the management of urinary tract infections and male genitalia, monotherapy is generally given to urinary tract infection patients who do not experience anatomical structural abnormalities3. While combination therapy is usually used to achieve effective drug action, because the right combination will provide better clinical benefits. In addition, combination therapy can also provide a synergistic effect and inhibit the emergence of bacterial resistance to the antibiotics used28.

In choosing antibiotics as therapy in urinary tract infection patients, there are generally several things that are taken into consideration in order to achieve optimal therapy, including antibiotic sensitivity, the risk of side effects, and the risk of bacterial resistance to antibiotics. Therefore, to achieve this, the selection of treatment with monotherapy or combination therapy can be carried out4.

**Evaluation of the use of antibiotics in quantity in DDD units**

In this study, the dosage form of antibiotics with peroral and parenteral routes had the same Defined Daily Dose value. During 2019, there are 11 types of antibiotics from 5 classes of antibiotics used in urinary tract infection patients, namely penicillin antibiotics, cephalosporins, fluoroquinolones, carbapenems, and other groups.

During the year 2019 from January to December, the total number of inpatient days (Length of Stay) of 115 patients was 552 days shown in table 4. the total LOS used in this study is for the calculation of DDD as a divisor with the DDD standard value from WHO.

The quantity of antibiotic use at RSU X East Jakarta in units of DDD/100 patient-days is shown in table 4. The quantity of antibiotic use that had the highest amount in 2019 was levofloxacin. DDD calculation for levofloxacin in 2019 reached 44.07 DDD/100 patient-days. This showed that there were 44 patients from all study subjects who consumed 1 DDD levofloxacin of 0.5 grams daily.

Levofloxacin is a third-generation fluoroquinolone broad-spectrum antibiotic with better activity against gram-positive bacteria and has a lower level of bacterial resistance to antibiotics than other fluoroquinolones, this is because many studies show that as many as 20-30% of bacteria that cause urinary tract infections are resistant to fluoroquinolone antibiotics, especially ciprofloxacin29,30.

Levofloxacin is an antibiotic recommended as empirical therapy in urinary tract infection patients, because levofloxacin can reach expected levels both in serum and in urine, besides levofloxacin is also included in the list of national formularies in 2018 as a therapy for urinary tract infections28,31.

The mechanism of action of levofloxacin as an antibiotic is by inhibiting the formation of bacterial DNA by inhibiting topoisomerase II (DNA gyrase which functions to maintain superhelical bacterial DNA needed for DNA replication and transcription, DNA repair, recombination, and transition) and bacterial topoisomerase IV so as to prevent relaxation of DNA chains needed for transcription and replication.

Levofloxacin has a peak action of 1-2 hours, excreted through the kidneys, and has a relatively long half-life of 6-8 hours, so it can be given at a dose once a day32,33.

Levofloxacin is a third-generation fluoroquinolone group broad-spectrum antibiotic with better activity against gram-positive bacteria and has a lower level of bacterial resistance to antibiotics than fluoroquinolone and others.

The results of other studies showed that about 20-30% of bacteria that cause urinary tract infections are resistant to fluoroquinolone antibiotics, especially ciprofloxacin 29.30.

**Antibiotic Use Profile Based on DU 90%**

Drug Utilization (DU) 90% is obtained by dividing the number of DDD/100 patient-days, based on the type of antibiotic used at RSU X in East Jakarta by the total DDD/100 patient-days of all antibiotics used then at 100% times. The percentage of antibiotic use is further cumulative and sorted from the highest percentage to the lowest percentage.

Drugs that enter the DU segment 90% are drugs that enter the accumulation of 90% on use. The DU profile of 90% of antibiotic use based on antibiotic type in RSU X 2019 can be seen in table 6.

Table 6 shows that antibiotics that fall into the segment of 90% use (DU 90%) consist of levofloxacin (45.60%), ceftriaxone (21.54%), cefoperazon (11.33%), amoxicillin clavulanate (9.00%). While antibiotics included in the 10% DU segment are meropenem (3.56%), cefixime (3.03%), cefoperazon sulbactam (1.87%), ampicillin sulbactam (1.50%), cefotaxime (1.26%), phosphomycin (1.03%), and cefepim (0.28%). The results of this study are different from the research conducted at Dr. Moewardi hospital which showed that antibiotics with 90% DU in the hospital were ceftriaxone (63.97%), levofloxacin (24.42%), ciprofloxacin (4.34%), meropenem (3.49%), cefoperazon + sulbactam (2.76%), cephaloline (0.58%), and ceftazidim (0.44%)17. This difference can occur because, among others, there are differences in the number of samples in the study.

This research has obtained Ethical Approval from the RS X Ethics Committee Team in East Jakarta in 2019.

**CONCLUSION**

Antibiotics used in urinary tract infection patients at the inpatient installation of RSU X in East Jakarta in 2019 as many as 11 types of antibiotics In single form (Levofloxacin, Seftriaxone, Sefoperazon, Meropenem, Cefixim, Sefotaxime, Phosphomycin, Sefepim, whereas, in the form of a combination of Clavulanate amoxicillin, Sefoperazon sulbactam, and Ampicillin sulbactam, 2) The results of quantitative analysis obtained total DDD / 100 patients-days was 96.65% with each DDD / 100 value patient-days levofloxacin 44,07 %, ceftriaxone 20,82 %, cefoperazon 10,95 %, amoxicillin clavulanate 8,69 %, meropenem 3,44 % cefixime 2,93 % sefoperazon sulbaktam 1,81 %, ampicillin sulbactam 1,45 % cefotaxime 1,22 % phosphomycin 1,00 %, and cefepim 0,27 %. 3) Antibiotics included in the 90% DU segment are levofloxacin 45.60%, ceftriaxone 21.54%, cefoperazon 11.33%, and amoxicillin clavulanate 9.00%.

**BIBLIOGRAPHY**

Apriyanti, Y.F. (2023) ‘APPLICATION OF THE ATC/DDD METHOD FOR ANTIBIOTIC EVALUATION IN INDONESIA’, *Medical Sains: Jurnal Ilmiah Kefarmasian*, 8(3), pp. 1323–1344.

Beadini, Albin *et al.* (2023) ‘URINE ANALYSIS AND URINARY TRACT INFECTIONS IN THE REGION OF THE POPULATION OF TETOVO’, *ACTA MEDICA BALKANICA International Journal of Medical Sciences*, 8(15–16), pp. 43–50.

Hikmawati, I. and Setiyabudi, R. (2021) ‘Epidemiology of COVID-19 in Indonesia: common source and propagated source as a cause for outbreaks’, *The Journal of Infection in Developing Countries*, 15(05), pp. 646–652.

Homey, K. (2018) ‘The flight from womanhood: The masculinity-complex in women, as viewed by men and women’, in *Female Sexuality*. Routledge, pp. 107–121.

Insani, Y. and Wunaini, N. (2018) ‘Hubungan jarak mata dan intensitas pencahayaan terhadap computer vision syndrome’, *Jurnal Manajemen Kesehatan Yayasan RS. Dr. Soetomo*, 4(2), pp. 153–162.

Karuniawati, A., van Doorn, H.R. and Hamers, R.L. (2022) ‘Optimizing antibiotic use in Indonesia: A systematic review and evidence synthesis to inform opportunities for intervention’.

Mantu, S.A. (2015) ‘Citizenship in times of terror. Citizenship deprivation in the UK’.

Morris, A.M. (2014) ‘Antimicrobial stewardship programs: appropriate measures and metrics to study their impact’, *Current treatment options in infectious diseases*, 6, pp. 101–112.

Noori, M. *et al.* (2023) ‘A Retrospective Cross-sectional Study on Prevalence and Susceptibility Pattern of Bacterial Pathogens Causing Urinary Tract Infections at a Teaching Hospital in Tehran, Iran’, *Archives of Pediatric Infectious Diseases*, 11(2).

Öztürk, R. and Murt, A. (2020) ‘Epidemiology of urological infections: a global burden’, *World journal of urology*, 38, pp. 2669–2679.

Ramaraj, R. (2014) ‘A Study on Nosocomial Infection in Intensive Medical Care Unit-incidence, pattern and etiology’. Tirunelveli Medical College, Tirunelveli.

Sykes, J.E. and Westropp, J.L. (2014) ‘Bacterial infections of the genitourinary tract’, *Canine and feline infectious diseases*, p. 871.

Talebi Bezmin Abadi, A. *et al.* (2019) ‘World Health Organization report: current crisis of antibiotic resistance’, *BioNanoScience*, 9, pp. 778–788.

Tanwar, H. *et al.* (2018) ‘Anti-inflammatory activity of the functional groups present in Hippophae rhamnoides (Seabuckthorn) leaf extract’, *Inflammopharmacology*, 26, pp. 291–301.

Walsh, C. and Collyns, T. (2017) ‘The pathophysiology of urinary tract infections’, *Surgery (Oxford)*, 35(6), pp. 293–298.

Yulia, R., Mariza, J.W. and Herawati, F. (2020) ‘Bacterial profile and antibiotic use in pneumonia patients at dr. Soetomo general hospital’, *Current Respiratory Medicine Reviews*, 16(1), pp. 21–27.

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