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EVALUATION OF ANTIBIOTIC USE USING THE ATC/DD AND DU 90% METHODS IN OUTPATIENT PATIENTS IN PUSKESMAS RI TENAYAN RAYA

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ABSTRACT

Infectious diseases are one of the health problem that threaten developing countries, including Indonesia. Riau as one of the provinces with its coastal coverage is not spared from this problem. Inaccurate use of antibiotics is found in the wider community, which can be a cause of negative risks such as antibiotic resistance. Antibiotics are drugs that are used to treat diseases caused by microbes. The improper use of antibiotics can lead to a risk of resistance. Resistance can be avoided using antibiotics. This study aimed to classify antibiotic use using ATC codes and determine the quantity of antibiotic use in outpatients by calculating the DDD. This research method was observational, with a descriptive design and retrospective data collection using secondary data by searching medical records. The sample in this study consisted of outpatients at the Tenayan Raya Inpatient Health Center Outpatient Installation between January and December 2022 who received antibiotic therapy with an ATC code and DDD value in accordance with the provisions of the WHO *Collaborating Center, using a* total sampling technique.The results of the study showed that based on the ATC/DDD and DU 90% methods, there were 3 antibiotics with the highest quantity of use, namely amoxicillin at 165,92 DDD/1000 KPRJ with a percentage of 67,02%, ciprofloxacin at 41,07 DDD/1000 KPRJ with a percentage of 16,59 %, and cefixime as much as 14,69 DDD/1000 KPRJ with a percentage of 5,93%.

Keywords: antibiotics, ATC/DD, DU 90%, resistance

INTRODUCTION

Antibiotics are a mixed class of microbes with antimicrobial properties that inhibit or stop the biochemical cycle in a creature, especially during contamination by microorganisms. Antibiotics are natural compounds produced by fungi/microorganisms (Katzung, 2018). Excessive and inappropriate use of antibiotics can lead to antibiotic resistance. Antibiotic resistance is a condition in which anti-infective agents can no longer prevent/treat diseases, because microbes cannot respond to antibiotic agents. Anti-microbial barriers can make microorganisms that contaminate the human immune system and are difficult to treat (*World Health Organization*, 2020).

Experts estimate that by 2050, approximately 10 million people will be at risk of developing antibiotic resistance (Kementerian Kesehatan RI, 2016a). Deaths due to antibiotic use are mostly caused by hypersensitivity reactions, overgrowth of microbes that are resistant to the antibiotic drugs used, and irrational drug use (Irianto, 2013). Microbial resistance to antibiotics (abbreviation: antimicrobial resistance, AMR) has become a global medical condition, with various negative impacts that can reduce the quality of health services. Resistance can be attempted by not using antibiotics carefully, while the spread

cycle can ideally be controlled by controlling contamination (Kementerian Kesehatan RI, 2021).

Anatomical therapeutic chemical (ATC) and Defined Daily Dose (DDD) classification systems are units of measurement of drug use in research and development of drug use recommended by the WHO as international standards for drug use evaluation research. The Defined Daily Dose was the average maintenance dose per day used for primary indications in adults. The Defined Daily Dose is only owned by drugs that have an ATC code *(World Health Organization*, 2022).

The ATC and DDD methods were used to quantitatively evaluate the use of antibiotics. The goal is to classify antibiotics according to organ systems, chemical properties, and their function in pharmacotherapy based on ATC and then based on standards appointed by the WHO, namely, calculating the average number of antibiotics used through DDD (Kementerian Kesehatan RI, 2015). The ATC/DDD strategy can be combined with 90% Drug Utilization (DU) to determine the group of drugs with high usage in health centers. A DU value of 90% can be used as a reference to determine the nature of recommendations and compliance with rules and formularies (*World Health Organization*, 2022).

Based on previous research, the 90% ATC/DDD &; DU method has been carried out by a number of researchers, including Perdaka dkk.(2020) at Puskesmas X Jambi City in outpatients showing that the antibiotic results that have the highest DDD value are amoxicillin with DDD / 1000 KPRJ values of 45,13 DDD / 1000KPRJ in the 2017 period & 46,27 DDD / 1000KPRJ in 2018, antibiotics that enter the DU 90% segment in the health center are amoxicillin oral tablets 500 mg and 250 mg and Cephalosporins oral capsules 500 mg. Another study by Aleksander dkk. (2020) at the Paal V Health Center in Jambi city on outpatients found that amoxicillin was the one that pocketed the highest amount of DDD compared to other antibiotics. The DDD value of amoxicillin antibiotics is 36,84 DDD/1000 KPRJ, 3,61 DDD/1000 KPRJ & 43,3 DDD/1000 KPRJ in the 2017-2019 period, antibiotics enter the DU segment 90% only amoxicillin oral tablets 500 mg and 250 mg, ciprofloxacin oral tablets 500 mg, chloramphenicol oral capsules 250 mg and Cephalosporins oral capsules 500 mg.

Additionally, a study conducted by Andriani et al.. (2021) at the Aur Duri Jambi Health Center in outpatients in the 2016-2018 period used the most therapy, namely amoxicillin, with the highest number of 39,39 DDD/1000 KPRJ. The antibiotics that enter the 90% DU segment at the Aur Duri Health Center based on data are amoxicillin oral tablets 500 mg and 250 mg and ciprofloxacin (500 mg). In addition, the study conducted by Jani (2022) at the Health Center Sidomulyo Pekanbaru included outpatients using the ATC/DDD &; DU 90% method, there were 3 anti-biotics with the highest quantity of use, namely amoxicillin oral tablets 500 mg and 250 mg as much as 21,58 DDD/1000 KPRJ, ciprofloxacin oral tablets 500 mg as much as 11,57 DDD/1000 KPRJ, and cephaloxil oral capsules 500 mg as much as 4,47 DDD/1000 KPRJ.

Owing to the high prevalence of antibiotic use in patients, researchers want to evaluate the use of antibiotics with ATC/DDD and DU 90% to determine the type and amount of antibiotics used and to understand the picture of antibiotic use at the RI Tenayan Raya Pekanbaru Health Center. The purpose of this study was to understand the classification of antibiotic use with the ATC code and the quantity of antibiotic use in outpatients with DDD calculations. Furthermore, evaluation and control of drug use can be performed.

Based on the first survey that has been conducted by researchers, the RI Tenayan Raya Pekanbaru Health Center is a health center with a fairly high antibiotic prescription. In addition, this health center has not carried out studies on the use of antibiotics with the ATC/DDD & DU 90% method. The increasing use of antibiotic drugs and the lack of exploration in several Regional Health Centers in Indonesia, especially in Pekanbaru City, mean that scientists need to conduct studies to assess the use of antibiotics using ATC/DDD techniques. & DU 90% at Puskes RI Tenayan Raya Pekanbaru. It is hoped that this study can

be used in the future as a source of additional information and consideration in the provision of therapy, monitoring, and evaluation of antibiotic use at the RI Tenayan Raya Pekanbaru Health Center.

RESEARCH METHODS

Time and Place

This research will be conducted from March to August 2023 at the RI Tenayan Raya Pekanbaru Health Center, after processing an ethical review letter. Based on the results of the researcher's survey, the use of antibiotics in this health center is quite high so this chosen as a research location.

Types of research

This descriptive observational study used retrospective data from outpatients at RI Tenayan Raya Pekanbaru Health Center in 2022. Retrospective sampling was chosen in this study because it allows researchers to evaluate the assessment of antibiotic use in the past year and the results of the study obtained can be a source of information for antibiotic use policies

Review Research Ethics

This research was approved an ethical review by the Medical and Health Research Ethics Unit of the Faculty of Medicine, University of Riau with letter number B/041/UNI9.5.1.1.8/UEPKK/2023.

Tools

The guidelines that have been set by WHO, can be seen on the following official WHO website link: (https://www.whocc.no/atc_ddd_index_and_guidelines/guidelines/) and Microsoft Excel application.

Materials

The research materials used were the medical records of patients receiving antibiotic therapy according to the provisions of the WHO ATC/DDD on Outpatients of the RI Tenayan Raya Pekanbaru Health Center from January to December 2022 and observation sheets.

Population and sample

The population used in this study was medical record data of patients who received antibiotic therapy from January to December 2022 who pocketed the ATC code according to the ATC classification published by the WHO and had DDD values and by the provisions of the WHO Collaborating Center. Data were collected using total sampling techniques. The sample in this study was the same as the population of 717 medical records of patients who received antibiotic therapy at the Outpatient Installation of the RI Tenayan Raya Health Center from January to December 2022.

Research Procedure

1. Sample assignment
2. Data collection includes: antibiotic name, dose, route of administration, dosage form &; number of uses
3. Data Processing & Analysis

Data Analysis

The data analysis used in this study was a descriptive analysis to determine the classification of anti-biotics with code naming based on the Anatomical Therapeutic Chemical system and measurement of anti-biotic use to determine the value of DDD using the Defined Daily Dose based on guidelines set by WHO and combined with DU 90% based

on patient characteristics, ATC classification, total antibiotics used, number of KPRJ, calculation of the quantity of antibiotic use based on DDD (Defined Daily Dose), percentage of antibiotic use, and segment DU 90%.

RESULTS AND DISCUSSION

Based on **Table I** found the most data on patients who received antibiotic therapy, namely women as much as 59% with the highest type of infection, namely Acute Respiratory Infection (ARI) at 41%.

Table I. Patients Demographics based on Gender and Age

No	Gender	Number of Patients	Percentage (%)
1	Woman	423 People	59%
2	Man	294 People	41%
	Total	717 People	100%
No	**Age Range**	**Number of Patients**	**Percentage (%)**
1	Late Adolescence (18 – 25 Years)	185 People	26%
2	Early Adulthood (26 – 35 Years)	152 People	21%
3	Late Adulthood (36 – 45 Years)	160 People	23%
4	Early Elderly Age (46 – 55 Years)	122 People	17%
5	Late Elderly Age (56 – 65 Years)	67 People	9%
6	Old Age (>65 Years)	31 People	4%
7	**Total**	717 People	100%

The main causes of contracting diseases due to bacterial infections can be genetic factors, immunity or immune system, environment, diet, and lifestyle of a person (Vascarya dkk., 2016). In this study, women received more antibiotic therapy (59%) than men (41%). Women are more at risk of developing common diseases than men because they have weak immune systems (Ingersoll, 2017). Women also experience many dental and oral diseases such as dental caries due to salivary and IgA secretion, which is a salivary protein that prevents caries in women less than in men until the risk of caries becomes (Jyoti dkk., 2019). In addition, women are also more susceptible to UTIs than men, which may be due to a number of factors, such as female urinary tract anatomy, menopause, and sexual activity. Women have a narrower urethra than men, and the area of the female urinary organs is closer to the buttocks, so that bacteria more easily reach and infect the bladder (Dipiro *et al*., 2015).

Based on research that has been conducted, it is known that the number of patients in late adolescence, namely 18-25 years, find more antibiotic therapy than other age ranges, with a percentage of (26%). This age is also called the dynamic age because many individuals at this age carry out various activities outside the home, so they are more often faced with unclean air and consume various types of unhealthy or less clean food (Khairunnisa dkk., 2016). More frequent exposure to air contamination from smoke or gas can cause ARI (Putra dan Wulandari, 2019). In addition, the high consumption of unclean foods can be caused by microbial contamination. Food can be contaminated with organisms due to several factors, including food stained with dirt from living things that roam around it, vegetables and natural products buried in polluted soil, and food that is not washed (Pratiwi, 2014).

TableII. Infeksi Patient characteristics by Type of Infection

No.	Types of Infection		Number of Patients	Total Patients	Percentage (%)
1.	ISPA	ISPA Bronchitis	177 53	354	41,89%

2.	Dental and oral diseases	Otitis Media	46	269	31,83%
		Pharyngitis	43		
		Sinusitis	22		
		Chronic Bronchitis	7		
		Tonsillitis	6		
		PWO	56		
		Pulpitis	54		
		Radix Gangrene	38		
		Dental Abscess	35		
		PW	34		
		Exodontia	22		
		Chronic Periodontitis	8		
		Acute Apical Periodontitis	5		
		Impacted Teeth	5		
		Periodontitis	4		
		Dental polyps	2		
		Chronic Apical Periodontitis	2		
		Axillary Abscess	2		
		Gingivitis	1		
		Pulp Gangrene	1		
3.	UTI	UTI	101	102	12,07%
		Urethritis	1		
4.	Vulnus	Vulnus Laseratum	18	19	2,24%
		Vulnus Excoriation	1		
5.	Cellulitis		32	32	3,78%
6.	Abscess		16	16	1,89%
7.	Conjunctivitis		13	13	1,53%
8.	Hordeolum		10	10	1,18%
9.	Rhinitis		9	9	1,06%
10.	Fluor Albus		6	6	0,71%
11.	Febris		5	5	0,59%
12.	Otitis External		4	4	0,47%
13.	Gonorrhea		4	4	0,47%
14.	Typhoid fever		2	2	0,23%
15.	Scabies		1	1	0,11%
16.	KLL		1	1	0,11%
17.	Mastitis		1	1	0,11%
18.	CSOM		1	1	0,11%
Total			845	845	100%

The results showed that the most common infection in patients receiving antibiotic therapy in 2022 was ARI, comprising upper and lower respiratory tract infections (41,89%.

Table III. Types of Antibiotics Based on ATC code and DDD Value

Type of Antibiotic	ATC code	DDD Value
Amoxicillin	J01CA04	1,5 gram
Ciprofloxacin	J01MA02	1 gram
Cefixime	J01DD08	0,4 gram
Cefadroxil	J01DB05	2 gram
Metronidazole	J01XD01	1,5 gram
Doxycycline	J01AA02	0,1 gram
Azithromycin	J01FA10	0,3 gram

During the period from January to December 2022, there were 7 types of antibiotics were administered orally at the RI Tenayan Raya Health Center. Antibiotic drug use information obtained from the checkpoint was then characterized based on the ATC settings. The characterization was then described in a list of drugs obtained against the background of the historical use of the drug in short-term patients. The reason for drug coding was to make it easier to recognize the drug to be used. There were 7 types of antibiotic agents with different ATC codes.

TableIV. Types of Antibiotics Based on Dosage Strength and Class

Class of Antibiotics	Antibiotics	Amount
Beta Lactams (Penicilin)	Amoxicilin tab 250 mg	570 tab
	Amoxicilin tab 500 mg	5.895 tab
Quinolones	Ciprofloxacin tab 500 mg	1.020 tab
Beta Lactams (Generation III Cephalosporins)	Cefixime caps 100 mg	730 caps
Beta Lactams (Generation I Cephalosporins)	Cefadroxil caps 500 mg	510 caps
Imidazole Derivatives	Metronidazole tab 500 mg	110 tab
Tetracycline	Doxycycline caps 100 mg	90 caps
Macrolides	Azithromycin tab 500 mg	40 tab

Based on the results of studies that have been carried out, there are 7 classes of antibiotics from 7 types of preparations used by outpatients at the RI Tenayan Raya Health Center in 2022. The antibiotic group used was the beta-lactam (penicillin) group with the active substance amoxicillin with 2 kinds of dosages strengths, namely amoxicillin in the form of 250 mg tablets used as many as 570 tablets and amoxicillin in the form of 500 mg tablets used as many as 5.895 tablets.

The quinolone group with the active substance ciprofloxacin used was ciprofloxacin in the form of tablets with a dosage strength of 500 mg and 1,020 tablets. The beta-lactam group (generation III cephalosporin) with the active substance cefixime used was a capsule-shaped cefixime with a dosage strength of 100 mg and a total use of 730 capsules. The beta-lactam group (cephalosporin generation I) with the active substance cep-halophiles were capsule-shaped cephalopods with a dosage strength of 500 mg, and 510 capsules were used.

The Imidazole derivative group with the active substance was metronidazole in the form of tablets with a dosage strength of 500 mg, and 110 tablets were used. The tetracycline group, with the active substance used, was doxycycline in the form of capsules with a dosage strength of 100 mg, and 90 capsules were used. The macrolide group with the active substance used azithromycin in the form of tablets with a dosage strength of 500 mg, and 40 tablets were used.

High use of antibiotics in the beta-lactam group can be effective against several respiratory tract infections, urinary tract infections, and other comorbidities. However, the use of this material requires extraordinary consideration because it can develop resistance

from extended spectrum beta-lactamase (ESBL)-producing microorganisms (Sholih dkk., 2015).

Table V. Calculation of The Quantity of Antibiotic Use

Type of Antibiotic	Number of Doses (gram)	DDD WHO (gram)	Total DDD (gram)	DDD/1000 KPRJ	Percentage DDD/1000 KPRJ
Amoxicillin 250 mg Amoxicillin 500 mg	3.090	1,5	2.060	165,92	67,02%
Ciprofloxacin 500 mg	510	1	510	41,07	16,59%
Cefixime 100 mg	73	0,4	182,5	14,69	5,93%
Cefadroxil 500 mg	255	2	127,5	10,26	4,14%
Metronidazole 500 mg	55	1,5	36,67	2,95	1,19%
Doxycycline 100 mg	9	0,1	90	7,24	2,92%
Azithromycin 500 mg	20	0,3	66,6	5,36	2,16%
Total				247,55	100%

After the data on the type of antibiotic used at the RI Tenayan Raya Health Center were known, the quantity of use was calculated. The amount of antibiotic used was estimated by duplicating the anti-biotic power by the amount of anitico-biotic agent used. The multiplication results are then divided by DDD, which was determined by the WHO collaborating center for statistical methodology to determine the total DDD usage. The number of DDD/1000 outpatient visits was obtained from the total DDD usage divided by the total number of outpatient visits and multiplied by 1000. A total DDD/1000 KPRJ for all antibiotic drugs was used to determine the quantity of antibiotic use at the RI Tenayan Raya Health Center in 2022.

The quantity of antibiotic used was calculated using DDD measurement units with DDD units / 1000 KPRJ. The total DDD/1000 KPRJ is then calculated as a percentage and then accumulated from largest to smallest to observe the types of antibiotics that enter the 90% DU segment. A DU of 90% was obtained from antibiotic use data that had been grouped based on ATC/DDD. Furthermore, the calculation of antibiotic use from highest to lowest was performed by utilizing DU 90%. DU 90% was obtained after calculating DDD/1000 KPRJ antibiotics by dividing DDD/1000 KPRJ antibiotic drugs by the total DDD/1000 KPRJ of all antibiotic drugs used and then multiplying by 100%. Furthermore, the percentage obtained was sorted from the highest to the lowest use, and the 90% segment was obtained, namely, the highest antibiotic use.

According to Sari and Safitri (2016), the greater the value of DDD/1000KPRJ means that it shows a high level of antibiotic use in 1000 visits of patients. If the use of antibiotics increases, this is a global problem and a health risk, especially with high levels of resistance (Sholih dkk, 2015). The small amount of antibiotics used shows that doctors are becoming more specific when choosing treatment for patients to be closer to the standard of using ingenious antibiotic drugs (Mahmudah dkk., 2016). Wise use of antibiotics is necessary only when there is an infection caused by bacteria. One sign of infection is fever (Kementerian Kesehatan RI, 2016c).

The results of the study showed that the most widely used antibiotic was the beta-lactam (penicillin) group, namely amoxicillin amounting to 165,92 DDD/1000 KPRJ with a percentage of 67,02% meaning that the results of the data were in 1000 patient visits 165 patient visits found 1 DDD amoxicillin per year. The results obtained are the same as those of Jani (2022), Aleksander dkk (2020), and Andriani dkk (2021) that amoxicillin has a DDD/1000 KPRJ higher than other antibiotics in basic health facilities, namely community health centers.

In research that has been done, amoxicillin is widely used for various types of diseases originating from dental poly, this can occur because pulp and perical diseases, gum

disease, periodontal tissue and alveolar bone in teeth are included in the ten most common diseases at the RI Tenayan Raya Health Center in 2022. Among them such as tooth abscess which is a collection of pus that has spread from the tooth to the surrounding tissue and generally comes from infection, pulpitis which is inflammation of the dental pulp that triggers pain which is a reaction to the bacterial toxin of dental diaries which is usually caused by tooth decay, gingivitis which is inflammation of the gums that is usually caused by bacteria or tartar or plaque, Next there is periodontitis, which is inflammation of deeper periodontium tissue which is a continuation of the dominant gingival inflammation caused by plaque & tartar buildup (Kementerian Kesehatan RI, 2012), Furthermore, there is Periapical Abscess Without Sinus (PWO) or periapical abscess without sinus and Periapical Abscess With Sinus (PW) or periapical abscess with sinus, which is an abscess that appears at the tip of the tooth root (Kementerian Kesehatan RI, 2014), there is also pericoronitis which is an inflammation of the soft tissue around the crown of the tooth that is erupting. This can be caused by plaque buildup and food debris between teeth and gums (Kementerian Kesehatan RI, 2012). The selection of amoxicillin for pulp and perical disease, gum disease, periodontal tissue, and alveolar bone is appropriate because it is effective against bacteria that often cause odontogenic infections (Suardi, 2014).

The second largest use of antibiotics is the quinolone group, namely ciprofloxacin as much as 41,07 DDD/1000 KPRJ, with a percentage of 16,59% meaning that in 1000 patient visits, there were 41 patient visits with 1 DDD of ciprofloxacin per year. Ciprofloxacin is the most widely used drug for the diagnosis of UTIs. The fluoroquinolone group is the initial empirical therapeutic antibiotic for UTIs. Ciprofloxacin is a fluoroquinolone antibiotic that was first introduced and has a broad spectrum with indications of respiratory tract infections, urinary tract infections, intra-abdominal infections, bone and joint infections, and skin and soft tissues. It can be used in the treatment of meningitis up to Multi-Drug Resistant Tuberculosis (MDR) (Kementerian Kesehatan RI, 2019). In addition, ciprofloxacin is also used in typhoid fever patients. Typhoid fever is a very intolerable disease of the small intestinal tract with side effects in the form of fever for 7 days or more, digestive system problems, weakening of consciousness and serious difficulties such as Sepsis. Sepsis (septicaemia) is a dangerous disease that can occur when the whole body responds to an illness. Typhoid fever is caused by Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B, and Salmonella paratyphic C. Salmonella typhi enters the human body through the mouth along with food and drinks contaminated by feces or urine of typhoid fever sufferers and people affected by typhoid fever. Known as a carrier of typhoid fever (Rahmat dkk., 2019). Ciprofloxacin is highly recommended for typhoid fever because it is relatively cheap, more tolerant and quickly causes good effects in typhoid fever patients (Suwandi dan Sandika, 2017).

The third largest use of antibiotics is the beta-lactam group (cephalosporins generation III), which is a cefixime of 14,69 DDD / 1000KPRJ with a percentage of 5,93% meaning that in 1000 patient visits 14 patient visits find 1 DDD fixime per year. Sefixime is used for the treatment of otitis media because based on pharmaceutical care is a 2nd line antibiotic, according to the guidelines for the right indication of drugs for otitis media (Kementerian Kesehatan RI, 2016c). In addition, cefixime is also given to patients with cellulitis abscess treatment, which is an acute infection of the hook caused by Streptococcus bacteria (Sullivan and De Barra, 2018). The choice of this antibiotic is appropriate because cefixime is a 3rd generation cephalosporin class antibiotic that has greater gram-negative activity and good Streptococcus activity (Katzung, 2018).

The next use of antibiotics is the beta-lactam group (cephalosporins generation I), namely Cephalosporins as much as 10,26 DDD / 1000KPRJ with a percentage of 4,14% meaning that in 1000 patient visits 10 patient visits find 1 DDD Cephalosporins per year. Cephalosporins is given to patients diagnosed with ARI such as pharyngitis and sinusitis because Cephalosporins is a second-line therapy, the selection of the second line is adjusted to the patient's condition if allergic to the first line, namely amoxicillin in ARI patients (Kementerian Kesehatan RI, 2016c). In addition, Cephalosporins is also given to UTI

patients, this choice of Cephalosporins antibiotic therapy is appropriate as an alternative therapy with a dose of 500mg twice a day which is recommended only for women without complete cystitis (IAUI, 2020). Cephalosporins is an antibiotic that acts on the membrane or cell wall of bacteria. Cephalosporins inhibits the formation of mucopeptides needed for the synthesis of bacterial cell walls. Cephalosporins are more stable against many beta-lactam bacteria and therefore have a wider spectrum of activity. Cephalosporins are inactive against enteroccupica &; Listeria monocytogenes (Katzung, 2018).

Imidazole derivatives group, namely Metronidazole as much as 2,95 DDD / 1000KPRJ with a percentage of 1,19% means that in 1000 patient visits 2 patient visits get 1 DDD metronidazole per year. Metronidazole can be given to patients diagnosed with a tooth abscess, gangrene radix or dead tissue from the tooth root left in the gums and dental deposits which are a buildup of dental plaque that is a breeding ground for bacteria in the mouth (Kementrian Kesehatan RI, 2022). The reason for administering this antibiotic is that metronidazole is a bactericidal agent that is highly active against most anaerobes and can maintain activity against anaerobic Gram-negative bacilli resistant to penicillin (Shweta dan Krishna, 2013). Metronidazole is also prescribed to patients diagnosed with fluorine albus with the recommended treatment, namely a single dose of oral Metronidazole 500 mg twice a day (Mojgan *et al*., 2021), this is the right choice for bacterial Vaginos infection caused by Gardnerella vaginalis bacteria (Kementrian Kesehatan RI, 2022).

The tetracycline group, namely doxycycline as much as 7,24 DDD / 1000KPRJ with a percentage of 2,92% means that in 1000 patient visits 7 patient visits get 1 DDD doxycycline per year. In this health center, the use of oral doxycycline is given to patients with a diagnosis of flour albus which is characterized by thick white discharge from the reproductive organs caused by an infectious disease in the female reproductive organs Chlamydia caused by Chlamydia trachomatis bacteria that spread through genital fluids (Marlina, 2017). In addition, doxycycline is also prescribed for patients with a diagnosis of Gonorrhea combined with Metronidazole, this dual therapy is recommended to reduce the development of bacterial resistance (Adhata, 2022). In outpatient patients Doxycycline is given for the treatment of lower abdominal pain due to chlamydiosis and Metronidazole is used as a treatment against anaerobic bacteria (Kementerian Kesehatan RI, 2016[b]). The mechanism of action of this drug is by inhibiting protein synthesis by binding to the 30S ribosomal subunit & allegedly also to 50S which inhibits bacterial growth. Doxycycline is a broad-spectrum antibiotic that is effective against both Gram-positive and Gram-negative bacteria (Irianto, 2013).

The macrolide group, namely azithromycin as much as 5,36 DDD / 1000KPRJ with a percentage of 2,16% means that in 1000 patient visits 5 patient visits get 1 DDD azithromycin per year. Azithromycin is used for gonorrhea in patients in combination with cefixime. This is an appropriate indication because azithromycin is very sensitive to the bacterium Neisseria gonorrhea. Azithromycin works by inhibiting bacterial protein synthesis by binding reversibly to ribosome subunit 50 (Syahidi dkk, 2016). Cefixime is a 3rd generation cephalosporin antitoxin taken orally. Cefixime works by suppressing transpeptidase compounds that are responsible for the interaction of bacterial cell wall unification. Cefixime also has a wide spectrum of action against various bacteria, including gram-negative bacteria. The combination therapy of azithromycin and cefixime antibiotics produced synergistic results and reduced mortality due to treatment failure, compared and used as monotherapy (Parisa dkk., 2022). Azithromycin is also used for the treatment of Non-Gonooccal Urethritis, which is inflammation of the urethra caused by Gram-negative bacteria Chlamydia trachomatis which is transmitted through sexual contact with a single dose of 1 gram per oral (Kementerian Kesehatan RI, 2016[b]). In addition, azithromycin is used also for patients with tonsillitis and pharyngitis. Streptococcus pyogenes is the most frequent cause of tonsillitis and bacterial pharyngitis, so the most widely used antibiotic is penicillin. If the patient has a history of allergy to penicillin, azithromycin can be an option (Az-zahro dkk., 2023).

Table VI. Use of Antibiotics Included in the Segment DU 90%

Type of Antibiotic	DDD/1000 KPRJ	Percentage DDD/1000 KPRJ	Cumulative Percentage	DU 90%
Amoxicillin 250 mg Amoxicillin 500 mg	165,92	67,02%	67,02%	90%
Ciprofloxacin 500 mg	41,07	16,59%	83,62%	
Cefixime 100 mg	14,69	5,93%	89,56%	
Cefadroxil 500 mg	10,26	4,14%	93,70%	
Metronidazole 500 mg	7,24	2,92%	96,62%	10%
Doxycycline 100 mg	5,36	2,16%	98,78%	
Azithromycin 500 mg	2,95	1,19%	100%	
Total	247,55	100%		100%

The 90% DU method shows a grouping of drugs that fall within the 90% usage segment, which is often used in conjunction with ATC/DDD. A DU of 90% indicates the amount of medication used for up to 90% of all drugs prescribed after the DDD calculation. The 10% segment includes selected drugs used for rare conditions in patients with a history of drug intolerance/side effects. The 90% DU method has been proposed as a single method for assessing the quality of the prescribed drugs. The principle of DU 90% is to focus on drugs that are widely prescribed or used.

Antibiotics in the 90% DU portion had a tremendous resistance potential. A perception shows that there is a relationship between the level of antibiotic wear and the frequency of resistance (Hasrianna dkk., 2015). Resistance is the adverse result of the improper use of antibiotics with unclear indications, improper portion/duration of use, improper method of use, unclear treatment status, and excessive use of antibiotics. Checking with this technique is very helpful in the process of preparing drugs because this information shows utilization for one year, which may not be very different from use in the next year.

From the results of the evaluation of antibiotics used in outpatients at the RI Tenayan Raya Health Center, it can be seen from Table 6 that there was an order of antibiotic use from the largest to the smallest, and the results of 3 antibiotics belonging to the 90% DU segment were obtained, namely amoxicillin, ciprofloxacin, and cefixime. Antibiotics that fell into the 10% segment were cephalosporins, doxycycline, azithromycin, and metronidazole. Antibiotics that enter the DU segment 90% indicate high use of these antibiotics. This shows that health centers must always monitor the use of antibiotics administered to patients.

Based on previous research that has been done, it was found that some diseases are not caused by bacterial infections, but can also be due to viral and fungal infections. For example, the most common type of infection is acute respiratory infection, but not all acute respiratory infections can be caused by bacteria, some of which are caused by viruses. Other diseases such as flour albus can also be caused by fungal infections. Giving antibiotics for infections other than bacterial infections can cause the use of antibiotics that are not by indication, which can be one of the risk factors for resistance. Resistance can also occur because of a lack of public knowledge about the factors that affect the occurrence of antibiotic resistance. People often buy antibiotics without a doctor's prescription and do not spend time on antibiotics until the possibility of antibiotic resistance occurs.

Some bacteria, such as S. aureus, have experienced resistance to amoxicillin, which can be mediated by a decrease in the amount of Penicilline Binding protein (PBP-1A) produced by bacteria or a decrease in the affinity of amoxicillin on Penicilline Binding protein (Setiawati, 2015). The incidence of bacteria resistant to ciprofloxacin is the bacteria Enterobacter aerogenes, Acinetobacter baumanii, Klebsiella ozaena, Raoultella ornithynolytica, Morganella morganii &; and Staphylococcus saprophyticus followed by Escherichia coli (84,6%) to handle it requires higher concentrations of ciprofloxacin to interfere with the synthesis of resistant diisolate DNA compared to the parent strain, a

finding that shows the relative insensitivity of DNA gyrase to ciprofloxacin (Muslim dkk., 2020). In addition, Acinetobacter spp. and Staphylococcus spp. strains showed resistance to cefixime, which illustrates the high activity of antibiotic use in the area (Yohana dan Wulur, 2021).

Based on the use of antibiotics at the RI Tenayan Raya Health Center in 2022, many antibiotic drugs are used because the RI Tenayan Raya Health Center is a basic health service; therefore, most JAMKESMAS and BPJS are given standard prescriptions with portions as needed. If the disease worsens, additional portions of antibiotics will be given, replaced with another antibiotic class, or referred to a clinic for better health services. If the use of antibiotics increases, this is a global problem and a threat to health, especially the high incidence of resistance. The use of antibiotics should be minimized during infection treatment. The small quantity of antibiotic use shows that doctors are increasingly selective in choosing therapy for patients, so that it is closer to the principle of wise use of antibiotics. It is important to monitor antibiotics that fall into the 90% DU segment to prevent resistance. It is expected that health workers authorized to administer drugs must control, monitor, and properly evaluate the delivery of antibiotics at the RI Tenayan Raya Health Center.

CONCLUSION

Based on a study conducted on the evaluation of antibiotic use in outpatients at the RI Tenayan Raya Health Center in 2022 with the ATC/DDD &; DU technique of 90%, it can be concluded that there are three antibiotics with the highest quantity of use, namely amoxicillin as much as 165,92 DDD / 1000 KPRJ with a percentage of 67,02%, ciprofloxacin as much as 41,07 DDD / 1000 KPRJ with a percentage of 16,59%, and cefixime as much as 14,69 DDD / 1000 KPRJ with a percentage of 5,93%. The Tenayan Raya inpatient health center is designed to continue to provide education and information and monitor the use of antibiotics to prevent an increased risk of antibiotic resistance and monitor the availability of antibiotics that enter the 90% DU segment, and the need for further qualitative research with the Gyssens method related to the use of antibiotics in the RI Tenayan Raya Health Center to determine the rationality of its use and conduct ongoing research to evaluate the profile of long-term antibiotic use.

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