

Application of ATC/DDD Methodology to Evaluate of Antibiotic Use in a Trauma Centre General Hospital in Batam

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ABSTRACT

Wise use of antibiotics will prevent bacterial growth and reduce prolonged hospitalization. Actions to reduce the impact of antibiotic resistance can be carried out by evaluating antibiotics in terms of quantity and quality, quantitative evaluation using the (DDD) Defined Daily Dose method. The purpose of this study was to determine the general profile of antibiotic use quantitatively in hospitalized patients at a Riau Islands General Hospital in the trauma center ward. This study is observational non-experimental, data was taken retrospectively, from July to September 2023. Data analysis of this study used the quantitative method (ATC) Anatomical Therapeutic Chemical Classification / (DDD) Defined Daily Dose with a sample size of 138 patient medical records that met the inclusion criteria. Based on the results of the study that has been carried out, there are 17 types of antibiotics with a total value of 46,876 DDD / 100 patient days. The three largest antibiotics were ceftriaxone 21,126 DDD/100 patient days, metronidazole 6,790 DDD/100 patient days, and levofloxacin 3,426 DDD/100 patient days. The most common route of administration was intravenous.

INTRODUCTION

Antimicrobial resistance occurs when germs such as bacteria, viruses and fungi develop the ability to defeat drugs designed to kill bacteria or no longer respond to antimicrobial drugs. In this case the germs are not killed and continue to grow. Thus increasing the spread of disease, disability, and death (WHO, 2023). According to the World Health Organization (WHO), antibiotic resistance is a global health threat, killing 1.27 million people worldwide and nearly 5 million deaths in 2019. The CDC's 2019 Antibiotic Resistance Threat Report, *Clostridioides difficile* bacteria infected more than 3 million people and killed around 48,000. The 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report, the highest number in the world in cases of antibiotic resistance is from the Southeast Asia region (WHO, 2022).

The AMC surveillance methodology is based on the Anatomical Therapeutic Chemical Classification (ATC) classification system and the Defined Daily Dose (DDD) methodology which have been WHO's references for monitoring and researching drug use to improve the quality of drug use since 1981. The increase in antibiotic sales increased by 10% in Covid-19 cases every month, such as cephalosporins 0.2%-0.3%, penicillins 0.4%-0.6% (Nandi et al., 2023). Antibiotic resistance if not addressed immediately will become a silent pandemic and threaten global health. Antibiotics are prescribed for 44-97% of patients in hospitals, often unnecessarily or inappropriately (Rubin et al., 2005). Social and economic factors are thought to contribute to inappropriate antibiotic use and result in resistance in developing countries (Okeke et al., 1999).

In a study at one of the hospitals in Indonesia, the average use of antibiotics was 39 DDD/100 days, and only 21% of prescriptions were considered appropriate. There is no accurate data to determine the amount of antibiotic use and the appropriateness of hospital prescriptions in Indonesia. The Antimicrobial Resistance In Indonesia study conducted between 2000-2005 on 2,494 people in the community showed that 43% of *Escherichia coli* were resistant to various types of antibiotics, including ampicillin (34%), cotrimoxazole (29%), and chloramphenicol (25%). In 781 patients treated in the hospital, 81% of *Escherichia coli* were resistant to ampicillin (73%), cotrimoxazole (56%), chloramphenicol (4.3%), ciprofloxacin (22%), and gentamicin (18%). In seeking evaluation of antibiotic use to prevent resistance, quantitative or qualitative methods can be used, quantitative evaluation can use the Defined Daily Dose (DDD) method. This method is used to determine the average daily dose of drugs (WHO, 2003).

THEORETICAL REVIEW

Antibiotics are drugs that kill or inhibit the growth and reproduction of bacteria to combat bacterial infections in humans and animals. Antibiotics can be classified into several groups based on their chemical structure such as Beta-lactams, for example penicillins (ampicillin, amoxicillin), cephalosporins (cefadroxil, ceftriaxone), carbapenems (meropenem, imipenem), aminoglycoside groups, for example gentamicin, streptomycin, amikacin, neomycin. Macrolide groups, for example erythromycin, azithromycin,

tetracycline groups, for example doxycycline, quinolone groups, for example ciprofloxacin, levofloxacin and other groups such as chloramphenicol, clindamycin, vancomycin, sulfonamides. Based on the type of activity, antibiotics are divided into two, the first is bacteriostatic, an antimicrobial agent that can produce bacterial replication or inhibit bacteria from proliferating, and the host's immune system kills bacteria with erythromycin, tetracycline, sulfonamides, and clindamycin. Both bactericidal antimicrobial drugs that have the ability to kill bacteria such as quinolone, rifampicin, and metronidazole. Antibiotics based on pharmacokinetic properties: time-dependent antibiotics antibiotic efficacy depends on the length of time the drug concentration is above the Minimum Inhibitory Concentration (MIC) at the site of infection and concentration-dependent antibiotics antibiotic efficacy depends on the high concentration of the drug compared to the MIC. The principles of antibiotic use and therapy include appropriate indications, appropriate types, appropriate doses and duration, appropriate routes, monitoring and de-escalation (Patel, 2023)

Principles of Antibiotic Use and Therapy

Principles of antibiotic use and therapy for empirical, prophylactic and definitive therapy : 1) Empirical Therapy : Treatment initiated before the specific causative organism is identified, based on clinical judgment and likely pathogens. Clinical Assessment: Consider the site of infection, patient history, local epidemiology, and common pathogens. Broad-Spectrum Antibiotics: Use broad-spectrum agents or combinations to cover a range of potential pathogens until specific identification. 2) Prophylactic Therapy : Administration of antibiotics to prevent infection in situations where there is a high risk but no established infection. Targeted Use: Indicated in scenarios like surgery (e.g., clean-contaminated procedures), immunosuppressed patients, or exposure to specific pathogens (meningococcal exposure). Timing : For surgical prophylaxis, administer antibiotics within 30–60 minutes before incision to ensure adequate tissue levels. Short Duration: Limit therapy duration to prevent the emergence of resistance (usually no more than 24 hours post-surgery). Appropriate Agent Selection: Choose antibiotics effective against the most likely pathogens for the situation (cefazolin for many surgical procedures). 3) Definitive Therapy : Antibiotic treatment tailored to a specific pathogen identified through microbiological testing. Narrow-Spectrum Antibiotics : de-escalate from broad-spectrum to narrow-spectrum agents based on culture and sensitivity results. Optimize dosage : use the appropriate dose, route, and duration to maximize efficacy and minimize toxicity. Resistance minimization : Avoid unnecessary combinations or prolonged courses to reduce resistance risks (Leekha et al., 2011).

Antibiotic Resistance

As a result of antibiotic resistance, microorganisms such as bacteria, viruses, fungi, or parasites have developed resistance to the treatment of diseases caused by antimicrobials or also called Antimicrobial Resistance (AMR), which were previously susceptible to disease treatment, then the

efficacy of antimicrobials is threatened. Controlling and preventing the unwise use of antibiotics is very important to prevent antibiotic resistance, which is a global threat to public health including the evaluation of antibiotic use (WHO, 2024). Government efforts to prevent antibiotic resistance include: forming an Antimicrobial Resistance Control Program team to assist hospital directors in implementing wise antibiotic use, increasing laboratory capacity for surveillance, strengthening cross-sector coordination and regulatory frameworks, partnering with veterinary pharmaceutical companies to facilitate the implementation of Antimicrobial stewardship strategies, partnering with Indonesian journalists to convey key messages to a wider audience (Kemenkes, 2017)

Evaluation of Antibiotic Use Using the ATC/DDD Method

In calculating antibiotic evaluation, the World Health Organization (WHO) has established a specific method to classify and measure antibiotic use. This a quantitative tool used to measure antibiotic consumption. It is expressed as the assumed average maintenance dose per day for a drug used in its main indication in adults, Metrics :

- DDD/100 bed-days: Used in hospital settings to compare antibiotic use across departments or hospitals.
- DDD/1,000 inhabitants/day: Common in community settings for population-level analysis.

Steps : identify the antibiotic used and determine its WHO-assigned DDD value, than calculate the total amount of the antibiotic consumed (in grams or units) and than compute the DDD using the formula :

$$\text{DDD per 100 bed-days} = \left(\frac{\text{Total antibiotic used (in DDDs)}}{\text{Number of bed-days}} \right) \times 100$$

For population-level analysis:

$$\text{DDD per 1,000 inhabitants/day} = \left(\frac{\text{Total antibiotic used (in DDDs)}}{\text{Population size}} \right) \times 1,000$$

This method allows for benchmarking and monitoring trends in antibiotic consumption. Antibiotic classification is carried out using the Anatomical Therapeutic Chemical Classification (ATC) method, while the amount of use is measured using the Defined Daily Dose (DDD) method per 100 patient days. The Drug Utilization 90% (DU90%) method is used to group drugs that are included in the 90% most common uses, complemented by an analysis of ATC/DDD drug use. DU 90% is important in highlighting aspects of control, evaluation of antibiotic use and in aspects of drug procurement planning (WHO, 2024).

METHODOLOGY

This study is a non-experimental (observational) study using a quantitative study design through retrospective secondary data search of

inpatient medical records in the surgical and internal medicine wards, antibiotic evaluation using Defined Daily Dose (DDD) at a General Hospital in the Riau Islands for the period July - September 2023, data processed using Microsoft excel. The sample in this study is the population that meets the inclusion and exclusion criteria. Inclusion criteria : adult patients over >18 years old, digital medical record files must have complete data including patient identity (name, age, gender, financing status, date of admission and discharge, diagnosis, name of antibiotic, number of preparations, strength of preparation). Antibiotic usage data was analysed quantitatively using Anatomical. Therapeutic Chemical (ATC), Defined Daily Dose (DDD), and Drug Utilisation 90% (DU 90%) methods.

RESULTS AND DISCUSSION

The results of research that has been conducted on inpatients in a Riau Islands General Hospital for the period July - September 2023, in the trauma centre wards using the ATC /DDD method, based on Table 1 The number of inpatients in the surgical ward in one of the General Hospitals in the Riau Islands is 400 people in a 3-month period, 35% is a percentage of the number of antibiotics or 138 prescriptions that use antibiotics. The percentage that did not use antibiotics was 66% or 262 patients out of a total percentage of 100%.

Table 1. Respondent characteristics

Characteristics	Totally	Percentage
Gender :		
Male	83	60%
Female	55	40%
Age :		
19 - 25	24	17%
26 - 40	32	23%
41 - 65	71	51%
>66	11	8%
Recipe antibiotics :		
Antibiotics	138	35 %
Without Antibiotics	262	66%

Based on research that has been conducted on inpatients at a General Hospital in the Riau Islands during the period July - September 2023, in the trauma centre wards, data on the number of patients based on gender and patient age data can be obtained Based on the results of research that has been conducted, female inpatients is 55 patients with a percentage of 40%, and male patients are 83 people with a percentage of 60%, a total of 138 patients with a total percentage of 100%.

From the results of the study, it is known that the most common diseases in one of the inpatient wards in a General Hospital in Riau Islands. The first most common diagnosis was head injury, the second most common

was fracture, the third most common was tumour, followed by abscess, hernia, appendicitis, arthritis, gallstones, kidney stones, cancer, haemorrhoids, cholelithiasis, diabetes plus abdominal pain, diabetes plus ulcer, renal failure, hepatitis, chemotherapy, abdominal pain, bowel obstruction, surgical bleeding, appendicitis, sinusitis, diabetes + fistula + abscess, diabetes + hypokalemia, diabetes + lymphadenitis coli, diabetes + gangrene. Trauma patients due to brain injury were dominated by adult males, the main cause was traffic accidents.

Table 2. Patient Diagnosis

Diagnosis	Totally	Diagnosis	Totally
Head injury	22	Diabetes + ulcer	2
Fracture	11	Kidney failure	2
Tumours	10	Hepatitis	2
Abscess	5	Chemotherapy	2
Hernia	5	Abdominal pain	2
Appendicitis	3	Intestinal blockage	2
Arthritis	3	Surgical bleeding	2
Gallstones	3	Appendicitis	2
Kidney stones	3	Sinusitis	2
		Diabetes +Fistula+	
Cancer	3	Abscess	1
Haemorrhoids	2	Diabetes+ Hypokalemia	1
		Diabetes +	
Cholelithiasis	2	lymphadenitis	1
Diabetes + abdominal pain	2		

The patient's injuries vary, with mild brain injury, moderate brain injury and severe brain injury patients. Prophylactic antibiotics are used in sterile surgery. Intravenous ceftriaxon antibiotics are often used in patients due to injury. Some antibiotics given such as cefixime, ampicillin, amokicillin, levofloxacin, gentamicin, amikacin, clindamicin (Ritter, 2024).

Table 3. Classification of Antibiotics Based on ATC Code

Drug name	Strength of preparation	ATC Code	Route
Amikacin	500 mg	J01GB06	P
Azithromycin	500 mg	J01FA10	O
Cefixime	100 mg	J01DD08	O
	200 mg	J01DD08	O
Cefoperazone	1000 mg	J01DD12	P
Cefotaxime	1000 mg	J01DD01	P
Ceftazidime	1000 mg	J01DD02	P
Ceftizoxime	1000 mg	J01DD07	P

Ceftriaxone	1000 mg	J01DD04	P
Ciprofloxacin	500 mg	J01MA02	O
	1200 mg	J01CR02	P
Co Amoxiclav	625 mg	J01CR02	O
Doripenem	500 mg	J01DH04	P
Levofloxacin	500 mg	J01MA12	O
Meropenem	1000 mg	J01DH02	P
Metronidazole	500 mg	J01XD01	P
Moxifloxacin	400 mg	J01MA14	P
Vancomycin	500 mg	J01XA01	P

P : *parenteral*, O : *oral*

Table 3 not all antibiotics have ATC codes, such as picalpreparations, WHO has recommended as a global standard for antibiotic calculation. According to the Ministry of Health, there are generally several routes of antibiotic administration such as intravenous (IV), parenteral and oral. (Permenkes RI, 2021). The Anatomical Therapeutic Chemical (ATC) classification system, developed by the World Health Organization (WHO), assigns codes to medicines based on their therapeutic use and chemical properties. However, not all antibiotics have an ATC code for several reasons : a) Newly developed antibiotics : some antibiotics may not yet have an atc code assigned because they are newly developed or recently approved and are awaiting classification. b) Limited or niche use : antibiotics developed for very specific or rare infections, or those used in limited geographical regions, might not have an atc code. c) Non-human use : antibiotics used exclusively in veterinary medicine or agriculture generally do not receive atc codes under the system designed for human medicines. d) Combination products : some antibiotic combinations may not have unique atc codes if they are not widely used or if classification is pending. The WHO periodically updates the ATC/DDD (Defined Daily Dose) system, so the absence of an ATC code for a specific antibiotic might reflect delays or pending review processes (WHO, 2018).

Table 4. Total number of DDD/100 patient days

Antibiotic	ATC Code	DDD	DDD/hospitalisation*100
Ceftriaxone	J01DD04	364	21,126
Metronidazole	J01XD01	117,00	6,790
Levofloxacin	J01MA12	59,00	3,424
Meropenem	J01DH02	50,00	2,902
Doripenem	J01DH04	45,07	2,616
Moxifloxacin	J01MA14	38	2,205
Cefotaxime	J01DD01	29	1,654
Amoxicillin clavulanate	J01CR02	28,36	1,646
Ceftizoxime	J01DD07	23,75	1,378
Vancomycin	J01XA01	19	1,103
Azithromycin	J01FA10	10	0,580

Ciprofloxacin	J01MA02	7	0,406
Ceftazidime	J01DD02	6,5	0,377
Cefixime	J01DD08	5	0,290
Cefoperazone	J01DD12	3,5	0,203
Amikacin	J01GB06	3	0,174

Table 4 above, the highest total amount of antibiotic use is the antibiotic ceftriaxone at 21.126 DDD/100 days of inpatients. Second metronidazole as much as 6,790 DDD/100 patient days, Third Levofloxacin 3,424 DDD/100 patient days, then carbapenem goals namely meropenem at 2,902 DD/100 patient days, doripenem at 2, 616 DDD/100 patient days. The least use is amikacin at 0.174 DDD/100 patient days, The high value of total DDD/100 patient days indicates that the higher the level of antibiotic use. The total Length Of Stay (LOS) of patients was 1,723 days. The percentage of antibiotic use was calculated from the total DDD / hospitalisation multiplied by 100 patient days, and obtained the highest antibiotic was ceftriaxone 21.126 DDD/100 patient days, second metronidazole 6.79 DDD/100 patient days, third levofloxacin 3.424 DDD/100 patient days, fourth meropenem 2.902 DDD/100 patient days, fifth doripenem 2,616 DDD/100 patient days, sixth moxifloxacin 2,205 DDD/100 patient days, seventh cefotaxime 1,654 DDD/100 patient days, amoxicillin clavulanate 1,646 DDD/100 patient days, ceftizoxime 1,378, vancomycin 1,103. DDD/100 patient days. Ceftriaxone is a class of cephalosporin antibiotics used as prophylactic antibiotics, the general mechanism of action of cephalosporins is to inhibit the microbial cell wall system. The results of this study are almost similar to the research conducted by (Lakoh et al., 2023) The highest antibiotic consumption was ceftriaxone, followed by levofloxacin and metronidazole. Given the high level of antibiotic consumption in the WATCH category of the AWaRe classification, surveillance of antibiotic consumption and implementation of hospital-based antibiotic governance and stewardship in this situation are needed. The use of ceftriaxone prophylactic antibiotics was 55.7%, generation III and IV cephalosporins are not recommended in order to avoid resistance. (Oktaviani, 2015) Another factor being the highest use is ceftriaxon has a DDD value of 2. And also ceftriaxone is a broad spectrum antibiotic that can be used in most infections, so its use is also high. The high usage of ceftriaxone in Indonesia highlights the need for a qualitative evaluation of antibiotic use to promote rational prescribing practices and combat antimicrobial resistance (AMR). This evaluation can help identify patterns of misuse, overuse, and gaps in adherence to clinical guidelines (Limato et al., 2022).

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of research from hospitalisation in one of the wards at the General Hospital in Riau Islands, 17 kinds of antibiotics were obtained with intravenous and oral routes of use, namely ceftriaxone, metronidazole, levofloxacin, meropenem, doripenem moxifloxacin, cefotaxime, amokicillin clavulanate, ceftizoxime, vancomycin, azithromicin, ciprofloxacin, ceftazidime, cefixime, cefoperazone, and amikacin. The highest DDD value was ceftriaxon

with a total of 21,126 DDD/100patient days. The order of highest antibiotic use was ceftriaxone, metronidazole, and levofloxacin.

FURTHER STUDY

This study is only an initial evaluation of the description of antibiotic use in one location. Qualitative antibiotic use evaluation research should be conducted to see the rationality of the most dominant antibiotic use

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