



EVALUATION OF ANTIBIOTIC USE WITH THE ATC/DDD METHOD AND DU 90% ON RESPIRATORY TRACT INFECTION PATIENTS

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ABSTRACT

Drug availability is one of the factors in the success of pharmaceutical services at the community health center (Puskesmas) as a Primary Health Facility (FKTP). The aim of this study was to determine the quantity of antibiotic use using the ATC/DDD method and DU 90%, as well as the percentage of antibiotic prescription conformity with the National Formulary (Fornas). The method used was an observational cross-sectional study with a descriptive approach. Data were collected retrospectively for the period of May to October 2024 at Khomba Health Center, Jayapura Regency. The results of this study indicate that the most commonly used antibiotic was Amoxicillin with a value of (1996.36 DDD/1,000/year). The antibiotic included in the DU 90% segment was Amoxicillin, and the level of prescription conformity with the National Formulary (Fornas) reached 100%.

Keywords: antidiabetics; ATC/DDD; DU 90%; ISPA

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INTRODUCTION

Acute respiratory infections (ARI) are a cause of increasing morbidity and mortality in diseases globally. Around 4 million people die from acute respiratory infections each year, of which 98% of deaths are caused by ARI. Mortality rates in infants, children and the elderly are quite high, especially in low- and middle-income countries. Acute respiratory infections are one of the most common causes of consultation or treatment in health care facilities, especially in children's services (World Health Organization, 2020). The prevalence of ARI based on the 2020 Indonesian Health Profile shows that the DKI Jakarta area is 53%, Banten Province 46%, West Papua 45.7%, East Java Province 44.3% and Central Java Province 42.9%. Based on the 2018 Basic Health Research (Riskesdas) data, there has been a decrease in the prevalence of ARI in Indonesia, where in 2013 it was recorded at 25% of cases and in 2018 it was 9.3% (Riskesdas, 2018). Health Profile Data in Jayapura Regency shows that ARI is in second place in terms of mortality at 28.68% (31,914 cases) in 2022 (Jayapura Regency Health Office, 2021). The use of antibiotics is recommended if there are clinical signs and symptoms indicating a bacterial infection. The use of antibiotics has the potential to be excessive if there are no clinical signs and symptoms indicating a bacterial infection. In a study reported by WHO (World Health Organization), it was found that more than 50% of prescribed antibiotics were ineffective and/or unnecessary (Kon & Rai, 2016). The results of previous studies at Kendari City health centers showed that the number of antibiotic prescriptions exceeded the WHO standard value, which was 30% (Ihsan et al., 2020).

The use of antibiotics lately is often found in private pharmacies in Kendari City without a doctor's prescription, with a low level of knowledge about antibiotics so that this can cause resistance problems due to irrational use of drugs, one of which is caused by use that is not in

accordance with the patient's clinical condition and the use of antibiotics without a doctor's prescription. Other causes are mainly the ease of people obtaining antibiotics without consideration and recommendations from doctors and pharmacists. The purchase of antibiotics at health facilities, especially pharmacies, is carried out by the community for self-medication without receiving adequate explanation of the rules of use and proper indications (Ihsan & Akib, 2016). From the description above, researchers see the need to evaluate the use of antibiotics because excessive use of antibiotics can increase resistance in communities and this is a national and global focus (Seppala H. et al, 1997). A study analyzing antibiotic consumption patterns is needed to increase the rationality of antibiotic use. WHO has determined that ATC/DDD and DU 90% are standard methods for drug use studies (American Diabetes Association (ADA), 2023). So it is hoped that this study can increase awareness of the use of antibiotics for health workers and local governments in an effort to increase rationality in the use of antibiotics in the community, especially in the Jayapura district. This study aims to evaluate antibiotic consumption patterns in ISPA patients at one of the Jayapura District health centers using the ATC / DDD analysis method and integrated with DU90%.

METHOD

This study is a non-experimental descriptive study with retrospective data collection using an observational cross-sectional design . The subjects in this study were prescription data of ISPA patients who visited the Khomba Health Center, Jayapura Regency, in the period May-October 2023. This study has obtained *ethical clearance* with number 43/I/2024/Bioethics Commission, Faculty of Medicine, Sultan Agung Islamic University, Semarang. The inclusion criteria in this study were vulnerable patients aged ≤ 18 and ≥ 18 years with a diagnosis of ISPA, while the exclusion criteria included incomplete or illegible prescription data and ISPA patients with comorbidities . The sample size in this study was obtained using the Slovin formula:

$$N = \frac{N}{1 + N(e)^2}$$

A total sample of 275 prescriptions was obtained. Data analysis used the ATC/DDD method integrated with DU 90% based on the *WHO Collaborating Center for Drug Statistics Methodology guidelines*. (https://www.whocc.no/atc_ddd_index/) The data is presented in the form of a table including data on the quantity of antibiotic drug use in ISPA patients and drug consumption patterns as well as the DDD value/1,000 *patient days* . The steps in calculating drug consumption with DDD units are as follows: search for ATC code on each drug based on ATC/DDD index. Calculate DDD value and DDD/1,000 patients for outpatient or community drug then sort the DDD/1,000 patient values from the largest to the smallest value and calculate the consumption of drugs that fall into the DU 90% and 10% segments (Kemenkes RI, 2017) in analyzing the suitability of antibiotic drug prescriptions for ISPA patients by looking at the percentage of drug suitability based on the National Formulary (Fornas).

RESULT

Characteristics of research subjects

In general, this study aims to determine the description of antibiotic use in patients with Acute Respiratory Tract Infections (ARI) at the Khomba Health Center, Jayapura Regency, for the period May-October 2023, seen from the type of antibiotic used and the quantity of use based on *the Define Daily Dose (DDD)* . Characteristics of research subjects on the use of antibiotic drugs in patients ISPA based on gender and age aims to see the comparison of the percentage of the number of prescriptions. The characteristics of the research subjects can be seen in table 1.

Table 1.
Characteristics of ISPA Patients (n=275)

Characteristics	f	%
Age (years)		
≤18	85	31
≥18	190	69
Gender		
Man	101	37
Woman	174	63

Evaluation of Quantity of Use and DU Profile 90%

The purpose of this study was to evaluate the use of antibiotics in patients suffering from ARI at the Khomba Health Center in Jayapura Regency. To see the pattern of drug use that falls into the DU 90% and 10% segments, the DDD unit was used in DDD units per 1,000 patient days. DU 90% shows the number of drug items that fall into the DU 90% and 10% segments, and shows the priority of drug procurement because drugs that fall into the 90% segment must be in accordance with the National Formulary (Fornas).

Table 2.
Types of antibiotics used

Group	ATC Code	Antibiotics	Preparation
Penicillin	J01CA04	Amoxicillin	Tablet syrup
Cephalosporin	J01DB05	Cefadroxil	Tablet syrup
Macrolides	J01FA01	Erythromycin	Tablet

Table 3.
Quantity of antibiotic use

Name of prescribed medication & Strength	ATC Code	DDD/1,000 days of care	Percentage (%)	Cumulative percentage (%)	DU 90%
Amoxicillin tab 500 mg Amoxycillin syr 125mg/5ml	J01CA04	1,996.36	89.6%	89.6%	90%
Cefadroxil tab 500 mg Cefadroxil syr 125mg/5ml	J01DB05	122,72	5,5%	95,1%	10%
Erytromicin tab 500mg	J01FA01	109,09	4,9%	100%	

Use of Antibiotic Drugs with National Formulary

According to WHO, one of the indicators of rational drug use is to see the suitability of drugs with the Formulary or treatment guidelines. Table 4 shows data on the suitability of antibiotics used at the Khomba health center in Jayapura district.

Table 4.
Compliance of antibiotics used

Group	Antibiotics	Preparation	Compliance
Penicillin	Amoxicillin	Tablet syrup	√ √
Cephalosporin	Cefadroxil	Tablet syrup	√ √
Macrolides	Erythromycin	Tablet	√

DISCUSSION

Table 1 shows the results of the study in accordance with the report by (Chen et al., 2014) which showed that people under the age of 18 years had more cases of acute respiratory infections (ARI) than people under the age of 18 years. Patients under the age of 18 years had a lower presentation of ARI events, namely 31% (85 patients) and 69% (190 patients). The results of research by (Maidi et al., 2024) show that the distribution of patients based on age is more dominant in the elderly. This is related to the body's immunity in the elderly starting to decline so that the body's immune response ability will decrease (Salsabila et al., 2024). One additional risk factor is increasing age, which has an impact on oropharyngeal secretions as well as a weakened immune response and comorbid disease factors (Tamayo et al., 2016). Women are more likely to experience ARI, especially sinusitis, tonsillitis, and otitis externa. These results are supported by research conducted by (Wulandari et al., 2021) showing that the characteristics of ISPA patients are more female than male at the Pengandonan Community Health Center, Pagaralam City. Other research also shows that the characteristics of ISPA patients are more female than male patients, namely research from (Mugopal et al., 2021) in Semarang urban and rural health centers, where 53.5% more female ISPA patients in rural health centers compared to 47.4% male patients, likewise in urban health centers 50.6% of ISPA patients were female more than male patients 49.6% while men are more likely to experience croup, otitis media, and lower respiratory tract infections (Falagas et al., 2007). This may be influenced by physical, lifestyle, behavioral, and socioeconomic differences between men and women. ARI can also increase due to the role of sex hormones in regulating the immune system (Reichert et al., 2009).

Tables 2 and 3 show that the most widely used antibiotic in the period May-October 2023 was Amoxicillin (1,996.36 DDD/1000 Patient days). This is because Amoxicillin can be absorbed well and is widely distributed in body fluids and tissues and food also cannot interfere with the absorption of the drug. The use of Amoxicillin in research at the Khomba Health Center, Jayapura Regency is available in 2 different forms and strengths, namely amoxicillin dry syrup 125 mg/5 ml and amoxicillin tablets 500 mg with the rules of use for pediatric patients amoxicillin syrup 3 x a day 1 tablet and pulveres 3 x 1 pack, while for children and adults who can swallow tablets, amoxicillin is prescribed with a strength of 250 mg and 500 mg depending on the patient's weight. Amoxicillin dry syrup is given to patients in a reconstituted form (water has been added to the limit mark) so that when the drug is given to the patient, it is accompanied by information to shake it first before use and the antibiotic should not be stored for more than 7 days. Amoxicillin antibiotics are mostly given to be used for 5 days. The rules for using syrup and powder dosage forms are adjusted to the patient's age and weight (Winda, 2018). The rules for using antibiotics are influenced by the frequency of drug use, if the antibiotic has a rule of use 3 times a day, then the drug is taken with an interval of 24 hours / 3, namely 8 hours between taking the prescribed antibiotics. The mechanism of drug absorption is when the drug enters the body, it will go through the ADME (Absorption, Distribution, Metabolism and Excretion) system. Drugs that are included in the therapeutic index will provide a therapeutic effect. If the drug level in the body is below the therapeutic index, the drug will not provide a therapeutic effect, conversely if the drug level in the body is above the therapeutic index, an overdose can occur (Khairinnisa et al., 2020).

The choice of amoxicillin in ARI therapy is because amoxicillin has a working mechanism under certain conditions as a bacteriostatic and can also be bactericidal, namely by damaging the bacterial cell wall containing complex mucoproteins against microbes (Pradina and Hanifa, 2022). Amoxicillin is the first choice in the treatment of ARI, because it is included in the group of broad-spectrum antibiotics that can inhibit gram-positive and negative bacteria

which are bacteria that cause secondary infections in ARI (Zaini et al., 2019). Amoxicillin is generally used as empiric therapy in most antibiotic cases. This antibiotic is the first line for ISPA patients (Riska Aulia, 2017). The antibiotic Amoxicillin is the most effective and most widely used antibiotic and is free from toxic properties (Dewi et al., 2020). Contraindications to the use of amoxicillin can occur in patients who are hypersensitive or allergic to penicillin, anaphylaxis or serious skin reactions such as Stevens-Johnson syndrome (Wasilah et al., 2022). For patients who are allergic to penicillin, an alternative cephalosporin group can be given, namely cefadroxil which has a broad spectrum for gram-positive and negative bacteria. Cephalosporins are indicated for the treatment of upper and lower respiratory tract infections, urinary tract infections, skin and soft tissue infections, so the use of cefadroxil for the treatment of upper respiratory tract infections is in accordance with the expected indications (Ekasari & Hastuti, 2022). The results of other research conducted at the Boliyohuto Community Health Center, Mootilango Community Health Center, and Bilato Community Health Center, Gorontalo Regency showed that the antibiotic therapy was mostly given amoxicillin at 17%, Cotrimoxazole 0.6%, Cefadroxil 0.6% and Ciprofloxacin 0.5% (Tuloli et al., 2024). These results are in line with research conducted by (Falevi, 2022), where amoxicillin ranks first in the treatment of upper respiratory tract infection (80.2%), in accordance with the Basic Treatment Guidelines at Community Health Centers which state that amoxicillin is the first line drug choice for pharyngitis, tonsillitis, sinusitis, and otitis media. Amoxicillin is preferred compared to other β -Lactam groups because it has a good antimicrobial effect against *Streptococcus*, *Haemophilus influenzae* and *Pseudomonas aeruginosa* bacteria.

The next most widely used antibiotic is cefadroxil (122.72 DDD/1,000 Patient days). Cefadroxil is a first-generation cephalosporin, which is sometimes inactive against methicillin-resistant staphylococcal strains, *E. coli*, *Klebsiella pneumoniae* and *proteus mirabilis*. Oral administration of cefadroxil can cause absorption in the intestine to vary. Where the concentration in urine is usually very high, but in some tissues, the concentration varies and is usually lower than in serum with a half-life of 1.4 hours. In patients with impaired renal function, the dose of the drug must be reduced, so cefadroxil is rarely used in the treatment of respiratory tract infections. Beta-lactam antibiotics such as amoxicillin and cefadroxil have common side effects, such as redness and diarrhea. In addition, both drugs have a high potential for allergies, so people should be careful when using them to avoid unwanted side effects (Heta & Robo, 2018). The use of penicillin antibiotics also often causes hypersensitivity reactions. At the Khomba Health Center, Jayapura Regency, amoxicillin was only used for three days in antibiotic treatment, and is one of the antibiotics included in the use of 90 percent of drugs, with a total percentage of 89.6 percent. Treatment of mild acute respiratory infections does not require antibiotics; symptoms such as runny nose, sore throat, cough, sneezing, and nasal congestion can heal on their own (Zoorob, Sidani, Fremont, & Kihlberg, 2012).

The right dose and duration of antibiotic therapy can control bacterial resistance. Medical personnel usually do not take into account the long-term impacts, such as the emergence of resistant germs. Antibiotics must be used wisely, meaning with clear indications. Antibiotic misuse is now a major problem in Indonesia and throughout the world (Sitepu et al., 2020). Excessive use of antibiotics, especially with broad-spectrum antibiotics, increases antibiotic resistance. The correct length of administration of antibiotics is very important and needs to be considered to prevent resistance to antibiotics (Ningrum & Gunawan, 2023). Research conducted by (Sugiharta, 2018) at the East Bogor Community Health Center showed that there were still many cases of ARI that were given antibiotics for less than 5 days (76.19%).

The reason for the long administration time which does not follow these rules is because the amoxicillin syrup available at the community health center is not sufficient for use for at least 5 days. Inappropriate duration of antibiotic administration will ultimately result in the overall antibiotic dosage regimen not being met, and will increase antibiotic resistance (Sugiharta, 2018). Table 4 shows that all types of antibiotic drug use prescribed to patients with acute respiratory infections in 2023 were in accordance with the Fornas applied by the Khomba Health Center. This means that the data on antibiotic drug use at the Khomba Health Center, Jayapura Regency in 2023 was in accordance with the Fornas.

CONCLUSION

According to the evaluation analysis of antibiotic use in ISPA patients at the Khomba Health Center, Jayapura Regency, it was found that Amoxycillin was included in the DU 90% segment. In addition, the analysis of the evaluation of the suitability of antibiotic use with Fornas has reached 100%.

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