

Quantitative Evaluation Of Antibiotic Usage In ICU Ward at West Nusa Tenggara Province Hospital in 2018

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Abstrak. Angka resistensi antibiotik di rumah sakit dan pelayanan kesehatan lainnya meningkat. Ruang *Intensive Care Unit* (ICU) memiliki angka kejadian resistensi yang cukup tinggi sebesar 11,6-22,5%. Penelitian ini bertujuan untuk mengetahui profil penggunaan antibiotik pada pasien ruang ICU di RSUD Provinsi NTB tahun 2018. Penelitian ini merupakan penelitian deskriptif *cross sectional* dengan mengumpulkan data rekam medik pasien secara retrospektif. Sampel dalam penelitian ini sebanyak 64 pasien yang memenuhi kriteria inklusi. Metode analisis penggunaan antibiotik menggunakan sistem defined daily dose DDD/100 pasien-hari. Hasil penelitian menunjukkan terdapat 37 pasien laki-laki dan 27 pasien perempuan. Pasien dewasa sejumlah 48 orang dan lansia 16 orang. Jumlah kasus tertinggi dari 11 pengelompokan kasus yaitu kasus bedah saraf sebanyak 30 pasien. Total lama hari perawatan semua pasien 621 hari dengan rentang hari perawatan 1-69 hari dan nilai tengah 6 hari. Berdasarkan hasil perhitungan terdapat 17 jenis antibiotik yang digunakan pasien di ruang ICU RSUD Provinsi NTB tahun 2018. Nilai DDD/100 *patient-days* lima antibiotik yang umum digunakan adalah seftriakson (60,71), levofloksasin (29,15), meropenem (16,10), metronidazol (11,00), dan amikasin (6,24). Persentase kelima antibiotik tersebut berturut-turut yaitu 45,44; 21,82; 12,05; 8,24; dan 4,67%. Nilai DDD/100 *patient-days* semua antibiotik berada pada rentang 60,71- 0,05 DDD/100 *patient-days*

Kata kunci: Antibiotik, ATC/DDD, ICU, DDD/100 patient-days

Abstract. The number of antibiotic resistances in hospitals and healthcare is increasing. The resistances prevalence rate in Intensive Care Unit (ICU) room is 11,6-22,5%. This research aim is to evaluate the usage of antibiotics of patients in ICU at West Nusa Tenggara Provincial Hospital in 2018. This research is observational and applies a cross-sectional design that collects data retrospectively, with the total number of samples are 64 patients who met inclusion criteria and employs DDD/100 *patient-days* system analysis method. The result of this study shows, among 64 patients; there are 37 male and 27 female patients; 48 adult and 16 elderly patients. Among 11 groups of cases, the highest case is neurosurgery with 30 patients. The total length of stay (LOS) of all patients is 621 days, where the range of LOS is 1-69 days, and the median value is 6 days. According to the calculation, there are 17 types of antibiotics used in the ICU room of West Nusa Tenggara Hospital in 2018. Five varieties of most used antibiotics based on their DDD/100 patient-days are ceftriaxone (60,71), levofloxacin (29,15), meropenem (16,10), metronidazole (11,00), dan amikacin (6,24). The percentage value of those antibiotics respectively is 45,44; 21,82; 12,05; 8,24; dan 4,67%. Based on all types of antibiotics, the range value of DDD/100 patient-days is 60,71- 0,05 DDD/100 patient-days

Keywords Antibiotic, ATC/DDD, ICU, DDD/100 patient

Backgrounds

Antibiotic resistance is a condition when bacteria continue to grow despite the administration of antibiotics. Resistance can be natural or acquired. Natural resistance occurs without prior exposure to antibiotics while acquired resistance is caused by exposure to antibiotics¹ (Kee and Hayes, 1996). Antibiotic resistance causes longer treatment time,

increased costs, also resulting in disability and death. The usage of antibiotics is an important factor causing antibiotic resistance worldwide. More than 50% of antibiotic prescriptions are prescriptions that are not needed or the prescription is not optimally effective². Several rates of resistance to this antibiotic have been recorded. The incidence of resistance in the United States in 2019, recorded more than 2.8

million people experiencing antibiotic resistance and more than 35,000 people died from it³. In 2016 antimicrobial resistance and antimicrobial usage surveillance study has been conducted at 8 hospitals, it was found that resistance increased significantly from 45-89%. There are several ways that can be done to overcome resistance, one of which is to apply the use of antibiotics wisely².

Evaluation of antibiotics usage is an indicator of quality in applying the wise use of antibiotics. This analysis can be done qualitatively with the Gyssens method or quantitatively with the defined daily dose (DDD)/100 patient-days⁴. In a study conducted by Rogues et.al (2007), found that the rate of *Staphylococcus aureus* resistance was correlated with the consumption of ciprofloxacin⁵. This shows that there is a relationship between the level of antibiotic consumption and bacterial resistance.

The DDD method will provide an overview of the estimated use of antibiotics so that trends in drug use can be seen and allow comparisons between population groups. This method will provide standardized, representative and stable data on drug use. The DDD value describes the level of drug utilization that plays a role in improving the quality of drug use⁶.

Research on the quantitative analysis of antibiotics using the DDD method in the ICU is still limited even though the incidence of resistance is 11.6-22.5%⁷. In the Province of West Nusa Tenggara, not many research has been conducted related to the use of antibiotics quantitatively using the DDD method. Study on the use of antibiotics in the West Nusa Tenggara Provincial Hospital. A total of 120 samples of patient medical records were used, the results obtained were ceftriaxone as the most dominant antibiotic used 28.1 DDD/100 patient-days. However, this study was conducted in an inpatient setting and has not been carried out in the ICU⁸. Therefore, this study aims to examine the quantitative profile of antibiotic use in the ICU room at the NTB Provincial Hospital in 2018 using the DDD/100 patient-days method.

Research Methods

This research is descriptive observational research with a cross sectional research design that collects data through patient medical records retrospectively. The study was conducted in January-March 2021 at the Regional General Hospital of the West Nusa Tenggara. The population in this study were ICU room patients at the West Nusa Tenggara Provincial

Hospital in 2018. The sampling technique used was a non-probability sampling technique with total sampling type. Inclusion criteria were adult patients aged 19 years, patients receiving antibiotic prescriptions, complete and clearly legible patient medical records. While the patient exclusion criteria were patient medical records that were available but could not be reached. Data collected from medical records in the form of patient sociodemographic data (gender, and age of the patient), clinical profile of the patient (patient diagnosis, length of treatment, and patient outcomes), and use of antibiotics (DDD value/100 patient-days of all types of antibiotics). and percentage of antibiotic use from DDD value). The use of antibiotics is calculated by the ATC/DDD classification system using the guidelines from the World Health Organization (WHO).

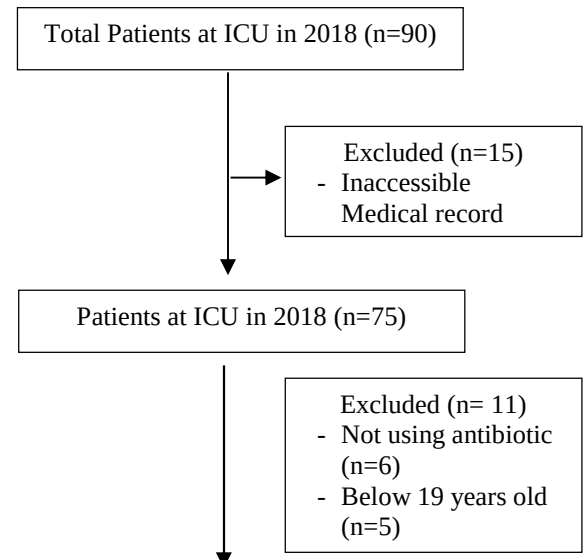
$$\text{DDD antibiotic} = \frac{\text{Antibiotic usage quantity} \times \text{dosage}}{\text{DDD in WHO}}$$

$$\text{DDD 100 patient-days} = \frac{\text{Total amount of DDD}}{\text{total length of stay}} \times 100$$

The analysis was carried out by calculating and processing the patient's antibiotic use data using the Ms. Excel version 2010. The stages of data processing include: data grouping sociodemographic aspects and clinical profiles of patients, Classification of antibiotics in the ATC system, and Calculation of the DDD/100 patient-days value and percentage of antibiotics. Data analysis was carried out and presented descriptively to see data on the use of all types of antibiotics. This research has received ethical approval from the research ethics committee of the NTB Provincial Hospital with the number: 070.1/04/KEP/2021. This research also obtained a research permit from the NTB Provincial Hospital with the number: 070/16/001/RSUDP NTB.

Results

The samples that meet inclusion criteria were 64 samples. The data collection process as diagrams below



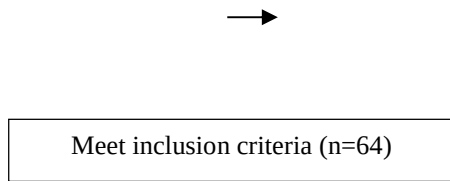


Figure 1. Research data collection flow

In this study, 90 patients were treated in the ICU room of the West Nusa Tenggara Provincial Hospital in 2018. We found that 64 patients met the inclusion criteria. From 64 patients, the number of male patients was 37 patients and female patients were 27 patients with the percentages of 58% and 42%, respectively. There were 48 adult patients (aged 19-60 years) and 16 elderly patients (>60 years). This is because the sampling was carried out in the ICU room which was not in the PICU or NICU room and the criteria for the patients studied and the criteria for the patients studied were 19 years.

From this research, it was found that there were 80% surgical cases and 20% non-surgical cases. The most dominant surgical cases based on the results of the study were neurosurgery cases with a percentage of 46.8% (n=30), followed by digestive surgery cases and obstetric surgery cases (12.50%).

Table 1. basic characteristics of the patient (n=64)

Age	Total (n)	%
19-60 years old	48	75%
> 60 years old	16	25%
Gender	Total (n)	%
Male	37	58%
Female	27	42%
Case Characteristic	Total (n)	%
Neurosurgery	30	46,88
Digestive Surgery	8	12,50
Obstetric and Gynecologic	8	12,50
Neurology	5	7,81
Internal Medicine	5	7,81
Pulmonology	2	3,13
Orthopedics Surgery	2	3,13
Oncology Surgery	1	1,56
Mouth Surgery	1	1,56
Head and Neck Surgery	1	1,56
Cardio	1	1,56

To calculate the DDD of antibiotics, it is necessary to classify all types of antibiotics in the ATC system. Classification can be done by accessing

information through the WHO website at: https://www.whocc.no/atc_ddd_index/. The results of the classification of antibiotics used in the ICU room of the NTB Provincial Hospital in 2018 are presented in Table 2.

Table 2. Classification of ATC Antibiotics

Antibiotic	ATC Code
Ceftriaxone	J01DD04
Levofloxacin	J01MA12
Meropenem	J01DH02
Metronidazole	J01XD01
Amikacin	J01GB06
Vancomycin	J01XA01
Cefoperazone & beta-lactamase inhibitor	J01DD62
Cefoperazone	J01DD12
Cefotaxime	J01DD01
Moxifloxacin	J01MA14
Cefixime	J01DD08
Azithromycin	J01FA10
Ceftazidime	J01DD02
Clindamycin	J01FF01
Amoxicillin	J01CA04
Gentamycin	J01GB03
Imipenem dan enzyme inhibitor	J01DH51
Trimethoprim and sulfamethoxazole	J01EE01
Gentamycin	D06AX04

Antibiotics used in the ICU room consist of single and combination antibiotics. The single antibiotics used were 16 types of antibiotics and the combination preparations were 3 types of antibiotics. The use of antibiotics for systemic use were 18 types antibiotics and 1 antibiotic for topical use.

Table 3. Quantitative usage of Antibiotics in the ICU ward

Antibiotics and route of administration	Total Dosage	DDD WHO	Total DDD	DDD/ 100 Patient-Days
Ceftriaxone (iv)	754	2	377	60,71
Levofloxacin (iv)	90,5	0,5	181	29,15
Meropenem (iv)	300	3	100	16,10
Metronidazole (iv)	102,5	1,5	68,33	11,00
Amikacin (iv)	38,75	1	38,75	6,24
Vancomycin (iv)	33	2	16,5	2,66
Cefoperazone dan beta-lactamase inhibitor (iv)	56	4	14	2,25
Cefoperazone (iv)	36	4	9	1,45

Cefotaxime (iv)	33	4	8,25	1,33
Moxifloxacin 9iv)	1,6	0,4	4	0,64
Cefixime (po)	1,4	0,4	3,5	0,56
Azithromycin (iv)	1,5	0,5	3	0,48
Ceftazidime (iv)	10	4	2,5	0,40
Clindamycin (iv)	3	1,8	1,67	0,27
Amoxicillin (po)	2	1,5	1,33	0,21
Imipenem and enzyme inhibitor (iv)	1	2	0,5	0,08
Gentamycin (iv)	0,08	0,24	0,33	0,05
Total			829,67	133,60

Total Length of Stay: 621 days; (iv) intravenous; (po) per oral; dan (g) gram; (DDD/100 *patient-days*) total amount DDD/total length of stay

Based on the research data, it was found that the 5 most dominant antibiotics used in the ICU room of the West Nusa Tenggara Provincial Hospital in 2018 were ceftriaxone, levofloxacin, meropenem, metronidazole, and amikacin. The value of DDD/ 100 patient-days in the ICU room at the NTB Provincial Hospital in 2018 is presented in Figure 1

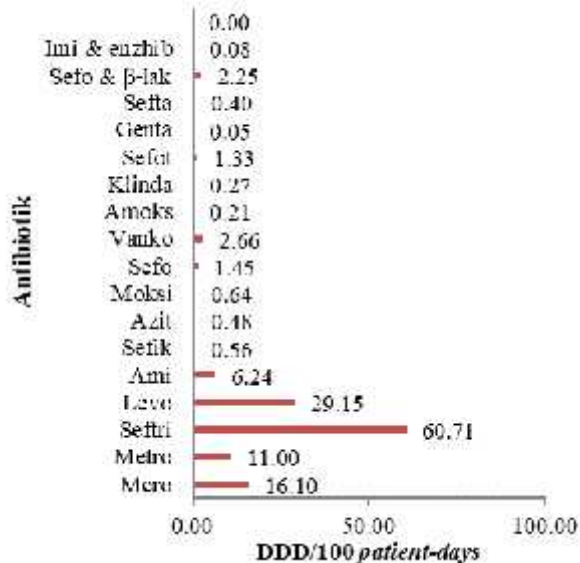


Figure 2. 1. Graph of DDD/100 patient-days of antibiotics in the ICU

(Mero) meropenem; (Metro) metronidazole; (Seftri) ceftriaxone; (Levo) levofloxacin; (Ami) amikacin; (Sefik) cefixime; (Azit) azithromycin; (Moksi) moxifloxacin; (Sefo) cefoperazone; (Vanko) vancomycin; (Amoks) amoxicillin; (Klinda) clindamycin; (Sefot) cefotaxime; (Genta) gentamycin; (Seftri) ceftazidime; (Sefo & β lak) Cefoperazone dan β-lactamase inhibitor; dan (imi & enzhib) imipenem dan enzyme inhibitor.

Discussion

Ceftriaxone was the most used antibiotics in ICU ward. The used of ceftriaxone in the NTB Provincial Hospital is generally for prophylactic antibiotics in cases of neurosurgery and digestive surgery. There were 26 cases of neurosurgery and 6 cases of digestive surgery using ceftriaxone as prophylactic antibiotics. Ceftriaxone is one of the antibiotics of choice for neurosurgical prophylaxis⁹. In the guidelines for the use of antibiotics used at the West Nusa Tenggara Provincial Hospital for prophylactic procedures in neurosurgery, generally the recommended antibiotic of choice is third-generation cephalosporins so that the use of ceftriaxone is in accordance with the guidelines¹⁰. Ceftriaxone can penetrate the blood-brain barrier, this penetration will increase the systemic inflammatory response when fighting infection¹¹.

In case of digestive surgery, ceftriaxone was used in patients with a diagnosis of appendicitis in 4 cases, gastric and intestinal perforation in 3 cases, and 1 case of hernia. Ceftriaxone was generally combined with metronidazole. In the guidelines for the use of antibiotics used at the NTB Provincial Hospital for prophylactic procedures in digestive surgery for appendectomy, gastroduodenal and herniorrhaphy procedures, there was no recommendation for ceftriaxone antibiotics, but in procedures for small bowel surgery with obstruction the use of cephalosporins was recommended¹⁰.

Levofloxacin is the second most common antibiotic used in the ICU room at the NTB Provincial Hospital. Levofloxacin is generally given for indications of community pneumonia, bacteremia or sepsis, and others. Based on the results obtained, in eleven cases levofloxacin was used concurrently with ceftriaxone and in 4 cases as ceftriaxone replacement therapy in some neurosurgery cases. In addition, levofloxacin was also used to treat 3 patients with a diagnosis of pneumonia and 2 patients with a diagnosis of sepsis. In the guidelines for the use of antibiotics used in the West Nusa Tenggara Provincial Hospital, there was no reason to use levofloxacin with ceftriaxone simultaneously in neurosurgery cases. In pneumonia patients, levofloxacin is recommended as therapy in the guidelines, while for sepsis, information on the recommendations for antibiotics to use is not listed in the guidelines¹⁰. However, the antibiotic levofloxacin is included in the empirical therapy of the quinolone class of antibiotics in the management of sepsis¹².

Meropenem has the third highest use of antibiotics in the ICU. Meropenem broad spectrum antibiotic, therefore it is effective against Gram-positive, Gram-negative and anaerobic bacteria. The use of meropenem antibiotics in the ICU room of the West Nusa Tenggara Provincial Hospital in 2018 was a substitute for antibiotic therapy of ceftriaxone or levofloxacin in 12 cases of neurosurgery patients. Meropenem has good penetration ability in cerebrospinal fluid so that it can be used as an alternative therapy in these cases¹³. In addition, meropenem was used in 7 patients with a diagnosis of sepsis and 3 patients with a diagnosis of pneumonia. In the guidelines for the use of antibiotics in the Provincial Hospital, the use of meropenem to treat pneumonia is generally carried out if levofloxacin therapy and a combination of cefoperazone and beta-lactamase inhibitors are not effective, while for the diagnosis of sepsis there is no antibiotic recommendation¹⁰. In the national guidelines for medical services for the management of antibiotic sepsis, carbapenems are included in empirical antibiotics for sepsis and antibiotics are used if the bacteria causing sepsis are resistant to antibiotics¹⁴.

After meropenem, metronidazole is the antibiotic with the highest use. This antibiotic is one of the main therapies in the treatment of anaerobic bacterial infections. The use of metronidazole in the ICU room of the West Nusa Tenggara Provincial Hospital in 2018 was generally for prophylaxis in 8 cases of digestive surgery with 6 cases of patients being given a combination with ceftriaxone and 2 cases of patients being used together with meropenem. Metronidazole was used in 2 patients with a diagnosis of appendicitis, 5 patients with gastric and intestinal perforation, and 1 patient with hernia. In the guidelines for the use of antibiotics used in the West Nusa Tenggara Provincial Hospital for prophylactic procedures for digestive surgery in appendectomy and herniorrhaphy procedures the use of metronidazole is recommended. However, the gastroduodenal procedure did not find metronidazole recommendations. The antibiotics ceftriaxone and meropenem in the three procedures above were not found to be recommended for use¹⁰. Metronidazole in certain cases suspected of involving bacteria can be combined with cephalosporins for surgical prophylaxis¹⁴.

Amikacin is another antibiotic that also frequently used. Amikacin has the widest spectrum of action of all aminoglycosides, including gram-negative and gram-positive bacteria¹⁵. This antibiotic is used for the treatment of serious infections including sepsis¹⁶. The use of amikacin in the ICU is as a therapy to

treat 2 cases of nosocomial pneumonia patients. Amikacin in the guidelines for the use of antibiotics is recommended for pneumonia patients¹⁰. This antibiotic is included in the line of therapy for the treatment of nosocomial pneumonia¹⁷.

Based on studies that have been carried out regarding the use of antibiotics in the ICU, several studies found the use of the five most dominant antibiotics used in the ICU room. In a study conducted by Putri et al., 2019, regarding the antibiotic profile in ICU patients at Dr. Soedarso Pontianak obtained a DDD value of ceftriaxone of 76.15 DDD/100 patient-days and metronidazole 23.28 DDD/100 patient-days¹⁸. In a study on the rationality of the use of antibiotics at RSUP Dr. Kariadi Semarang conducted by Yuniftiadi., 2010, ceftriaxone has a DDD value of 62.2 DDD/100 patient-days¹⁹.

Furthermore, studies related to the use of antibiotics in the ICU of tertiary hospitals in West Java showed the consumption of levofloxacin antibiotics was 143.18 DDD/100 bed-days, meropenem was 49.88 DDD/100 bed-days, and metronidazole 16.99 DDD/100 bed-days²⁰. In a study related to antibiotic consumption and patient resistance patterns in the ICU at a tertiary hospital in Delhi, India, the use of levofloxacin was 62.7 bed-days, meropenem was 49.5 DDD/100 patient-days, metronidazole was 100.9 DDD. /100 patient-days, and amikacin 39.1 DDD/100 bed-days²¹.

In this study we used method of classification and calculation of ATC/DDD which is a method of calculating the use of antibiotics recommended by WHO and the ministry of health for audits of antibiotic consumption. However, this study has limitation which are using retrospective data so that it only relies on written medical record data and cannot confirm directly with health workers who write patient medical records; and DDD/100 patient-days method used can only present data on the use of antibiotics quantitatively, not qualitatively

Summary

The profile of the use of 17 antibiotics in ICU patients at the West Nusa Tenggara Provincial Hospital for the January-December 2018 period was in the range of 60.71 DDD/100 patient-days to 0.05 DDD/100 patient-days.

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