Original Research Article

Evaluation of the use of antibiotics using the anatomical therapeutic chemical/defined daily dose and Gyssens methods in pneumonia patients at a tertiary care general hospital in Medan

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ABSTRACT

Background: The impact of irrational antibiotic usage in pneumonia patients is an increase in resistance, an increase in drug side effects, and a failure of therapy that causes patients' health to deteriorate, lowering their quality of life and raising their treatment costs. The primary objective of this study is to assess the extent to which antibiotics are being used rationally in the inpatient facility of a private tertiary care hospital located in Medan.
Methods: The present study employs an observational design with a prospective cross-sectional approach, carried out within the timeframe of September to November 2022. The evaluation of antibiotic utilization was conducted utilizing the anatomical therapeutic chemical (ATC)/defined daily dose (DDD) methodology and the Gyssens methodology.
Results: The findings of the study indicate that a significant proportion of individuals diagnosed with pneumonia fell between the age range of 46 to 55 years, comprising 23.4% of the overall patient population. Moreover, the male gender was found to be the most prevalent, accounting for 55.81% of the 278 patients who satisfied the inclusion criteria. The findings from the evaluation of antibiotic utilization, employing the ATC classification system and DDD methodology, yielded a rate of 145.72 DDD per 100 days of care. Ceftriaxone exhibited the highest value, reaching 87.59 DDD/100 days of treatment. The evaluation of the Gyssens approach yielded a total of 254 patients who were administered antibiotics in an appropriate manner (category 0), while 24 patients were found to have received unsuitable antibiotics (categories I-VI).
Conclusions: Based on the findings of this study, it can be inferred that the utilization of antibiotics within the hospital under investigation remains inadequate in terms of both quantity and quality.

Keywords: Pneumonia, Gyssenes, ATC/DDD, Antibiotics

INTRODUCTION

Pneumonia is an infectious condition resulting from the invasion of microorganisms, including bacteria, viruses, fungi, and parasites, which induce inflammation inside the lungs and respiratory system. Indonesia exhibits a notable prevalence of pneumonia inside its borders. According to data from Regional Health Research, there was an observed rise in the prevalence of pneumonia from 2.1% to 2.7% till the conclusion of 2022.[1,2]

According to data obtained from the World Health Organization (WHO), there was an observed rise in the prevalence of pneumonia cases, with an increase from 2.1% in 2007 to 2.7% in 2013. The heightened incidence of pneumonia was observed mostly among the demographic of individuals aged 65 years and older, as well as those with pre-existing comorbidities.[3]

Pneumonia is an infectious condition resulting from the inhalation of particles that penetrate the lower respiratory

tract. The introduction of these particles can result in pulmonary injury as a consequence of bacterial, viral, and mycoplasma infections. Pneumonia is a pathological condition that is commonly managed with the use of antibiotic therapy.[4]

The inappropriate prescription of antibiotics and the excessive and repetitive utilization of antibiotics might result in the development of antibiotic resistance.[5] Research conducted in the field of American research has revealed that a significant proportion, ranging from 30% to 50%, of cases exhibit instances of improper treatment indication, medication selection, or length of antibiotic therapy.[3] The phenomenon of antibiotic resistance is associated with elevated expenses for medical treatment, extended durations of hospital stays, and heightened rates of patient fatality. Bacterial resistance to antibiotics can be defined as the inability of a maximum dosage of an antibiotic to effectively inhibit bacterial growth. This phenomenon arises as a result of the utilization of antibiotics that deviate from the recommended guidelines.[5]

The assessment of antibiotic utilization serves as a key metric for evaluating the effectiveness of antibiotic resistance control initiatives within hospital settings. The assessment of antibiotic utilization can be conducted by qualitative and quantitative methodologies. There are multiple approaches available to ensure appropriate and prudent use of medications. These methods include quantitative measures such as the defined daily dose (DDD) method, which relies on anatomical therapeutic chemicals (ATC) classification. Additionally, qualitative assessments can be conducted using the Gyssens method. This method evaluates antibiotic utilization based on criteria such as the accuracy of indications, correct dosage, appropriate duration of administration, suitable intervals between drug administrations, as well as safety and affordability for patients, taking into account cultural patterns and test results.[7] The ATC categorization system is utilized to categorize medications based on their therapeutic and pharmacological characteristics. The DDD serves as the standard unit of measurement for quantifying medication consumption in accordance with the ATC classification system. The DDD serves as a quantitative measure representing the average daily dosage of a medication when administered as the primary treatment for adult patients.[8]

Existing literature indicates that the assessment of antibiotic usage using the ATC/DDD methodology has revealed that ceftriaxone, levofloxacin, and azithromycin, which are three specific types of antibiotics, exhibit DDD/100 patient days values that beyond the guidelines set by the World Health Organization (WHO). The DDD/100 patient days values for the antibiotics are as follows: ceftriaxone at 83.80, levofloxacin at 27.47, and azithromycin at 3.52 DDD/100 patient days.[9] In a recent study conducted at Gatot Subroto Army Hospital in 2021, a prospective approach was employed to collect data from patient medical records and conduct interviews with

patients directly at the inpatient facility. The study focused on the period between September and November 2019. The findings of the study, which utilized the Gyssens method, revealed that out of the total sample, 28 patients demonstrated appropriate antibiotic usage (category 0), while 15 patients exhibited inappropriate antibiotic usage (categories I-VI).[10]

Antibiotics are considered the initial treatment modality for community-acquired pneumonia. It is imperative to exercise vigilance in monitoring the utilization of antibiotics in order to promote rational antibiotic usage, mitigate the emergence of antibiotic resistance, and yield favorable clinical outcomes. Aligned with the initiatives of the World Health Organization (WHO) and the Ministry of Health, the implementation of an antimicrobial stewardship program is highly recommended to enhance the judicious utilization of antimicrobial agents, particularly within hospital settings. In the year 2021, community-acquired pneumonia exhibited a notable prevalence, ranking as the tenth most prevalent disease within the Medan General Hospital. The present study seeks to assess the utilization of antibiotics in community-acquired pneumonia patients in a private public hospital in Medan, employing the ATC/DDD and Gyssens methodologies to quantify the extent of antibiotic usage.

METHODS

A prospective cross-section descriptive study design was used for this investigation. The necessary information was gathered from pneumonia patients' prescriptions and medical records at the Mitra Medika General Hospital in Medan during the September 2022–November 2022 period. This study was authorized by the University of Sumatera Utara's Health Research Ethical Committee (FK USU-RSUP HAM/2022). This study used the Anatomical Therapeutical Chemical (ATC)/DDD and Gyssens techniques to assess the usage of antibiotics in patients and to ascertain the amount of antibiotic use in pneumonia therapy. Patients receiving antibiotic therapy and having a diagnosis of pneumonia were the study's inclusion criteria. Patients who were pregnant, had HIV, or had cancer were excluded. During the study period, 278 patients with a diagnosis of pneumonia fulfilled the inclusion criteria. The patient's age, gender, and kind of medication were all noted on the data collection sheet. Records on the types of drugs used to treat pneumonia include the dosage, number of uses, and dosage form.

The ATC classification is based on the antibiotic code, the DDD calculation of each antibiotic is obtained by the total number of drugs that say in milligrams. The results of the use of antibiotics per patients were carried out using DDD/100 patients-days. Data from the DDD/100 patients-days calculations were changed in the form of percentages and then cumulative. The assessment results can be classified into many categories, as depicted in Gyssens' flowchart. Category 0 (appropriate and rational utilization of antibiotics), Category I-VI (inappropriate antibiotic

usage). Category I (inadequate timing of antibiotic administration), category II (refers to the delivery of an improper dosage, interval, method of administering of antibiotics), category III (refers to the excessive duration of antibiotic administration, where antibiotics are given for a longer or shorter duration than required), category IV (involves the incorrect selection of antibiotics, wherein alternative medications that possess greater efficacy, a higher level of safety, more cost-effective and a more limited range alternatives are available but not chosen), category V (There is insufficient evidence to support the administration of antibiotics), category VI (refers to a situation where the available evidence is insufficient to make an assessment on the usage of antibiotics). All analyses patient's characteristics were done using Microsoft excel version 2016.

This natural medicine is obtained from an e-catalog. This research is disastrous by the organizers of research and ethics at the University of Sumatera Utara. It was carried out in accordance with ethical standards provided by the University of Sumatera Utara, Faculty of Pharmacy.

RESULTS

Patient characteristics

The study yielded a total of 278 patients who met the inclusion criteria. The data presented in Table 1 is observable. The study yielded a total of 278 patients who met the inclusion criteria. The data below illustrates the observed phenomena shown in (Table 1).

Table 1: Patient characteristics.

Characteristics	N	Percentage (%)
Age		
17-25	20	7.2
26-35	32	11.5
36-45	45	16.2
46-55	65	23.4
56-65	61	22
>65	55	19.7
Gender		
Male	160	57.56
Female	118	42.44
LOS		
3-5	109	39.21
6-8	116	41.72
9-11	38	13.67
12-14	15	5.40

Treatment profile of pneumonia patients

Based on ATC code

The research done at a private tertiary care hospital in Medan during the period of September to November 2022

involved the categorization of data into four groups based on the ATC code for antibiotics. Displays the utilization of antibiotics in the treatment of individuals diagnosed with pneumonia in (Table 2).

Table 2: ATC codes for antibiotic use.

Class antibiotics	ATC code	Antibiotics	Dosage	Dosage (g)
Beta lactam	J01D D04	Ceftriaxone	Intra venous	1
Fluoroqui-nolone	J01M A12	Levofloxacin	Intra venous	0,5
Macrolides	J01F A10	Azithromycin	Oral	0,5
Monobact-am	J01D H02	Meropenem	Intra venous	1

Based on the type of antibiotic use

Based on the results of research on pneumonia patients at a private tertiary care hospital in Medan during the period of September to November 2022. Patient data was distributed into 6 antibiotic groups, namely single antibiotics levofloxacin and ceftriaxone, combination antibiotics namely meropenem-ceftriaxone, meropenem-levofloxacin, levofloxacin-ceftriaxone and ceftriaxone-azithromycin. The data bellow on the types of antibiotic use in the treatment of pneumonia is shown in Table 3.

Table 3: Type of antibiotic use.

Antibiotic type and group	Antibiotic name	Quant-ity
Single		
β lactams	Cefriaxone	189
Fluroquinolones	Levofloxacine	19
Combination		
Monobactam-betalactam	Meropenem-ceftriaxone	26
Fluroquinolone-β lactam	Levofloxacin-ceftriaxone	19
Monobactam-fluroquinolone	Meropenem-levofloxacine	13
β lactam-macrolides	Ceftriaxone-azithromycine	12
Total		278

Based on the number of antibiotics used

Based on the results of research on pneumonia patients at a tertiary care hospital in Medan during the period of September to November 2022, patient data was distributed into 4 antibiotic groups, namely meropenem, levofloxacin, azithromycin and ceftriaxone.

The data on the number of antibiotics used in the treatment of pneumonia is shown in Table 4.

Evaluation of the use of antibiotics using the ATC/DDD method

According to the findings from a study conducted at a tertiary care general hospital in Medan between September to November 2022, as presented in Table 5, it was observed that the utilization of antibiotics exhibited the highest frequency among the four categories of prescribed antibiotics, amounting to a total of 145.72 defined daily doses (DDD) per 100 patient days. The data below illustrates the observed phenomena shown in Table 5.

Evaluation of the use of antibiotics using the Gyssens method

The Gyssens method is a methodology employed to evaluate the appropriateness of antibiotic usage. The therapeutic approach for the treatment of community-acquired pneumonia in this healthcare facility pertains to the guidelines provided by the Indonesian Lung Doctors Association (PDPI) in 2014 and the Indonesian Ministry of Health in 2021. Presents the outcomes of the assessment conducted on the utilization of antibiotics employing the Gyssens methodology show in (Table 6).

Table 4: Number of antibiotics used.

Antibiotics	Dosage (g)	Preparations	Total usage	(%)
Ceftriaxone	1	Injection	3.120	75.24
Meropenem	1	Injection	514	12.39
Levofloxacin	0.5	Injection	461	11.12
Azithromy-cine	0.5	Tablets	52	1.25
Total			4.147	100

Table 5: Antibiotic usage by ATC/DDD method.

ATC code	Antibiotics	Total usage (g)	DDD standard value (WHO) (g)	Total LOS (days)	DDD/100 patient days
J01DH02	Ceftriaxone	3120	2		87.59
J01MA12	Levofloxacine	345.75	0.5	1781	38.83
J01FA10	Meropenem	514	2		14.43
JO1DD04	Azithromycine	26	0.3		4.87
Total					145.72

Table 6: Antibiotic use of the Gyssens method for pneumonia patients.

Category	Description	N	%
VI	Incomplete data	0	0
V	Antibiotics not indicate	0	0
IVa	There is a more effective alternative	12	4.32
IVb	There is a non-toxic alternative	0	0
IVc	There is a cheaper alternative	0	0
IVd	There is a narrower spectrum alternative	0	0
IIIa	Antibiotic administration is too long	0	0
IIIb	Administering antibiotics for too short a period of time	0	0
IIa	Inappropriate dose	7	2.52
IIb	Inappropriate interval	5	1.79
I	inappropriate timing	0	0
0	Not included in categories I-IV	254	91.37

DISCUSSION

The data shown in Table 1 illustrates that among a cohort of 278 individuals diagnosed with pneumonia, the predominant proportion of patients at private tertiary care institutions in Medan were male, accounting for 42.44% of the total, while female patients constituted a comparatively lower number. This disparity in risk can be attributed to the anatomical variation in respiratory tract size between males and females, with males generally exhibiting smaller respiratory tracts. Additionally, disparities in endurance levels between males and females may contribute to the differential risk observed.[12] The prevalence of the smoking habit is predominantly observed among males in comparison to females. Both individuals who actively smoke and those who are exposed to secondhand smoke are at risk of developing pneumonia. This susceptibility arises from the inhalation of cigarette smoke, which contains a multitude of chemicals that have detrimental effects on health. These chemicals disturb the body's natural defense mechanisms, impairing its ability to combat bacteria or viruses that are responsible for causing pneumonia.[4]

According to the observed characteristics of the age group, it was determined that the age range of 45-55 years exhibited the highest incidence of pneumonia cases. This particular age group accounted for a total of 65 patients, or

approximately 23.4% of the overall population under study. Age is a significant determinant in the development of pneumonia, since there is a positive correlation between age and the occurrence of pneumonia. In addition to the older population, toddlers are also vulnerable to contracting this particular pneumonia infection. However, in contrast to older individuals, this disparity may be mostly attributed to the numerous health problems that are commonly associated with advanced age, such as diminished lung function and a weakened immune system. It is important to acknowledge that individuals aged 60 years and above have a progressively deteriorating prognosis, with a doubling effect observed for each successive decade.[5]

The duration of hospitalization has a strong correlation with both the acuteness of the patient's ailment and their financial means or insurance coverage. The findings of this study indicate that the majority of community pneumonia patients had a length of stay ranging from 6 to 8 days, accounting for 41.72% of the sample. Conversely, the smallest proportion of patients had a length of stay between 12 and 14 days, representing only 5.40% of the total. The data suggests that individuals diagnosed with pneumonia and admitted to private tertiary care institutions in Medan between September and November 2022 had an average duration of hospitalization ranging from 6 to 8 days. The duration of hospitalization for patients with community-acquired pneumonia varies between 5 and 10 days, as reported by the Indonesian Ministry of Health. The cohort of hospitalized individuals for a duration exceeding 10 days encompasses geriatric patients who present with many medical conditions, one of which is accompanied by the presence of acute respiratory distress syndrome (ARDS).[3] Additional research has demonstrated that individuals afflicted with bacterial infections typically experience a hospitalization period lasting approximately 7 to 10 days. This duration is subject to various factors, including the presence of comorbid conditions, the occurrence of sequelae, and the overall severity of the illness.[13]

The ATC codes of antibiotics used in the treatment of pneumonia are presented in Table 2. Ceftriaxone is classified under the ATC code J01DD04, indicating its categorization as an anti-infective agent for systemic use. J01 refers to an antibiotic agent that is administered systemically, while J01D denotes a beta-lactamase antibacterial agent. J01DD refers to a class of antibiotics known as third-generation cephalosporins. J01DD04 refers to ceftriaxone, which is classified as an antibiotic. The ATC code is a drug classification system that categorizes the active constituents of medications based on their specific target organ or system of action, as well as their therapeutic, pharmacological, and chemical characteristics.[8]

Table 3 presented above illustrates the categorization of antibiotics provided by medical professionals, namely into two distinct groups: single antibiotics and combination antibiotics. Among the cohort of 189 patients, ceftriaxone had the highest level of utilization as the sole type of antibiotic. The microorganisms responsible for pneumonia are challenging to detect, thereby prompting the administration of empirical antibiotics as an initial therapy approach. Therefore, β-lactam antibiotics are frequently employed. In the study, it was observed that meropenem-ceftriaxone had the highest utilization rate among the cohort of 26 patients. The administration of a combination of antibiotics is employed with the objective of expediting bacterial eradication and achieving synergistic outcomes, particularly in cases when the duration of treatment extends beyond a single day. In essence, the efficacy of combination therapy surpasses that of monotherapy with a single medicine on the initial day of treatment.[14] As to the 2021 guidelines set forth by the Ministry of Health of the Republic of Indonesia, the administration of antibiotics for non-intensive care unit (ICU) hospitalization is recommended to include the administration of ceftriaxone and levofloxacin as single agents. The administration of a combination of inpatient antibiotics during ICU hospitalization may involve the use of levofloxacin-ceftriaxone or ceftriaxone-azithromycin.[3]

Table 4 displays the distribution of antibiotic utilization in a tertiary care general hospital in Medan. It reveals that ceftriaxone was the most often prescribed antibiotic, accounting for 75.24% of the total usage. Conversely, azithromycin had the lowest utilization rate, representing just 1.25% of the total antibiotic usage. Ceftriaxone belongs to the third generation of cephalosporins and is derived from β-lactam. Ceftriaxone exhibits a wide range of antibacterial activity against both gram-positive and gram-negative pathogens.[6] When compared to other preparations in the cephalosporin class, ceftriaxone exhibits significant efficacy against gram-positive pathogens like *Streptococcus sp.* and *Streptococcus pneumoniae*, as well as gram-negative organisms such as *Branhamella catarhalis*, *Escherichia coli*, *Proteus sp.*, and *Haemophilus influenza*.[7] The method of action of this substance is bactericidal. Ceftriaxone exhibits high stability and demonstrates effective inhibition of B-lactamases generated by a wide range of organisms. The recommended dosage of ceftriaxone is 1-2 grams per day. Ceftriaxone is primarily eliminated via the biliary system, and therefore does not necessitate dosage adjustment in the presence of renal impairment. Hence, it is advisable to administer third-generation cephalosporin-class antibiotics, such as ceftriaxone, for the purpose of empirical therapy in cases of pneumonia infection.[8]

The findings of this study align with prior research examining the assessment of antibiotic utilization among pneumonia patients at Jombang Hospital in 2019, specifically focusing on the administration of third-generation cephalosporin medicines, such as ceftriaxone.[9] The study conducted in 2017 demonstrated that third-generation cephalosporin medicines, specifically ceftriaxone, continued to exhibit the most effective outcomes in addressing pneumonia-related issues.[10]

Table 5 displays the evaluation of the use of antibiotics using the ATC/DDD method amounting to a total of 145.72 defined daily doses (DDD) per 100 patient days. Ceftriaxone exhibits the greatest numerical value among antibiotics, specifically 87.59 DDD/100 patient days. The preference for ceftriaxone in the treatment of pneumonia is attributed to its heightened antibacterial efficacy against gram-positive bacteria, expanded distribution volume, and prolonged half-life.[12] The term "DDD value" refers to the findings that suggest a high prevalence of antibiotic usage in tertiary care general hospitals in Medan. These findings imply that the utilization of antibiotics in this context is still characterized by a lack of rationality. In order to facilitate future antibiotic prescription decisions, it is imperative to address this aspect. In comparison to a study conducted at a hospital in Germany, the utilization of antibiotics among patients diagnosed with sepsis and pneumonia in the hospital resulted in a cumulative usage of 67.1 to 51.0 defined daily doses (DDD) per 100 patient days.[15] A higher degree of antibiotic utilization over a 100-day hospitalization period is indicated by a bigger total value of DDD/100 days of hospitalization, above the standard set by the World Health Organization (WHO). Conversely, a smaller DDD number corresponds to a lower likelihood of antibiotic resistance. Another study additionally shown that the limited utilization of antibiotics indicated that physicians exhibited greater selectivity in their treatment choices for patients, aligning more closely with the notion of judicious antibiotic use.[16]

Additionally, a separate investigation disclosed a substantial utilization of antibiotics at Dr. Moewardi Hospital, amounting to 111.87 defined daily doses (DDD) per 100 patient days.[17] This study aligns with prior studies conducted at Jombang Hospital about the administration of antibiotics to hospitalized patients with a defined daily dose (DDD) value of 83.25 DDD/100 days of hospital stay. In contrast, the DDD value pertaining to the utilization of antibiotics among pneumonia patients at Wava Husada Kepanjen Hospital exhibited no statistically significant variation, amounting to 88.95 DDD/100 days. The observed discrepancy can be attributed to variations in the duration of hospital stays among patients, leading to distinct computations of length of stay (LOS) for each individual.

The Gyssens method is a methodology employed to evaluate the appropriateness of antibiotic usage. This evaluation encompasses various aspects, such as the accuracy of indications, the effectiveness of antibiotic selection based on factors like efficacy, toxicity, cost, spectrum, duration of administration, dosage, interval, route, and timing of administration.[18,19] The medical record data that was collected was found to be comprehensive, thereby indicating the absence of any instances falling under category VI. Antibiotics administered without indication refer to the administration of antibiotics that do not align with the patient's clinical condition. This includes the use of antibiotics for individuals who lack symptoms and signs of infection, and

are not intended for preventative purposes.[14] Category V did not include any cases due to the exclusive utilization of medical records with a diagnosis of community pneumonia in the analysis of medical record data.

Within the realm of category IVa, an alternative of greater efficacy exists. The findings indicate that there were a total of 12 instances where antibiotics were utilized more effectively. Specifically, the use of single levofloxacin in community pneumonia was deemed inappropriate as the initial treatment option. This conclusion is based on Izadi's study conducted in 2018, which revealed that the combination of ceftriaxone and azithromycin demonstrated comparable efficacy to levofloxacin monotherapy in the management of community pneumonia necessitating hospitalization.[20]

Category IV B includes alternative antibiotics that have lower toxicity or are considered safer, indicating that the antibiotics prescribed are not recommended due to the patient's clinical condition. The clinical conditions under consideration encompass the laboratory results of the patient's SGOT, SGPT, BUN, and creatinine. The safety of administering antibiotics to individuals with pneumonia suggests the absence of any instances falling within category IV B.

Within category IVC, there exist alternative antibiotics that are more cost-effective, indicating the continued availability of generic antibiotics at lower prices. The assessment of non-generic antibiotics is a comparative analysis of the costs associated with branded antibiotics containing identical active components. Based on the findings of the research, it was observed that all categories of antibiotics examined exhibited availability of generic variants at affordable price points.

Within the realm of in vitro diagnostics (IVD), there are additional antibiotics that possess a more limited range of activity. Specifically, these antibiotics are evaluated to determine their appropriateness for usage based on the findings of patient culture tests. The medical records analyzed in this study did not include patient culture findings due to the use of antibiotics for empirical therapy. The assessment of category IV D was conducted through an evaluation of the utilization of broad-spectrum antibiotics for empirical therapy. The evaluation results indicated a lack of instances of antibiotic utilization within category IV D. The administration of ceftriaxone, levofloxacin, meropenem, and azithromycin to patients is consistent with the recommended guidelines for the use of broad-spectrum antibiotics.

Category III A refers to the excessive duration of antibiotic use, whereas category III B pertains to the insufficient duration of antibiotic use. Prolonged antibiotic usage refers to the administration of antibiotics beyond the recommended term of antibiotic therapy by the patient. Prolonged antibiotic use refers to the situation wherein patients do not adhere to the recommended length of

antibiotic medication. The duration of therapy for patients diagnosed with pneumonia is determined based on established clinical recommendations. Based on the guideline provided by the PDPI (2014), the typical length of antibiotic administration for empirical therapy of community-acquired pneumonia (CAP) is approximately five days.[21] As per the guidelines provided by the Indonesian Ministry of Health (2021), the recommended period of antibiotic treatment for pneumonia patients receiving non-intensive care unit (ICU) treatment is 3-5 days.[3] Conversely, for pneumonia patients receiving ICU care, the recommended duration of antibiotic treatment is 7-10 days.[3] The duration of single and combination antibiotic regimens is neither excessively lengthy nor insufficiently brief. The analysis yielded a finding that no instances were classified as IIIA and IIIB.

Category II A refers to the utilization of antibiotics at improper dosages, when there is a discrepancy between the prescribed dose of antibiotics and the recommended range of antibiotic doses as outlined in the relevant guidelines. According to the findings of the evaluation, it was observed that out of the total instances examined, seven cases failed to meet the Gyssens criteria. These seven cases represent a proportion of 2.52% out of the total number of cases evaluated. The reason for this discrepancy is that the physician administered a levofloxacin infusion dosage of 750 mg every 12 hours, although the PDPI guideline from 2014 suggests a dosage of 750 mg every 24 hours.[21] The antibiotics prescribed by the physician deviated from the established criteria as a result of taking into account the patient's clinical condition and elevated leukocyte levels.

Category II B refers to the utilization of antibiotics at irregular intervals of administration, indicating that antibiotics are being used at intervals that lack consistency. This phenomenon can lead to fluctuations in medication concentrations within the bloodstream, so preventing the attainment of the desired steady-state drug levels required for effective eradication of bacteria by antibiotics. Administration intervals that are shorter than the specified duration may result in elevated drug concentrations within the body, hence increasing the risk of drug toxicity. Exceeding the specified delivery intervals may result in diminished drug concentrations within the body or drug levels falling below the minimal threshold required to elicit therapeutic effects. Consequently, bacteria may develop resistance due to insufficient drug levels that are unable to effectively eradicate these microorganisms. A comparative analysis was conducted to assess the discrepancy in the administration interval of antibiotics, specifically by comparing the documented administration interval in the medical record with the guidelines provided by the PDPI (2014) and the Indonesian Ministry of Health (2021).[3,21] According to the findings of the evaluation, a total of five instances (1.79%) were identified whereby antibiotics were used inappropriately. Specifically, these cases involved the administration of a combination of levofloxacin and ceftriaxone, as well as the use of ceftriaxone as a single agent. The administration of

antibiotics at improper intervals by nurses was observed and documented by researchers during a study conducted at a tertiary care general hospital in Medan.

Category II C refers to the inappropriate administration of antibiotics, specifically when the route of administration does not align with the prescribed route outlined in the guideline being followed. This study focuses on evaluating the precision of the route of administration, specifically by comparing the route of administration documented in the medical record with the route of administration recommended in the guideline. The preferred method of antibiotic delivery for hospitalized patients with pneumonia is the parenteral route, specifically through intravenous injection (PDPI, 2014; the Indonesian Ministry of Health, 2021).[3,21] All instances of antibiotic utilization successfully underwent the *Gyssens* assessment, with none falling under the classification of IIC.

Category I, referred to as the utilization of antibiotics, lacks timeliness, indicating that the timing of antibiotic administration does not align with the recommended schedule for drug administration. The evaluation of drug administration timeliness in this study involved a comparison between the recorded time of antibiotic administration on the Drug Administration Sheet in the medical record and the duration of antibiotic usage. According to the findings of the review, there were no instances of inappropriate antibiotic usage occurring within the specified timeframe.

Category 0, referred to as sensible antibiotic usage, encompasses the appropriate utilization of antibiotics based on the clinical requirements of patients. This entails the use of cost-effective and high-quality antibiotics, specifically those that possess narrow-spectrum properties and exhibit low levels of toxicity. The appropriate utilization of antibiotics is contingent upon several factors, including the administration of suitable doses, adherence to acceptable intervals of administration, adherence to right duration of administration, adherence to appropriate method of administration, and adherence to appropriate time of administration. According to the data presented in Table 6, the utilization of antibiotics in a rational manner (classified as category 0) among patients diagnosed with pneumonia amounted to 254 instances, representing a percentage of 91.37%.

The findings from the assessment of antibiotic usage quality, conducted using the Gyssens method, revealed that 254 patients (91.37%) appropriately utilized antibiotics. Conversely, 24 patients (8.63%) in categories I-V demonstrated inappropriate antibiotic usage. The rationality of antibiotic usage remains questionable.

A prior study conducted at Zainoel Abidin Banda Aceh Hospital examined the assessment of antibiotic utilization by the Gyssens approach. The findings revealed that around 35,1% of antibiotic usage was deemed reasonable,

while the remaining 64,29% was categorized as irrational.[22] In contrast, a study conducted at the UGM Academic Hospital examined the assessment of antibiotics and revealed that 84.93% of antibiotic usage was deemed illogical, while 15.07% was considered suitable and sensible.[23] Several research findings evaluating the utilization of antibiotics in various clinical settings suggest a negative correlation between the extent of antibiotic usage and its rationality. There are other variables that can contribute to this phenomenon, including patient non-adherence to medication regimens, the inappropriate use of antibiotics, inadequate management of drug processing in healthcare facilities, and the administration of antibiotic doses that do not align with patient requirements. Hence, it is imperative to exercise caution when administering antibiotics to individuals who require such treatment, in order to mitigate the development of antibiotic resistance.[24]

Previous studies undertaken by researchers have demonstrated that the use of empirical antibiotics can enhance clinical outcomes in individuals with pneumonia. Hence, it is crucial to prioritize the rationale of the antibiotics administered to mitigate the potential morbidity and death associated with pneumonia.[25]

CONCLUSION

Based on the evaluation results of the ATC/DDD method and the Gyssens method conducted for the use of antibiotics, it can be concluded that the use of antibiotics in hospitalized pneumonia patients in one of the tertiary care hospitals in Medan is still not rational in quantity and quality. This is evidenced by the high percentage of ATC/DDD scores and the percentage of Gyssens assessment categories IVA, IIA, IIB. It is expected that hospitals should conduct blood culture examinations and look at the germ map of the cause of pneumonia so that appropriate antibiotics can be given in an effort to control antibiotic resistance in Indonesia.

ACKNOWLEDGEMENTS

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