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Original Article

EVALUATION OF QUANTITATIVE AND QUALITATIVE USE OF ANTIBIOTICS IN COMMUNITY HEALTH CENTERS, BOYOLALI DISTRICT, INDONESIA

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ABSTRACT

Objective: This study evaluated the quantity and quality of antibiotic use in hospitalized patients and outpatients at the Boyolali District Health Center.

Methods: This research is a non-experimental study that collects data by purposive sampling. The inclusion criteria were inpatients and outpatients at the two community health centers in the Boyolali district. Data were analyzed quantitatively using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) method and qualitatively using the Gyssens method.

Results: During the study period, 123 hospitalized patients and 338 outpatients met the inclusion and exclusion criteria. The majority of hospitalized patients were women (53.7%) aged 46-65 (30.1%) with a length of stay ≤4 d (56.9%). In comparison, most outpatients were women (61.5%) aged 26-45 (26.9%). The total Defined Daily Dose (DDD)/100 patients-days aged<18 who were hospitalized was 24.3; the most antibiotic was Cefotaxime (36.6%). The total DDD/100 patients days aged ≥ 18 who were hospitalized was 89.7; the most common antibiotic was Thiamphenicol (42.1%). Meanwhile, the most frequently prescribed antibiotic in outpatient was Amoxicillin, 85.3% (age<18 y) and 50.2% (age ≥18 y). Based on Gyssen's analysis, most of the antibiotic administration was in criterion IIIB; namely, the administration of antibiotics was too short.

Conclusion: It is necessary to increase the rationality of the use of antibiotics both in inpatients and outpatients.

Keywords: Antibiotic, ATC/DDD, Quantitative analysis, Gyssens, Qualitative analysis

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INTRODUCTION

Infectious disease is still a significant public health problem, especially in developing countries. One of the drugs to overcome this problem is antimicrobials, including antibacterial/antibiotics, antifungals, antivirals, and anti-protozoa. Antibiotics are the drugs most widely used in infections caused by bacteria. However, prescription and inappropriate antibiotic use will increase the incidence of resistance, which has become a national and global focus [1-3].

World Health Organisation (WHO) states that antibiotic resistance is a serious threat in all parts of the world. Resistance is defined as the absence of inhibition of bacterial growth by systemic administration of antibiotics at regular doses [3, 4]. Antibiotic resistance can have a significant negative impact on the provision of healthcare services, the quality of patient's lives, the length of hospital stays, the difficulty of treatment, medical costs, the length and complexity of illnesses, the number of doctor visits, the use of potent and expensive drugs, and the morbidity and mortality rate [2–9]. Therefore, it is necessary to monitor the use of antibiotics to ensure rational use over time and prevent irrational use of antibiotics as early as possible [10, 11]. Various studies have found an inaccuracy in the use of antibiotics of 40-62%. In addition, research on the quality of antibiotic use in various parts of the hospital found that 30% to 80% were not based on indications [1, 3]. Improper prescribing of antibiotics is the cause of epidemics of resistant bacteria. WHO has stated the importance of studying the factors associated with the problem of antibiotics, including strategies to control the incidence of resistance [12]. One of the strategies WHO recommends is to conduct surveillance on the use of antibiotics at health facilities and report them regularly [12, 13].

Puskesmas is a health service unit that reaches the village's depths. Puskesmas (Indonesian for "Community Health Center") are government-mandated community health clinics located throughout Indonesia. The Indonesian Ministry of Health oversees them and provides sub-district-level healthcare to the population. People who live far from cities make community health care the first priority in getting health services, so it is necessary to evaluate the use of antibiotics in patients in community health care quantitatively and qualitatively. The quantitative use of the ATC/DDD method is recommended by the WHO to assess drug use [14]. This method is carried out by calculating the Defined Daily Dose (DDD) used per 100 patient days for hospitalized patients and the DDD/1000 population for outpatients to determine the type and amount of antibiotics used [15]. Qualitatively evaluate the use of antibiotics using the Gyssens Algorithm. Gyssens algorithm was developed in 1992 to assess the classification of prescriptions in the category of inappropriate use, which will provide a qualitative evaluation of antimicrobial administration. This algorithm is in the form of classified questions to organize and simplify the evaluation process so that it helps categorize antibiotic prescriptions [16].

MATERIALS AND METHODS

Study design

This research is a non-experimental study with purposive sampling according to inclusion and exclusion criteria. This study used medical record data from the two community health centers in Boyolali, Indonesia. Analyzed quantitatively with the ATC/DDD method and qualitatively with the Gyssens method.

Tools and materials

The tools used in the study are Gyssens diagrams and some guidelines. The guidelines used to evaluate antibiotic therapy are Guidelines for the control of typhoid fever (2006), patterns of management of acute diarrhea in pediatrics (2006), current medical diagnosis and treatment (2017), technical guidelines for leptospirosis control (2017), pocket book of rabies tropical module (2016), Carranza's periodontology clinical guidelines (2012), pharmaceutical care for respiratory infections, and the WHO collaborating center for drug statistics methodology [17–19]. In addition, data were obtained from patients' medical records. Before the study, research approval was obtained from the health research ethics committee, the medical faculty of Universitas Muhammadiyah Surakarta No.2833/B.1/KEPK-FKUMS/II/2020.

Data collection

The data used in this study were secondary data derived from patients' medical records. The population of this study was all inpatients and outpatients who received antibiotic therapy at two community health centers in the Boyolali district. The sampling method used purposive sampling following the inclusion and exclusion criteria. Inclusion criteria are hospitalized and outpatients receiving antibiotics, while the exclusion criteria are patients with two or more infectious diseases, death, and forced discharge. The sample was taken from January to December 2019. Data were obtained from the medical records of patients consisting of medical record number, demographic characteristics (age, sex, height, weight), patient diagnosis, history of the disease, medical history (antibiotic name, dose, frequency, route, duration of antibiotic administration), laboratory data (blood test, serum glutamate-pyruvate transaminase, and serum glutamic-oxaloacetic transaminase, SrCr, and supporting examinations such as chest X-ray, culture examination results (if any), and Length of Stay (LoS).

Data analysis

The data were analyzed and presented descriptively. Antibiotic use was assessed or evaluated quantitatively by calculating the DDD per 100 patient days [15]. In the hospitalized patients, the number of antibiotic uses was calculated by multiplying the frequency with the length of stay of the patient receiving antibiotics, the total strength of the antibiotics used (strength x number of antibiotic use), the total per group, and LoS by summing all patient days. Quantitative analysis was performed using the Defined Daily Doses method. The quantity of antibiotics used for hospitalized patients is expressed in DDD/100 patient-days:

$$\frac{\text{DDD}}{100}\text{patient} - \text{days} = \frac{\text{the number of grams of antibiotic used by the patient}}{\text{DDD WHO standard in gram}} \text{ x } \frac{100}{\text{total LoS}}$$

The quantity of antibiotics used for outpatients is expressed in the DDD/1000 patient population:

$$\frac{\text{DDD}}{1000}\text{population} = \frac{\text{Total DDD Antibiotic}}{\text{Total number of patients}} \times 1000$$

Qualitative analysis of antibiotics used the Gyssens method. Gyssens' algorithm is in the form of questions that are classified to organize and simplify the evaluation process so that it helps categorize antibiotic prescriptions [16]. Assessment of antibiotic use was obtained from the amounts contained in categories 0 and I-VI expressed as a percentage. Category 0 is the appropriate use of antibiotics; Category I-IV is inappropriate antibiotic use.

RESULTS

During the study period, 123 hospitalized patients and 338 outpatients met the inclusion and exclusion criteria. The majority of hospitalized patients were women (53.7%), aged 46-65 (30.1%), with a length of stay ≤4 d (56.9%), and were diagnosed with typhoid (81.3%). Likewise, in outpatients, with the majority being women (61.5%) aged 26-45 y (26.9%), with the most diagnoses of acute periapical periodontitis (23.4%) followed by influenza (18.3%) and typhoid (16.6%). The respondents' characteristics are shown in table 1.

Table 1: Characteristics of inpatients and outpatients

Characteristics		Inpatients n=123 (%)	Outpatients n=338 (%)
Gender	Male	57 (46.3)	130 (38.5)
	Female	66 (53.7)	208 (61.5)
Age (year)	≤5	10 (8.1)	70 (20.7)
	6-17	23 (18.7)	44 (13.0)
	18-25	18 (14.6)	48 (14.2)
	26-45	28 (22.8)	91 (26.9)
	46-65	37 (30.1)	58 (17.2)
	>65	7 (5.7)	27 (8.0)
Diagnosis	Tooth abscess	-	25 (7.4)
	Acute Bronchitis	-	18 (5.3)
	Acute nasopharyngitis	-	13 (3.8)
	Acute Otitis Media	-	32 (9.5)
	Acute Pharyngitis	-	31 (9.2)
	Acute Periapical Periodontitis	-	79 (23.4)
	Animal bite	-	1 (0.3)
	Combustion	-	1 (0.3)
	Cystitis	-	8(2.4)
	Dengue Fever	1 (0.8)	-
	Acute Diarrhea	4 (3.3)	-
	Febris	6 (4.9)	-
	Gastritis	1 (0.8)	-
	Gastroenteritis	4 (3.3)	-
	Haemorrhoid	-	2 (0.6)
	Skin infection	-	2 (0.6)
	Urinary tract infection	-	1 (0.3)
	Influenza	-	62 (18.3)
	Upper respiratory infection	2 (1.6)	-
	Leptospirosis	-	1 (0.3)
	toothache	-	4 (1.2)
	Superficial Injuries Involving	-	1 (0.3)
	Susp. Tifoid	1 (0.8)	-
	Tifoid	100 (81.3)	57 (16.9)
	Vertigo	4 (3.3)	-
Length of stay (day)	≤4	70 (56.9)	-
	5-9	53 (43.1)	-

Quantitative evaluation of antibiotic use with ATC/DDD

Evaluation of the quantity of antibiotic use was calculated using the DDD method with the unit DDD/100 patient-days, which describes the number of patients who received the DDD in inpatients. Outpatients are calculated using the DDD unit/1000 population to determine the quantity of antibiotic use in 1000 outpatient visits for a year. The results of the quantitative assessment of the use of antibiotics in inpatients and outpatients in patients aged<18 y and ≥18 y can be seen in tables 2 and 3, respectively.

Table 2: Results of quantitative analysis of antibiotic use in inpatients and outpatients<18 y

ATC	Antibiotic	Inpatients (n=33)			Outpatients (n=114)		
		DDD	DDD/100 *patient-days*	(%)	DDD	DDD/1000 *population*	%
J01CA04	Amoxicillin	6.6	1.4	5.8	32.5	2.9	85.3
J01BA01	Chloramphenicol	21.57	4.5	18.5	1.8	0.2	5.9
J01BA02	Thiamphenicol	35.63	7.5	30.9	1.7	0.2	5.9
J01DD01	Cefotaxime	42.7	8.9	36.6	-	-	-
J01DD08	Cefixime	9	1.9	7.8	-	-	-
J01DB05	Cefadroxil	0,56	0.1	0.4	0.3	0.003	0.9
P01AB01	Metronidazole	-	-	-	1.3	0.1	2.9
	Total DDD		24.3			3.4	

Table 3: Results of quantitative analysis of antibiotic use in inpatients and outpatients ≥18 y

ATC	Antibiotic	Inpatients (n=90)			Outpatients (n=224)		
		DDD	DDD/100 *patient-days*	%	DDD	DDD/1000 *population*	%
J01BA01	Chloramphenicol	36.1	12.9	14.4	2.2	0.2	0.8
J01BA02	Thiamphenicol	201.0	42.1	46.8	12.3	1.1	4.2
J01CA04	Amoxicillin	42.0	8.8	9.8	148.6	13.2	50.2
J01DB05	Cefadroxil	6.50	2.7	3.0	2.0	0.2	0.8
J01DD01	Cefotaxime	42.7	15.5	17.4	-	-	-
J01DD08	Cefixime	26.0	5.4	6.0	3.0	0.3	1.1
J01MA02	Ciprofloxacin	6.4	2.3	2.6	39.2	3.5	13.3
J01AA02	Doxycycline	-	-	-	18.0	1.6	6.1
P01AB01	Metronidazole	-	-	-	68.3	6	22.8
J01FF01	Clindamycin	-	-	-	0.8	0.06	0.2
J01EE03	Trimethoprim-Sulfamethoxazole	-	-	-	1.5	0.1	0.4
	Total		89.7			26.3	

The most widely used antibiotic for inpatients aged<18 y is Cefotaxim, with usage of 8.9 DDD/100 patient-days, which means that in 100 d of hospitalization in community health centers, nine patients with a diagnosis of infection receive Cefotaxim therapy according to the definitive daily dose per days and for patients ≥18 y, namely Thiamphenicol with 42.1 DDD/100 patient-days. On the other hand, the least used antibiotic in hospitalized patients aged <18 y is Cefadroxil with 0.1 DDD/100 patient-days, and for patients ≥18 y, namely Ciprofloxacin with 2.3 DDD/100 patient-days.

While the use of antibiotics in outpatients is calculated by DDD/1000 patient population, the total use of antibiotics in outpatients aged ≥18 y with the widely used antibiotic, namely Amoxicillin, was 13.2 DDD patients/1000 patient populations. For every 1000 patient populations, 13-14 patients received Amoxicillin therapy. For patients aged <18 y, namely Amoxicillin with 2.9 DDD patients/1000 patient population. The least used antibiotic was Clindamycin 0.06 DDD/1000 patient population.

Qualitative evaluation of antibiotic use within the gyssens category

The results of evaluating the quality of antibiotic use for inpatients and outpatients using the Gyssens method can be seen in table 4.

Table 4: The results of a qualitative analysis of the use of antibiotics

Code	Category	<18 y				≥18 y			
		Inpatients (n=33)		Outpatients (n=114)		Inpatients (n=90)		Outpatients (n=218)	
		No	%	No	%	No	%	No	%
V	Antibiotics are not indicated	4	7.8	39	32.2	17	11.9	38	17.1
IVA	Other antibiotic options are more effective	5	9.8	5	4.1	39	27.3	41	18.5
IVC	There are other, less expensive, antibiotic options	10	19.6	1	0.8	24	16.8	1	0.5
IVD	Other antibiotic options are narrower in the spectrum	9	17.6	-	-	19	13.3	1	0.5
IIIB	Antibiotic duration is too short	20	39.2	73	60.3	28	19.6	126	56.8
IIA	Incorrect dose of antibiotics	2	3.9	-	-	12	8.4	-	-
IIB	Incorrectly administering antibiotics in terms of frequency	1	2.0	-	-	3	2.1	2	0.9
0	Proper and appropriate administration of antibiotics			3	2.5	1	0.7	13	5.9

Table 4 shows a qualitative evaluation of antibiotic use in hospitalized and outpatient patients aged<18 and ≥18 y. In hospitalized patients under 18 y, the results of a qualitative assessment of the use of antibiotics were mostly in category IIIB, i. e., the duration of antibiotics was too short (39.2%), followed by the IVC category, i. e., there were other cheaper antibiotic options. In outpatients, more than half of the patients (60.3%) were in category IIIB; namely, the duration of antibiotics was too short, followed by 32.2% administration of antibiotics was not indicated. In adult patients, 27.3% were in category IVA, i. e., there was a more effective choice of antibiotics, and 19.6% were in category IIIB (the duration of antibiotics was too short). Whereas in outpatient adult patients, more than half of the patients (56.8%) were in the IIIB category (the administration of antibiotics was too short) and IVA (there were more effective antibiotic options), as much as 18.5%.

DISCUSSION

Antimicrobial resistance is a threat worldwide, so controlling antimicrobial resistance is an urgent action. One of the strategies used in antimicrobial resistance control programs is to control the development of resistant microbes due to selection pressure by antibiotics through the wise use of antibiotics. The application of wise use of antibiotics is carried out through surveillance of patterns of use of antibiotics, as well as reporting them periodically [12]. Surveillance is essential for informing policies and infection control and prevention responses, assessing antimicrobial resistance spread, and monitoring the impact of local, national, and global strategies [13]. Ideally, antibiotic therapy is based on definitive, but due to limited laboratory facilities in community health centers, antibiotic therapy is given empirically.

In this study, the total DDD/100 patients in<18-year hospitalization was 24.3, with the most frequently prescribed antibiotic being Cefotaxime. Whereas in adult inpatients, the total DDD/100 patients was 89.7, with the highest prescription of antibiotics, namely Thiamphenicol. Based on the AWaRe antibiotic classification grouping, Thiamphenicol is an ACCESS group of antibiotics available in all healthcare facilities and used for treating common bacterial infections. In contrast, Cefotaxime is a group of WATCH class of antibiotics. WATCH class antibiotics are only available in advanced health care facilities for special indications or when ACCESS group antibiotics are ineffective. This group of antibiotics has a higher ability and potential to cause resistance, so it is prioritized as the main target of surveillance and monitoring programs. This class of antibiotics should only be prescribed by a specialist doctor or specialist dentist, reviewed by a pharmacist, and approved by an infection consultant doctor; if an infection consultant doctor is not available, approval is given by a member of the Antimicrobial Resistance Control Committee determined by the hospital leadership. Community health centers are first-level health service centers only available and can access ACCESS class antibiotics. Therefore, Cefotaxime should not exist and be inaccessible in community health centers [20–22].

In outpatients, the most commonly prescribed antibiotic was Amoxicillin, with a population DDD/1000 per day of 3.4 in patients<18 y and 26.3 in patients ≥18 y. This result aligns with previous research, which stated that Amoxicillin was the most widely used in all community health centers in the North Gorontalo district, Indonesia. Amoxicillin is an ACCESS category antibiotic available in basic health facilities and is a broad-spectrum beta-lactam antibiotic commonly used for respiratory infections [20, 23-25].

A qualitative analysis of antibiotic use using the Gyssen method shows that most antibiotics were used in category IIIB, meaning that the antibiotics' duration is too short. Based on the guidelines for controlling typhoid fever, the choice of antibiotics that can be given is chloramphenicol for 14 d (adults) and 10-14 d (children), Ceftriaxone for 3-5 for adults and five days for children, Ampicillin and Amoxicillin 14 d for adults and ten days for children, and co-trimoxazole for adults 14 d and children ten days, quinolone group for seven days, Cefixime for ten days, and Tiamfenicol for 5-7 d [26]. In this study, patients diagnosed with typhoid received appropriate antibiotics, namely Amoxicillin, Chloramphenicol, and Thiamphenicol, but the duration was three days. Likewise, in the diagnosis of acute periapical periodontitis, antibiotic therapy was given for three days, whereas according to the guidelines, administration of Amoxicillin or Metronidazole is recommended for eight days [17]. In previous research, it was stated that more than half (59.02%) categorized the IVA (as irrational, as there is a more effective antibiotic) [27].

In outpatients aged<18 y, as many as 32.2% of antibiotics were included in category V, and antibiotics were not indicated. In adult patients, approximately 11-17% of the use of antibiotics is not indicated, including the use of antibiotics in the diagnosis of influenza. Influenza is usually caused by a virus. Antibiotics cannot cure viral infections. Antibiotics are helpful in some cases of secondary bacterial infections but do not affect the influenza virus [28]. According to an observational study, prescribing antibiotics to influenza patients has no clinical benefit. Patients treated with antibiotics and those not treated with antibiotics had similar durations of illness, secondary visit rates, and missed work days. Due to their potential side effect and role in the spread of bacteria resistant to antibiotics, antibiotics are not necessary for the initial treatment of influenza [29]. A retrospective study of pediatric patients also discovered that those who received an antibiotic or an antibiotic plus antiviral had longer hospital stays than those who received an antiviral alone [30]. Inaccurate knowledge also occurs in a society that antibiotics can cure viral infections. According to surveys, 64% of participants wrongly believed that colds and influenza could be treated with antibiotics. Most influenza cases are self-limiting, but some can be treated with antiviral medication [28, 31, 32].

Applying an Antimicrobial Stewardship Program (ASP) is very important in reducing the irrational use of antibiotics. In a study, it was stated that the application of an antimicrobial stewardship program could reduce the number of antibiotics used pre-post ASP from 90.84 DDD/100 patients-days to 61.42 DDD/100 patients-days and increase the prudent use of antibiotics from 31.25% to 62.5% pre-post ASP, respectively [33].

Strengths and limitations of study

This study was conducted in twelve months so that it might be able to describe the use of antibiotics in the year the panel was conducted. However, data collection was carried out retrospectively so that existing medical record data could not be reconfirmed, and researchers had difficulty knowing doctors' reasons regarding the consideration of choosing antibiotics. Suggestions from the results of this study are that it is necessary to carry out quantitative and qualitative audits on an ongoing basis to see the latest developments in the use of antibiotics, to improve the quality, and reduce the quantity of antibiotic use so that antibiotics can be used appropriately and rationally. Researchers suggest future research using prospective data collection.

CONCLUSION

Total DDD/100 patient days were 24.3 (age<18 y with the most prescriptions of Cefotaxime) and 89.7 (aged ≥ 18 with Thiamphenicol being the most frequently prescribed antibiotic). The total DDD/1000 population in patients aged<18 y was 3.4, and for patients aged ≥18 y was 26.3, with the most antibiotics received by patients being Amoxicillin, 85.3%, and 50.2%, respectively. Based on Gyssen's analysis, most of the antibiotic administration was in criterion IIIB; namely, the administration of antibiotics was too short. Intervention is needed to increase the rationality of the use of antibiotics, for example, with the strategy of implementing an antimicrobial stewardship program.

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Nil

AUTHORS CONTRIBUTIONS

HK: conceptual or design of the work, analysis, interpretation of data, critical for important intellectual content, and final approval of the version to be published. RHA: collected data, analyzed, drafted the work, revised, and gave final approval for the version to be published. KU: collected data, analyzed, drafted the work, revised, and finally approved the version to be published. WII: interpretation of data, critical for important intellectual content, project administration, and final approval of the version to be published.

CONFLICT OF INTERESTS

Declared none

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