ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

Jurnal Kefarmasian Indonesia
Available online at https://jkefarind.com/index.php/jki
Original Research Article
JKI

Evaluation of the Use of Antibiotics in the COVID-19 Ward at A North Jakarta Hospital

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ARTICLE INFO

Article history:
Received 02 February 2023
Revised 26 June 2023
Accepted 18 July 2023
Published online 31 August 2023

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DOI: https://doi.org/10.22435/jki.v13i2.6539

Citation: Arrang ST, Buntoro L, Notario D. Evaluation of the use of antibiotics in the covid-19 ward at a North Jakarta hospital. Jurnal Kefarmasian Indonesia. 2023;13(2):113-120.

ABSTRACT

The misuse of antibiotics can lead to antibiotic drug resistance, which can increase morbidity and mortality. In order to stop the emergence of antibiotic drug resistance, the WHO recommends routinely assessing the usage of antibiotics. When the COVID-19 epidemic broke out, antibiotic consumption significantly increased compared to the prior year. The panic buying phenomenon also appeared during the COVID-19 pandemic. As a result of this circumstance, medications like antibiotics become rare. The abuse of antibiotics during the COVID-19 pandemic may have contributed to the spread of antibiotic resistance more frequently. This study was conducted to evaluate and describe the use of antibiotic drugs in COVID-19 ward patients at a North Jakarta regional hospital for the period April 2020 – April 2021. This study was an observational study design. The Gyssens method and the Anatomical Therapeutic Chemical/Defined Daily Doses (ATC/DDD) methodology, respectively, evaluate the effectiveness of antibiotic use on a quantitative and qualitative level. There were 24 different types of antibiotics used, and 161 respondents all met the criterion for inclusion. The most widely used antibiotic was azithromycin, with a DDD/100 patient days value of 25.15. According to Gyssen's evaluation, 92.6% of antibiotic usage was rational and 7.4% was irrational.

Keywords: Evaluation of antibiotic use; Infection; COVID-19 ward; ATC/DDD; Gyssens

INTRODUCTION

Antibiotic-resistant bacteria are a global health concern in many regions of the world. Selection pressure, which is directly linked to the usage patterns of antibiotics and the development of resistant bacteria, is the mechanism that results in bacterial resistance to antibiotics.[1] According to one study, the levofloxacin class, ciprofloxacin, and clindamycin all have high rates of antibiotic resistance in the United States (78.6%, 68.4%, and 48.5%, respectively). The prescription of antibiotics is connected to this trend of levofloxacin resistance.[2] The Indonesian Ministry of Health claims that improper or non-indicated antibiotic use is one of the factors contributing to the rise in antibiotic resistance.[3] Additionally, Indonesia has seen an increase in the prevalence of antibiotic resistance .[4]

In comparison to the prior year, antibiotic use dramatically rose after the COVID-19 epidemic through April 2020.[5] About half of the COVID-19-infected hospital patients receive ceftriaxone, usually in combination with azithromycin and about 80% of these patients are also given antibiotics. Azithromycin and ceftriaxone use has increased in hospitals, linked to increased COVID-19 cases.[6] For COVID-19 patients, both moderate and severe, antibiotic therapy is advised in the COVID-19 management protocol versions I and II.[7]

During the COVID-19 epidemic, the phenomenon of panic buying also happened.

People purchase COVID-19 prevention and treatment medications even when they don't require them out of concern for a medicine shortage or a lack of access to these medications. Drugs like antibiotics, vitamins, and antivirals become scarce and useless as a result of this phenomenon.[8] The likelihood of an increase in the incidence of antibiotic resistance is increased by the overuse of antibiotics during the COVID-19 pandemic. Antibiotic resistance, increased risk of side effects, risk of illness complications, lengthened hospital stays, and increased risk of death are all consequences of improper antibiotic usage.[9] Evaluating antibiotic use is one of the things that may be done to guarantee the prudent use of antibiotics.[3] Determining trends of antibiotic prescribing in patients in the COVID-19 ward during the COVID-19 pandemic is therefore necessary by evaluating the usage of antibiotics.

MATERIALS AND METHODS

The study is descriptive. Retrospective data collection was used to gather information on antibiotic use from the medical records of COVID-19 inpatients from April 2020 to April 2021. Adult COVID-19 ward patients who were over 18 years old, received antibiotic medication and had complete medical record data met the criterion for inclusion. The School of Medicine and Health Sciences Ethics Committee, Atma Jaya Catholic University of Indonesia, issued research ethics with No: 08/02/KEP-FKIKUAJ/2022.

There are two approaches used to evaluate the usage of antibiotics: qualitative and quantitative methods. Analyzing antibiotic use quantitatively using the ATC/DDD (Anatomical Therapeutic Chemical/Defined Daily Doses) approach and qualitatively using the Gyssens method.[3,10] The Gyssens method evaluates several aspects, including accuracy in choosing the type, dose, duration of administration, time of administration, and price of antibiotics. The flow of assessment using the Gyssens method can be seen in Figure 1.[1]

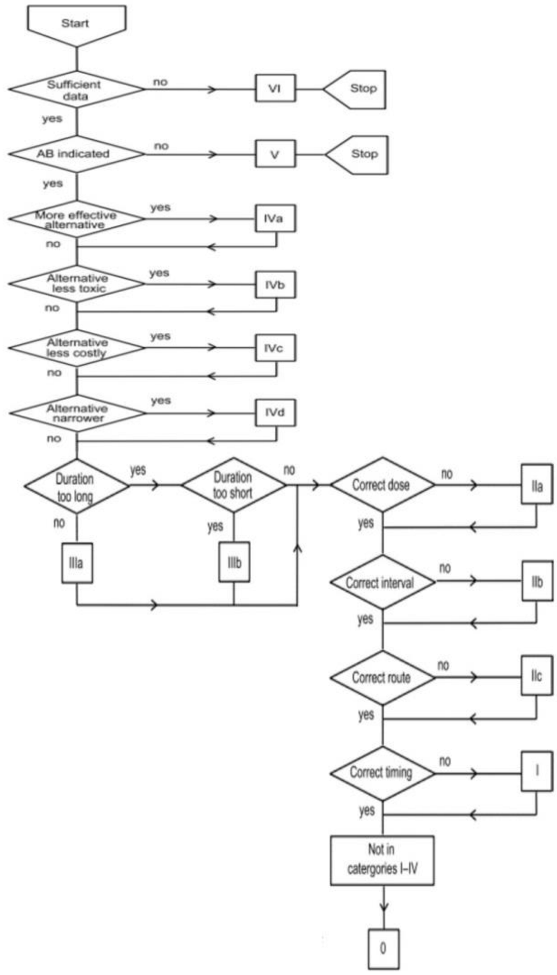

Figure 1. Gyssens Flowchart[1]

Table 1 displays the outcomes of the Gyssens method's qualitative analysis, categorizes for easy viewing. The term "rational" refers to something that falls into category 0, whereas "irrational" refers to something that falls within categories I through V.[1]

Data on the antibiotic type, dose, duration of administration, administration route, and length of hospital stay (LOS) are needed for the quantitative evaluation of antibiotics. The ATC/DDD method's quantitative evaluation of antibiotic use is reported as DDD/100 patient days. The following patient data is used or the DDD/100 patient days calculation:[1]

$$= \frac{number\ of\ antibiotic\ used\ by\ the\ patient\ (gram)}{WHO\ DDD\ standard\ in\ gram}\ x\ \frac{100}{total\ LOS}$$

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

Table 1. Gyssens categories

Categories	Description
0	Appropriate antibiotics usage
I	Inappropriate timing of antibiotics usage
II A	Inappropriate antibiotics dosage
II B	Inappropriate interval of antibiotics usage
II C	Inappropriate antibiotics administration route
III A	Antibiotics are administered for too long
III B	Antibiotics are administered for too short
IV A	There is a more practical option
IV B	There is a less toxic option
IV C	There is a cheaper option
IV D	There is a narrower antibiotics spectrum
V	No indication of antibiotics
VI	Incomplete data

RESULTS AND DISCUSSION

For the months of April 2020 and April 2021, there were 401 patients in the COVID-19 ward at one of the North Jakarta regional hospitals. A total of 240 patients' COVID-19 inpatient ward data were removed, and 161 met the inclusion criteria (Figure 2). In addition to the COVID-19 virus, the respondents also have illnesses from pneumonia, TB, and urinary tract infections (UTIs).

Age, COVID-19 severity, gender, and other demographic information about the study participants were listed in Table 2. Fifty-two percent of the research participants were men, 65.2% had mild COVID-19 symptoms, and 42.9% were adults (aged 26 to 45).

Table 2. Characteristics of research subjects

Characteristics	Frequency (N)	Percentage (%)
Gender		
Male	85	52.8
Female	76	47.2
COVID-19 severity level		
No symptoms	0	0
Mild	105	65.2
Moderate	52	32.3
Severe	4	2.5
Age (year)		
17 - 25	21	13
26 - 45	69	42.9
46 – 54	17	10.6
55-90	54	33.5
>90	0	0

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

There are 24 types of antibiotics used in inpatient COVID-19 wards for the April 2020-April 2021 period, including azithromycin, amoxicillin, ampicillin, cefepime, cefixime, cefotaxime, ceftazidime, ceftriaxone, ciprofloxacin, co-trimoxazole, ethambutol, gentamicin, imipenem, isoniazid, levofloxacin, meropenem, metronidazole, moxifloxacin, ofloxacin, pyrazinamide, rifampicin, cefazolin, ceftizoxime, and piperacillin-tazobactam. The majority of antibiotics supplied to COVID-19 ward patients in one of the North Jakarta regional hospitals for the months of April 2020 and April 2021 were azithromycin, according to the results of the quantitative evaluation of antibiotic use, which were assessed using the ATC/DDD approach. Azithromycin's DDD/100 Patient-Days result was 25.15, which indicates that 25 patients used the antibiotic within a period of 100 days. Higher levels of antibiotic use are associated with higher values of DDD/100 patient days.[11] Levofloxacin is the second-most often used antibiotic, with a DDD/100 patient days of 10.78. Table 3 displays the data for DDD/100 patient days for several medications.

Table 3. The Quantitative evaluation of antibiotic use by ATC/DDD method

Antibiotics	ATC Code	DDD WHO (gram)		DDD Total	DDD/100 Patient-days
		Parenteral	Oral		
Azithromycin	J01FA10	0.5	0.3	89	25.15
Levofloxacin	J01MA12	0.5	0.5	43.61	10.78
Cotrimoxazole	J01EE01	0.4	0.4	15.6	7.25
Moxifloxacin	J01MA14	0.4	0.4	21.45	5.24
Meropenem	J01DH02	3	-	16.58	4.07
Ofloxacin	J01MA01	0.4	0.4	13	2.57
Cefixime	J01DD08	-	0.4	8.33	1.95
Ethambutol	J04AK02	1.2	1.2	13.96	1.76
Ceftriaxone	J01DD04	2	-	8	1.49
Isoniazid	J04AC01	0.3	0.3	12.75	1.44
Rifampicin	J04AB02	0.6	0.6	10.19	1.14
Amoxicillin	J01CA04	3	1.5	3.31	1.13
Ceftazidime	J01DD02	4	-	9	0.87
Ciprofloxacin	J01MA02	0.8	1	3	0.81
Pyrazinamide	J04AK01	-	1.5	7.25	0.78
Cefazoline	J01DB04	3	-	3.5	0.67
Ampicillin	J01CA01	6	2	3	0.57
Metronidazole	J01XD01	1.5	-	3	0.57
Imipenem	J01DH51	2	-	5	0.49
Cefotaxime	J01DD01	4	-	2.25	0.31
Gentamicin	J01GB03	0.24	-	1.34	0.24
Ceftixozime	J01DD07	4	-	1.13	0.22
Cefepime	J01DE01	4	-	1	0.18
Piperacillin Tazobactam	J01CR05	14	-	0.65	0.12

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

Since azithromycin was one of the antibiotics recommended at the time for COVID-19 patients, it is the most commonly utilized antibiotic in the COVID-19 ward.[7] Patients in this study not only have COVID-19 but also other infectious disorders including pneumonia. Additionally, there are indications for the use of azithromycin in the treatment of bacterial infections, such as community-acquired pneumonia (CAP).[12] According to Wahidah et al.'s research (2020) on the evaluation of antibiotic use at Dr. A. Dadi Tjokrodipo Bandar Lampung, azithromycin is the third most commonly prescribed antibiotic for children patients with pneumonia infection.[13] In patients with pneumonia infection, azithromycin and levofloxacin were the third and fourth most commonly used antibiotics, according to research by Prasetyo et al. (2018) on the review of antibiotic use at DKT Hospital, Kediri City.[14] According to Hanifah et al.'s research (2021) conducted in a private hospital in Bandung, azithromycin and levofloxacin were the most widely utilized antibiotics.[15]

Antibiotics of the macrolide class, such as azithromycin, work as immunomodulators in pulmonary infectious illnesses by lowering the pathogenicity of bacteria by preventing communication between bacteria, controlling their movement through quorum sensing, and building biofilms. By reducing the volume and viscosity of sputum, macrolide drugs initially increase host resistance.[16]

Azithromycin has a mechanism of action inhibiting protein synthesis by damaging the peptidyl chain elongation. Viruses require an acidic environment for endosome maturation and function. Azithromycin is a weak base and accumulates intracellularly in endosomal and lysosomal vesicles, which can increase pH levels and potentially block endocytosis or viral genetic release from lysosomes, thereby limiting viral replication.[17] By enhancing the immune response to viruses and controlling the expression of the MDA5 and RIG-I genes, which are involved in virus recognition, azithromycin can decrease the number of viruses that enter cells.[18] Azithromycin can suppress the spike-ACE2 interaction of SARS-CoV-2 in addition to boosting the body's immunological response.[19] Levofloxacin is the second most often used antibiotic. Levofloxacin is also the antibiotic of choice for treating COVID-19 infection in COVID-19 patients issue I (April 2020).[7] Levofloxacin (a fluoroquinolone) works by binding to DNA gyrase and topoisomerase IV to prevent DNA replication. Levofloxacin is believed to have antiviral properties, namely through binding to the primary protease (Mpro) of SARS-CoV-2 to prevent viral replication.[20,21] The antibiotics azithromycin and levofloxacin can be used as therapy because in vitro and in vivo tests show that they reach high concentrations in the lungs and have antiviral, immunomodulatory, and antibacterial benefits against co-infection or infection with commensal anaerobic bacteria in the lungs, such as Prevotella spp. empiric for pneumonia caused by COVID-19.[18,20,22]

Table 4 displays the findings of a Gyssens method-based qualitative evaluation of antibiotics. Antibiotics were utilized 92.6% rationally and 7.4% irrationally. There were 3.1% inappropriate timing of antibiotics usage, and 4.3% of antibiotics were administered for too long.

Several studies similar to this study, research conducted by Putra et al. (2021) at Diponegoro National Hospital during the COVID-19 pandemic era, where 13.5% of no indication of antibiotics, 51.1% of antibiotics were given irrationally, and 35.4% of antibiotics were given rationally.[23] Research by Anggraini et al. (2020) at the Kanjuruhan Hospital in Malang Regency in patients with urinary tract infections showed only 20% rational use of antibiotics, while 2.86% of antibiotics were inappropriate timing of antibiotics usage, 28.57% inappropriate antibiotics dosage, 34.59% inappropriate interval of antibiotics usage, 11.42% antibiotics were administered for too short and 2.86% there was a more practical option for antibiotics.[24]

Research by Wibowo et al. (2020) at Hasan Sadikin General Hospital in Bandung in post-cesarean section patients from January to December 2018 showed 59.5% no indication

Table 4. The qualitative evaluation of antibiotic use by Gyssens method

Gyssens Categories		Frequency (N)	Percentage (%)
0	Appropriate antibiotics usage	149	92.6
I	Inappropriate timing of antibiotics usage	5	3.1
II A	Inappropriate antibiotics dosage	0	0
II B	Inappropriate interval of antibiotics usage	0	0
II C	Inappropriate antibiotics administration route	0	0
III A	Antibiotics is administered for too long	7	4.3
III B	Antibiotics is administered for too short	0	0
IV A	There is a more practical option	0	0
IV B	There is a less toxic option	0	0
IV C	There is a cheaper option	0	0
IV D	There is a narrower antibiotics spectrum	0	0
V	No indication of antibiotics	0	0
VI	Incomplete data	0	0
Rationality Categories			
Rational (0)		149	92.6
Irrational (I - V)		12	7.4

of antibiotics and 40.5%, there were more practical options for antibiotics.[25] Research by Yusuf et al. (2022) at Bhayangkara Bandung Hospital in pneumonia patients from July to December 2019 showed that 12% there was a less toxic option for antibiotics, 4% inappropriate interval of antibiotics usage, and 84% appropriate antibiotics usage.[26] The use of antibiotics in a hospital in North Jakarta in this study was classified as rational compared to other hospitals. This hospital has an antimicrobial resistance control committee (PPRA) and clinical pharmacists who monitor the use of antibiotics. This hospital also monitors, evaluates, and reports on antibiotics regularly every month.

The limitation of this study is that the study was conducted retrospectively using medical record data so that a qualitative evaluation of the use of antibiotics in terms of cost-effectiveness could not be carried out. Another area for improvement is not being able to classify the use of empirical and definitive antibiotics because microbial culture examination was not carried out in all patients, and this study was only conducted in one ward, so it could not describe the widespread use of antibiotics in this hospital.

If other researchers carry out similar studies related to the quality of antibiotic use, it can be done prospectively, so that some of the criteria from the Gyssens method can be evaluated, such as in terms of cost (cost-effectiveness), and can collaborate with other health workers (doctors) in determining the rationale for using antibiotics.

CONCLUSION

The qualitative evaluation of the use of antibiotics in inpatients on the COVID-19 ward in a North Jakarta regional hospital for the April 2020-April 2021 period was classified as rational. The quantitative evaluation showed that azithromycin was the most widely used antibiotic.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgments

The authors are grateful to Atma Jaya Hospital, for the encouragement and permission to collect data.

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