PRESCRIPTION OF ANTIBIOTICS FROM ACCESS GROUP ACCORDING TO AWARE CLASSIFICATION: DATA FROM COMMUNITY PHARMACIES IN SLEMAN REGENCY YOGYAKARTA

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ABSTRACT

Antibiotic resistance is the most challenging problem in the 21st century. Therefore, the WHO released a classification of antibiotics into the Access, Watch, and Reserve (AWaRe) group, with the aim of optimizing the use of the access group to at least 60%. The objective of this study was to determine the profile of antibiotic prescriptions at community pharmacies in Sleman Regency, Yogyakarta, during the period 2019–2022, based on the AWaRe classification. A Cross-sectional survey was designed to collect data on antibiotic prescriptions from community pharmacies across four regions of the Sleman Regency. Each antibiotic was classified in accordance with the AWaRe classification and the quantity of prescribed antibiotics was calculated in DDD units following the ATC/DDD method. This study found that in terms of the antibiotic agents, 10-13 antibiotic from the Access group (52%–62%) were prescribed during the study period. Meanwhile, in terms of quantity expressed in DDD units, 52.38% and 61.90% of prescribed antibiotics were from the Access group, according to the AWaRe classification released by the WHO and the Indonesian Ministry of Health, respectively. In conclusion, antibiotic prescriptions at community pharmacies in Sleman Regency, Yogyakarta, have reached the target of optimizing the use of access groups according to the Indonesian Ministry of Health, but were still slightly below the target of the WHO.

Keywords: Antibiotic Prescription; ATC/DDD; AWaRe Classification; Community Pharmacy

INTRODUCTION

Antibiotic resistance has become a major global problem, which is estimated to cause 10 million deaths per year by 2050 (Browne et al., 2021; Murray et al., 2022). Annually, utilization of antibiotics tends to grow; between 2000 and 2015, the average annual consumption of antibiotics climbed by 39%, and the overall use increased by 65% (Klein et al., 2021). Developing nations, also called low- and middle-income countries (LMICs), are the main contributors to the increase in antibiotic use. Compared to hospitals, the prescription of antibiotics at the community level is comparatively inappropriate. While most antibiotic consumption occurs in the community, most antibiotic control efforts mainly target hospitals (Cunha & Ashar, 2018; Jackson et al., 2019). The consumption of antibiotics in primary healthcare varies between industrialized and poor nations; according to multiple studies, the gap is estimated to be between 8 and 10% (Sulis et al., 2020).

Monitoring and evaluation of antibiotic use is required to reduce the risk of antibiotic resistance. Antibiotic use can be evaluated both statistically and qualitatively to ascertain its use profile and quality (Kallen et al., 2019). Recommendations for health policymakers can be derived from an evaluation of antibiotic use. The Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD), as a global methodology, is typically used for quantitative drug evaluation, including for the evaluation of antibiotics use (Apriyanti & Saepudin, 2023).

The National Action Plan and Global Action Plan (GAP) are required to stop the negative impacts of antibiotic resistance. The WHO GAP for classifying antibiotics into the AWaRe (Access, Watch, and Reserve) classification needs to be applied in all countries globally to optimize the utilization of antibiotics from the Access group to at least 60% (Mugada et al., 2021). The Regulation of the Minister of Health of the Republic of Indonesia also includes antibiotic optimization methods with the AWaRe classification in accordance with the WHO's AWaRe classification. To slow the progression of antibiotic resistance in the community, the Association of Indonesian Pharmacists in the region of Yogyakarta also released a circular letter mandating that all pharmacies sell antibiotics only with a doctor's prescription. Therefore, community pharmacies play an important role in ensuring the appropriate use of antibiotics (Permenkes RI, 2021; Zawahir et al., 2019).

Sleman Regency is one of the regencies in Yogyakarta Province that has more health facilities than other regencies, including community pharmacies. By 2022, there were more than 200 community pharmacies in Sleman Regency. However, research to capture the profile of antibiotic prescriptions has not been widely conducted, specifically after the issuance of the antibiotic AWaRe classification in the national guidelines for antibiotic use released in Subdistricin 2021. The objective of this study was to capture the profile of antibiotic prescriptions at community pharmacies in Sleman Regency, Yogyakarta, in accordance with the AWaRe classification by the WHO and Indonesian Ministry of Health.

RESEARCH METHODS

This study was a cross-sectional survey that collected retrospective data on antibiotic prescriptions from community pharmacies in the Sleman Regency, Yogyakarta. Data were collected from 10 community pharmacies representing 4 regions of Sleman Regency, for the period of 2019 to 2022. Sleman Regency was chosed for this study because it has a dense population with quite a lot of health facilities so that it is necessary to improve and evaluate pharmaceutical services including antibiotic prescribing. The study was approved by the Health Research Ethics Committee of the Medical Faculty Universitas Islam Indonesia, with an approval IDE of 23/Ka. Kom.Et/70/KE/II/2023.

A purposive technique was used to select the pharmacies involved in this study. The main criteria for selecting pharmacies were the availability of antibiotic sales based on prescriptions from January 1, 2019, to December 31, 2022, and sales data can be accessed either from sales record books or computers. The number of pharmacies sampled from each region of the Sleman Regency was calculated based on the number of pharmacies in the area with the fewest pharmacies where 1 pharmacy was sampled. For other regions, the number of pharmacies sampled was multiple, as listed in **Table I**.

Table I. Selection of Community Pharmacy Involved in this Study

Region	Subdistrict	Number of Pharmacies (N)	Sample (n=N/23)
North Sleman	Tempel, Turi, Cangkringan, Pakem, Ngaglik	45	2
West Sleman	Godean, Minggir, Seyegan, Moyudan	23	1
Center Sleman	Sleman, Mlati, Depok Gamping	116	5
East Sleman	Ngemplak, Kalasan, Prambanan, Berbah	34	2
		218	**10**

This study included all antibiotics with ATC code J01 in the ATC classification. Information about antibiotic prescriptions was retrieved from both the pharmacy's drug sales system and prescription records. Data on antibiotics include brand and generic names of the antibiotics, dosage form and strength, route of administration, and quantity of prescribed antibiotics. The quantity of each prescribed antibiotic was then calculated in DDD unit by dividing the total prescription of each antibiotic in gram by the definitive DDD from the WHO website https://atcddd.fhi.no/atc_ddd_index.

$$DDD = \frac{quantity\ of\ prescribed\ antibiotic\ (gram)}{Defined\ DDD\ (gram)}$$

The quantity of antibiotics was then converted into percentages to create a 90% antibiotic utilization profile (DU90%) for each year by dividing the amount of each antibiotic by the total amount of antibiotics used during the year. The antibiotics that were used in the 90% cumulative usage area can be sorted by percentage, with the highest proportion being used first and decreasing to the lowest percentage. This allows for the determination of DU90%.

The final data on the number of antibiotic prescriptions and the DU 90% segment were classified according to the AWaRe classification of the WHO and the Ministry of Health of the Republic of Indonesia. A one-way ANOVA test was conducted to compare the antibiotic prescriptions from the access group during the study period (2019-2022), using an alpha value of 5%.

RESULTS AND DISCUSSION

This study found that 21 antibiotics were prescribed at community pharmacies during the study period. Overall, the total quantity of antibiotic prescriptions expressed in DDD units each year over the study period increased with a peak in 2021 (16387 DDD), but then decreased in 2022, as shown in **Figure 1**.

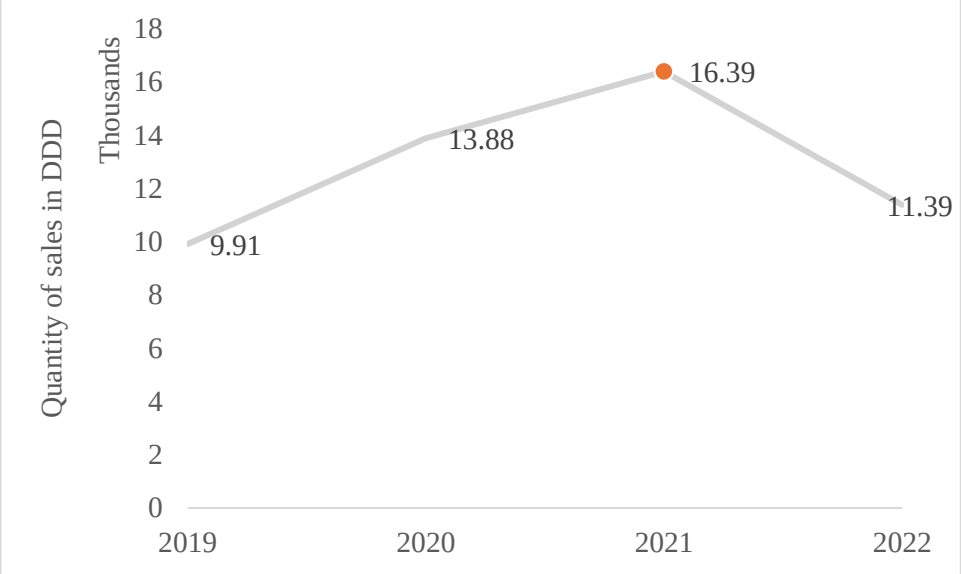

Figure 1. Total Quantity of Antibiotics Prescription at The Community Pharmacies Each Year Over Four Years Period of 2019 – 2022

Eight subgroups of antibiotics were used based on the ATC classification. Antibiotics from the quinolone subgroup (J01M), including fluoroquinolones (J01MA) and other quinolones (J01MB), were the most prescribed antibiotics during the study period, followed by the subgroup of beta-lactams (penicillins/J01C) and the macrolide, lincosamide,

and streptomycin subgroup (J01F), as presented in **Table II**. The antibiotics included in the beta-lactam (penicillin) subgroup were penicillin (J01CA) and a combination of penicillin and beta-lactamase inhibitors (J01CR). Amoxicillin (J01CA04) was the most commonly prescribed antibiotic with a total DDD of 16,179 (31.38%) among the 10 pharmacies during the study period, followed by cefixime (J01DD08) with a total DDD of 9,255 (17.95%), azithromycin with a DDD of 7754.33 (15.04%), ciprofloxacin with a DDD of 5009.5 (9.72%), metronidazole with a DDD of 2327.33 (4.51%). Erythromycin, sultamycin, clarithromycin, chloramphenicol, and moxifloxacin were the least frequently prescribed antibiotics during the study period.

Table II. Total DDD of Antibiotics Dispensed in Community Pharmacies Based on Pharmacological Subgroups

ATC code	Pharmacological Subgroup	Number of antibiotic agents used	Total consumption peryear (DDDs)				
			2019	2020	2021	2022	Total
J01A	Tetracyclines	2	224.00	302.50	793.00	695.50	2015.00
J01B	Amphenicols	2	45.42	31.33	0.00	5.50	82.25
J01C	Beta-lactam antibacterial, penicillin	4	3041.92	5062.58	5775.42	3902.00	17781.92
J01D	Other beta-lactam	2	2337.75	3190.50	3216.75	2674.00	11419.00
J01E	Sulphonamides and trimethoprim	1	222.75	166.25	179.50	81.75	650.25
J01F	Macrolides, lincosamides, streptogramins	4	1434.83	2362.10	3755.00	1941.75	9493.68
J01M	Quinolone antibacterial	5	2094.50	2086.50	2138.00	1470.50	7789.50
J01X	Other antibacterial	1	507.33	675.33	529.67	615.00	2327.33
Total of antibiotic agents used		**21**					

Figure 2 shows the antibiotic prescription levels of the access and watch groups, estimated based on the total DDD. Of the total 51558.93 DDD of antibiotic prescriptions, the percentage of access group antibiotic prescriptions according to WHO from 2019-2022 was 50.61%, 52.48%, 50.10%, and 54.14%, respectively. The proportions of access group antibiotic prescriptions according to the Indonesian Ministry of Health were 62.68%, 63.97%, 59.34%, and 61.93%, respectively.

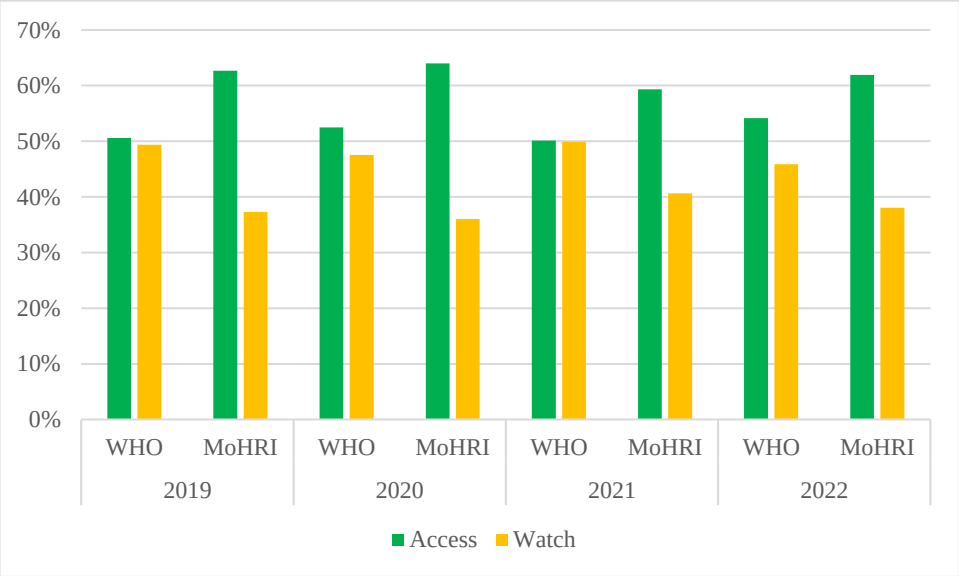

Figure 2. The Proportional Antibiotics Prescription (DDDs) of The AWaRe Classification at Community Pharmacies Each Year During The Period of 2019 – 2022

Figure 3 indicates that during the study period, 10 out of all prescribed antibiotics formed the drug utilization 90% (DU90%) profile, with amoxicillin, cefixime, and azithromycin being the most frequently prescribed antibiotics. In contrast, co-amoxiclav, clindamycin, and doxycycline were the least frequently prescribed drugs.

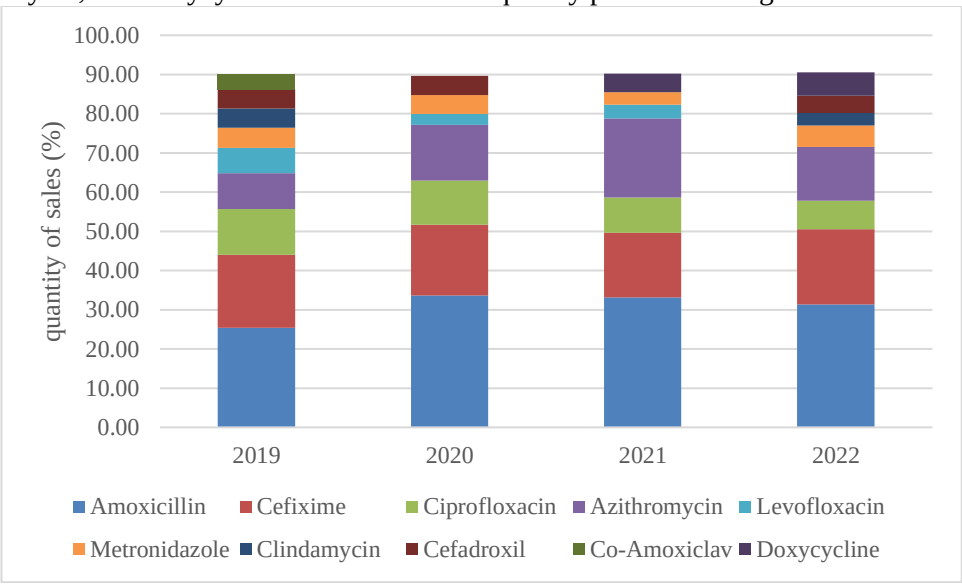

Figure 3. DU90% Profiles of Antibiotics Prescription at Community Pharmacies Each Year During The Period of 2019 – 2022

To the best of our knowledge, this is the first study to investigate the profile of antibiotic prescriptions by collecting data from community pharmacies in the Sleman Regency. According to both the WHO and Indonesian Ministry of Health AWaRe classification, this study found that more than 50 percent of prescribed antibiotics were from the access group. This finding is slightly different from those reported in Bangladesh, India, and Italy, where the Watch group was used much more frequently than the Access group (Galimberti et al., 2022; Islam et al., 2022; Senthilkumar et al., 2020). In terms of antibiotic use in the community, the access group should be prioritized as both first-line treatments because of their low risk of promoting bacterial resistance (WHO, 2021).

This study found that the beta-lactam subgroup, which includes penicillin, is the most prescribed class of antibiotics annually. Mild-to-moderate community-acquired pneumonia and infectious diarrhea are among the respiratory tract illnesses that can be treated with these medicines (Muin & Widayanti, 2023). The WHO encourages all health facilities worldwide to optimize the use of antibiotics from the access group by considering antibiotic properties and their abilities against infections. Penicillin antibiotics have diverse characteristic in regard to their antibacterial and pharmacokinetic profiles; therefore, they should be used appropriately (Roberts & Zembower, 2021). Macrolides and other beta-lactam antibiotics were the second and third most prescribed antibiotics, respectively. Similar findings have also been reported in Vietnam, Jordan, and Egypt, where pharmacists are encouraged to dispense these antibiotics because of their relative safety and efficacy (Haddadin et al., 2019; Nguyen et al., 2020; Sabry et al., 2014).

Approximately 33–48% of antibiotics from the Watch group were found in this study, including third-generation cephalosporins (cefixime), macrolides (azithromycin, erythromycin, and clarithromycin), and fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin, and moxifloxacin). A similar finding was also reported by another study from Congo conducted in 2022, which found that 42.30% of the Watch group antibiotics were third-generation cephalosporins, with fluoroquinolones and macrolides (Kakumba et al., 2023). These findings indicate that some second-line antibiotics are widely prescribed by general practitioners. These broad-spectrum antibiotics should be prescribed with precaution because of their higher risk of promoting antibiotic resistance, and they should only be prescribed for the treatment of more severe infections by specialists (WHO, 2021). The prescription of Watch antibiotics found in this study was much better than that reported by Kazakhstan, which reported that more than 60% of prescribed antibiotics were prescribed by the Watch group (Zhussupova et al., 2021).

The overuse of cefixime, a third-generation cephalosporin, may increase the risk of gram-negative bacterial resistance, nephropathy, and Clostridium difficile infection (Macy & Contreras, 2015; Slimings & Riley, 2014). In a study on the use of macrolide antibiotics in several countries in Asia, an association was found between an increase in macrolide antibiotic resistance rates (erythromycin 66.8%, azithromycin 67.2%, and clarithromycin 64.7%) and *Streptococcus pneumoniae* bacteria (Chae et al., 2022). The increase in prescription sales of cephalosporins and macrolides from 2019 to 2021 could be related to the impact of the Covid-19 pandemic because the use of these antibiotics is the standard of therapy of the Indonesian Lung Doctors Association (PDPI, 2020). These findings are similar to those of previous studies in several countries, such as China, Italy, France, and America, with an increased consumption of azithromycin antibiotics during the covid-19 pandemic (Al-Hadidi et al., 2021).

Among the eight pharmacological subgroups of antibiotics found in this study, quinolone antibiotics were the most prescribed antibiotics (23.80%). Broad-spectrum antibiotics or quinolones are effective against gram-positive and gram-negative bacteria, including anaerobes and mycobacteria. Quinolones are often used to treat gastrointestinal, respiratory, and urinary tract infections (Pham et al. 2019).

While antibiotics from the access group were still dominant within the DU90% segment (including amoxicillin, metronidazole, clindamycin, cefadroxil, co-amoxiclav, and doxycycline), no antibiotics were found in the reserve group in this study. This is understandable because antibiotics from the Reserve group are all available in parenteral dosage forms and are used only for very severe conditions.

Based on statistical analysis using ANOVA with the purpose of determining whether there is a significant difference in terms of the prescription of antibiotics from the access group each year during the study period based on the AWaRe classification released by the Ministry of Health and WHO, it was found that there was a difference with a p-value < 0.05. This indicates that different classifications result in different pictures of antibiotic use, especially in terms of quantity. However, other factors such as prescriber attitudes or disparities in cultural and educational backgrounds may also contribute to this tendency in

the context of antibiotic use (Piovani et al., 2014). Therefore, studies on antibiotic use using the AWaRe classification should clarify which AWaRe classification is being used in the study.

This study provides valuable data on antibiotic consumption profiles, which can inform policy decisions to optimize stewardship programs. By understanding patterns of antibiotic use, local governments can allocate health resources more efficiently. If there is a trend of excessive or inappropriate use of antibiotics, corrective measures can be taken to reduce waste and prioritize the use of funds for other aspects of health. Each region has unique characteristics related to public health and the environment. Research in Sleman District will provide specific data relevant to local conditions. The results of this study can serve as a basis for more targeted and effective health policies.

One important strength of this study is that it is the first to analyze antibiotic consumption in community settings in Yogyakarta using the AWaRe classification. The findings of this study can strengthen the strategy to optimize the use of antibiotics by the access group, especially in community settings. However, this study also has some limitations with regard to the limited number of community pharmacies involved, which might affect the accuracy and validity of antibiotic prescription profiles.

CONCLUSION

The prescription of antibiotics from Access group at community pharmacies in Sleman Regency is slightly below the target of WHO if the classification of antibiotics follows WHO AWaRe classification, but it is within the target if the classification of antibiotics follows the AWaRe classification released by the Ministry of Health, Republic of Indonesia.

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