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Prescribing Patterns of Antibiotics According to the WHO AWaRe Classification during the COVID-19 Pandemic at a Teaching Hospital in Lusaka, Zambia: Implications for Strengthening of Antimicrobial Stewardship Programmes

Steward Mudenda [1,*], Eustus Nsofu [1], Patience Chisha [1], Victor Daka [2], Billy Chabalenge [3], Webrod Mufwambi [1], Henson Kainga [4], Manal H.G. Kanaan [5], Ruth L. Mfune [2], Florence Mwaba [6], Mildred Zulu [6], Rabecca Tembo [6], Wizaso Mwasinga [7], Kennedy Chishimba [8], Grace Mwikuma [9], Ngula Monde [10], Mulemba Samutela [11], Harriet K. Chiyangi [12], Shafiq Mohamed [13] and Scott K. Matafwali [14]

1 Department of Pharmacy, School of Health Sciences, University of Zambia, Lusaka P.O. Box 50110, Zambia
2 Department of Public Health, Michael Chilufya Sata School of Medicine, Copperbelt University, Ndola P.O. Box 71191, Zambia
3 Department of Medicines Control, Zambia Medicines Regulatory Authority, Lusaka P.O. Box 31890, Zambia
4 Department of Veterinary Epidemiology and Public Health, Faculty of Veterinary Medicine, Lilongwe University of Agriculture and Natural Resources, Lilongwe 219, Malawi
5 Department of Agriculture, Technical Institute of Suwaria, Middle Technical University, Baghdad 8998+QHJ, Iraq
6 Department of Pathology and Microbiology, School of Medicine, University of Zambia, Lusaka P.O. Box 50110, Zambia
7 Department of Disease Control, School of Veterinary Medicine, University of Zambia, Lusaka P.O. Box 32379, Zambia
8 Department of Environmental Health, School of Medicine, Eden University, Lusaka P.O. Box 37727, Zambia
9 Department of Pathology, Kitwe Teaching Hospital, Kitwe P.O. Box 20969, Zambia
10 Department of Biomedical Sciences, Tropical Diseases Research Centre, Ndola P.O. Box 71769, Zambia
11 Department of Biomedical Sciences, School of Health Sciences, University of Zambia, Lusaka P.O. Box 50110, Zambia
12 Department of Clinical Studies, School of Veterinary Medicine, University of Zambia, Lusaka P.O. Box 32379, Zambia
13 Remedium Pharmaceuticals Limited, Libowa Street No. 48, Salama Park, Lusaka P.O. Box 51227 RW, Zambia
14 Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK
* Correspondence: steward.mudenda@unza.zm; Tel.: +260-977549974

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Abstract: Irrational and inappropriate prescribing of antibiotics is a major problem that can lead to the development of antimicrobial resistance (AMR). In Zambia, there is insufficient information on the prescribing patterns of antibiotics according to the World Health Organization (WHO) AWaRe classification. Therefore, this study assessed the prescribing patterns of antibiotics using the AWaRe classification during the COVID-19 pandemic at the University Teaching Hospital in Lusaka, Zambia. A cross-sectional study was conducted using 384 patient medical files at the University Teaching Hospital in Lusaka, Zambia, from August 2022 to September 2022. All antibiotics were classified according to the WHO "AWaRe" tool and assessed for appropriateness using the 2020 Zambian Standard Treatment Guidelines. Of the 384 patient medical files reviewed, antibiotics were prescribed 443 times. The most prescribed antibiotics were ceftriaxone (26.6%), metronidazole (22.6%), amoxicillin (10.4%), amoxicillin/clavulanic acid (5.6%), and azithromycin (5%). The prescribing of 42.1% of "Watch" group antibiotics was greater than the recommended threshold by the WHO. Most antibiotics were prescribed for respiratory infections (26.3%) and gastrointestinal tract infections (16.4%). The most prescribed antibiotic was ceftriaxone, a Watch antibiotic. This is a worrisome observation and calls for strengthened antimicrobial stewardship and implementation of the AWaRe framework in prescribing antibiotics.

Keywords: AWaRe classification; antibiotics; ceftriaxone; prescribing patterns; antimicrobial stewardship; Zambia

1. Introduction

Antibiotics have been used widely in preventing and managing infections since the discovery of penicillin in the 1920s [1,2]. This discovery changed the course of medicine and reduced infection-related mortality [1,3,4]. However, in recent times, there have been concerns over the inappropriate prescribing patterns of the Access, Watch and Reserve (AWaRe) antibiotics which has partly contributed to the development of antimicrobial resistance (AMR) [5–8].

The inappropriate prescribing of antibiotics can lead to an increase in antimicrobial-resistant infections, leading to increased morbidity, mortality, and healthcare costs [9–12]. The impact of AMR is arguably greatest in low-income countries, which face the double burden of fewer antibiotic choices and higher rates of infectious diseases [13–24]. Further, antibiotic-resistant infections commonly occur in hospitals because of the nature of the activities, such as large numbers of susceptible patients and invasive procedures taking place in the hospital environment [25]. Rational prescribing and dispensing practices serve to combat this global public health challenge by preventing antibiotic overuse and misuse [26–28]. Monitoring of prescriptions and antibiotic utilisation can identify the problems and provide feedback to prescribers, dispensers, and other stakeholders to create awareness about the irrational use of antibiotics [27,29,30].

The COVID-19 pandemic had severely impacted healthcare systems and other facets of people's lives worldwide [31,32]. Another inescapable impact of this pandemic is the increased and inappropriate use of antibiotics leading to a rise in AMR [33–36]. During the pandemic, the World Health Organization (WHO) guidelines recommended that until there is a strong clinical suspicion of a secondary bacterial illness, antibiotics should not be provided [37], but in many settings, antibiotics remained a strong part of the COVID-19 management protocols [38–40]. A review by Langford and colleagues revealed that as many as 70% of patients with COVID-19 received antimicrobials as out-patients or in-patients [41]. Consequently, the high use of antibiotics during the COVID-19 pandemic may exacerbate the global challenge of AMR [42–47].

The AWaRe tool was developed by the WHO Expert Committee on Selection and Use of Essential Medicines to address the global spread and burden of AMR, antibiotic-related adverse effects and drug costs [6,48–50]. The AWaRe classification divides the antibiotics into three categories; Access (first-choice antibiotics that are typically narrow-spectrum and have less potential for resistance, i.e., amoxicillin, cefalexin, chloramphenicol, and nitrofurantoin), Watch (broader-spectrum antibiotics such as fluoroquinolones, macrolides, and second-and third-generation cephalosporins), and Reserve (last-resort option antibiotics classes such as linezolid, imipenem, meropenem, aztreonam, and colistin) [51]. The number one goal of the AWaRe classification of antibiotics is to have all countries report antibiotic use by 2023 [51]. The second goal is to limit at least 60% of global antibiotic consumption to the "Access" group of antibiotics [6,51]. The tool also emphasises the limited use of Watch and Reserve antibiotics [5,50,52].

The AWaRe tool is part of antimicrobial stewardship (AMS) that promotes the rational prescribing, dispensing, and use of antibiotics [5,52]. The WHO developed it to help address the problem of AMR [48,50]. Therefore, AMS programmes are critical in reducing AMR and eventually its consequences [27,53–55]. So far, the tool has proven helpful in some countries that have adopted it, such as the United Kingdom, Bangladesh, Brazil and Germany [50]. Countries can use the AWaRe tool to monitor their antimicrobial usage patterns and promote rational prescribing [48]. Thus, the WHO AWaRe tool ensures that the best antibiotic, correct dose, route of administration and duration is chosen for common infections that affect children and adults [49].

In Zambia, there is a paucity of information about the prescribing patterns of antibiotics based on the AWaRe classification. However, studies done in community pharmacies have reported increased dispensing of antibiotics without using prescriptions [18,56,57]. Therefore, it is against this background that the present study assessed the prescribing patterns of antibiotics according to the WHO AWaRe classification during the COVID-19 pandemic at the University Teaching Hospital (UTH) in Lusaka, Zambia.

2. Results

2.1. Sociodemographic Characteristics of Participants

A total number of 384 patient medical files were included in this study. Most files 57.3% (n = 220) were for female patients, and the majority, 71.1% (n = 273), were above 18 years of age. Most reviewed files, 53.6% (n = 206), were for outpatients (Table 1).

Table 1. Sociodemographic characteristics of patients based on the reviewed medical files.

Variable	Characteristics	Frequency (n = 384)	Proportion (%)	95% CI
Gender	Male	164	42.7	37.7–47.8
	Female	220	57.3	52.2–62.3
Age (years)	<12	49	12.8	9.7–16.6
	12–18	62	16.1	12.7–20.3
	>18	273	71.1	66.2–75.5
Category of Patient	In-patients	178	46.4	41.3–51.5
	Out-patients	206	53.6	48.5–58.7

NB: n = Sample size; % = proportion of medical files; 95% CI = Confidence interval.

2.2. Commonly Prescribed Antibiotics for the Reviewed Patient Files

Ceftriaxone (26.6%) was the most frequently prescribed antibiotic followed by metronidazole (22.6%), amoxicillin (10.4%), amoxicillin/clavulanic acid (5.6%), and azithromycin (5%) (Table 2). Of the 443 antibiotics prescribed, 233 (52.6%) were prescribed for in-patients while 210(47.4%) were prescribed for out-patients. Overall, 108 injectables and 125 oral antibiotics were prescribed for in-patients while 21 injectables and 189 oral antibiotics were prescribed for out-patients (p = 0.001).

Table 2. Commonly prescribed antibiotics at the University Teaching Hospital.

Name of Antibiotic	Frequency (n = 443)	Percent (%)	95% CI	AWaRe Classification
Amoxicillin	46	10.4	7.78–13.70	Access
Amoxicillin/clavulanate	25	5.6	3.8–8.3	Access
Cloxacillin	22	5.0	3.2–7.5	Access
Metronidazole	100	22.6	18.8–26.8	Access
Sulfamethoxazole/trimethoprim	15	3.4	2.0–5.6	Access
Azithromycin	22	5.0	3.2–7.5	Watch
Ceftriaxone	118	26.6	22.6–31.1	Watch
Cefuroxime	11	2.5	1.3–4.5	Watch
Ciprofloxacin	20	4.5	2.9–7.0	Watch
Levofloxacin	7	1.6	0.7–3.4	Watch
Linezolid	6	1.4	0.6–3.1	Reserve
Other Access antibiotics	38	8.5	6.2–11.7	Access
Other Watch antibiotics	13	2.9	1.6–5.1	Watch
Total	443	100		

n = Number of commonly prescribed antibiotics; 95% CI = Confidence interval.

2.3. Prescribing of AWaRe Antibiotics for In- and Out-Patients

According to the AWaRe classification, the "Access" group of antibiotics was prescribed at 55.5% (n = 246), followed by the "Watch" group at 43.1% (n = 191) and lastly, the "Reserve" group had a proportion of 1.4% (n = 6). Most in-patients compared to out-patients received more Watch antibiotics (1.9:1) and Reserve antibiotics (5:1) but fewer Access antibiotics (1:1.5) (Table 3).

Table 3. Distribution of prescribed antibiotics according to the WHO AWaRe classification for in- and out-patients.

Indicator	Access	Watch	Reserve
AWaRe category	246	191	6
In-patients	96	122	5
Out-patients	144	63	1
p-value	0.002	0.001	0.077

2.4. Average Number of Prescribed Antibiotics per Prescription

In most patients, 84.9% (*n* = 326) received one antibiotic, followed by those who received two antibiotics 14.8% (*n* = 57), and lastly, three antibiotics 0.3% (*n* = 1). Of the total 206 out-patients, 98% (*n* = 201) received one antibiotic, while 70% (*n* = 125) and 29% (*n* = 52) out of the 178 in-patients received one and two antibiotics, respectively. This resulted in an average of 1.2 antibiotics per prescription (Table 4).

Table 4. Number of antibiotics per prescription.

Indicator	Frequency			*p*-Value
Number of antibiotics	1	2	3	0.001
In-patients	125	52	1	0.001
Out-patients	201	5	0	

2.5. Common Diseases for Which Antibiotics Were Prescribed

The most diseases for which antibiotics were prescribed included those of the respiratory tract 26.3% (*n* = 101), gastrointestinal tract (GIT) 16.4% (*n* = 63), ear, nose, and throat 10.2% (*n* = 39), and skin and soft tissue 9.1% (*n* = 35) as depicted in Table 5.

Table 5. Diseases for which antibiotics were prescribed.

Disease Condition	Frequency (*n* = 384)	Percentage (%)	95% CI
Respiratory tract infections	101	26.3	22.0–31.1
GIT infections	63	16.4	12.9–20.6
Ear, eyes, nose and throat infections	41	10.7	7.9–14.3
Skin and soft tissue infections	35	9.1	6.5–12.6
Bone and joint infections	32	8.3	5.9–11.7
Urinary tract infections	24	6.3	4.1–9.3
Pelvic inflammatory disease	21	5.5	3.5–8.4
Sexually transmitted infections	13	3.4	1.9–5.9
Septicemia	12	3.1	1.7–5.5
Others	42	10.9	8.1–14.6
Total	384	100	

n = number of diseases prescribed for antibiotics; 95% CI = Confidence interval.

2.6. Adherence to Prescribing Indicators by Dose, Frequency, and Duration of Treatment

Of the 384 patient medical files, antibiotic prescribing was appropriate by dose 382(99.5%), frequency 383(99.7%), duration 372(96.9%) and indication 380(98.6%) as depicted in Table 6.

Table 6. Appropriateness of the prescribed antibiotics by dose, frequency, and duration of treatment.

Variable	Appropriate *n* (%)	Inappropriate *n* (%)	*p*-Value
Dose	382(99.5)	2(0.5)	0.001
Frequency	383(99.7)	1(0.3)	0.001
Duration	372(96.9)	12(3.1)	0.001
Indication	380(98.6)	4(1.04)	0.001

3. Discussion

This study assessed the prescribing of antibiotics according to the WHO AWaRe classification at the University Teaching Hospital in Lusaka, Zambia. The current study found that the most prescribed antibiotic was ceftriaxone (26.5%), a third-generation cephalosporin classified under the 'Watch group' in the WHO AWaRe. This is similar to previous studies conducted in Zambia in primary healthcare hospitals [58] and first- and second-level hospitals [59]. These findings could be due to the broad-spectrum activity of ceftriaxone which increases its use empirically and for prophylaxis [60–63]. This finding is slightly higher than the recent 24.2% reported in a worldwide survey [64] but less than the 39.6% that was reported in an earlier study in Pakistan [65]. A study in the United Arab Emirates found that Cefaclor was the most prescribed antibiotic [66]. The excessive use of third-generation cephalosporins is worrisome as it predisposes to the development of extended-spectrum beta-lactamase (ESBL)-producing microorganisms [67–69].

Further, our study indicated that azithromycin, another 'Watch' antibiotic, was among the most prescribed antibiotics. These results are consistent with findings from studies conducted in some countries [38,70,71], India [72], Malaysia [73], Eastern Mediterranean countries [43], and Zambia inclusive [58,59]. The reasons for the similarities could be attributed to an increase in respiratory tract infections during the pandemic many of which were suspected to be COVID-19 [74,75]. Early in the pandemic, antibiotics such as azithromycin were widely prescribed as part of the management of COVID-19 [76,77]. This finding calls for the need to promote rational prescribing and strengthening of AMS programmes in healthcare facilities [78–80].

Furthermore, the reasons attributed to increased prescription of the Watch group antibiotics (broad-spectrum antibiotics) might be due to fear of treatment failure if Access group antibiotics were to be used, availability of these medicines, demands and expectations of the patients [81]. Therefore there is a need for healthcare authorities to improve the availability of Access group antibiotics and encourage the reduction in the use of the Watch group antibiotics since these antibiotics have a higher rate of resistance [81–83].

Our study also found that the "Access" group of antibiotics was the most prescribed (55.5%), compared to the "Watch" (43.1%) and "Reserve" (1.4%) groups of antibiotics. Similar results were reported from other studies that were conducted in Ghana [84], where 45–52% of the prescribed antibiotics were from the Access group, and in India [82], where 53.31% of the antibiotics were from the Access group. The overall prescribing of antibiotics in our study is lower than the WHO recommendations, which state that more than 60% of all prescribed antibiotics must be from the Access group [51]. This could be due to the unavailability of first-line groups of antibiotics in some set-ups [85]. Our findings differ from a Bangladesh study in which 64.0% of the patients were treated with antibiotics from the Watch group, 35.6% were treated with antibiotics from the Access group, and only 0.1% were treated with antibiotics from the Reserve group [86]. In a Caribbean study, no Reserve antibiotics were prescribed for the patients [87]. Our results and those from similar studies indicate a different trend or pattern in the prescribing of these AWaRe antibiotics.

Furthermore, our study found that most prescriptions (84.9%) (98% out-patients and 70% in-patients) had one prescribed antibiotic translating into an average of 1.2 antibiotics per prescription. The average number of antibiotics per prescription found in our study is lower than the WHO prescribing indicators which state that each prescription should contain an average of 1.6–1.8 antibiotics [70]. This low average of prescribed antibiotics per prescription indicates appropriate prescribing practice, and it decreases poly pharmacy and drug-drug integration or side effects. These findings corroborate reports from other studies that were conducted in Congo [88], which found an average of 1.4, Eritrea [89], which reported an average of 1.2, India [72], where an average of 1.12 was reported, and Pakistan [90], where an average of 1.4 was reported. In contrast, other studies reported a higher average of prescribing antibiotics [91–93]. Given these findings, it is recommended that hospitals implement AMS programmes for outpatients as well. Additionally, specific guidelines should be established to promote the appropriate prescribing of antibiotics in outpatient departments.

Our study also found that adherence to prescribing patterns using the STG was 99.5% by dose, 99.7% by frequency, 96.9% by duration, and 98.6% by indication. However, despite high adherence to the STG was not 100% for the measured doses, frequency, duration, and indication indicators. These findings are similar to those that were reported in Ethiopia at Lumane Primary Hospital [94] and Tanzania across six referral hospitals [95]. In contrast to our findings, a study in Indonesia reported that 15% of all prescriptions were inappropriate regarding the dose, frequency, and duration of antibiotic treatment [96]. Low adherence to the STG was also reported in Ethiopia [97]. This calls for increased educational programmes to continue and improve adherence to STGs and good practices [7,98–102].

Our study examined antibiotic prescribing patterns at a referral hospital during the COVID-19 pandemic. These findings can help promote rational and appropriate antibiotic prescribing and strengthen AMS programmes, which may reduce the overuse of antibiotics. However, it is important to note that our study did not include children under the age of 12 years, so the generalisability of these findings to this vulnerable population is limited.

4. Materials and Methods

4.1. Study Design, Site, Period and Population

This was a cross-sectional study that was conducted at the University Teaching Hospital in Lusaka, Zambia. Data collection was done from August 2022 to September 2022. The study site is a national referral hospital offering specialised healthcare services across populations in Zambia. This study was conducted by reviewing medical files for in- and out-patients, and all patient medical files where antibiotics were prescribed between January 2021 and December 2021 were included in the survey. In Zambia, all prescription only medicines which include antibiotics are prescribed by registered prescribers including physicians, clinical officers, clinical licentiates, and nurses. Hence, all antibiotics for in- and out-patients are prescribed by these registered prescribers.

4.2. Sample Size Determination and Sampling Technique

The sample size was estimated using Cochran's formula, as explained by Charan and Biswas [103]. A conservative prevalence of 50% and a margin of error of 5% at a 95% confidence level were used in estimating the minimum sample size required. This resulted in an estimated sample size of 384. All medical files that had antibiotics prescribed were retrieved and checked for completeness of the information. All files that were used in the study were then selected using simple random sampling to increase the chances of every file being sampled.

4.3. Data Collection

Data was collected using an adapted validated tool from a similar study [6]. Data collected from patients' medical files included sociodemographic information such as age, gender, and patient category (in or out-patient). We also collected information such as the name of the antibiotic prescribed, dose and treatment duration, and the disease condition for which the antibiotic was prescribed (Table S1). Adherence to prescribing antibiotics by dose, frequency, and duration was done according to the 2020 Zambian Standard Treatment Guidelines (STG) [104]. Classification of antibiotics into the AWaRe groups was done based on 2021 WHO AWaRe tool [51]. Overall, 384 patient medical files were used in this study.

4.4. Data Analysis

The collected data were entered into Microsoft Excel 2013 and exported to IBM Statistical Package for the Social Sciences (SPSS) version 22.0 for statistical analysis. The results were presented in the form of frequency tables. The variables were considered significant at $p < 0.05$, and all tests were performed at a 95% confidence level.

5. Conclusions

This study found that antibiotics were widely used at the University Teaching Hospital during the COVID-19 pandemic, though, most were prescribed appropriately. A high prescription of Watch antibiotics was noted, and ceftriaxone was the most prescribed antibiotic. These results are of great concern and highlight the need for strengthened antimicrobial stewardship at the University Teaching Hospital in Lusaka, Zambia. Overall, our study findings demonstrate high adherence to the measured prescribing indicators during the COVID-19 pandemic.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/pharma2010005/s1, Table S1: Data Collection Tool.

Author Contributions: Conceptualization, S.M. (Steward Mudenda) and E.N.; methodology, S.M. (Steward Mudenda) and E.N.; software, S.M. (Steward Mudenda); validation, S.M. (Steward Mudenda), E.N., W.M. (Webrod Mufwambi), H.K. and S.K.M.; formal analysis, S.M. (Steward Mudenda); investigation, S.M. (Steward Mudenda) and E.N.; resources, S.M. (Steward Mudenda); data curation, S.M. (Steward Mudenda), E.N., P.C., V.D. and B.C.; writing—original draft preparation, S.M. (Steward Mudenda).; writing—review and editing, S.M. (Steward Mudenda), E.N., P.C., V.D., B.C., W.M. (Webrod Mufwambi), H.K., M.H.G.K., R.L.M., F.M., M.Z., R.T., W.M. (Wizaso Mwasinga), K.C., G.M., N.M., M.S., H.K.C., S.M. (Shafiq Mohamed) and S.K.M.; visualization, S.M. (Steward Mudenda), E.N., H.K., F.M., M.Z., R.T., W.M. (Wizaso Mwasinga), K.C., G.M., N.M., M.S., H.K.C. and S.M. (Shafiq Mohamed); supervision, S.M. (Steward Mudenda); project administration, S.M. (Steward Mudenda); funding acquisition, S.M. (Steward Mudenda). All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: Ethical approval was obtained from the University of Zambia Health Sciences Research Ethics Committee (UNZAHSREC) with an approval number of 202211231186. Permission to conduct the study was sought from the management at the University Teaching Hospital. This research was conducted ethically regarding privacy, confidentiality and respect for autonomy.

Informed Consent Statement: Informed consent to use the patient files was obtained from the hospital management and healthcare workers who were working at the time of the study. Patient const was waived because the files were for patients who had been discharged and were home. Additionally, informed consent to publish the findings of the study was obtained from the hospital management.

Data Availability Statement: The data supporting the reported results can be made available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflict of interest.

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