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Antibiotic consumption at community pharmacies: A multicenter repeated prevalence surveillance using WHO methodology

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Abstract

Background: Antibiotics are losing their effectiveness because of the rapid emergence of resistant bacteria. Unnecessary antimicrobial use increases antimicrobial resistance (AMR). There are currently no published data on antibiotic consumption in Pakistan at the community level. This is a concern given high levels of self-purchasing of antibiotics in Pakistan and variable knowledge regarding antibiotics and AMR among physicians and pharmacists.

Objective: The objective of this repeated prevalence survey was to assess the pattern of antibiotic consumption data among different community pharmacies to provide a baseline for developing future pertinent initiatives.

Methods: A multicenter repeated prevalence survey conducted among community pharmacies in Lahore, a metropolitan city with a population of approximately 10 million people, from October to December 2017 using the World Health Organization (WHO) methodology for a global program on surveillance of antimicrobial consumption.

Results: The total number of defined daily doses (DDDs) dispensed per patient ranged from 0.1 to 50.0. In most cases, two DDDs per patient were dispensed from pharmacies. Co-amoxiclav was the most commonly dispensed antibiotic with a total number of DDDs at 1018.15. Co-amoxiclav was followed by ciprofloxacin with a total number of 486.6 DDDs and azithromycin with a total number of 472.66 DDDs. The least consumed antibiotics were cefadroxil, cefotaxime, amikacin, and ofloxacin, with overall consumption highest in December.

Conclusion: The study indicated high antibiotic usage among community pharmacies in Lahore, Pakistan particularly broad-spectrum antibiotics, which were mostly dispensed inappropriately. The National action plan of Pakistan on AMR should be implemented by policymakers including restrictions on the dispensing of antimicrobials.

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Introduction

Antibiotics, which have revolutionized medicine and saved millions of lives worldwide, are losing their efficacy because of the rapid emergence of antimicrobial resistance (AMR).[1,2] Moreover, growing rates of AMR are now increasing morbidity, mortality, and costs.[3–7] In 1962, the first case of methicillin-resistant *Staphylococcus aureus* (MRSA) was identified. Since then, pharmaceutical companies have developed many new potent antibiotics. However, fewer new antibiotics are now being discovered and marketed in recent years, enhanced by considerable commercial opportunities for new medicines for immunological diseases, cancer, and orphan diseases versus new antibiotics.[4,8–10] Over time though, the effectiveness of the newer potent antibiotics has reduced due to their inappropriate use along with the emergence of multidrug-resistant strains of *S. typhi* and carbapenem-resistant *Enterobacteriaceae*.[2,11] Despite significant attempts to optimize antibiotic use in the community and hospital settings, AMR rates continue to increase enhanced by excessive and inappropriate utilization of antibiotics in both individuals and the population at large.[12,13] Community pharmacies provide major primary health care facilities in most low monthly income countries (LMICs), which is enhanced during the pandemics, that is, COVID-19.[14] Consequently, the surveillance of dispensing behavior among private community pharmacies, who have an important role in delivering primary care especially in LMICs, is essential. Injudicious and high use of antibiotics, especially in ambulatory care where most infections are seen, increases the utilization of broad-spectrum and more expensive antimicrobials enhancing AMR.[15] As a result, there are ongoing antimicrobial stewardship programs globally, regionally, and nationally to improve antibiotic utilization rates with AMR, a worldwide problem.[16–22]

The discrepancies and differences in the consumption of antibiotics among European countries prompted the World Health Organization (WHO) to organize its first meeting on drug Consumption in Oslo in 1969, which led to the development of the WHO European Drug Utilization Research Group (DRUG).[23] However, regular research on antibiotic consumption is now undertaken by the European Centre for Disease Prevention and Control (ECDC) as well as the WHO Europe group using a range of indicators.[24–26] To ascertain antibiotic consumption on an individual level (per person basis), the World Bank studied consumption patterns among six selected countries including China, India, the United Kingdom, the United States, Germany, and France from 2000 to 2010. The findings showed that antibiotic consumption increased in which cephalosporin increased in consumption by 36% and other broad-spectrum penicillins accounted for a 55% increase in consumption.[27] Other recent estimates suggest that worldwide antibiotic consumption increased by 65% between 2000 and 2015 principally driven by increased utilization in developing countries.[28,29] Consequently, activities to reduce inappropriate prescribing and dispensing of antibiotics especially in the community are urgently needed with antibiotic consumption appreciably increasing over the years.[30,31] This is especially important at this time with the WHO concerned about inappropriate prescribing and dispensing of antibiotics during the current COVID-19 pandemic and has issued guidance to try and reduce such behavior to decrease antibiotic consumption.[32,33]

The emergence and prevalence of resistant microbes are reported to be highest among Asian countries where they are found to be spreading both in communities and hospitals.[34] One of the reasons for the increasing spread of AMR in this region is the high rate of irrational use of antibiotics.[35–38] The first step in developing strategies to reduce inappropriate prescribing and dispensing of antibiotics in ambulatory care is to determine actual utilization patterns and compare these with suggested quality indicators alongside any ongoing initiatives.[39–46] However, determining utilization patterns in LMICs can be challenging with commercial utilization data typically only available in higher income countries.[44] This has resulted in the development of different approaches to measure utilization rates including import data as well as exit surveys.[40,47] Currently, in Pakistan, there is a scarcity of data on the pattern of antibiotics dispensed and their consumption at the community pharmacy level hampering the development of future strategies to reduce unnecessary prescribing and dispensing of antibiotics. Within this context, this present repeated prevalence survey aimed to assess the utilization of antibiotics from different community pharmacies in Lahore and to ascertain consumption patterns by measuring the number of dispensed defined daily doses (DDDs) per customer. This is a different approach to WHO and The International Network for Rational Use of Drugs (INRUD) criteria that typically just measures the extent of antibiotics being prescribed per patient [48–50] as there are concerns whether such approaches measure the quality of prescribing.[51] In addition, we wanted to assess utilization rates of different classes following the publication of guidance from the WHO and others, including more recently WHO Access, Watch, Reserve (AWaRe) antibiotic listing.[40,44,52–54] This builds on our recently published point prevalence survey of antibiotic use in the hospitals of Pakistan.[55] Community pharmacies are very important in Pakistan given high rates of patient co-payments for medicines, appreciable self-purchasing of antibiotics in the community, and concerns with antibiotics being dispensed.[56,57]

Method

Study design and centers

A multicenter repeated prevalence survey was conducted among community pharmacies in Lahore from October

2017 to December 2017 using the WHO methodology for the global program on surveillance of antimicrobial consumption.[58] This includes measuring consumption rates using the WHO DDD methodology.[59] Lahore is the capital city of Punjab, and it is one of the wealthiest cities of Pakistan with a Gross Domestic Product (GDP) of US$277.2 billion and GDP per capita of US$1641 in 2018, with a population of approximately 10 million. We chose Lahore for this study as community pharmacies in Lahore are undergoing radical changes as this city harbors well-established pharmacy chains as well as independent pharmacies. In addition, if there were concerns with inappropriate prescribing and dispensing of antimicrobials in the main provincial capital city, such concerns are likely to be seen throughout Pakistan. Five community pharmacies in Lahore were enrolled for the study from different geographical areas of Lahore.

Inclusion and exclusion criteria

Our study included both oral and parenteral antibacterial agents excluding vaginal, ophthalmic, or other topical antibacterial agents because these dosage forms are mainly associated with AMR.

Variables

Pharmacy name, generic name, brand name, strength, dosage form, route, volume dispensed, pack size, and grams of drug dispensed were recorded.

Data collection and analysis

First, we reviewed the inventory of antibiotics in each selected pharmacy. One-day antibiotic sales data were collected consecutively for 3 months in each pharmacy. The data of antibiotics consumed per day were extracted from the pharmacy management system named Wasila Inventory Management Software® (Abuzar Consultancy, Pvt, Ltd), which is the reliable inventory management software used in Pakistan. Different parameters were checked including the brand name, generic name, dosage form, strength, and quantity of dispensed antibiotics, respectively. Consumption data were obtained from different community pharmacies, measuring the number of packs dispensed per day. Data were entered in Microsoft Excel sheets including the name of all the variables, and statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 24 version. Antibiotic consumption was measured using the Anatomical Therapeutic Chemical Classification (ATC)/DDD system developed by WHO.[59,60] The DDD is defined as the average maintenance dose per day for a drug used in adults for its primary indication. DDDs enable comparisons to be made between different hospitals, pharmacies, and even countries.[40,45,18,61,62] We were not able to ascertain DIDs (DDDs per 1000 inhabitants per day) as there was no reliable denominator. However, measuring DDDs per patient for the different antibiotics dispensed does permit assessing utilization patterns against suggested quality indicators. A DDD is only assigned for medicines that already have an ATC code. According to the ATC/ DDD methodology, collected data were analyzed, where the number of DDDs of drugs was determined from the number of grams dispensed. The number of DDDs is equal to the total grams used divided by the DDD value in grams. The total grams of the antibacterial used are calculated by summing up the amounts of the active ingredient in different formulations and pack sizes.

Results

Antibiotics in tablet dosage form were the most commonly dispensed from the selected community pharmacies (Table 1). There was considerable variation in the total number of DDDs dispensed per patient, ranging from 0.1 to 50.0 DDDs. In most of the cases observed in the study, two DDDs were dispensed per patient. Table 2 and Figure 1 describe the consumption patterns of the antibiotics dispensed, which differed significantly during follow-up. Co-amoxiclav (J01CR02) was the most commonly dispensed antibiotic with a total number of DDDs of 1018.15 (24.3%) among the five pharmacies during the data collection period, followed by ciprofloxacin (J01MA02) with a total number of DDDs of 486.6 (11.6%). Azithromycin (J01FA10) was the third most commonly dispensed antibiotic with a total number of DDDs of 472.66, and the highest number of dispensed DDDs of azithromycin was also in December 2017, that is, 247.5 (6%) DDDs. That was followed by levofloxacin (J01MA12) with a total number of DDDs of 344.5 (8.2%), clarithromycin (J01FA09) with a total number of DDDs of 324.52 (7.7%), and cefixime (J01DD08). Cefadroxil, meropenem, cefotaxime, amikacin, and ofloxacin were found to be least dispensed during the period mentioned.

Discussion

To our knowledge, this is the first prevalence survey that presents data on antibiotic consumption among community pharmacies in Lahore, Pakistan. We believe the highest consumption of broad-spectrum antibiotics is due to a belief in better coverage against potential bacteria in the absence of any formal resistance pattern data. However, this remains to be seen. Interestingly, the dispensing of these antibiotics were found to be increased in November and December, which may be due to increased respiratory tract infections despite the vast majority being viral in origin.[15,63] Consequently, antibiotics never prove completely beneficial for patients experiencing viral upper respiratory tract infections (URTIs) and should be reserved.[15] This excessive use of broad-spectrum antibiotics raises concerns

Table 1. Overall antibiotic consumption.

Parameters	October 2017	November 2017	December 2017	Total
No. of DDDs				
Mean ± SD	3.29 ± 3.24	2.97 ± 4.14	3.62 ± 4.34	3.30 ± 3.97
Median (range)	2.25 (0.1–20.0)	1.50 (0.1–50.0)	2.50 (0.1–35.0)	2.00 (0.1–50.0)
Total	1287.09	1245.7	1651.61	4184.43
Dosage form				
Tablet, n (%)	241 (61.7)	254 (60.5)	262 (57.4)	757 (59.8)
Capsule, n (%)	108 (27.6)	93 (22.2)	125 (27.4)	326 (25.9)
Injection, n (%)	22 (5.6)	33 (7.9)	36 (7.90)	91 (7.4)
Suspensions, n (%)	15 (2)	26 (6.2)	28 (6.1)	69 (5.5)
Infusion, n (%)	19 (0.6)	5 (1.2)	0	24 (2.1)
Syrup, n (%)	3 (0.8)	8 (1.9)	5 (1.1)	16 (1.3)
Route				
Oral	367 (93.9)	381 (90.9)	423 (92.1)	1168 (92.3)
Parenteral	24 (6.1)	38 (9.1)	34 (7.9)	98 (7.8)

DDD: defined daily dose.

Table 2. Number of DDDs dispensed at community pharmacies.

Antibiotics	October 2017		November 2017		December 2017		Total	
	Mode (range)	Total	Mode (range)	Total	Mode (range)	Total	Mode (range)	Total
Co-amoxiclav (J01CR02)	8.3 (4.9–20.0)	266.9	10.6 (7.3–38.1)	339.0	7.5 (1.4–30.4)	412.8	15.2 (1.4–38.1)	1018.9
Ciprofloxacin (J01MA02)	7.0 (2.3–13.0)	138.8	1.0 (0.3–21.0)	158.0	5.5 (2.9–35.0)	189.9	3.0 (0.3–35.0)	486.6
Azithromycin (J01FA10)	5.0 (0.8–10.0)	149.0	1.0 (0.8–3.0)	75.3	5.0 (1.6–13.0)	247.5	5.0 (0.8–13.0)	472.7
Levofloxacin (J01MA12)	8.0 (3.5–13.0)	145.0	2.0 (2.0–22.0)	88.5	3.0 (0.5–10.0)	104.0	2.0 (0.5–22.0)	337.5
Clarithromycin (J01FA09)	2.0 (0.5–2.0)	84.5	3.0 (0.5–5.0)	80.0	3.0 (0.5–15.0)	159.5	3.0 (0.5–15.0)	324.0
Cefixime (J01DD08)	10.0 (6.0–20.0)	118.10	10.0 (6.0–12.0)	135.0	4.5 (4.5–10.0)	37.50	14.5 (4.5–20.0)	290.6
Amoxicillin (J01CA04)	2.7 (1.7–6.2)	52.2	1.0 (0.5–50.0)	142.0	1.0 (0.3–7.5)	61.8	1.0 (0.3–50.0)	255.9
Metronidazole (J01XD01)	2.0 (0.2–4.2)	66.6	1.0 (0.2–4.2)	57.2	2.0 (0.2–7.0)	62.3	1.0 (0.2–7.0)	186.1
Doxycycline (J01AA02)	3.0 (3.0–3.0)	66.0	10.0 (2.0–20.0)	47.0	10.0 (1.0–20.0)	59.0	10.0 (1.0–20.0)	172.0
Moxifloxacin (J01MA14)	2.0 (1.0–14.0)	36.0	1.0 (1.0–5.0)	16.5	2.0– (1.0–7.0)	45.0	2.0 (1.0–14.0)	97.5
Cephradine (J01DB09)	2.3 (0.5–5.3)	29.8	0.3 (0.1–7.0)	26.9	0.3 (0.3–3.8)	13.00	0.3 (0.1–7.0)	69.6
Erythromycin (J01FA01)	1.0 (0.5–3.0)	15.7	0.5 (0.5–3.5)	13.0	0.5 (0.5–2.5)	12.3	0.5 (0.5–3.5)	41.0
Rifaximin (A07AA11)	9.3 (9.3–14.0)	23.3	9.2 (9.2–9.2)	9.2	3.3 (3.3–3.3)	6.7	3.3 (3.3–14.0)	39.2
Ceftriaxone (J01DD04)	0.5 (0.5–1.0)	9.3	0.5 (0.5–1.0)	11.0	0.5 (0.3–2.5)	17.50	0.5 (0.3–2.5)	37.8
Cefuroxime (J01DC02)	NU	NU	0.5 (0.5–2.0)	28.5	1.0 (1.0–1.0)	1.0	0.5 (0.5–21.0)	29.5
Cefaclor (J01DC04)	1.5 (1.5–4.5)	6.0	0.5 (0.5–1.5)	2.0	1.5 (1.5–3.0)	6.00	1.5 (0.5–4.5)	14.0
Ampicillin (J01CA01)	NU	NU	NU	NU	10.0 (10.0–10.0)	10.0	10.0 (10.0–10.0)	10.0
Clindamycin (J01FF01)	0.5 (0.5–1.6)	5.0	4.0 (4.0–4.0)	4.0	0.25 (0.3–.05)	0.8	0.5 (0.3–4.0)	9.8
Linezolid (J01XX08)	1 (1.0–1.0)	1.0	2.0 (2.0–5.0)	7.00	NU	NU	1.0 (1.0–5.0)	8.0
Vancomycin (J01XA01)	0.5 (0.5–1)	1.5	0.3 (0.3–1.0)	1.50	NU	NU	0.3 (0.3–1.0)	3.0
Piperacillin-tazobactam (J01CR05)	NU	NU	0.3 (0.3–1.2)	1.5	0.3 (0.3–1.0)	1.3	0.3 (0.3–1.9)	2.9
Lincomycin (J01FF02)	NU	NU	NU	NU	0.5 (0.6–1.1)	2.2	0.5 (0.6–1.1)	2.2
Ofloxacin (J01MA01)	NU	NU	NU	NU	1.5 (1.5–1.5)	1.5	1.5 (1.5–1.5)	1.5
Amikacin (J01GB06)	0.5 (0.1–0.5)	1.10	NU	NU	0.1 (0.1–0.1)	0.3	1.0 (0.1–0.5)	1.4
Cefotaxime (J01DD01)	NU	NU	0.3 (0.3–0.5)	1.0	0.1 (0.1–0.3)	0.31	0.3 (0.1–0.5)	1.3
Meropenem (J01DH02)	0.5 (0.5–0.5)	0.5	0.3 (0.3–0.3)	0.5	NU		0.3 (0.3–0.5)	1.0
Cefadroxil (J01DB05)	NU	NU	NU	NU	1.0 (1.0–1.0)	1.00	1.0 (1.0–1.0)	1.0

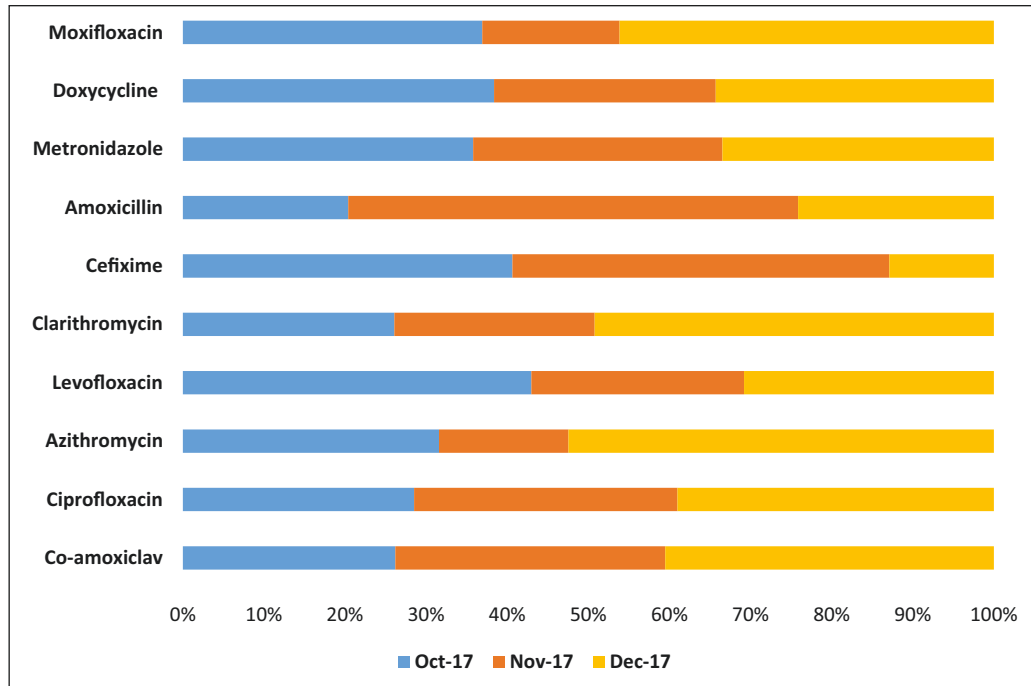DDD: defined daily dose, NU: Not Used.

Figure 1. Percentage consumption data of top 10 antibiotics.

regarding inappropriate use.[64] Ideally, these antibiotics must be used as the second-line agents because these are not recommended as the first-line agent for the management of respiratory tract infections and are part of the WHO AWaRe list. Interestingly, this study reported frequent dispensing of metronidazole, despite less number of total DDDs. This dispensing pattern can be attributed partly since the dosing frequency of metronidazole is high. The common practice seen in this aspect is that patients usually take one or two doses of metronidazole for diarrhea and later discontinue the course once relieved of their symptoms. This is witnessed as a commonly irrational practice in Pakistan, and we will be following this up in future research.[56] Compare the aforementioned with another finding of this study that one or two DDDs of co-amoxiclav are rarely dispensed because co-amoxiclav is typically available in packing size of six tablets. The tablets of co-amoxiclav are sold as a full pack and are seldom dispensed in units that increase DDD.

The National Action Plan of Pakistan for antibiotics recommends and emphasizes the rational use of antibiotics in the country. Despite this, many reserves and watch group antibiotics in the WHO AWaRe list appear to be consumed in Pakistan for simple infections as well as for prophylaxis.[55,56] The irrational use of fluoroquinolones is rising in Pakistan not only causing serious side effects but also increasing the risk of AMR,[65] enhanced by high self-purchasing of antibiotics in Pakistan.[63] According to the critically important antimicrobials (CIA) list of the WHO, quinolones are classified as the main priority class of antibiotics and should be used cautiously. The US FDA has indicated that fluoroquinolones should be only used in those patients left with no other treatment options.[66] Contrary to this, fluoroquinolones are repeatedly used for uncomplicated infections such as upper respiratory infections and diarrhea in Pakistan.[55] This has raised concerns regarding the appropriate use of antibiotics through antibiotic stewardship programs (ASPs). Evidence has shown that ASPs have contributed to decreasing both unnecessary antibiotic consumption as well as expenditures in the high-income countries; however, recognizing difficulties with undertaking ASPs in LMICs, especially in ambulatory care.[31,67–72] Overall, we believe the community pharmacists must be vigilant about the rational use of antibiotics because they are conveniently accessible and they are an integral part of the healthcare system of any country.[73–76] Consequently, they should be part of any future AMS programs within countries to improve future antibiotic utilization.[77] The restricted use of antibiotics can be executed by campaigns of general public awareness and through policy-making including regulations banning the sale of antibiotics in the Watch and Reserve list as well as enhancing the education of pharmacists accompanied by appropriate guidelines.[78–80] This is seen as preferable to fining pharmacists for dispensing antimicrobials without a prescription as seen in some countries especially where there are high co-payments and where community pharmacists are the principal healthcare professional available.[15,81]

The widespread practice of selling antibiotics inappropriately over the counter or without any prescription is one of the major problems at community pharmacies because of poor law enforcement and needs to be addressed.[37,63] A

lack of a sustainable health care system and failure regarding enforcement of any regulation are some of the reasons for unauthorized over-the-counter sales of antibiotics.[15,82] Unnecessary self-medication with antibiotics may go along to reduce the irrational use of broad-spectrum antibiotics,[63] thereby helping to reduce the emergence of AMR. Moreover, incomplete antibiotic prescription, dosing frequency, duration, and other patient-related factors also promote inappropriate use of antibiotics and need to be tackled with future educational programs among both pharmacists and patients.[83,84] This includes dispensing parenteral antibiotics among community pharmacists, which should be avoided given their necessity as well as possible complications from needle administration. Such use in ambulatory care is likely driven more by incentives in the system than actual clinical need.[85] Moreover, the study conducted in Jordan reported that 46% of the patients self-medicated antibiotics.[86] Studies conducted in Malta Lithuania revealed the prevalence of self-medication to be 19% and 22%, respectively.[87,88] Furthermore, a study in Europe revealed that Greece had one of the highest rates of antibiotic consumption in Europe as outpatients with macrolides and cephalosporins being the most frequently used antibiotics.[89]

We are aware that there are several limitations with this study. First, we did not calculate the consumption and expenditures of antibiotics according to patient demographic factors and clinical conditions. Second, we cannot generalize the findings of the data because we conducted this study in only a few pharmacies in one city of Pakistan. Finally, there could be some underestimation of the consumption of some antibiotics because only 1 day of data was collected from each pharmacy. Nonetheless, we believe that this study provides good baseline data for policymakers, and we are planning future studies to address some of the concerns. Our study identified potential indicators for quality improvement. These included reduced dispensing of incomplete course of antibiotics. In addition, reduce the total consumption of commonly dispensed antibiotics including co-amoxiclav, ciprofloxacin, and other broad-spectrum antibiotics where there are concerns under the AWaRe list.

Conclusion

Our study indicated high antibiotic usage at different community pharmacies, particularly for broad-spectrum antibiotics, that is, azithromycin. The National Action Plan of AMR should be implemented by policymakers to address issues of inappropriate prescribing and dispensing of antibiotics and must ensure the rational use of antibiotics by the public. Moreover, the National Action Plan of AMR has to design a law to minimize the self-purchasing of antibiotics at community pharmacies. Awareness of the irrational use of broad-spectrum antibiotics should

be increased among physicians, pharmacists, and patients. The unauthorized over-the-counter sale of antibiotics should be avoided in a community pharmacy where possible.

Author contributions

Zikria Saleem: Formal analysis; Methodology; Supervision; Writing – original draft.
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Brian Godman: Methodology; Supervision; Writing – review & editing.
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Furqan Khurshid Hashmi: Resources.
Mohamed Azmi Hassali: Writing – review & editing.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was acquired from the Human Ethics Committee of University College of Pharmacy, University of the Punjab, Lahore (HEC/1000/PUCP/1925AMCC).

Patient consent

The study design is non-experimental and involves neither patient examination nor any intervention advised or made. This study is based on a non-experimental study design; therefore, patient consent is not required for such type of study.

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