Antimicrobial Dispensing Sans Legitimate Prescription from Community Pharmacies in Lahore, Pakistan: Implications for Antimicrobial Resistance

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Abstract

Background: The use of antimicrobials and their acquisition from pharmacies without prescription is on the rise in low-and middle-income countries contributing towards the emergence of antimicrobial resistance (AMR). The study aims to determine factors influencing the non-prescription dispensing of antibiotics from community pharmacies and implications in AMR.

Methods: A questionnaire-based cross-sectional survey was conducted from January 2019 to September 2019 in Lahore city of Pakistan. The data were analyzed using a statistical package for social sciences (SPSS) version 22. The association of the knowledge, attitude, and practice with demographic parameters were determined using correlation and chi-square test.

Results: The majority of the respondents were male pharmacists (84.5%) working as staff pharmacists (45.5%). Among the respondents, 75.9% considered AMR as a global health threat, however, 52.1% facilitated antimicrobial dispensing without prescriptions. Respondents stated that non-prescription antimicrobial dispensing was to make medical consultation easy (42%) and satisfy the demand of the patients (30.1%). Yet participants recognized the value of patient education concerning drug interactions 42.6%, culture and sensitivity test 31.5%, and full course of antimicrobials 40.8%. Participants were not agreed to dispense antimicrobials in cold and flu (58.1%), influenza (57.8%), abdominal pain (50%), and fever (60.7%). They practiced dispensing in diarrhea (62.2%), urinary tract infections (68.1%), ear infection (56.9%), and sore throat (64%). For qualification with all knowledge variables, a significant association was obtained. For marital status and qualification with practice variables, P-value was found significant.

Conclusion: Interventions should be done to halt these irrational practices which have a negative impact on public health. Educational interventions are required for the public. Strict enforcement of rules and regulations, Drug Sale Rules 2007, and implementation of Pakistan's National Action Plan on AMR is required.

Background

Antimicrobial resistance (AMR) is one of the greatest threats to public health; responsible for increased morbidity and mortality as well as the increased healthcare costs [1, 2]. The World Health Organization (WHO) has recognized the importance of AMR for a long, therefore, in 2001 Global Strategy for Containment of Antimicrobial Resistance has provided a framework of interventions to slow the emergence, and reduce its spread [3]. AMR has been declared as a global emergency, in line with that at the 68th World Health Assembly in May 2015 endorsed a Global Action Plan to combat AMR and control the escalation in the trend [4]. The incidence of AMR is more prevalent in developing countries due to poor enforcement of laws and lack of substantial surveillance systems resulting in a high incidence of resistance [5]. AMR can be attributed to irrational use of antibiotics such as; unnecessary, suboptimal (duration, frequency, indication, dose), and extensive use of broad-spectrum antibiotics [6, 7].

In low-and middle-income countries (LMICs) dispensing of antibiotics without prescription is common [8]; as it is a convenient, time saving, and cheap way of obtaining the drugs without physician consultation [9], consequently promoting the irrational practice which has long-term effects on patient's health [10].

Pakistan is the sixth most populous country and is categorized as LMIC with a Human Development Index (HDI) value of 0.560 [11]. The healthcare system of Pakistan is under the constantly increasing burden of communicable- as well as non-communicable diseases and a majority of the healthcare spending is out of pocket [12, 13]. In this context, the public finds it easy to get their medicines from a local retail drug store or pharmacy without having a legitimate prescription from a medical practitioner. Even antibiotics can be acquired as over the counter (OTC) medicines. A study reported a high number of broad-spectrum antibiotics dispensed through community pharmacies, subsequently leading to AMR [14].

The present study aims to evaluate the dispensing of antimicrobials without prescription and evaluation of the knowledge, attitudes, and practices of community pharmacy staff about the dispensing of antimicrobials sans legitimate prescriptions.

Methodology

Ethics approval

The research has been performed in accordance with the Declaration of Helsinki. The ethics approval was granted by the Humans Ethics Committee (HEC) University College of Pharmacy, University of the Punjab, Lahore (No: HEC/UCP/2045-19). Informed consent to participate in the study was obtained from participants.

Study design

A cross-sectional study was carried out in community pharmacies in Lahore, Pakistan from January 2019 to September 2019, principally targeting antimicrobials dispensing without prescription.

A questionnaire was developed comprising of four sections; demographics of participants, knowledge, attitude, and practices of antibiotic dispensing. The knowledge section was based on the concept of the participants. The attitude section proclaims the thinking of the participant. The practice section presents what the respondents perform. Both attitude and practice sections contained statements on a five-point Liker-Scale (1 = strongly disagree to 5 = strongly agree).

The face and content validity of the questionnaire was carried out by three experts at the university. The reliability analysis yielded a Cronbach alpha value of 0.80.

Sample size

Online sample size calculator "Raosoft" was used for calculating sample size with a margin of error 5% and CI 95%. For 3500 pharmacies in Lahore [15], the sample size was 347 pharmacies. The pharmacies

were randomly selected and pharmacy staffs engaged in drug dispensing; the manager-pharmacy, staff pharmacist, and dispenser were included.

Data analysis

Data were analyzed by IBM SPSS version 22. Frequencies and percentages were calculated for the demographic variables. The association of the knowledge, attitude, and practice with demographic parameters were determined using correlation and chi-square test.

Results

A total of 400 questionnaires were distributed among the community pharmacies out of which 336 were returned (response rate = 84%). The majority of the study respondents were male pharmacists 84.5% (n = 284). About 34.8% (n = 117) had work experience of fewer than 2 years while 20.2% (n = 68) had more than 10 years of experience at community pharmacies. Most of the respondents were staff pharmacist 45.5% (n = 153) whereas 35.7% (n = 120) were managers. Only 18.8% (n = 63) were technicians. Table 1.

Table 1
Demographics of the study population (N = 336)

Demographics		Frequency (n)	Percentage (%)
Gender	Male	284	84.5
	Female	52	15.5
Marital Status	Single	169	50.3
	Married	167	49.7
Age (years)	18–27	163	48.5
	28–37	115	34.2
	38–47	46	13.7
	> 47	12	3.6
Job status	Manager	120	35.7
	Staff Pharmacist	153	45.5
	Technician	63	18.8
Experience (years)	< 2	117	34.8
	3–5	70	20.8
	6–10	81	24.1
	> 10	68	20.2
Qualification	Intermediate	87	25.9
	Graduate / Master	45	13.4
	Diploma of Pharmacy	13	3.9
	B.Pharm / PharmD	191	56.8

The overall knowledge of the community pharmacy staffs regarding antimicrobials as powerful medicines to fight bacterial infection, prescription-only medicines (PoM) status, the optimal duration of treatment, and pharmacists' advice to patients regarding the use of antimicrobials to strictly adhere to the treatment regimen were evaluated. A majority of participants responded to AMR as a public health problem, given in Table 2

Table 2
Knowledge of antibiotics (N = 336)

Statements	Options	n (%)
Antibiotics are powerful medicines that help to fight against	Bacteria	274 (81.5)
	Virus	26 (7.7)
	Fungi	1 (0.3)
	Parasites	2 (0.6)
	Do not know	33 (9.8)
In which category antibiotics fall?	Over the counter	24 (7.1)
	Prescription only Medicine	252 (75)
	Controlled medicine	30 (8.9)
	Do not know	30 (8.9)
What is the course of duration of antibiotic treatment?	Less than 3 days.	4 (1.1)
	3 Days	58 (17.3)
	5 Days	154 (45.8)
	7 Days	106 (31.5)
	Do not know	14 (4.2)
In all cases where antibiotics are dispensed, it is essential that patients be advised about complying with the treatment?	Yes	261 (77.7)
	No	44 (13.1)
	Do not know	31 (9.2)
Use of antibiotic is rational in minor ailment / self-limiting diseases?	Yes	111 (33)

Statements	Options	n (%)
	No	194 (57.7)
	Do not know	31 (9.2)
Antibiotic resistance is an important public health problem.	Yes	255 (75.9)
	No	43 (12.8)
	Do not know	38 (11.3)

The attitude and practices of community pharmacists towards dispensing of antibiotics were evaluated on a five-point Likert scale (1 = strongly disagree to 5 = strongly agree). Eight questions were asked to test users' attitudes toward the selling of antibiotics, which are depicted in Tables 3 and 4.

Table 3
Attitude towards dispensing the antibiotic (N = 336)

Statements	Strongly Disagree n(%)	Disagree n(%)	Neutral n(%)	Agree n(%)	Strongly Agree n(%)
Non-prescribed dispensing of antibiotic is a rational medical practice	125 (37.2)	94 (28)	35 (10.4)	48 (14.3)	34 (10.1)
Antibiotics are sometimes dispensed without a medical prescription because the patient is known to have difficulty in obtaining a medical consultation.	44 (13.1)	45 (13.4)	62 (18.5)	141 (42.0)	44 (13.1)
In case of non-prescribed dispensing, personal experience is the source of deciding dosage regimen?	45 (13.4)	62 (18.5)	60 (17.9)	124 (36.9)	45 (13.4)
Antibiotic resistance is getting worse and it is only getting worse. There is nothing I can do.	47 (14.0)	81 (24.1)	65 (19.3)	75 (22.3)	68 (20.2)
When dispensing, possible interaction between the antibiotic and other drugs should be assessed.	26 (7.7)	31 (9.2)	63 (18.8)	143 (42.6)	73 (21.7)
Antibiotics are sometimes dispensed even if not indicated because no time to explain the reasons.	55 (16.4)	70 (20.8)	85 (25.3)	101 (30.1)	25 (7.4)
There is a need for culture analysis before dispensing antibiotics in clinically complicated conditions.	28 (8.3)	34 (10.1)	64 (19)	104 (31.0)	106 (31.5)
Completing the course of antibiotic therapy is crucial in preventing antibiotic resistance.	22 (6.5)	24 (7.1)	51 (15.2)	102 (30.4)	137 (40.8)

Table 4
Practice towards antibiotic dispensing (N = 336)

	Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)
Fever	116 (34.5)	88 (26.2)	39 (11.6)	68 (20.2)	25 (7.4)
Cold and flu	92 (27.4)	103 (30.7)	32 (9.5)	82 (24.4)	27 (8)
Influenza	104 (31)	90 (26.8)	52 (15.5)	57 (17)	33 (9.8)
Sore throat	32 (9.5)	33 (9.8)	56 (16.7)	162 (48.2)	53 (15.8)
Diarrhoea	30 (8.9)	32 (9.5)	65 (19.3)	131 (39)	78 (23.2)
Abdominal pain	64 (19)	104 (31)	83 (24.7)	69 (20.5)	16 (4.8)
Otitis media (ear infection)	29 (8.6)	47 (14)	69 (20.5)	141 (42)	50 (14.9)
Urinary tract infection (UTIs)	31 (9.2)	29 (8.6)	47 (14)	151 (44.9)	78 (23.2)

Association of knowledge of antibiotic with demographics was evaluated using correlation and chi-square, given in Table 5

Table 5
Association of knowledge of antibiotic with demographics

STATEMENT	Gender	Age	Marital status	Job	Experience	Qualification
Action of antibiotic	0.182 (0.001)	2.089 (0.554)	-0.049 (0.372)	-0.102 (0.063)	-0.151 (0.006)	0.454 (0.000)
Category of antibiotic	0.057 (0.297)	3.795 (0.284)	0.107 (0.051)	-0.108 (0.049)	0.066 (0.227)	0.188 (0.001)
Duration of antibiotic treatment	0.054 (0.321)	2.423 (0.489)	0.096 (0.078)	-0.088 (0.107)	-0.009 (0.875)	0.166 (0.002)
Advise the patient for complying with antibiotic treatment	0.111 (0.042)	11.633 (0.009)	-0.210 (0.000)	-0.067 (0.221)	-0.179 (0.001)	0.183 (0.001)
Use of antibiotic; minor ailment / self-limiting diseases?	0.116 (0.033)	2.885 (0.410)	-0.114 (0.038)	0.024 (0.656)	-0.078 (0.156)	0.175 (0.001)
Antibiotic resistance; public health problem.	0.183 (0.001)	13.379 (0.004)	-0.117 (0.001)	-0.075 (0.170)	-0.230 (0.000)	0.483 (0.000)

Table 6 shows the association of attitude towards dispensing of antibiotics with demographic parameters was evaluated, given in Table 6.

Table 6
Association of attitude towards dispensing antibiotic with demographics

STATEMENTS	Gender	Age	Marital status	Job	Experience	Qualification
Non-prescribed dispensing of antibiotic is rational medical practice.	-0.008 (0.887)	13.514 (0.333)	-0.006 (0.916)	-0.050 (0.364)	-0.042 (0.446)	0.166 (0.033)
Patient is known to have difficulty in obtaining medical consultation.	0.026 (0.638)	30.002 (0.003)	0.076 (0.165)	-0.021 (0.700)	0.048 (0.384)	-0.086 (0.115)
personal experience; the source of deciding dosage regimen	0.076 (0.167)	18.503 (0.101)	-0.024 (0.655)	-0.077 (0.158)	-0.016 (0.776)	0.018 (0.747)
Antibiotic resistance is getting worse.	-0.156 (0.004)	23.647 (0.023)	-0.247 (0.000)	0.000 (0.995)	-0.291 (0.000)	0.300 (0.000)
Possible interaction between antibiotic and other drugs.	-0.029 (0.590)	17.949 (0.117)	0.059 (0.281)	0.000 (0.997)	0.039 (0.474)	-0.150 (0.006)
Antibiotics are sometimes dispensed even if not indicated.	0.140 (0.010)	9.359 (0.672)	-0.130 (0.017)	0.079 (0.150)	-0.049 (0.373)	0.051 (0.347)
Need of culture analysis	-0.033 (0.545)	15.601 (0.210)	-0.056 (0.308)	-0.004 (0.935)	-0.022 (0.682)	-0.100 (0.068)
Duration of antibiotic treatment preventing antibiotic resistance	0.005 (0.933)	14.888 (0.248)	-0.024 (0.655)	0.003 (0.962)	-0.083 (0.127)	-0.088 (0.106)

The association of dispensing behavior of dispensing staff with demographics was evaluated as shown in Table 7.

Table 7
Association of dispensing behavior of dispensing staff with demographics

Pathological conditions	Gender	Age	Marital status	Job	Experience	Qualification
Fever	0.177 (0.001)	28.730 (0.004)	-0.153 (0.005)	0.007 (0.898)	-0.086 (0.116)	0.247 (0.000)
Cold and flu	0.078 (0.152)	12.541 (0.403)	-0.193 (0.000)	-0.067 (0.223)	-0.151 (0.006)	0.321 (0.000)
Influenza	0.116 (0.033)	11.590 (0.479)	-0.142 (0.009)	-0.047 (0.387)	-0.070 (0.201)	0.269 (0.000)
Sore throat	0.075 (0.173)	29.402 (0.003)	-0.139 (0.001)	-0.054 (0.325)	-0.088 (0.107)	0.174 (0.001)
Diarrhea	0.166 (0.002)	19.271 (0.082)	-0.070 (0.201)	0.010 (0.854)	-0.069 (0.204)	0.132 (0.016)
Abdominal pain	0.177 (0.001)	22.590 (0.031)	-0.161 (0.003)	0.102 (0.062)	-0.109 (0.046)	0.106 (0.051)
Otitis media (ear infection)	0.072 (0.191)	17.130 (0.145)	0.008 (0.881)	0.000 (0.996)	0.015 (0.790)	0.064 (0.243)
Urinary tract infection (UTIs)	0.031 (0.576)	12.371 (0.416)	-0.023 (0.670)	0.019 (0.734)	0.060 (0.277)	-0.011 (0.835)

Discussion

The destructive properties of AMR are already demonstrating themselves across the globe. With the emergence of resistant strains of bacteria, non-prescribed antibiotic dispensing (NPAD) is also considered a relevant factor to deal with. It imparts a substantial role in the prevalence of AMR globally both in the community and hospital settings [16]. Various studies all over the world presented NPAD with a significant proportion [17–22]. The different studies reported that a majority of pharmacies encountered claims of visitors with self-medication of antibiotics and about half of them dispensed antibiotics without any due requirements [23, 24]. A similar trend is observed in this study. The results of this study focus on the attributes that lead to NPAD at the community pharmacies.

Out of 336 respondents, most of them were pharmacy graduates (56.8%) and working either as a manager or staff pharmacist. The majority of the pharmacy staff had an experience of fewer than two years in community pharmacies. Not every pharmacy visited had a pharmacist at that very time, so the place was revisited. The unavailability of a licensed pharmacists in the pharmacy might contribute towards NPAD in a haphazard way and hence AMR.

As far as policy perspective in Pakistan is concerned, the Drug Act 1976/ Drug Regulatory Authority Act 2012 provides the legislative impetus for the sale of medicines only under the supervision of a registered pharmacist [25, 26]. Despite the act being in place, the sales of antibiotics are poorly regulated because

of poor enforcement by the concerned authority. In the Punjab province of Pakistan, pertinent rules are formulated for the regulation of drug sales by way of retail; known as the Punjab Drug Rules 2007. These rules have barred the sale of certain drugs without any prescription and have categorized drugs into different schedules *viz* Schedules B, C, D, E, F, and G. The Schedule-D, permits the sales of drugs strictly on the prescription of a registered medical practitioner [27]. All the antibiotics have been included in this schedule. Therefore, the increasing trend of antimicrobial dispensing without prescription can be attributed to poor enforcement of existing laws in our study setting with a subsequent high rate of AMR.

Knowledge of the participants was good on a marking scale but still, a fair portion (21.1%) depicted poor knowledge about antibiotic use and dispensing which adds to unnecessary and over-dispensing of antibiotics [28]. Our study revealed that 75% of the pharmacy staff were well aware of the PoM status of antibiotics. The majority of the respondents (75.9%) in this study agreed that AMR is a serious public health problem. However, dispensers supply antibiotics as OTC even after knowing their PoM status. Our study also reveals the same scenario. It is, therefore, necessary that the 'PoM' status of antimicrobials is enforced especially concerning to the sales from community pharmacies, to create an enabling environment for health behavior. A coordinated approach amongst stakeholders, including healthcare workers, patients, and policy-makers on the issue of AMR is needed [29]. The multipronged approach with intra- as well as inter-professional coordination can ensure compliance with the national action plan on AMR.

The difference of opinion is detected among respondents whether to use antibiotics for minor ailments or not. A good portion of participants stated that antibiotics dispensing without prescription renders ease to patients who visit pharmacies and for those who find it difficult to access healthcare facility either due to lack of time or affordability [30]. Different studies across the globe evince a good perception of pharmacy staff regarding the use of antibiotics but still, they do dispense without physician's order without any reluctance [31]. Our findings are found coherent with these facts. Results showed a prominent agreement of proper guidance of patients regarding disease state of the patient, drug interactions, and emphasis on the complete course of antibiotics treatment; which is contradictory to the findings of Asian countries as retrieved by the public opinion about practices of pharmacy staff, especially the pharmacists [32]. About one-third of the respondents stated to dispense antibiotics even in self-limiting and viral infections which is irrational. On average, 60% of the respondents agreed to provide antibiotics in infectious diseases if the patient gives a direct visit to their pharmacy as soon as the symptoms appear where only symptomatic treatment can bring out relief. The view of respondents in our study coincided with the fact that there is a need for proper laboratory tests for pathogen identification and sensitivity analysis for initiating antibiotics, but their practice of NPAD doesn't match with this. Such practice accounts for irrational use of antibiotics in the community as indicated by National Institute for Health & Care Excellence (NICE) guidelines [33]. Moreover, guidelines suggest using diagnostic tools for assessing the severity of disease which will eventually reduce over-use of antibiotics and avoid the emergence of AMR [34–36].

Interventions are always a choice for improvement [37]. Good pharmacy practice (GPP) is a landmark standard for achieving rational, cost-effective, and responsible use of medicines to counter abuse of

antibiotics and halt AMR. In Pakistan, in regards to AMR, the Ministry of National Health Services Regulations & Coordination Government of Pakistan (MNHSRC) devised a National Action Plan in the year 2017; in which weak curricula of professional education and lack of AMR awareness among professionals are pinpointed as weaknesses of the system [38]. Our findings are in line with the results presented in a study conducted in the physicians of Lahore which, iterate awareness about antibiotics to all the stakeholders of the healthcare profession [39]. Another study in Lahore demonstrated that low-dose and extensive use of broad-spectrum antimicrobials due to ease of access from pharmacies is responsible for high rates of AMR in Pakistan [40]. A study conducted by Saleem et al in Lahore demonstrated that co-amoxiclav, levofloxacin, ciprofloxacin, and third-generation cephalosporins were among the most widely consumed antimicrobials from private healthcare institutions and pharmacies [41]. If the use of such antimicrobials goes unchecked, it results in more resistant strains of microorganisms such as the outbreak of extensively drug-resistant (XDR) Typhoid in Hyderabad, Pakistan in 2016 [42].

According to a broad brush estimate of the global economic cost of antimicrobial drug resistance by 2050, the continually escalated resistance by 2050 will contribute to the death of 10 million people per year. There will be a reduction of 2-3.5% in Gross Domestic Product (GDP) which would cost the world up to 100 trillion United States Dollar [43].

In this context, the role of health authorities is very important; the Government of Pakistan should prioritize the issue of escalating AMR and formulate its containment strategies, however, there have not been sufficient resources allocated so far for this [44]. Efforts should be made to educate healthcare professionals who deal with drugs such as; pharmacists and physicians regarding the appropriate use of antibiotics to reduce the likelihoods of AMR [45]. Moreover, the pharmacists should be present in the pharmacies and should educate the visitors about self-care and AMR as well. The patients or the public also need to be educated for the use of antibiotics upon prescription by the registered medical practitioner [46].

Strengths And Limitations

This study signifies the importance of pharmacists and other staff involved in dispensing antimicrobials at community pharmacies. The study setting is the second-largest city in Pakistan, the center of culture, business, and education, and has a structured and well-defined network of pharmacies with the highest number of pharmacists working in the city. This study is limited to only one city in Pakistan. Therefore, the findings of this may not be correlated to the scenario of the whole of Pakistan.

Conclusion

Lack of enforcement of already existing laws is responsible for extravagant use of antimicrobials sans legitimate prescription and has led to antimicrobial resistance. This demands strict enforcement of the Drug Regulatory Authority of Pakistan Act 2012, Punjab Drug Rules 2007, and Pakistan's National Action

Plan on antimicrobial resistance. Pharmacy personnel should be trained and aware of dispensing practices as well as the patients should be educated regarding the use of antimicrobials.

Abbreviations

AMR: Antimicrobial Resistance

DRAP: Drug Regulatory Authority of Pakistan

HDI: Human Development Index

HEC: Humans Ethics Committee

LMICs: Low-and Middle-Income Countries

MNHSRC: Ministry of National Health Services Regulations & Coordination Government of Pakistan

NICE: National Institute for Health & Care Excellence

NPAD: Non-Prescribed Antibiotic Dispensing

OTC: Over the Counter

PoM: Prescription only Medicines

WHO: World Health Organization (WHO)

XDR: Extensively Drug Resistant

Declarations

Ethics approval and consent to participate

The research has been performed in accordance with the Declaration of Helsinki. The ethics approval was granted by the Humans Ethics Committee (HEC) University College of Pharmacy, University of the Punjab, Lahore (No: HEC/UCP/2045-19). Informed consent to participate in the study was obtained from participants.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing conflict of interest.

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Authors' contributions

Furqan K. Hashmi: Conceptualization, Methodology, Formal Analysis, Investigation, Data Curation, and Writing - original draft preparation. Mash'hood Mahmood Khan: Resources, Validation, Investigation, and Project Administration. Saif Ullah Khan: Data Curation. Sitaram Khadka: Methodology, Writing- Reviewing and Editing. Hamid Saeed: Visualization, Writing- Reviewing and Editing. Muhammad Islam: Formal Analysis, Investigation. Naveel Atif: Data curation, Investigation, Writing- Reviewing and Editing. Usman Malik: Investigation, Writing- Reviewing and Editing. *Muhammad Fawad Rasool*: Supervision. Husaam-ul-Haq Mansoor: Formal Analysis. Muhammad Majid Aziz: Validation. Zineb Riboua: Writing- Reviewing and Editing.

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