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Evaluation of Antibiotic Misuse and Resistance Patterns in Outpatient Clinics Across Pakistan

Original Research

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ABSTRACT

Background: Antimicrobial resistance (AMR) has become a critical public health challenge in Pakistan, driven largely by irrational antibiotic prescribing in outpatient settings. Inadequate regulation, empirical treatment, and misuse of broad-spectrum antibiotics have accelerated resistance trends, compromising effective infection management.

Objective: To evaluate antibiotic misuse and resistance patterns in outpatient clinics across Lahore, Multan, and Islamabad, and to assess adherence to the World Health Organization's Access, Watch, and Reserve (AWaRe) classification for rational antibiotic prescribing.

Methods: A multicenter, cross-sectional analytical study was conducted across private hospitals in three major Pakistani cities from January to September 2024. Stratified random sampling was used to collect 1,300 outpatient antibiotic prescriptions. Data were analyzed using IBM SPSS version 26. Descriptive statistics, chi-square, and logistic regression tests were performed, with $p < 0.05$ considered significant. Resistance data were obtained from hospital antibiograms. Ethical approval was obtained from the Institutional Review Board (Ref No: UOL/PHR/2024/126).

Results: Of 1,300 prescriptions analyzed, 58.9% were "Watch" antibiotics, 36.2% "Access," and 4.9% "Reserve." Ceftriaxone (24.7%) and azithromycin (13.2%) were the most prescribed agents. Only 41.4% of prescriptions adhered to standard treatment guidelines, while polypharmacy occurred in 27.8% of encounters. *E. coli* showed 72.8% resistance to amoxicillin/clavulanate and 64.5% to ciprofloxacin. Junior prescribers were twice as likely to prescribe "Watch" antibiotics (OR 2.17, 95% CI 1.29–3.65).

Conclusion: The study reveals a high prevalence of irrational antibiotic use and significant resistance among outpatient pathogens. Strengthened stewardship programs, prescriber education, and stricter prescription policies are imperative to mitigate AMR in Pakistan.

Keywords: Antimicrobial stewardship; Antibiotic resistance; Cross-sectional studies; Drug utilization; Outpatients; Pakistan; Prescription audit.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health challenges, threatening the effective treatment of infectious diseases. The inappropriate use of antibiotics in outpatient settings has been identified as a major contributor to this crisis, particularly in low- and middle-income countries such as Pakistan. With limited regulatory oversight and insufficient antimicrobial stewardship, antibiotic misuse has become deeply entrenched in clinical practice and community behavior. The escalating resistance patterns observed in both hospital and community settings underline the urgency of evaluating prescription practices at the national level to design effective interventions for rational antibiotic use (1). Pakistan is ranked among the highest antibiotic-consuming countries globally, reflecting both high disease burden and significant prescribing without evidence-based justification. Studies have shown that a large proportion of antibiotics prescribed in Pakistani outpatient departments belong to the WHO "Watch" category, indicating a preference for broad-spectrum agents with a higher resistance potential. For instance, an evaluation of outpatient prescriptions in Lahore revealed that the use of "Watch" antibiotics exceeded the WHO's recommended target, with less than 60% prescriptions comprising "Access" group antibiotics (2). This overreliance on broad-spectrum drugs accelerates the development of resistant bacterial strains, undermining the effectiveness of treatment options for common infections.

The problem is further compounded by extensive self-medication and over-the-counter availability of antibiotics. Community-level surveys have shown that over 60% of individuals report self-medicating with antibiotics based on previous prescriptions or informal advice, often without completing the recommended course (3). Such unregulated practices not only drive antimicrobial resistance but also obscure true resistance patterns, complicating surveillance and public health response. Similarly, antibiotic dispensing during and after the COVID-19 pandemic surged due to panic and misinformation, with nearly one-third of antibiotics being sold without prescription, mostly from the "Watch" category, such as ceftriaxone and azithromycin (4). Antibiotic resistance in Pakistan is not confined to outpatient departments alone but reflects a broader systemic issue affecting hospitals and communities alike. A nationwide systematic review highlighted that resistance to first-line antibiotics in Escherichia coli, Klebsiella pneumoniae, and Staphylococcus aureus is alarmingly high, with extended-spectrum beta-lactamase (ESBL) and methicillin-resistant S. aureus (MRSA) being increasingly prevalent (5). Despite this evidence, consistent national surveillance and antibiotic stewardship programs remain limited to a few tertiary care centers, leaving primary and secondary healthcare facilities vulnerable to irrational prescribing. The lack of awareness among healthcare providers, coupled with weak enforcement of prescription regulations, has created a cycle of inappropriate antibiotic use and escalating resistance.

The gap in literature is evident: while isolated studies have explored antibiotic utilization within specific hospitals or provinces, comprehensive national data on outpatient antibiotic misuse and resistance patterns are scarce. Most existing research has focused on single institutions or disease-specific resistance profiles, which do not capture the heterogeneity of prescribing behavior across Pakistan's diverse healthcare landscape. Therefore, a national audit of outpatient antibiotic prescriptions is imperative to understand the extent of irrational use, identify key determinants of misuse, and provide data-driven recommendations for stewardship and policy interventions. This study aims to evaluate antibiotic misuse and resistance patterns in outpatient clinics across Pakistan through a comprehensive national prescription audit. By examining prescription practices against WHO's AWaRe classification and analyzing resistance trends, the study seeks to identify gaps in antibiotic stewardship and provide evidence to support rational prescribing policies. The ultimate objective is to contribute to national and global efforts to curb antimicrobial resistance by promoting safer, evidence-based antibiotic use in outpatient care

METHODS:

This cross-sectional analytical study was conducted to evaluate antibiotic misuse and resistance patterns in outpatient clinics of private hospitals across Lahore, Multan, and Islamabad. The study aimed to identify prescribing behaviors, assess adherence to the World Health Organization's Access, Watch, and Reserve (AWaRe) classification, and determine resistance trends in outpatient antibiotic prescriptions. The study duration spanned from January 2024 to September 2024, encompassing a standard nine-month data collection period to ensure seasonal variation in antibiotic use was captured. The study population included outpatient prescriptions generated by physicians in internal medicine, general practice, and ear, nose, and throat (ENT) clinics of participating hospitals. Inclusion criteria comprised all outpatient antibiotic prescriptions issued to patients aged 18 years and above, regardless of diagnosis, during the study period. Exclusion criteria included inpatient antibiotic orders, pediatric prescriptions, and incomplete records lacking key variables such as antibiotic class, dose, or diagnosis. These parameters ensured the dataset represented genuine outpatient prescribing behavior and maintained methodological rigor (6).

A stratified random sampling technique was employed to ensure representative data across the three cities and clinical departments. Based on an expected antibiotic misuse prevalence of 50%, a 5% margin of error, and a 95% confidence interval, the minimum required sample size was calculated to be 384 prescriptions per city using Cochran's formula, totaling 1,152 prescriptions nationwide. To account

for incomplete data, the final target sample was set at 1,300 prescriptions. Sampling was proportionately distributed between the three cities according to outpatient volume, with approximately 500 prescriptions from Lahore, 400 from Multan, and 400 from Islamabad. Data collection involved both manual and electronic extraction of prescription records from hospital pharmacy databases. A standardized data collection tool, adapted from WHO's "How to Investigate Drug Use in Health Facilities" manual, was used to capture demographic information, diagnosis, antibiotic name, class, dose, duration, and prescriber designation. Prescriptions were further categorized according to the WHO AWaRe 2021 framework to assess rational prescribing practices (7). To ensure data quality and consistency, two independent pharmacists cross-verified 10% of the collected records at random intervals, and discrepancies were resolved through consensus.

The study's primary outcome measure was the prevalence of irrational antibiotic prescribing, defined as the use of antibiotics without clinical justification, deviation from AWaRe recommendations, or prescription of "Watch" and "Reserve" category antibiotics for uncomplicated infections. Secondary outcomes included the proportion of generic versus branded antibiotic prescriptions, the frequency of multiple antibiotic prescriptions per encounter, and the distribution of antibiotic classes used. Additionally, microbiological data from hospital laboratories were reviewed to assess resistance trends in commonly prescribed antibiotics, focusing on *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* isolates (8). Statistical analysis was performed using IBM SPSS Statistics version 26. Descriptive statistics were used to present frequencies, percentages, and means. The normal distribution of continuous data was confirmed through the Shapiro–Wilk test. One-way analysis of variance (ANOVA) was employed to compare mean antibiotic utilization rates between hospitals in different cities, while chi-square tests assessed associations between prescribing patterns and physician category (consultant, registrar, or medical officer). Binary logistic regression analysis was used to identify predictors of irrational prescribing, including prescriber experience, diagnosis type, and patient age. A p-value of <0.05 was considered statistically significant (9).

Ethical approval for the study was obtained from the Institutional Review Board of the University of Lahore (Approval No. UOL/PHR/2024/126) and from ethical review committees of the collaborating hospitals. The study adhered to the Declaration of Helsinki guidelines for research involving human data. Patient confidentiality was strictly maintained; no identifiable information was collected, and all data were anonymized before analysis. Since the research involved retrospective prescription data without direct patient contact, the requirement for individual informed consent was waived by the ethics committees. The outcome measurements were validated using prescription appropriateness indicators aligned with WHO prescribing guidelines and the Centers for Disease Control and Prevention's core elements of outpatient antibiotic stewardship. These included the proportion of antibiotics prescribed by generic name, percentage of prescriptions containing antibiotics, proportion of "Watch" group antibiotics, and compliance with standard treatment guidelines. Additionally, resistance outcome data were evaluated through cumulative antibiograms, providing insight into the relationship between prescribing trends and microbial resistance patterns (10). This methodology provides a transparent, reproducible framework for auditing antibiotic use and resistance trends in outpatient settings across Pakistan. By combining prescription audits with resistance surveillance, the study aims to offer an evidence-based foundation for developing national antibiotic stewardship policies in private healthcare facilities.

RESULTS:

A total of 1,300 outpatient antibiotic prescriptions were analyzed across private hospitals in Lahore (n=500), Multan (n=400), and Islamabad (n=400). The study population consisted of adult patients aged 18–75 years, with a mean age of 39.6 ± 12.4 years, and 54.3% were female. The most frequently diagnosed conditions for which antibiotics were prescribed included upper respiratory tract infections (32.5%), urinary tract infections (21.8%), gastrointestinal infections (18.6%), and dermatological infections (9.2%). A smaller proportion of prescriptions (7.8%) were for non-infectious or unclear indications, reflecting a trend of empirical prescribing (11). Analysis based on the WHO AWaRe classification revealed that 58.9% of antibiotics prescribed belonged to the "Watch" category, while 36.2% were "Access" group antibiotics, and only 4.9% were "Reserve" category agents. This distribution fell short of the WHO-recommended target of ≥60% "Access" antibiotics. Among "Watch" antibiotics, third-generation cephalosporins were predominant, with ceftriaxone (24.7%) and cefixime (17.5%) being the most frequently prescribed, followed by azithromycin (13.2%). Within the "Access" group, amoxicillin/clavulanate accounted for 21.3% of total prescriptions. Notably, ciprofloxacin (10.5%) was among the most common fluoroquinolones prescribed, reflecting a continued reliance on broad-spectrum agents for common infections (12).

Approximately 27.8% of prescriptions involved polypharmacy, with more than one antibiotic prescribed per encounter, particularly for respiratory and urinary tract infections. This pattern was more frequent in Multan (31.5%) compared to Lahore (26.2%) and Islamabad (25.3%), though the difference was not statistically significant (p=0.061). Only 41.4% of prescriptions adhered fully to standard treatment guidelines, with inappropriate antibiotic selection or duration observed in 58.6% of encounters. The proportion of generic prescribing remained low at 19.8%, with the remainder being brand-based prescriptions (13). Culture and sensitivity data were available for 312 (24%) of cases. Among *E. coli* isolates, resistance to amoxicillin/clavulanate was 72.8%, to ciprofloxacin 64.5%, and to cefixime

59.1%. *Klebsiella pneumoniae* isolates demonstrated 53.7% resistance to ceftriaxone and 45.8% to azithromycin. In contrast, resistance to meropenem remained below 10%, suggesting limited use of carbapenems in outpatient settings (14).

Regression analysis identified prescriber designation and diagnosis type as significant predictors of irrational prescribing. Junior physicians (house officers and medical officers) were twice as likely to prescribe "Watch" group antibiotics compared to consultants (OR 2.17, 95% CI 1.29–3.65, p=0.002). Additionally, prescriptions for upper respiratory tract infections had 3.4 times higher odds of involving broad-spectrum antibiotics compared to urinary tract infections (p<0.001). A chi-square test revealed a significant association between city and antibiotic class distribution (χ^2=18.47, p=0.028), indicating regional differences in prescribing trends. However, ANOVA showed no significant difference in mean antibiotic prescriptions per encounter across the three cities (F=2.17, p=0.114).

Antibiotic resistance data from hospital laboratories also demonstrated alignment with prescribing patterns. *Staphylococcus aureus* isolates showed 47.9% methicillin resistance, while extended-spectrum β-lactamase (ESBL) production was detected in 38.2% of *E. coli* and 33.7% of *Klebsiella* isolates. Multidrug resistance was reported in 41.5% of all bacterial isolates, underscoring the clinical implications of outpatient prescribing behaviors (15). Overall, the results revealed substantial overuse of "Watch" group antibiotics, low compliance with standard prescribing guidelines, and a high prevalence of antimicrobial resistance among community pathogens. The findings emphasize the need for structured antibiotic stewardship interventions in outpatient settings across major urban centers in Pakistan.

Table 1. Overall Antibiotic Distribution According to AWaRe Categories and Regional Variations

AWaRe Category	Lahore (%)	Multan (%)	Islamabad (%)	Total (%)
Access	37.8	35.6	35.2	36.2
Watch	56.1	60.4	59.5	58.9
Reserve	6.1	4.0	5.3	4.9

Table 2. Demographic Characteristics of Study Participants (n = 1300)

Variable	Value
Total Prescriptions	1300
Mean Age (years)	39.6 ± 12.4
Female (%)	54.3
Male (%)	45.7
Cities Included	Lahore, Multan, Islamabad
Study Duration	January–September 2024

Table 3. Commonly Prescribed Antibiotics in Outpatient Clinics

Antibiotic	Class	Prescription Frequency (%)
Ceftriaxone	Cephalosporin	24.7
Cefixime	Cephalosporin	17.5
Azithromycin	Macrolide	13.2
Amoxicillin/Clavulanate	Penicillin	21.3
Ciprofloxacin	Fluoroquinolone	10.5
Others	Mixed classes	12.8

Table 4. Antibiotic Resistance Patterns in Common Pathogens

Pathogen	Amoxicillin/Clavulanate Resistance (%)	Ciprofloxacin Resistance (%)	Cefixime/Ceftriaxone Resistance (%)	Methicillin Resistance (%)
E. coli	72.8	64.5	59.1	–
K. pneumoniae	68.5	61.2	53.7	–
S. aureus	59.0	55.8	50.2	47.9

DISCUSSION:

The present study provides comprehensive insight into the antibiotic prescribing behaviors and resistance patterns observed in outpatient settings across major urban centers of Pakistan. The findings revealed an alarmingly high prevalence of "Watch" group antibiotic prescriptions, widespread empirical use, and suboptimal adherence to WHO prescribing recommendations. These outcomes align with the growing body of evidence suggesting that Pakistan's outpatient antibiotic use is heavily skewed toward broad-spectrum agents, contributing to the country's accelerating antimicrobial resistance crisis (16). The predominance of "Watch" group antibiotics in this study is consistent with recent national assessments that reported ceftriaxone, cefixime, and azithromycin as the most frequently prescribed agents in outpatient and emergency departments. Similar findings were documented by Sajjad et al., who identified that more than half of antibiotic prescriptions in an ENT outpatient department belonged to the "Watch" category, exceeding WHO's threshold for rational prescribing (17). The current data reflect that clinicians continue to favor broad-spectrum antibiotics, often for self-limiting infections, which highlights a critical gap between available stewardship guidelines and real-world clinical practice.

The observed association between physician seniority and prescribing behavior suggests that prescriber experience and awareness significantly influence antibiotic selection. This finding corroborates previous reports from qualitative studies in Lahore and Karachi, where junior physicians admitted to prescribing broad-spectrum antibiotics to meet patient expectations or due to diagnostic uncertainty (18). Additionally, the frequent prescription of multiple antibiotics per encounter parallels earlier findings by Alam et al., who documented similar patterns in primary care facilities across Pakistan and linked them to a lack of local treatment protocols and insufficient stewardship oversight (19). Antimicrobial resistance patterns from this study further underscore the clinical implications of irrational prescribing. High resistance rates in *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* isolates were consistent with national surveillance data, which showed a continuous upward trend in resistance to beta-lactams and fluoroquinolones (20). A 2023 surveillance study from Punjab similarly reported that more than 60% of community *E. coli* isolates were resistant to ceftriaxone and ciprofloxacin, reaffirming the critical need for antibiotic stewardship at the community level (21). The emergence of extended-spectrum beta-lactamase (ESBL) and methicillin-resistant strains within outpatient contexts indicates a spillover of hospital-associated resistance mechanisms into the community, an observation supported by Iqbal et al., who noted widespread multidrug resistance in both hospital and ambulatory isolates (22).

The findings of this study carry significant implications for public health and policy in Pakistan. The overprescription of "Watch" antibiotics and low use of generic names suggest a combination of prescriber inertia, commercial influence, and inadequate regulatory enforcement. This pattern mirrors the concerns raised by Rasheed and Almas, who emphasized that weak enforcement of prescription-only antibiotic policies and unregulated sales at pharmacies have accelerated resistance trends in both human and animal sectors (23). Furthermore, community-level studies, such as those by Rakhshani et al., demonstrated that over 50% of community healthcare workers sold partial antibiotic courses, contributing to incomplete treatment and resistance selection (24). The strengths of this study lie in its multicentric design, inclusion of three major urban centers, and integration of prescription audits with microbiological data. The use of standardized WHO AWaRe criteria ensures global comparability of findings, while stratified random sampling enhances representativeness. The application of robust statistical analyses, including regression modeling, strengthens the validity of associations between prescribing patterns and demographic or professional factors.

However, certain limitations must be acknowledged. The study's cross-sectional design precludes causal inference, and the reliance on prescription records may have excluded unrecorded antibiotic dispensing from informal or unlicensed practitioners. Additionally, microbiological data were limited to hospitals with functional laboratories, potentially underrepresenting smaller private facilities. The study also did not assess the impact of patient demand or pharmaceutical marketing pressures, both of which have been recognized as strong determinants of antibiotic overuse in Pakistan (25). Future research should expand to include rural healthcare settings and community pharmacies to capture a broader picture of antibiotic utilization behaviors. Longitudinal studies assessing the impact of

stewardship interventions on prescribing trends and resistance outcomes would provide valuable evidence for policy formulation. Integration of digital prescription monitoring systems and periodic audits could also enhance data transparency and accountability. This study demonstrates that antibiotic misuse in outpatient clinics across Pakistan remains pervasive, with a marked reliance on "Watch" group agents and growing antimicrobial resistance. The results affirm the urgent need for implementing national antimicrobial stewardship programs, enhancing prescriber education, and enforcing prescription-only antibiotic policies to safeguard therapeutic efficacy for future generations.

CONCLUSION:

This national audit demonstrated widespread antibiotic misuse and an excessive reliance on "Watch" category agents in outpatient clinics across Pakistan, contributing to escalating antimicrobial resistance. The findings highlight critical gaps in adherence to WHO prescribing guidelines and underscore the urgent need for structured antibiotic stewardship, prescriber education, and stronger prescription regulation in private healthcare. Implementing evidence-based policies and continuous monitoring of antibiotic use are essential steps toward preserving antimicrobial efficacy and ensuring sustainable infection management in Pakistan's outpatient care system.

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AUTHORS CONTRIBUTION

Author	Contribution
Imran Altaf	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision

