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Original Research Article

Assessment of antimicrobial resistance risks due to physician and patient practices: An observational study

Pradeep Battula[1]*, Bhupalam Pradeep Kumar[2]
[1]Department of Pharmaceutical Sciences, Jawaharlal Nehru Technological University Anantapur, Ananthapuramu, [2]Department of Pharmacy Practice, Raghavendra Institute of Pharmaceutical Education and Research (RIPER) – Autonomous, Anantapur, Andhra Pradesh, India

For correspondence:* ***Email:* *doctorbattulapradeep@gmail.com*

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Abstract

Purpose: *To assess the risk factors for antimicrobial resistance (AMR) by examining physician antibiotic prescribing patterns, and patient adherence.*
Methods: *A cross-sectional descriptive study was conducted across two sites. The study involved two components: physician-focused assessment of inappropriate antibiotic prescribing and patient-focused assessment of antibiotic adherence. Data were collected from patient records and structured forms, and were analyzed using descriptive statistics, with chi-square tests for categorical data. Statistical significance was defined as* $p < 0.05$.
Results: *The physician-focused study revealed that 40.49 % of antibiotic prescriptions had no indication, and 23.93 % involved drug-drug interactions. The risk of AMR due to inappropriate prescribing was 47.75 %, which decreased to 28.83 % following pharmacist intervention* ($\chi^2 = 147.61$, $p < 0.001$). *In the patient-focused study, 19.52 % of patients were non-adherent to prescribed antibiotics, contributing to an equivalent risk of AMR. A total of 72.67 % of the patients were male, with a mean age of 50.43 years. Most patients (97.5 %) lacked knowledge about AMR.*
Conclusion: *Inappropriate antibiotic prescribing and patient non-adherence are significant contributors to the development of AMR. Interventions by pharmacists significantly reduce the risk of AMR. The study highlights the need for improved antibiotic stewardship, patient education, and adherence to treatment guidelines to mitigate AMR risk. Locally developed guidelines and shorter antibiotic courses may also help address this growing concern.*

Keywords: *Antimicrobial resistance, Physician practices, Patient practice, Antibiotic prescribing, Pharmacist intervention*

INTRODUCTION

Bacterial infections remain a significant cause of mortality worldwide, with India experiencing one of the highest rates of infectious diseases. While antibiotics are essential in controlling these infections, their misuse has led to the emergence of antimicrobial resistance (AMR), a global health crisis [1]. Antimicrobial resistance, particularly prevalent in Southeast Asia, is responsible for approximately 7 million deaths annually and is projected to cause up to 10 million deaths per year by 2050. In the United States alone, AMR results in 23,000 deaths each year and contributes significantly to healthcare costs. It also accounts for 15 - 30 % of global health budgets [1]. The consequences of AMR are severe, including increased disease severity, treatment failures, prolonged hospital stays, higher mortality rates, increased healthcare costs, drug interactions, adverse effects, and death [2].

This study aims to assess the risk factors contributing to AMR, focusing on physician and patient practices, as well as the use of Complementary and Alternative Medicine (CAM) for treating infections.

METHOD

Study design and setting

This descriptive, cross-sectional study was conducted across two sites to evaluate the risk of AMR. Data for the study were collected from Santhiram Medical College and General Hospital (SRMC & GH) in Nandyal, and Sri Venkateswara Ramnarayan Ruia Government General Hospital (SVRRGGH) in Tirupati both in India. The study consisted of two components:

A physician-focused assessment to evaluate AMR risk through inappropriate antibiotic prescribing, drug interactions, and therapeutic duplication. After identifying inappropriate antibiotic use, researchers intervened to reduce the risk of AMR by discussing it with the prescribing physician. The rate of antibiotic prescribing before and after the intervention was determined as frequency of inappropriate prescribing over the total number of antibiotic prescriptions made.

A patient-focused study to examine the risk of AMR associated with non-adherence to prescribed antibiotics was also done.

Study instruments

The following were used as standards and guides to evaluate the objectives of the study:

Treatment guidelines for antimicrobial use in common syndromes - ICMR New Delhi Guidelines [3]; National treatment guidelines for antimicrobial use in infectious diseases [4]; National List of Essential Medicines (NLEM) [5]; WHO model list essential medicines – 23rd list [6], and WHO - AWaRe classification of antibiotics [7].

The WHO AWaRe classification of antibiotics was developed in 2017 by the WHO expert committee on selection and use of essential medicines as a tool to support antibiotic stewardship efforts at local, national and global levels, antibiotics are classified into three groups; *Access, Watch* and *Reserve,* taking into account the impact of different antibiotics and antibiotic classes on antimicrobial resistance, to emphasize the importance of their appropriate use.

Ethical approval

Ethical approval was obtained from IEC at Santhiram Medical College and General Hospital (IEC/2022/042) and Sri Padmavathi School of Pharmacy (SPSP/2022-2023/PDB/11).

Study participants

Participants included patients admitted to the hospitals with infections and receiving antibiotics. In the physician-focused study, data on antibiotic prescription and rationality were collected. The same patient cohort was used in the patient-focused study to gather adherence and satisfaction data.

Study population

This is a cross-sectional descriptive study with a population including patients who were admitted to the hospital with an infection and who received antibiotics.

Sample Size (n)

This was determined using Eq 1. Standard normal deviation corresponding to 95 % confidence interval (Z_{α}^{2}) = 1.96^2 or 3.841; p represents the estimated proportion of the population based on previous studies [12]; q = 1 - p; while E represents the margin of error allowed in the estimation which is 0.05 so E^2 = 0.0025.

$$n = \frac{Z_{\alpha}^{2} \times p \times q}{E^2} \quad \text{.........................} \quad (1)$$

(3.8416×0.7×0.3)/0.0025 = 322.69

Inclusion criteria

Patients were included if they were admitted to the hospital and prescribed antibiotics.

Exclusion criteria

Patients who had not given their consent for participation, and were not under follow-up, pregnant women, and case sheets with incomplete information and incomplete satisfaction survey were excluded from the study.

Data collection

Data were collected through patient records and a structured data collection form. Consent forms were provided, detailing the study's purpose, potential risks, and benefits. After obtaining consent, data on various factors such as antibiotic dosage, duration, prescribing patterns, treatment type, poly-pharmacy, culture sensitivity tests, drug duplication, potential drug interactions, inappropriate prescribing, adherence, and satisfaction with treatment were collected and analyzed to ensure the study objectives were met. Patient satisfaction was assessed based on a question on a 5-point Likert scale with 5 being the upper limit for satisfaction.

Data analysis

Data collected from the survey were entered into Microsoft Excel spreadsheet, sorted, checked and then exported into DATAtab statistical software. Descriptive statistics were performed on the primary data and results were presented in percentages and proportions. Chi-square test was used for categorical data. *P*-value < 0.05 was considered significant.

RESULTS

In the physician-focused study, the average number of antibiotics per prescription was 1.52 (range 1 - 5). The duration of time spent in the hospital ranged between 3 to 16 days. The longest duration of antibiotic use was 11 days. Analysis of 508 antibiotic prescriptions revealed that 40.49 % had no indication, 23.93 % had drug-drug interactions, 14.72 % had therapeutic duplications, and other issues like drug-food interactions and inappropriate prescribing were identified. Overall, 414 (81.5 %) of the prescriptions were prescribed empirically. Majority, 190 (57.07 %) of the prescriptions had one antibiotic, while 119 (35.74 %), 19 (5.71 %), 4 (1.2 %) and 1 (0.3 %) of the prescriptions had two, three, four, and five antibiotics respectively. Table 1 shows the drug-drug/food interactions observed in the study using Micromedex 20.0. Eighteen drug types and two foods were responsible for the 55 drug-drug/food interactions encountered. Of these 19 (34.5 %) had the potential for major severity, 34 (61.8 %), had moderate severity and 2 (3.6 %), had minor severity. Table 2 shows the antibiotics prescribed, category and essential medication assessment. A total of 25 antibiotics from 19 antibiotic drug classes were encountered in the study. The third-generation cephalosporins; 6/25 (24 %) constituted the most frequently prescribed antibiotic class. Based on the WHO AWaRe classification, of the 25 antibiotics prescribed, only 8 (32 %) were from the Access group, 14 (56 %) from the Watch group, 2 (8 %) from the Reserve group and 1 (4 %) was unclassified. Eight (32 %) of the antibiotics prescribed were not in the WHO Essential Medicines List (EML) 2023, and 11 (44 %) were not in the Indian National List of Essential Medicines (NLEM) 2022. The risk of AMR based on the frequency of inappropriate prescribing was 47.75 %, However, post-intervention, the risk of developing AMR reduced to 28.83 % demonstrating a significant reduction ($\chi^2 = 147.61$; $p < 0.001$).

Patient study: A total of 333 patients were surveyed, 72.67 % of them were male and 27.33 % were female. The mean age of the patients was 50.43 ± 15.92 years (95 % CI 48.72 – 52.14). The youngest patient admitted was 11 years old while the oldest was 84 years.

Out of the 333 patients, 19.52 % were non-adherent to antibiotic prescriptions, contributing to a 19.52 % risk of developing AMR. Of this proportion, 15.02 % of them omitted taking their antibiotics while 4.5 % delayed taking their antibiotics. Reasons for non-adherence to prescribed antibiotics are shown in Table 3. Almost all (97.5 %) of the patients did not know about antibiotic resistance. The average patient satisfaction score was 3.96 ± 0.59.

DISCUSSION

In the physician study, patients spent 3 - 16 days in the hospital, with the longest duration of antibiotic use being 11 days. Shorter hospital stays and excessive antibiotic use lead to AMR development. Some prescriptions consisted of multiple antibiotics contributing to AMR. The same was reported in Domez *et al* [8]. The antibiotics were majorly empirically prescribed by the physicians; Inappropriate prescriptions and lack of culture sensitivity tests were observed in the study, which highlights the need for better antibiotic management [9].

Similar studies have reported varying levels of inappropriateness: Adorka *et al,* reported 47.9 %, and Sulis *et al,* reported 49.9 % [10,11]. The prescribing of multiple antibiotics and polypharmacy also cause drug interactions and contribute to AMR. Interactions between drugs and food also impact the effectiveness of treatments and lead to AMR.

Table 1: Drug interaction observed in the prescriptions causing the AMR

Drugs involved in the interaction		Severity	Documentation	Summary of interaction	Frequency (%)
Drug 1/Food	***Drug 2***				
Amoxicillin + Clavulanic acid	Doxycycline	Major	Good	Decreased antibacterial effectiveness	2 (3.63)
Calcium/vitamin D	Doxycycline	Moderate	Good	Decreased effectiveness of tetracyclines	4 (7.3)
Calcium/vitamin D	Ciprofloxacin	Moderate	Good	Decreased ciprofloxacin efficacy	3 (5.45)
Sevelamer	Ciprofloxacin	Moderate	Excellent	Decreased bioavailability of Ciprofloxacin	2 (3.63)
Sucralfate	Ciprofloxacin	Moderate	Excellent	Decreased oral ciprofloxacin effectiveness	2 (3.63)
Piperacillin + Tazobactam	Doxycycline	Major	Good	Decreased antibacterial effectiveness	6 (10.90)
Iron/Folic acid	Ciprofloxacin	Moderate	Good	Decreased ciprofloxacin effectiveness	1 (1.81)
Multivitamin/Ascorbic acid	Doxycycline	Major	Fair	Decreased doxycycline efficacy	8 (14.54)
Cacl/Nacl	Doxycycline	Moderate	Good	Decreased effectiveness of tetracyclines	1 (1.81)
Phenytoin	Metronidazole	Major	Good	Decreased metronidazole plasma levels	3 (5.45)
Calcium/vitamin D/NaHCo3	Cefpodoxime	Moderate	Fair	Decreased cefpodoxime effectiveness	1 (1.81)
Ranitidine	Cefpodoxime	Moderate	Good	Decreased cefpodoxime effectiveness	1 (1.81)
Piperacillin + Tazobactam	Amikacin	Minor	Good	Loss of aminoglycosides efficacy	1 (1.81)
Iron/Folic acid	Doxycycline	Moderate	Good	Decreased tetracycline effectiveness	1 (1.81)
Amoxicillin + Clavulanic acid	Amikacin	Minor	Good	Loss of aminoglycosides efficacy	1 (1.81)
Diclofenac	Ciprofloxacin	Moderate	Excellent	Increased ciprofloxacin plasma concentration	2 (3.63)
Dairy foods	Ciprofloxacin	Moderate	Good	Decreased ciprofloxacin concentration	15 (27.27)
Food	Penicillin G	Moderate	Good	Decreased peak penicillin concentrations	1 (1.81)
Total					***55 (100)***

Table 2: Total antibiotics prescribed, category and essential medication assessment

Antibiotic	Class	ATC Code	AWaRe Category	WHO EML 2023	NLEM 2022
Amikacin	Aminoglycosides	J01GB06	Access	Yes	No
Amoxicillin + Pot. clavulanate	Beta-lactam/beta-lactamase-inhibitor	J01CR02	Access	Yes	Yes
Azithromycin	Macrolides	J01FA10	Watch	Yes	Yes
Cefditoren	Third-generation-cephalosporins	J01DD16	Watch	No	No
Cefixime		J01DD08	Watch	Yes	Yes
Cefoperazone + Sulbactam		J01DD12	Watch	No	No
Cefotaxime		J01DD01	Watch	Yes	Yes
Cefpodoxime Proxetil		J01DD13	Watch	No	No
Ceftriaxone		J01DD04	Watch	Yes	Yes
Ciprofloxacin	Fluoroquinolones	J01MA02	Watch	Yes	Yes
Clindamycin	Lincosamides	J01FF01	Access	Yes	Yes
Co-Trimoxazole	Sulfonamide-trimethoprim combinations	J01EE01	Access	Yes	Yes
Doxycycline	Tetracyclines	J01AA02	Access	Yes	Yes
Faropenem	Penems	J01DI03	Reserve	No	No
Framycetin	Aminoglycosides	D09AA01	NC*	No	No
Levofloxacin	Fluoroquinolones	J01MA12	Watch	No	No
Linezolid	Oxazolidinones	J01XX08	Reserve	Yes	No
Meropenem	Carbapenems	J01DH02	Watch	Yes	Yes
Metronidazole_IV	Imidazoles	J01XD01	Access	Yes	Yes
Metronidazole_Oral		P01AB01	Access	Yes	Yes
Ofloxacin	Fluoroquinolones	J01MA01	Watch	No	No
Penicillin G	Penicillins	J01CE08	Access	Yes	No
Piperacillin + Tozobactam	Beta-lactam/beta-lactamase-inhibitor, anti-pseudomonal	J01CR05	Watch	Yes	Yes
Rifaximin	Rifamycins	A07AA11	Watch	No	No
Vancomycin_IV	Glycopeptides	J01XA01	Watch	Yes	Yes

NC – Not categorized

Table 3: Reasons for non-adherence

Reason	Frequency	%
Vomiting	14	21.54
Stomach Pain	13	20.00
Nausea	10	15.38
Bitter taste	6	9.23
Forgot	5	7.69
Intentional	5	7.69
Dizziness	4	6.15
Nurse administration error	4	6.15
Diarrhea	2	3.08
Throat pain	2	3.08
Total	**65**	**100**

Battula and Kumar *et al,* explained the same concerning AMR development when taking antibiotics with other drugs and food [12]. Communicating and intervening with physicians help to reduce the inappropriate use of antibiotics. There was a significant reduction in the risk of AMR after the pharmacist interacted with the prescribing physician.

Patient's contribution to AMR development was estimated through patient's adherence. Some 19.52 % did not follow the physicians' orders, this includes 15.02 % omitted doses, and 4.5 % delayed doses. Reasons for non-adherence included mainly vomiting, stomach pain, and nausea. It has been reported earlier that antibiotics need sufficient concentration and time to kill bacteria [12]. Unfortunately, not taking the antibiotics at the proper time, frequency, and duration will lead to AMR. Majority of the patients did not know about antibiotic resistance. Patient education is essential to avoid AMR. Satisfaction levels were lower compared to other studies. The risk of AMR development through patients was about 19.22 %. The present study's level of satisfaction was 3.96 ± 0.59 on a 5-point Likert scale, which was lower than previous studies on antibiotic treatment by Cziner *et al,* (4.23) and Perera *et al,* (4.7) [13,14].

A recent study in India found that many patients prefer alternative therapies such as Ayurveda (62 %) and Unani (74 %) over allopathic medicine [15]. The reasons adduced for the preference include effectiveness, safety, and cost. Roy *et al* [16] illiterates have been reported to depend more on CAM [17].

The WHO standard targets that at least 60 % of antibiotics used should be from the Access group of antibiotics [7]. In this study only 32 % of the antibiotics prescribed were from the Access group contributing to the risk of AMR. A study conducted in Ghana found that 74 % of antibiotics used were from the Access group, 24 % were from the Watch group, and none were prescribed from the Reserve group. This demonstrates good practice as the reserve antibiotics should be used only in rare cases [18]. In this study 2 antibiotics were from the reserve group. This study shows that there was non-compliance with the Essential Medicines List (EML). Thirty-two percent and 44 % of antibiotics prescribed were not on the WHO and Indian National Essential Medicines List respectively. Other studies in countries such as Ethiopia (100 %), Eritrea (100 %), Lesotho (79 %), Pakistan (98.8 %), Nepal (67.1 %), and India have shown varying levels of compliance with the EML [8]. Some bacteria are becoming resistant to antibiotics, leading to an urgent need for new antibiotics, according to the WHO. WHO released a list of bacteria for which new antibiotics are needed to treat infections. However, pressure from patients and lack of facilities for testing contribute to the misuse of antibiotics. Even parents also pressure the physicians to prescribe antibiotics. Patients are also reasons for the misuse of antibiotics. Sometimes, the prescribing of antibiotics based on some factors like financial benefits from pharmaceutical companies or marketing influences lack of knowledge on guidelines also results in the development of AMR [19]. Locally developed guidelines for treatment and shorter antibiotic courses are recommended to address the issue as reported by Broad Spellberg *et al* [20]. Based on previous studies, healthcare professionals have good knowledge and attitude but poor practice. Trained clinical pharmacists effectively treat patients by understanding drug-related problems in prescriptions and ensuring drug safety [21].

Previous studies focused on inappropriate antibiotic prescriptions, but this study uniquely identifies factors contributing to the development of AMR, such as drug interactions, therapeutic duplications, and non-adherence. It examines the roles of physicians and patients in this issue and assesses the risk of AMR for certain antibiotics.

CONCLUSION

Inappropriate prescribing is just one cause of AMR. Other factors include drug interactions, duplication, and patients' non-adherence. Counseling, education interventions, and stewardship programs are necessary to prevent AMR. All stakeholders must take responsibility, and the government should enforce stricter regulations.

DECLARATIONS

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Ethical approval

Ethical approvals were obtained from the Institution Ethics Committees at Santhiram Medical College and General Hospital (no. IEC/2022/042) and Sri Padmavathi School of Pharmacy (no. SPSP/2022-2023/PDB/11).

Availability of data and materials

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

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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