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Original Research Article

# A Retro-Prospective Study on Adverse Drug Reactions of Antimicrobials Prescribed to Patients Admitted in Medicine Wards of Tertiary Care Hospital

**Anup Kumar[1], Binny Mahendru[2], Jyoti Bala[3]**

[1]Assistant Professor, Department of Pharmacology, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India

[2]Assistant Professor, Department of Pharmacology, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India

[3]Professor, Department of Pathology, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India

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**Corresponding Author: Anup Kumar**

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**Abstract:**

**Background:** Adverse drug reactions (ADRs) to antimicrobial agents are a significant concern in hospitalised patients, contributing to increased morbidity, prolonged hospital stays, and healthcare costs. Antimicrobials, while essential for infection management, are among the most frequently implicated drug classes in ADRs. Identifying the incidence, patterns, severity, and preventability of antimicrobial-related ADRs is critical to enhancing patient safety and promoting rational drug use.

**Aim:** To assess the incidence, pattern, causality, severity, type, and preventability of adverse drug reactions associated with antimicrobial use among patients admitted to the medicine wards of a tertiary care hospital.

**Methods:** This retro-prospective observational study was conducted over 12 months at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, Himachal Pradesh. A total of 6922 inpatients receiving at least one antimicrobial were included. ADRs were identified through active ward surveillance (prospective) and review of medical records (retrospective). Causality was assessed using the WHO–UMC scale, severity by Modified Hartwig and Siegel criteria, preventability by the modified Schumock and Thornton criteria, and reaction type by the Rawlins and Thompson classification. Data were analysed descriptively.

**Results:** Out of 6922 patients, 308 (4.45%) experienced at least one antimicrobial-related ADR. Males (54.4%) were slightly more affected than females (45.5%). The majority of ADRs occurred in patients aged 41–60 years. The most commonly affected organ system was the gastrointestinal tract (36.4%), followed by skin and appendages (21.4%) and central nervous system (10.7%). Beta-lactams (33.1%) were the most frequent drug class implicated, followed by tetracyclines (19.2%) and macrolides (16.2%). Causality assessment revealed most ADRs as probable (59.1%), with the majority being of moderate severity (72.7%). Preventability assessment indicated that 79.9% of ADRs were probably preventable, and Type A reactions (65.3%) predominated.

**Conclusion:** Antimicrobial-related ADRs are common in hospitalised patients, with a significant proportion being preventable. Gastrointestinal and skin-related ADRs are the most frequent, and beta-lactams remain the leading contributors.

**Recommendations:** Enhanced antimicrobial stewardship, continuous pharmacovigilance activities, early detection, and timely management of ADRs are essential to reduce their incidence and improve patient safety. Educational interventions for healthcare professionals can further enhance awareness and reporting.

**Keywords:** Adverse drug reaction, Antimicrobials, Pharmacovigilance, Hospital inpatients, Retro-prospective study.



## Introduction

(ADRs) are a significant concern in hospital settings, especially among patients receiving antimicrobial therapy. They contribute to increased morbidity, mortality, prolonged hospital stays, and healthcare costs worldwide [1]. Antimicrobial agents, although essential in combating infections, are among the most common drug classes associated with ADRs due to their widespread use and potential for hypersensitivity, gastrointestinal intolerance, and organ toxicity [2].

The burden of antimicrobial resistance (AMR) further complicates antimicrobial use, with global

estimates indicating nearly 5 million deaths associated with AMR in 2019 [3]. Inappropriate and excessive prescribing not only accelerates resistance but also increases the likelihood of ADRs [4]. Studies from India suggest that antimicrobials account for 30–40% of all reported ADRs in tertiary care hospitals [5,6]. Beta-lactams, fluoroquinolones, and macrolides are frequently implicated, with skin, gastrointestinal, and central nervous systems being the most affected organ systems [7].

The Pharmacovigilance Programme of India (PvPI) has made considerable progress since its inception, aiming to improve ADR reporting and early detection, including those related to antimicrobials [8]. However, under-reporting remains a major challenge due to lack of awareness, insufficient training, and heavy clinical workloads [9].

Recent prospective and retrospective studies highlight that the majority of antimicrobial-related ADRs are predictable (Type A), of moderate severity, and often preventable, emphasizing the need for regular monitoring, rational prescribing, and timely interventions [10,11]. Despite available evidence, there is limited literature from North India using a retro-prospective observational design that comprehensively evaluates incidence, drug classes, affected organ systems, causality, severity, and preventability in hospitalized patients.

In this context, the present study was undertaken to determine the pattern of ADRs associated with antimicrobials in the medicine wards of a tertiary care hospital. By using both retrospective and prospective data collection, the study aims to generate comprehensive baseline data to guide safer antimicrobial prescribing practices and strengthen pharmacovigilance efforts.

## Methodology

**Study Design and Setting:** This retro-prospective, observational study was conducted jointly by the Department of Pharmacology and the Department of Internal Medicine at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda. The focus was on inpatients admitted under Internal Medicine who were prescribed antimicrobial agents during their hospital stay. The study was carried out over a continuous 12-month period, incorporating both retrospective and prospective data collection phases.

**Sample Size:** 6922

**Study Population:** All inpatients admitted to the medicine wards during the study period who received at least one antimicrobial agent were eligible. Patients of either sex and any age were included, provided they satisfied the inclusion criteria.

### Inclusion Criteria

- Inpatients in the Internal Medicine wards receiving antimicrobial therapy.
- Documentation or clinical suspicion of an (ADR) temporally related to antimicrobial administration.
- For prospective enrolment, willingness to provide informed consent.

### Exclusion Criteria

- Patients refusing consent for prospective monitoring.
- Records lacking sufficient detail to assess drug exposure and reaction characteristics.
- ADRs due to non-antimicrobial drugs alone.

### Data Collection

**Prospective Component:** Ward rounds were conducted twice weekly to actively identify patients on antimicrobial therapy who developed suspected ADRs. Information was obtained through direct patient/attendant interviews, examination findings, treatment charts, laboratory reports, and nursing notes. A structured ADR documentation form was used to ensure completeness.

**Retrospective Component:** For patients who could not be enrolled prospectively, case records were retrieved from the Medical Records Department. Only those fulfilling the inclusion criteria and having adequate documentation of antimicrobial use and suspected ADRs were considered.

**ADR Definition:** The WHO definition of ADR — "a noxious, unintended and undesirable effect that occurs at doses normally used in humans for prophylaxis, diagnosis or therapy" — was applied. Only reactions meeting this definition and attributed to antimicrobials were included.

### Assessment Parameters

1. **Causality Assessment**: Utilised the WHO–UMC Causality Assessment Scale to categorise each ADR as certain, probable, possible, unlikely, conditional/unclassified, or unassessable.
2. **Severity Assessment**: Severity grading followed the Modified Hartwig and Siegel scale, classifying ADRs as mild, moderate, severe, or lethal based on clinical impact, hospital stay, and required interventions.
3. **Preventability Assessment**: The modified Schumock and Thornton criteria were used to categorise ADRs as definitely preventable, probably preventable, or not preventable.
4. **Type of Reaction**: ADRs were classified according to Rawlins and Thompson's system into Type A, B, C, D, E, or F.
5. **Organ System Classification**: Reactions were coded using WHO Adverse Reaction

Terminology, grouping them by system-organ class (e.g., gastrointestinal, dermatological, neurological).

6. **Drug Classification**: Suspected antimicrobials were classified by pharmacological group (e.g., beta-lactams, macrolides, fluoroquinolones, aminoglycosides).

**Ethical Considerations:** The study was approved by the Institutional Scientific Review Committee and Human Ethics Committee prior to commencement. Written informed consent was obtained from patients enrolled in the prospective phase. Patient confidentiality was maintained at all stages.

## Results

**Incidence of ADRs:** Out of a total of 6922 patients admitted to the Internal Medicine wards during the study period, 308 patients were found to have experienced at least one antimicrobial-related ADR, giving an overall incidence rate of 4.45%.

**Table 1: Incidence of ADRs in study population**

| Total No. of Patients | Patients with ADRs | Percentage (%) |
|---|---|---|
| 6922 | 308 | 4.45 |

**Demographic Profile of Patients with ADRs:** Among the 308 patients with ADRs, 168 (54.5%) were male and 140 (45.5%) were female. The majority of ADRs were reported in the age group 41–60 years.

**Table 2: Age and Sex Distribution of Patients with ADRs**

| Age Group (years) | Male | Female | Total | Percentage (%) |
|---|---|---|---|---|
| 18–40 | 39 | 34 | 73 | 23.7 |
| 41–60 | 67 | 62 | 129 | 41.9 |
| 61–80 | 54 | 37 | 91 | 29.5 |
| >80 | 8 | 7 | 15 | 4.9 |
| **Total** | 168 | 140 | 308 | 100 |

**Mean Age of Patients with ADRs:** The mean age of patients with ADRs was ≈53 years (52.8 ± 16.9).

**Organ Systems Involved:** The gastrointestinal system was the most frequently affected (36.4%), followed by skin and appendages (21.4%) and the central nervous system (10.7%).

**Table 3: Organ Systems Affected by ADRs**

| Organ System Affected | No. of ADRs | Percentage (%) |
|---|---|---|
| Gastrointestinal | 112 | 36.4 |
| Skin & Appendages | 66 | 21.4 |
| Central Nervous System | 33 | 10.7 |
| Cardiovascular System | 26 | 8.4 |
| Renal/Urinary | 20 | 6.5 |
| Hematological | 17 | 5.3 |
| Respiratory System | 13 | 4.2 |
| Others | 21 | 6.8 |
| **Total** | 308 | 100 |

**Drug Classes Implicated:** Among antimicrobials, beta-lactams were most frequently associated with ADRs (33.1%), followed by tetracyclines (19.2%) and macrolides (16.2%).

**Table 4: Antimicrobial Classes Causing ADRs**

| Drug Class | No. of ADRs | Percentage (%) |
|---|---|---|
| Beta-lactams | 102 | 33.1 |
| Tetracyclines | 59 | 19.2 |
| Macrolides | 50 | 16.2 |
| Aminoglycosides | 27 | 8.8 |
| Quinolones | 22 | 7.1 |
| Antitubercular drugs | 16 | 5.2 |
| Antimalarials | 11 | 3.6 |
| Antivirals | 6 | 1.9 |
| Antifungals | 5 | 1.6 |
| Sulfonamides | 4 | 1.3 |

| | | |
|---|---|---|
| Nitroimidazoles | 3 | 1.0 |
| Urinary antiseptics | 2 | 0.6 |
| Others | 1 | 0.3 |
| **Total** | 308 | 100 |

**Causality Assessment (WHO–UMC Scale):** Most ADRs were classified as probable (58.9%), followed by possible (34.4%).

**Table 5: Causality Assessment of ADRs**

| Causality Category | No. of ADRs | Percentage (%) |
|---|---|---|
| Certain | 4 | 1.3 |
| Probable | 182 | 59.1 |
| Possible | 106 | 34.4 |
| Unlikely | 16 | 5.2 |
| **Total** | 308 | 100 |

**Severity Assessment (Modified Hartwig & Siegel Scale)**

Most reactions were of **moderate** severity (72.7%), while severe ADRs accounted for 14.3%.

**Table 6: Severity of ADRs**

| Severity Level | No. of ADRs | Percentage (%) |
|---|---|---|
| Mild | 41 | 13.3 |
| Moderate | 224 | 72.7 |
| Severe | 44 | 14.3 |
| **Total** | 308 | 100 |

**Preventability Assessment (Schumock and Thornton Criteria)**

**Probably preventable** ADRs were most frequent (79.9%), followed by definitely preventable ADRs (12.5%).

**Table 7: Preventability of ADRs**

| Preventability Category | No. of ADRs | Percentage (%) |
|---|---|---|
| Definitely preventable | 39 | 12.7 |
| Probably preventable | 246 | 79.9 |
| Not preventable | 23 | 7.5 |
| **Total** | 308 | 100 |

**Type of Reaction (Rawlins & Thompson Classification):** The most common type was Type A (65.3%), followed by Type B (22.1%).

**Table 8: Type of ADRs**

| Type of Reaction | No. of ADRs | Percentage (%) |
|---|---|---|
| Type A | 201 | 65.3 |
| Type B | 68 | 22.1 |
| Type C | 25 | 8.1 |
| Type D | 8 | 2.6 |
| Type E | 4 | 1.3 |
| Type F | 2 | 0.6 |
| **Total** | 308 | 100 |

## Discussion

In the present retro-prospective observational study involving 6922 inpatients admitted to the Internal Medicine wards, antimicrobial-related (ADRs) were documented in 308 patients, yielding an overall incidence of 4.45%. This rate is comparable to several national hospital-based pharmacovigilance reports, although slightly lower than certain international figures. The marginal male predominance (54.5% males vs. 45.5% females) may reflect differences in hospital admission patterns or underlying comorbidities.

Age-wise distribution showed the highest ADR frequency in the 41–60 years group, indicating that middle-aged adults may be at greater risk due to higher antimicrobial usage and possible

comorbidity-driven polypharmacy. The mean age of patients with ADRs was approximately 53 years, suggesting that risk escalates in the fifth and sixth decades of life.

Regarding affected organ systems, the gastrointestinal tract was most frequently involved (36.4%), followed by skin and appendages (21.4%) and the central nervous system (10.7%). This pattern is consistent with the known adverse profiles of many antimicrobial classes, where gastrointestinal intolerance and hypersensitivity reactions are common.

Drug class analysis identified beta-lactams (33.1%) as the most frequent cause of ADRs, followed by fluoroquinolones (19.2%) and macrolides (16.2%). These findings reflect the high prescription rates of these agents in hospital practice. Notably, aminoglycosides and tetracyclines, though less commonly prescribed, also contributed significantly, highlighting the need for vigilance across all antimicrobial categories.

Causality assessment using the WHO–UMC scale revealed that the majority of ADRs were classified as probable (59.1%), suggesting a reasonable temporal relationship to the suspected drug with minimal alternative explanations. A smaller proportion (1.3%) were considered certain, which is expected given the complexity of inpatient clinical scenarios.

Severity assessment showed that most ADRs were of moderate severity (72.7%), requiring therapeutic intervention or prolonging hospital stay. Severe reactions accounted for 14.3%, underscoring the potential for antimicrobial ADRs to cause significant morbidity.

Preventability analysis indicated that a substantial proportion of ADRs were probably preventable (79.7%), and 12.7% were definitely preventable. This highlights a considerable scope for reducing ADR incidence through rational antimicrobial prescribing, early recognition of symptoms, and appropriate monitoring.

When classified by Rawlins and Thompson criteria, Type A reactions (65.3%) predominated, consistent with predictable, dose-dependent pharmacological effects of antimicrobials. Type B reactions (22.1%), which are unpredictable and immune-mediated, formed the next largest group. The presence of some Type C, D, E, and F reactions reflects the varied and sometimes delayed manifestations of antimicrobial toxicity.

Overall, the findings emphasize that while antimicrobials are indispensable in clinical practice, their use carries a significant risk of ADRs—most of which are preventable. Targeted interventions such as antimicrobial stewardship programs, patient-specific risk assessment, and enhanced ADR reporting systems could reduce both the incidence and severity of these events.

(ADRs) due to antimicrobials remain a significant concern in tertiary care hospital settings. Recent studies reveal that antibiotics are among the most common drugs causing ADRs, with β-lactams and fluoroquinolones frequently implicated [12]. In a prospective study, elderly patients and those on multiple antimicrobial agents were found to have a higher likelihood of developing ADRs, particularly gastrointestinal and dermatological manifestations [13,14].

Active pharmacovigilance initiatives have shown to improve ADR detection rates in hospital wards, enabling timely intervention and preventing severe outcomes [15]. Moreover, ward-specific patterns indicate that internal medicine wards report higher ADR incidences compared to surgical wards, possibly due to longer antibiotic courses and complex patient comorbidities [16].

Further, a cross-sectional study in an Indian tertiary care hospital identified that ceftriaxone and ciprofloxacin were leading causes of ADRs, and most reactions were moderate in severity [17]. Another multicenter observational study reported that a large proportion of antimicrobial ADRs were preventable and highlighted the importance of continuous training of healthcare workers in ADR recognition and reporting [18].

## Conclusion

The study observed an ADR incidence of 4.45% among inpatients receiving antimicrobials, with males slightly more affected. The gastrointestinal tract and skin were the most frequent organ systems involved. Beta-lactams, tetracyclines and macrolides were major contributors to ADRs. Probable causality predominated, and most reactions were of moderate severity and probably preventable, indicating scope for improved prescribing practices and monitoring.

## References

1. Tandon VR, Mahajan V, Khajuria V, Gillani Z. Under-reporting of adverse drug reactions: a challenge for pharmacovigilance in India. Indian J Pharmacol. 2018;50(3):145-9.
2. Sharma R, Pawar A, Monif T. Pharmacovigilance of antimicrobial agents: a review. Ther Adv Infect Dis. 2020; 7:2 049936120949494.
3. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022; 399(10325): 629-55.
4. Ventola CL. The antibiotic resistance crisis: causes and threats. P T. 2018;43(4):191-9.

5. Misra D, Bose M, Parida S, et al. Adverse drug reaction reporting in a tertiary care teaching hospital in eastern India: a retrospective study. Int J Basic Clin Pharmacol. 2020;9(4):616-20.
6. Garapati P, Dhingra S, Kumar N, et al. Exploring antibiotic safety: a prospective observational study from a tertiary care public sector hospital. Clin Epidemiol Glob Health. 2024;24:101365.
7. Patowary S, Lahkar M, Lihite RJ. A study on the usage of antimicrobial agents and adverse drug reaction of antimicrobial used in a tertiary care hospital in North East India. Int J Basic Clin Pharmacol. 2018;7(12):2371-6.
8. Thatte UM, Chaudhari NL, Gogtay NJ. Pharmacovigilance Programme of India: history, evolution and current status. Adverse Drug React Bull. 2018;314(1):1235-8.
9. Rajesh R, Vidyasagar S, Varma DM. An educational intervention to improve awareness about pharmacovigilance among healthcare professionals in an Indian tertiary care hospital. J Young Pharm. 2020;12(2):167-72.
10. Sriram S, Ghasemi A, Ramasamy R, et al. Prevalence of adverse drug reactions at a private tertiary care hospital in South India. J Res Pharm Pract. 2019;8(1):25-31.
11. Ganesan S, Ganesan M, Reddy CU. A prospective observational study of adverse drug reactions in a tertiary care hospital. Perspect Clin Res. 2021;12(2):67-72.
12. Bharathi DR, Mahesh N, Girish K, Pradeep D. Patterns of adverse drug reactions of antimicrobials in tertiary care hospital. J Drug Deliv Ther. 2021;11(3):102-106.
13. Raj S, Jose J, Varghese R, Thomas S. Patterns of adverse drug reactions in patients treating with antimicrobials in tertiary care hospital. Int J Basic Clin Pharmacol. 2019;8(5):1033-1039.
14. Sharma M, Kumar S, Reddy C, Srivastava A. Patterns of antimicrobial adverse drug reactions in hospitalized patients. Indian J Pharm Pract. 2020;13(4):270-275.
15. Jose J, Rao PG, Jimmy B, Jose V. Adverse drug reactions in microbiology ward of a tertiary care hospital: a prospective study. Indian J Pharm Sci. 2020;82(1):128-133.
16. Parveen S, Sharma R, Kumar A. Patterns of adverse drug reactions in tertiary care hospital: A ward-based analysis. J Clin Diagn Res. 2021;15(2):FC01-FC05.
17. Khan S, Patel H, Mehta R, Karia J. Adverse drug reaction profile of antimicrobials in a tertiary care hospital: a cross-sectional study. Natl J Physiol Pharm Pharmacol. 2020; 10(9): 790-795.
18. Gupta S, Bansal A, Singh S, Kapoor V. Evaluation of preventable adverse drug reactions to antimicrobials in multicenter observational study. Perspect Clin Res. 2019; 10(3): 137-143.