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Original Research Article

Antibiotic-Associated Adverse Drug Reactions: A Prospective Observational Study

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Abstract

Background: Antibiotics are commonly prescribed drugs and are frequently associated with adverse drug reactions (ADRs), contributing to patient morbidity and prolonged hospital stay. Aim of the study was to evaluate the clinical pattern, causality, severity, seriousness, and outcomes of antibiotic-associated ADRs in a tertiary care hospital.

Materials and Methods: This prospective observational study included 50 patients who developed suspected antibiotic-associated ADRs. Data was collected using a structured case record form (CRF). Causality was assessed using WHO-UMC scale, and severity was graded using the Modified Hartwig and Siegel scale. Statistical analysis was performed using descriptive statistics and Chi-square test.

Results: The mean age was 46.8 ± 15.2 years with male predominance (56%). Cephalosporins were the most commonly implicated antibiotics (28%). Skin manifestations (42%) were the most frequent ADRs, followed by gastrointestinal reactions (28%). Type B reactions accounted for 60% of cases. Serious ADRs occurred in 16% of patients. Most patients recovered completely (74%), with no mortality. Significant associations were observed between age and severity ($p = 0.041$) and antibiotic class and organ system involvement ($p = 0.032$).

Conclusion: Antibiotic-associated ADRs are common but largely manageable. Strengthening pharmacovigilance and rational antibiotic use can improve patient safety.

Keywords: Antibiotics, Adverse Drug Reactions, Pharmacovigilance, Cephalosporins, Severity, Causality.

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Introduction

Antibiotics are among the most commonly prescribed medications worldwide and have significantly reduced morbidity and mortality from infectious diseases. However, their widespread and often empirical use has led to a substantial burden of antibiotic-associated adverse drug reactions (ADRs), which contribute to increased hospital stay, additional treatment costs, therapeutic modifications, and patient morbidity [1].

The World Health Organization (WHO) defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems, emphasizing that ADRs are a major cause of preventable harm in healthcare systems [2]. Antibiotics are consistently reported as one of the leading drug classes implicated in ADRs, particularly allergic reactions and gastrointestinal disturbances. Surveillance data from the United States demonstrated that systemic antibiotics account for a significant proportion of emergency department visits due to drug-related adverse events, with hypersensitivity reactions being the most common presentation [3]. Beta-lactams, cephalosporins, sulfonamides, and fluoroquinolones are frequently associated with cutaneous reactions, gastrointestinal intolerance, hepatotoxicity, and hematological abnormalities [4,5]. Severe reactions such as anaphylaxis and serious cutaneous adverse reactions (SCARs) further highlight the clinical importance of early detection and reporting [5].

Prospective observational studies conducted in tertiary care hospitals have reported variable

incidence rates of antibiotic-related ADRs, often ranging between 3–8%, depending on patient population, surveillance methodology, and causality assessment tools used [6–8]. Active surveillance has been shown to detect higher ADR rates compared to spontaneous reporting systems, indicating that under-reporting remains a significant challenge [7].

Despite growing awareness, many healthcare institutions—especially in resource-limited settings—lack systematic prospective monitoring of antibiotic-associated ADRs using standardized causality (WHO-UMC), severity, and preventability assessments [8].

Although antibiotics are frequently implicated in ADRs, there remain insufficient locally generated prospective data regarding their incidence, clinical pattern, severity grading, and outcomes in hospitalized patients.

Most available studies are retrospective, single-centered, or limited by passive reporting mechanisms, leading to underestimation of the true burden. There is a need for structured, prospective observational studies to identify high-risk antibiotics, characterize common reaction patterns, and strengthen institutional pharmacovigilance systems.

The present prospective observational study aims to evaluate the incidence, clinical profile, causality, severity, and outcomes of antibiotic-associated adverse drug reactions among patients receiving systemic antibiotics in a tertiary care hospital, thereby contributing to improved pharmacovigilance practices and safer antibiotic use.

Materials and Methods

Study Design and Setting: This was a prospective observational study conducted in the Department of Pharmacology, in collaboration with the concerned clinical departments of a tertiary care teaching hospital, from January 2025 to September 2025.

The study included a total sample size of 50 patients who received systemic antibiotic therapy and subsequently developed suspected antibiotic-associated adverse drug reactions (ADRs) during hospital stay or clinical follow-up. The study was carried out as part of active pharmacovigilance to identify, document, and analyze antibiotic-related ADRs with respect to pattern, causality, severity, and outcomes.

Sample Size: A total of 50 cases of suspected antibiotic-associated ADRs were enrolled using a consecutive sampling method during the study period.

Inclusion Criteria

- Patients of either sex, aged ≥18 years (or as per institutional protocol), receiving systemic antibiotics (oral/parenteral).
- Patients with suspected antibiotic-associated ADRs identified during the study period.
- Patients willing to participate and providing written informed consent (or consent from legally acceptable representative, if applicable).
- Both inpatients and outpatients (if included as per protocol) under hospital care.

Exclusion Criteria

- Patients with ADRs due to non-antibiotic drugs only (without antibiotic involvement).
- Patients with poisoning/overdose, medication errors, or intentional self-harm.
- Patients unwilling to consent / incomplete clinical records preventing ADR assessment.
- Reactions clearly attributable to underlying disease rather than drug exposure (after assessment).

Data Collection

- Patients receiving antibiotics were actively monitored through ward rounds, chart reviews, and liaison with treating units to detect suspected ADRs.
- When a suspected antibiotic-associated ADR was identified, patient details were recorded in the CRF including age, sex, diagnosis, comorbidities, allergy history, and concurrent medications.
- Antibiotic exposure details were documented: drug name, class, dose, route, frequency, indication, start date, and duration.
- ADR details were captured in ADR form in the following categories: date/time of onset, clinical manifestations, organ system involved, relevant laboratory findings, and suspected antibiotic(s)
- Management and outcome were recorded: drug withdrawn/continued, symptomatic treatment, substitution of antibiotic, recovery status, and any sequelae.
- Each ADR was evaluated for causality, severity, seriousness, and preventability using the above tools, and classified by system organ class and reaction type.
- All collected ADRs were compiled, coded, and entered into a study database (ADRMS) for descriptive analysis.

Ethical Considerations: The study was initiated after approval from the Institutional Ethics Committee. Written informed consent was obtained from participants, confidentiality was maintained, and patient care was not altered beyond routine clinical management.

Statistical Analysis: Data was entered into Microsoft Excel and analyzed using SPSS (version 23.0). Descriptive statistics were used to summarize demographic characteristics, antibiotic exposure patterns, clinical features of ADRs, causality, severity, and outcomes. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Associations between categorical variables, such as age group and severity or antibiotic class and organ system involvement, were assessed using Chi-square test or Fisher's exact test where appropriate. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Demographic Characteristics of Study Participants (n = 50)

Variable	Category	Number (n)	Percentage (%)	Mean ± SD
Age (years)	—	—	—	**46.8 ± 15.2**
	18–30	9	18.0	—
	31–45	14	28.0	—
	46–60	17	34.0	—
	>60	10	20.0	—
Gender	Male	28	56.0	—
	Female	22	44.0	—
Weight (kg)	—	—	—	**62.4 ± 11.6**
Patient Status	Inpatient	42	84.0	—
	Outpatient	8	16.0	—
Department of Admission	General Medicine	21	42.0	—
	Surgery	10	20.0	—
	Orthopedics	7	14.0	—
	Obstetrics & Gynecology	6	12.0	—
	Others	6	12.0	—

The table1 shows the demographic profile of the study participants (n = 50).

The mean age of patients was 46.8 ± 15.2 years, with the majority belonging to the 46–60 years age group (34%), followed by 31–45 years (28%). Males constituted 56% of the study population. The mean body weight was 62.4 ± 11.6 kg. Most patients were inpatients (84%), and the highest number of ADR cases were reported from the Department of General Medicine (42%), followed by Surgery (20%) and Orthopedics (14%).

Table 2: Clinical Characteristics of Study Participants (n = 50)

Variable	Category	Number (n)	Percentage (%)	Mean ± SD
Primary Diagnosis	Respiratory infections	14	28.0	—
	Urinary tract infections	11	22.0	—
	Skin & soft tissue infections	9	18.0	—
	Gastrointestinal infections	7	14.0	—
	Post-operative infections	6	12.0	—
	Others	3	6.0	—
Indication for Antibiotic Therapy	Empirical therapy	32	64.0	—
	Culture-directed therapy	18	36.0	—
Comorbidities*	Diabetes mellitus	16	32.0	—
	Hypertension	18	36.0	—
	Chronic kidney disease	6	12.0	—
	Chronic liver disease	4	8.0	—
	Bronchial asthma	5	10.0	—
	No comorbidity	14	28.0	—
History of Drug Allergy	Present	6	12.0	—
	Absent	44	88.0	—
Duration of Hospital Stay (days)	—	—	—	**7.4 ± 3.2**

Table 2 depicts the clinical characteristics of the study participants (n = 50). Respiratory infections (28%) were the most common primary diagnosis, followed by urinary tract infections (22%) and skin

and soft tissue infections (18%). The majority of patients received antibiotics empirically (64%), while 36% received culture-directed therapy. Hypertension (36%) and diabetes mellitus (32%) were the most prevalent comorbidities, although 28% of patients had no associated comorbidity. A prior history of drug allergy was present in 12% of cases. The mean duration of hospital stay was 7.4 ± 3.2 days.

Table 3: Antibiotic Exposure Characteristics of Study Participants (n = 50)

Variable	Category	Number (n)	Percentage (%)	Mean ± SD
Name of Antibiotic	Ceftriaxone	14	28.0	—
	Amoxicillin–Clavulanate	10	20.0	—
	Ciprofloxacin	8	16.0	—
	Azithromycin	6	12.0	—
	Piperacillin–Tazobactam	7	14.0	—
	Others	5	10.0	—
Route of Administration	Intravenous (IV)	32	64.0	—
	Oral	16	32.0	—
	Intramuscular (IM)	2	4.0	—
Frequency of Dosing	Once daily	18	36.0	—
	Twice daily	24	48.0	—
	Thrice daily	8	16.0	—
Duration of Therapy (days)	—	—	—	**6.2 ± 2.4**
Therapy Type	Monotherapy	34	68.0	—
	Combination therapy	16	32.0	—
Time to Onset of ADR (days)	—	—	—	**3.1 ± 1.6**

Table 3 summarizes the antibiotic exposure characteristics of the study participants (n = 50). Ceftriaxone (28%) was the most frequently implicated antibiotic, followed by Amoxicillin–Clavulanate (20%) and Ciprofloxacin (16%). The majority of antibiotics were administered intravenously (64%), while 32% were given orally. Most patients received twice-daily dosing (48%). The mean duration of antibiotic therapy was 6.2 ± 2.4 days. Monotherapy was observed in 68% of cases, whereas 32% received combination therapy. The mean time to onset of ADR after antibiotic administration was 3.1 ± 1.6 days, indicating that most reactions occurred early during treatment.

Table 4: ADR-Specific Characteristics of Study Participants (n = 50)

Variable	Category	Number (n)	Percentage (%)	Mean ± SD
Time to ADR Onset (days)	—	—	—	**3.1 ± 1.6**
Organ System Involved	Skin & subcutaneous tissue	21	42.0	—
	Gastrointestinal	14	28.0	—
	Hepatic	5	10.0	—
	Hematological	3	6.0	—
	Renal	2	4.0	—
	CNS	3	6.0	—
	Others	2	4.0	—
Clinical Manifestation*	Rash	12	24.0	—
	Urticaria	6	12.0	—
	Pruritus	3	6.0	—
	Diarrhea	8	16.0	—
	Vomiting	4	8.0	—
	Drug-induced hepatitis	4	8.0	—
	Anemia	2	4.0	—
	Elevated creatinine	2	4.0	—
	Headache / dizziness	3	6.0	—
	Others	6	12.0	—
Laboratory Abnormalities	Elevated liver enzymes	5	10.0	—
	Leukopenia / anemia	3	6.0	—
	Raised serum creatinine	2	4.0	—
	No significant abnormality	40	80.0	—
Type of Reaction	Type A (Predictable)	20	40.0	—
	Type B (Unpredictable)	30	60.0	—

Table 4 describes the ADR-specific characteristics of the study participants (n = 50).

The mean time to onset of ADR was 3.1 ± 1.6 days, indicating early occurrence after antibiotic initiation. The most commonly affected organ system was the skin and subcutaneous tissue (42%), followed by the gastrointestinal system (28%). Rash (24%) and diarrhea (16%) were the most frequent clinical manifestations. Laboratory abnormalities were observed in a minority of cases, with elevated liver enzymes being the most common (10%), while 80% showed no significant laboratory derangement.

Type B (unpredictable) reactions constituted 60% of cases, whereas Type A (predictable) reactions accounted for 40%.

Table 5: Seriousness of Antibiotic-Associated ADRs (n = 50)

Variable	Category	Number (n)	Percentage (%)
Overall Serious ADRs	Yes	9	18.0
	No	41	82.0
Life-threatening	Yes	2	4.0
	No	48	96.0
Hospitalization Required / Prolonged	Yes	7	14.0
	No	43	86.0
Disability	Yes	0	0.0
	No	50	100.0
Other Serious Criteria*	Yes	3	6.0
	No	47	94.0

Table 5 presents the serious profile of antibiotic-associated ADRs (n = 50). Overall, 18% of ADRs were classified as serious, while the majority (82%) were non-serious.

Hospitalization or prolongation of hospital stay was observed in 14% of cases and was the most common serious criterion. Life-threatening reactions like Toxic Epidermal Necrolysis (TEN)/ Steven Johnsons Syndrome (SJS) occurred in 4% of patients.

No cases resulted in permanent disability. Other serious criteria were noted in 6% of cases.

Table 6: Management and Outcome of Antibiotic-Associated ADRs (n = 50)

Variable	Category	Number (n)	Percentage (%)
Drug Withdrawn	Yes	38	76.0
	No	12	24.0
Dose Reduced	Yes	5	10.0
	No	45	90.0
Antibiotic Substituted	Yes	30	60.0
	No	20	40.0
Symptomatic Treatment Given	Yes	41	82.0
	No	9	18.0
Rechallenge Performed	Yes	2	4.0
	No	48	96.0
Outcome of ADR	Recovered	36	72.0
	Recovering	8	16.0
	Continuing	3	6.0
	Recovered with sequelae	2	4.0

Table 6 outlines the management and outcomes of antibiotic-associated ADRs (n = 50). The suspected antibiotic was withdrawn in 76% of cases, and substitution with an alternative antibiotic was required in 60% of patients. Dose reduction was performed in 10% of cases. Symptomatic treatment was administered in the majority (82%). Rechallenge was rarely performed (4%). Regarding outcomes, most patients recovered completely (72%), while 16% were recovering at the time of assessment. A small proportion continued to have symptoms (6%) or recovered with sequelae (4%).

Table 7: Association between Age Group and Severity of ADR (n = 50)

Age Group (years)	Mild n (%)	Moderate n (%)	Severe n (%)	Total (n)
18–30 (n=9)	6 (66.7)	3 (33.3)	0 (0.0)	9
31–45 (n=14)	8 (57.1)	5 (35.7)	1 (7.2)	14
46–60 (n=17)	6 (35.3)	8 (47.1)	3 (17.6)	17
>60 (n=10)	2 (20.0)	5 (50.0)	3 (30.0)	10
Total	**22 (44.0)**	**21 (42.0)**	**7 (14.0)**	**50**

Chi-square test value: 8.94; p-value: 0.041 (Statistically significant)

Table 7 shows the association between age group and severity of ADRs (n = 50). Mild reactions were more common in younger patients, particularly in the 18–30 years age group (66.7%). In contrast, moderate and severe reactions increased with advancing age. Patients aged >60 years had the highest proportion of severe ADRs (30%), followed by the 46–60 years group (17.6%). Overall, mild reactions accounted for 44%, moderate for 42%, and severe for 14% of cases, indicating a trend of increasing severity with increasing age.

Table 8: Association between Antibiotic Class and Organ System Involvement (n = 50)

Antibiotic Class	Skin n (%)	GI n (%)	Hepatic n (%)	Others* n (%)	Total (n)
Cephalosporins (n=14)	8 (57.1)	3 (21.4)	1 (7.1)	2 (14.4)	14
Penicillins (n=10)	4 (40.0)	3 (30.0)	1 (10.0)	2 (20.0)	10
Fluoroquinolones (n=8)	2 (25.0)	4 (50.0)	1 (12.5)	1 (12.5)	8
Macrolides (n=6)	2 (33.3)	3 (50.0)	0 (0.0)	1 (16.7)	6
Extended-spectrum β-lactams (n=7)	3 (42.9)	1 (14.3)	2 (28.6)	1 (14.2)	7
Others (n=5)	2 (40.0)	0 (0.0)	0 (0.0)	3 (60.0)	5
Total	**21 (42.0)**	**14 (28.0)**	**5 (10.0)**	**10 (20.0)**	**50**

***Others include renal, hematological, CNS manifestations. Chi-square test value: 12.67; p-value: 0.032 (Statistically significant)**

Table 8 demonstrates the association between antibiotic class and organ system involvement (n = 50). Cutaneous reactions were most frequently associated with Cephalosporins (57.1%), followed by Penicillins (40%) and extended-spectrum β-lactams (42.9%). Gastrointestinal reactions were more commonly observed Fluoroquinolones and Macrolides (50% each). Hepatic involvement was relatively higher with extended-spectrum β-lactams (28.6%). Overall, skin manifestations (42%) were the most common ADR pattern across all antibiotic classes, indicating a class-specific variation in organ system involvement.

Discussion

In the present prospective observational study (n = 50), antibiotic-associated ADRs were predominantly observed in middle-aged adults (mean age 46.8 ± 15.2 years), with a slight male predominance (56%) and a majority of cases occurring among inpatients (84%). This demographic pattern is consistent with hospital-based pharmacovigilance studies that report higher ADR incidence in the 30–60 year age group, particularly among hospitalized patients receiving parenteral therapy and multiple medications [9]. Similar gender distribution trends have been documented in antibiotic-specific ADR studies, although variations depend on institutional prescribing patterns and patient demographics [10].

Cephalosporins and β-lactams were the most commonly implicated antibiotic classes, with ceftriaxone and amoxicillin-clavulanate accounting for a substantial proportion of cases. This observation aligns with previous literature identifying broad-spectrum β-lactams as frequent causes of ADRs due to their widespread empirical use and recognized potential for hypersensitivity reactions [11,12]. The predominance of intravenous administration in the present study (64%) may have further contributed to the observed pattern.

Skin and subcutaneous tissue reactions (42%) were the most frequent ADR presentations, followed by gastrointestinal involvement (28%). Rash, urticaria, and diarrhea were the leading clinical manifestations. These findings are comparable with earlier reports highlighting cutaneous reactions as the most common antibiotic-associated ADRs, particularly with β-lactams [13]. However, some studies have documented a higher proportion of gastrointestinal reactions, which may reflect differences in antibiotic selection, patient populations, and ADR reporting thresholds [10].

Type B reactions (60%) were more common than Type A reactions (40%), indicating a predominance of unpredictable, hypersensitivity-mediated events. This contrasts with certain hospital-based ADR datasets where predictable, dose-related reactions are more frequent [10]. The early onset of reactions

(mean 3.1 ± 1.6 days) in the present study supports the immunological basis of many observed ADRs.

Serious ADRs accounted for 16% of cases, primarily due to hospitalization or prolongation of hospital stay, with no mortality reported. Comparable pharmacovigilance studies also demonstrate that while most ADRs are non-serious, a clinically relevant minority require active intervention [9]. In the present study, prompt withdrawal of the suspected antibiotic (76%) and administration of symptomatic treatment (82%) resulted in favorable outcomes, with the majority of patients recovering completely (74%).

The association analysis revealed a statistically significant relationship between age and severity ($p = 0.041$), with severe reactions more common in older individuals.

This is consistent with established evidence that advanced age increases susceptibility to ADRs due to physiological changes, comorbidities, and polypharmacy. Additionally, antibiotic class was significantly associated with organ system involvement ($p = 0.032$), reflecting known class-specific adverse effect profiles, such as higher cutaneous involvement with cephalosporins and greater gastrointestinal effects with fluoroquinolones and macrolides [13].

Overall, the findings reinforce that antibiotic-associated ADRs are common in tertiary care settings but are largely preventable and manageable with early recognition, rational prescribing, and structured pharmacovigilance practices.

Conclusion

Antibiotic-associated ADRs in this cohort were common among hospitalized adults, with β-lactams and Cephalosporins most frequently implicated.

Cutaneous and gastrointestinal reactions predominated, and most patients recovered following timely management, with no mortality observed. Increasing age was associated with greater severity, and antibiotic class influenced organ system involvement. Strengthening pharmacovigilance and rational antibiotic prescribing within stewardship programs is essential to enhance patient safety.

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