e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(10); 691-698

Original Research Article

Evaluation of Antimicrobial Related Adverse Drug Reactions in Patients at Tertiary Care Hospitals, Central India

Swati Nilesh Chavan[1], Poonam Patel[2]

[1,2]Department of Pharmacology, Index Medical College & RC, Indore (M.P.)

Received: 01-08-2025 / Revised: 16-09-2025 / Accepted: 05-10-2025
Corresponding Author: Dr. Swati Nilesh Chavan
Conflict of interest: Nil

Abstract

Background: Antimicrobial agents are commonly prescribed in outpatient settings for various infections but can cause adverse drug reactions (ADRs) ranging from mild to life-threatening, increasing morbidity, hospital stays, and healthcare costs. This study analyzes antimicrobial-related ADRs in a tertiary care hospital in India, focusing on patient demographics, infection type, and treatment patterns, aiming to support rational antibiotic use and enhance patient safety.

Aims and Objectives: (1) To assess the adverse drug reactions (ADRs) occurring in patients treated with antimicrobial agents across different clinical conditions. (2) To assess antimicrobial-related adverse drug reactions (ADRs) based on age, gender, severity.

Materials and Methods: 200 patients were enrolled for evaluating adverse effects with antimicrobial agents. All patients were followed up by medical history, history of drugs, and any severity of ADR. Causality was graded by Naranjo scale.

Results: ADRs were most frequent in the 41–60 years group (32.6%), followed by 19–40 years (24.3%) and elderly patients (20%), with 8.7% in children, reflecting polypharmacy and reduced metabolism in older groups. ADRs were higher in males (69.5%) than females (30.5%), with severe cases more common in males (40 vs. 18). Respiratory (25.1%) and urinary tract infections (18.9%) were the leading indications for 275 antimicrobial prescriptions. Causality assessment by Naranjo's algorithm classified 47.82% ADRs as probable, 39.78% as possible, 4.57% as certain, and 7.83% as unlikely.

Conclusion: In conclusion, the study highlights that adverse drug reactions (ADRs) to antimicrobial agents were more prevalent among males and middle-aged individuals, with respiratory and urinary tract infections being the leading causes for antibiotic use. Most ADRs were classified as probable or possible based on Naranjo's algorithm, emphasizing the need for careful antibiotic prescribing, monitoring, and awareness to minimize ADR risk, especially in high-risk groups.

Key words: Adverse Drug Reactions; Antimicrobial agents; Naranjo Scale.

Introduction

Antibiotics and antitumor agents were identified as the most problematic drugs in terms of adverse drug reactions (ADRs), accounting for approximately 16% and 15% of cases, respectively. These findings highlight that a significant proportion of documented ADRs can be attributed to these drug classes, emphasizing the need for careful monitoring and judicious use to minimize patient risk [1]. Antimicrobial agents are often mentioned in ADR studies because their widespread and careless use has increased the incidence of ADRs. The various classes of antibiotics, which include penicillin's, cephalosporin's, sulphonamides, and aminoglycosides, etc, differ in respect of their mechanism of actions and adverse effects. Antibiotics are frequently used in daily practice to treat and prevent a variety of medical conditions [2].

The occurrence and characteristics of adverse drug reactions (ADRs) associated with antimicrobial therapy differ according to patient demographics, prescribing practices, and regional healthcare practices. In tertiary care hospitals, where a heterogeneous patient population is treated, recognizing these ADRs is critical for optimizing antimicrobial utilization and reducing potential risks.

Timely ADR reporting through pharmacovigilance programs is critical pharmacovigilance is a concept focused on the monitoring, evaluation, and prevention of adverse effects associated with the use of pharmaceutical products.

In India, strengthening ADR reporting through the Pharmacovigilance Programme of India (PvPI) and training healthcare workers has been shown to improve both the volume and quality of reports, ultimately supporting safer antimicrobial use [3]. High-quality reporting provides real-time data for causality assessment and prevents inappropriate re-exposure, thereby reducing treatment failures, resistance selection, and mortality.

ADRs are a major global health concern, contributing significantly to morbidity and mortality and straining healthcare systems, especially in resource-limited settings [5, 6].

Vigilant monitoring in OPDs is essential for timely detection and safe antimicrobial use. Due to limited data from central India, this study retrospectively analyzes regional ADRs in a tertiary care hospital, focusing on patient demographics, infection type, dosage form, and treatment duration.

Materials and Methods

Study Site: This study was carried out in Index Medical College Hospital & Research Centre, Indore located in central India.

Study Design: This is a prospective observational study and adopted both spontaneous reporting and an active surveillance pharmacovigilance methodology. Data collection based on drugs, doses, and duration of disease. Institutional Ethics Committee approval was taken.

Study Populations

Inclusion Criteria: The study included patients of all ages experiencing ADRs of any type or severity from antimicrobial agents in both outpatient and inpatient settings.

Exclusion Criteria: Case of poisoning, anti tubercular, antileprotic and antimalarial will be excluded.

Study Procedure: Structured forms were developed to document patient information, including separate patient appraisal and data collection forms for outpatients and inpatients.

These captured demographics, diagnosis, medication history, treatment details, ADR characteristics, laboratory results, severity, onset, management, and outcomes. An ADR assessment form recorded causality, severity, predictability, preventability, and associated costs. Data were collected through spontaneous reporting and intensive monitoring, with all healthcare personnel encouraged to report ADRs. Inpatients were monitored daily, while outpatients were assessed during visits. Follow-up included patient interviews and chart reviews to detect short- and long-term ADRs using objective (e.g., labs, vitals) and subjective (e.g., headache, rash) markers, with all findings documented in the designed forms. Causality assessment was done using the WHO-UMC causality assessment scale, and severity assessment was carried out using the Naranjo Scale[6,]

Results and Observations

A prospective observational study was conducted on the prescriptions of 200 patients visiting the Index Medical College Associated Hospital, Indore.

Age-wise distribution of adverse drug reactions (ADRs)

Table 1:

Age Group	Number of ADR Cases	Percentage (%)
0 – 12	40	8.7
13 – 18	30	6.5
19 – 40	112	24.3
41 – 60	150	32.6
> 60	92	20
Total	460	

Adverse drug reactions (ADRs) were reported across all age groups, with the highest incidence observed in individuals aged 41–60 years (32.6%), followed by those aged 19–40 years (24.3%) and elderly patients above 60 years (20%). Pediatric patients (0–12 years) contributed 8.7% of ADR cases, primarily linked to antibiotic use for common infections.

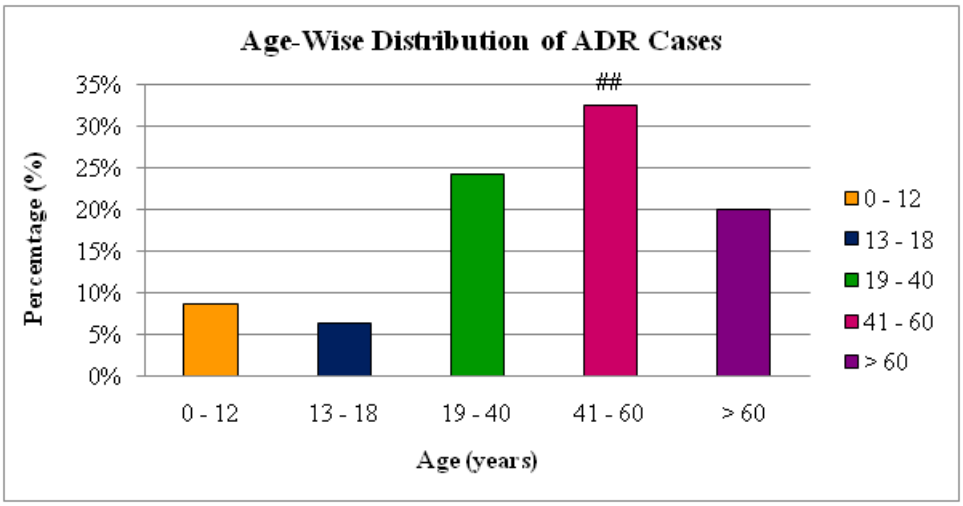

Figure 1: Age-Wise Distribution of ADR Cases

Middle-aged adults (41-60 years) had the highest ADR incidence (32.6%), likely due to long-term antibiotic use for chronic infections. Elderly patients (>60 years) experienced 20% of ADRs, often due to polypharmacy and drug interactions. Children (0-12 years) accounted for 8.7% of ADRs, mostly associated with penicillin and cephalosporins.

Gender Distribution of ADR Cases: Among 200 patients, ADR occurrence was significantly higher in males (69.5%) compared to females (30.5%).The higher prevalence of ADRs in males may be attributed to greater antibiotic usage, higher infection rates, and differences in drug metabolism.

Table 2: Gender Distribution of ADR Cases

Gender	Number of Patients	Percentage (%)
Male	139	69.5
Female	61	30.5
Total	200	

Males experienced significantly more ADRs (69.5%) than females (30.5%).The higher ADR rate in males may be due to higher antibiotic consumption and comorbidities requiring antimicrobial therapy. Females had a lower incidence but still reported significant moderate and severe ADRs.

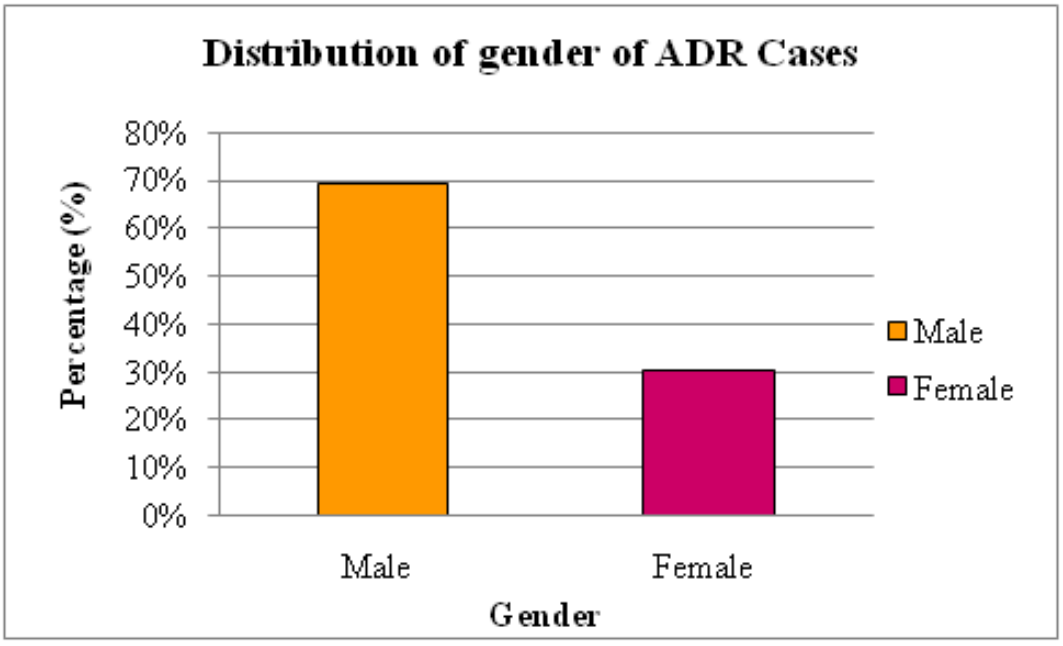

Figure 2: The distribution of gender of ADR Cases

Severity of ADRs by Gender

Table 3: Severity of ADRs by Gender

Gender	Mild ADRs (n=number)	Moderate ADRs (n=number)	Severe ADRs (n=number)	Total cases (%)
Male	185	95	40	320 (69.56)
Female	87	35	18	140(30.44)
Total	262	130	58	460

In this study, it was observed that males experienced a significantly higher number of severe adverse drug reactions (ADRs), with 40 cases reported, compared to 18 cases in females. However, when comparing both genders in cases of mild to moderate adverse drug reactions (ADRs), the frequency of ADRs was generally common, but the prevalence remained significantly higher in males.

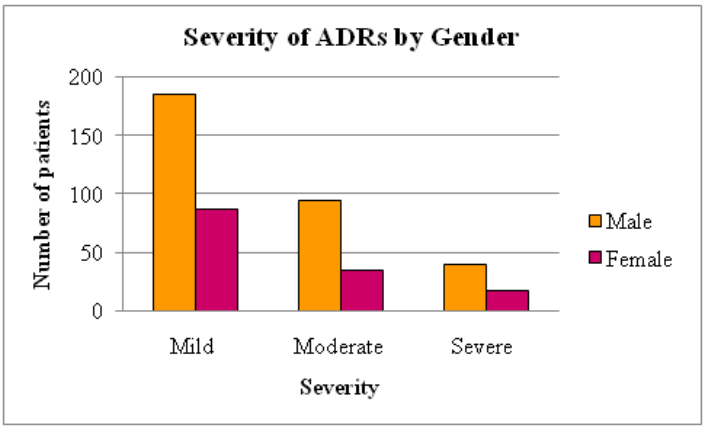

Figure 3: The distribution of gender of ADR Cases

Most Common ADR Symptoms by Antibiotic Class and Organ System Affected: Each antibiotic class was associated with specific ADR symptoms affecting different organ systems.

Among the 138 cases (30%) containing penicillin, the most prevalent adverse drug reactions (ADRs) included rash, diarrhea, and anaphylaxis, especially affecting the skin and gastrointestinal tract (GIT). Out of the 92 cases (20%) associated with cephalosporins, the most frequently reported adverse drug reactions (ADRs) included nausea, hypersensitivity, and rash, mainly impacting the gastrointestinal tract (GIT) and skin. However, fluoroquinolones, accounting for 69 cases (15%), primarily affected the gastrointestinal (GIT) and neurological systems, manifesting as nausea, seizures, and tendonitis.

Macrolides, responsible for 46 cases (10%), primarily affected the gastrointestinal (GIT) system and liver, leading to GI upset and hepatotoxicity. Similarly, aminoglycosides, also accounting for 46 cases (10%), caused adverse drug reactions (ADRs) such as nephrotoxicity and ototoxicity, impacting the renal system and central nervous system (CNS).

For other antimicrobial agents, including antibacterial drugs like sulfonamides and linezolid, a total of 69 cases (15%) were reported, affecting multiple organ systems and leading to a variety of adverse reactions.

Table 4: Most Common Symptoms by Antibiotic Class and Affected Organ System

Antibiotic Class	Common ADR Symptoms	Primary Organ System Affected	Number of Cases (%)
Penicillins	Rash, Diarrhea, Anaphylaxis	Skin, GI, Hypersensitivity	138 (30)
Cephalosporins	Nausea, Hypersensitivity, Rash	GI, Skin	92 (20)
Fluoroquinolones	Nausea, CNS Toxicity, Tendonitis	GI, Neurological	69 (15)
Macrolides	GI Upset, Hepatotoxicity	GI, Hepatic	46 (10)
Aminoglycosides	Nephrotoxicity, Ototoxicity	Renal, Neurological	46 (10)
Others	Mixed Symptoms	Multiple	69 (15)

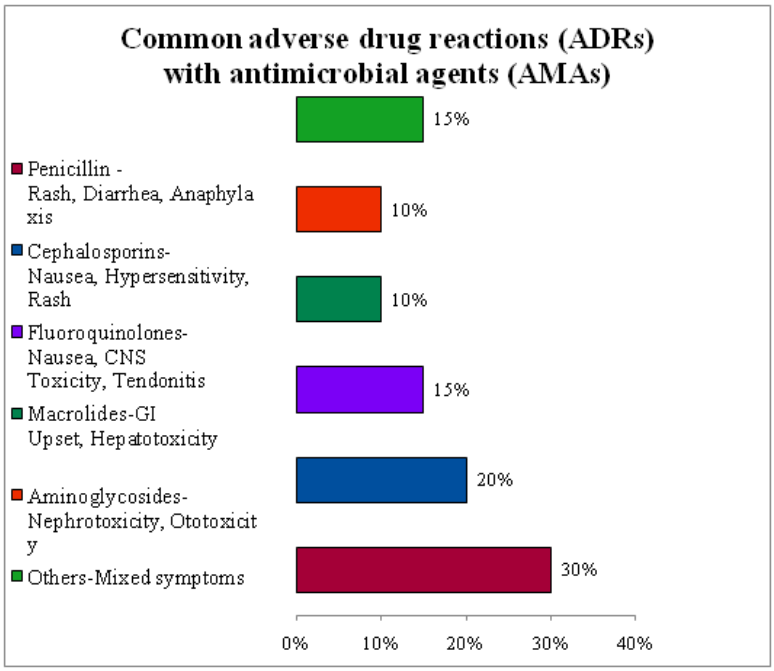

Figure 4: Common adverse drug reactions (ADRs) with antimicrobial agents (AMAs)

Causality classification of adverse drug reactions (ADRs): Antimicrobial medications, such as antibiotics, antiviral, antifungal, and antiparasitics are essential for combating infections. However, their usage is frequently linked to adverse drug reactions (ADRs), which can vary from minor side effects to serious, life-threatening complications. This report examines 460 adverse drug reactions (ADRs) identified in 200 patients, associated with 275 antimicrobial prescriptions, to assess causality, severity, and clinical outcomes. To evaluate the connection between antimicrobial drugs and ADRs, the Naranjo Algorithm, a probability-based assessment tool, was utilized.

In this report, classification was primarily conducted using the WHO-UMC scale:

- **Certain**: A clear link between the drug and ADR, supported by evidence.
- **Probable/Likely**: A strong association, but alternative causes exist.
- **Possible**: A suspected link, but other factors could contribute.
- **Unlikely**: Weak or no connection between the drug and ADR.

Table 5: Causality classification of adverse drug reactions (ADRs)

Causality Category	Number of ADRs	Percentage (%)
Certain	21	4.57
Probable/Likely	220	47.82
Possible	183	39.78
Unlikely	36	7.83

Causality assessment of adverse drug reactions (ADRs) was performed using Naranjo's algorithm, a standardized and widely accepted tool in pharmacovigilance for determining the likelihood that a specific drug caused a reported reaction. Based on the scoring criteria of this algorithm, 220 ADRs (47.82%) were categorized as probable, indicating a reasonable temporal relationship between the drug intake and the reaction, with no alternative explanation.

183 ADRs (39.78%) were classified as possible, suggesting that while the reaction could be linked to the drug, other factors might also have contributed. A smaller number, 21 ADRs (4.57%), were deemed certain, meaning the reaction had a clear and definitive causal association with the suspected drug, supported by dechallenge or rechallenge evidence.

Meanwhile, 36 ADRs (7.83%) were considered unlikely, implying that the adverse events were probably unrelated to the drug therapy. These findings emphasize the importance of systematic causality assessment in understanding drug safety and improving rational prescribing practices.

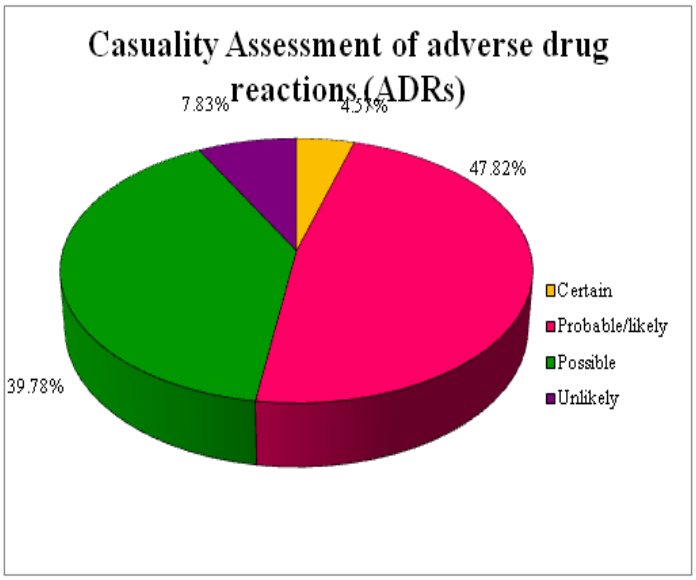

Figure 5: Causality classification of adverse drug reactions (ADRs)

Discussion

Pharmacovigilance, the systematic surveillance of adverse drug reactions (ADRs), plays a crucial role in tertiary care hospitals, especially in relation to antimicrobial agents. As referral centers, these tertiary care hospital or institutions frequently treat complex infections that require potent antimicrobials, heightening the risk of adverse drug reactions (ADRs). Establishing strong pharmacovigilance systems in these settings is essential for improving patient safety, optimizing treatment outcomes, and addressing antimicrobial resistance (AMR).

Monitoring adverse drug reactions (ADRs) is a multifaceted process influenced by various factors, including age, gender, affected organ systems, and prescription patterns. Understanding these variables is crucial for enhancing patient safety and optimizing pharmacotherapy [7].

Our findings indicate that ADR monitoring may vary based on factors such as age, gender, affected system, and prescription patterns.

According to our study findings, adverse drug reactions (ADRs) can present in multiple forms. Evidence from previous studies suggests that antimicrobial agents (AMAs) or antibiotics tend to act more rapidly in children and elderly individuals. Moreover, several studies have reported that ADRs are predominantly observed among the elderly population [8].

According to the study by A. Clavenna and M. Bonati et al. (2009), it was found that infants and very young children are particularly susceptible to adverse drug reactions (ADRs) because their drug metabolism systems are not yet fully developed [9]. However, in the current study, we observed that individuals aged 19 to 40 (24.3%) and 40 to 60 (32.6%) were more susceptible to antimicrobial agent (AMA)-related adverse drug reactions. This was primarily due to a lack of awareness and self-medication, which emerged as major contributing factors. Notably, this finding contrasts considerably with the previously mentioned studies.

Research has indicated that older adults, specifically those aged 60 and above, had a 20% incidence of developing adverse drug reactions. This was mainly attributed to poor patient compliance and polypharmacy, which were identified as key contributing factors. These findings are consistent with the observations reported by Delafuente JC et al. (2008) [8].

In the current study, a total of 460 adverse drug reactions (ADRs) were recorded, with antimicrobial agents accounting for 315 cases in males and 135 in females. The incidence was significantly higher in males, comprising 69.56% of the cases, while in females, it was 30.44%.

According to the review by Hari Singh Rathore et al. (2024) on the use of antimicrobial agents in the Indian population, adverse drug reactions were found to be more prevalent in males compared to females [10].

Park MA et al. (2007) reported that the female gender is correlated with a higher prevalence of adverse drug reactions (ADRs), with penicillin allergy being more frequently documented among adult female patients [11]. The findings of our current study contrast significantly with those of Park MA et al. (2007), as our data indicate a higher incidence of adverse drug reactions in males (69.5%) compared to females (30.5%) among a population of 200 patients [11].

In our study, penicillins (32.39%) were found to be linked with a higher frequency of adverse drug

reactions (ADRs) than cephalosporins (18.47%). However, the results reported by Dubrall D et al. (2022) were in contrast to our findings [12].

Interestingly, contradictory results were also observed in the Indian context. A retrospective study conducted over four years at PT JNM Medical College and its affiliated B.R. Ambedkar Hospital in Raipur, Chhattisgarh, showed that 54.33% of reported adverse drug reactions (ADRs) were associated with antimicrobial agents. Among these, cephalosporins accounted for 25.12% and penicillins for 18.84%. The majority of these ADRs were related to skin and subcutaneous tissue disorders (52.56%), with gastrointestinal disturbances following at 11.19% [10].

Following penicillins and cephalosporins, other antimicrobial agents (15%) such as tetracyclines and sulfonamides were also found to be associated with a higher incidence of adverse drug reactions (ADRs) in our observations.

Our observations showed that fluoroquinolones, aminoglycosides, and macrolides were responsible for adverse drug reactions (ADRs) in 13.92%, 10.87%, and 9.35% of cases, respectively. Gastrointestinal-related adverse drug reactions were observed with the use of macrolides, while kidney and ototoxicity were specifically noted with the use of aminoglycosides.

Macrolide antibiotics, including erythromycin, are frequently associated with gastrointestinal side effects. These adverse drug reactions often present as nausea, vomiting, abdominal discomfort, and diarrhea.

According to research by Periti P et al (1993), approximately 15% to 20% of patients treated with erythromycin experience gastrointestinal side effects [13].

The findings from the study by Periti P et al. (1993) are relatively consistent with the observations made in our study [13].

The distribution of causality assessment of ADRs of antimicrobial drug was done by according to Naranjo's algorithm. Antibiotics are generally used in a variety of conditions, ranging from mild to moderate infections and severe to life-threatening situations. However, in such cases, the dosage and route of administration may differ accordingly. According to our findings, the majority of cases (47.82%) were classified as 'probable/likely' based on causality assessment. This rating suggests that there was strong evidence supporting the adverse drug reactions (ADRs), although alternative causes were also identified. According to the causality assessment, 39.78% of the cases were classified under the 'Possible' category. As per the Naranjo causality scale, this classification indicates a likelihood of adverse drug reactions (ADRs), although the possibility of other contributing factors cannot be ruled out

According to the causality assessment, 7.83% of the cases were categorized as 'Unlikely'. As per the Naranjo algorithm, these adverse drug reactions (ADRs) showed little to no association with the suspected drug.

Only 4.57% of the cases were classified under the 'Certain' category according to the Naranjo algorithm. In this category, the Naranjo algorithm clearly states that the adverse drug reactions (ADRs) are directly linked to the drug, and we also found supporting evidence for this in our pharmacovigilance survey.

The current study revealed that the majority of cases fall under the 'Probable' and 'Possible' categories, and these cases or adverse drug reactions (ADRs) are generally non-preventable.

Similar findings were observed in the study by Iftikhar S et al. (2018), where a large number of cases were identified as non-preventable adverse drug reactions (ADRs) during causality assessment. These reactions were especially noted among adults and children, and the majority of them were classified under the 'Probable' and 'Possible' categories.

Among all age groups, the gastrointestinal tract was the most commonly affected organ system by antibiotic-related adverse drug events (ADEs) [14].

References

1. Novotny J, Novotny M. Adverse drug reactions to antibiotics and major antibiotic drug interactions. Gen Physiol Biophys 1999; 18:126-39.
2. Tripathi, K.D., 2007. Antimicrobial Drugs. Essentials of Medical Pharmacology, sixth ed. Jaypee Brothers, (pp. 667–682).
3. Lihite RJ, Lahkar M. An update on the Pharmacovigilance Programme of India. Front Pharmacol. 2015 Sep 22; 6:194. doi: 10.3389/fphar.2015.00194. PMID: 26441651; PMCID: PMC4585088.
4. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. Ann Pharmacother. 2008;42(7):1017-25.
5. Ramesh M, Pandit J, Parthasarathi G. Adverse drug reactions in a South Indian hospital—their severity and cost involved. Pharmacoepidemiol Drug Saf. 2003;12(8):687-92.
6. Naranjo CA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30: 239245.

7. Shamna M, Dilip C, Ajmal M, Linu Mohan P, Shinu C, Jafer CP, Mohammed Y. A prospective study on Adverse Drug Reactions of antibiotics in a tertiary care hospital. Saudi Pharm J. 2014 Sep;22(4):303-8. doi: 10.1016/j.jsps.2013.06.004. PMID: 25161373; PMCID: PMC4142362.
8. Delafuente JC. Pharmacokinetic and pharmacodynamic alterations in the geriatric patient. Consult Pharm. 2008 Apr;23(4):324-34. doi: 10.4140/tcp.n.2008.324. Erratum in: Consult Pharm. 2008 Aug;23(8):564. PMID: 18454589.
9. A Clavenna, M Bonati. Adverse drug reactions in childhood: a review of prospective studies and safety alerts. Arch Dis Child 2009; 94:724–728. doi:10.1136/adc.2008.154377.
10. Hari Singh Rathore, Mehul Soni, Bhoomi Soni, Narendra Bheemraj Parihar, Mahendra Singh Rathore, Adverse Drug Reactions Associated with Antibiotics In Indian Population: A Review, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 6, 241-252.
11. Park MA, Matesic D, Markus PJ, Li JT. Female sex as a risk factor for penicillin allergy. Ann Allergy Asthma Immunol. 2007 Jul;99(1):54-8. doi: 10.1016/S1081-1206(10)60621-7. PMID: 17650830.
12. Dubrall D, Schulz M, Schmid M, Sachs B. Descriptive analysis of adverse drug reaction reports for hypersensitivity reactions stratified in relation to different beta-lactam antibiotics. Allergol Select. 2022 Feb 3;6:42-60. doi: 10.5414/ALX02189E. PMID: 35141466; PMCID: PMC8822522.
13. Periti P, Mazzei T, Mini E, Novelli A. Adverse effects of macrolide antibacterials. Drug Saf. 1993 Nov;9(5):346-64. doi: 10.2165/00002018-199309050-00004. PMID: 8280403.
14. Iftikhar S, Sarwar MR, Saqib A, Sarfraz M. Causality and preventability assessment of adverse drug reactions and adverse drug events of antibiotics among hospitalized patients: A multicenter, cross-sectional study in Lahore, Pakistan. PLoS One. 2018 Jun 27;13(6):e0199456. doi: 10.1371/journal.pone.0199456. PMID: 29949616; PMCID: PMC6021047.