Original article

Pattern, Causality, Severity, and Preventability of Adverse Drug Reactions Reported in a Tertiary Care Teaching Hospital: A Prospective Observational Study

Dr. Balaji Patil*

Assistant Professor, Department of Pharmacology, RKDF Medical College Hospital and Research Centre, Bhopal
Corresponding author*

Abstract

Background: Adverse drug reactions are an important cause of morbidity, treatment interruption, prolonged hospital stay, and increased healthcare expenditure. Monitoring and reporting of adverse drug reactions are essential components of pharmacovigilance and rational drug use. Evaluation of pattern, causality, severity, and preventability of adverse drug reactions helps in improving patient safety and guiding clinicians toward safer prescribing.

Aim: To study the pattern, causality, severity, preventability, commonly implicated drug groups, clinical manifestations, and outcome of adverse drug reactions reported in a tertiary care teaching hospital.

Materials and Methods: A prospective observational study was conducted in the Department of Pharmacology during 2015. A total of 200 suspected adverse drug reaction reports received from various outpatient and inpatient clinical departments were analyzed. Patient demographic details, suspected drug, indication, route of administration, time of onset, clinical presentation, treatment given, outcome, and seriousness were recorded. Causality assessment was performed using WHO-UMC causality assessment scale and Naranjo adverse drug reaction probability scale. Severity was assessed using modified Hartwig and Siegel scale. Preventability was assessed using modified Schumock and Thornton criteria. Data were analyzed using descriptive statistics.

Results: Among 200 adverse drug reaction reports, females constituted 108 (54.0%) cases and males constituted 92 (46.0%) cases. The most commonly affected age group was 31–60 years. Antimicrobials were the most frequently implicated drug group, followed by non-steroidal anti-inflammatory drugs, antiepileptics, antihypertensives, antidiabetic drugs, and gastrointestinal drugs. Cutaneous reactions were the most common clinical presentation, followed by gastrointestinal, central nervous system, metabolic, and cardiovascular reactions. Most reactions were categorized as possible or probable. The majority were mild to moderate in severity. Most reactions were not preventable, while a clinically important proportion was probably preventable. Complete recovery was observed in most patients.

Conclusion: Adverse drug reactions are commonly encountered in hospital practice and require systematic monitoring. Antimicrobials and non-steroidal anti-inflammatory drugs were the commonest implicated drug groups, while cutaneous reactions were the most frequent clinical presentation. Strengthening pharmacovigilance activities, regular training of healthcare professionals, rational prescribing, and patient counseling can reduce preventable adverse drug reactions and improve medication safety.

Keywords- Adverse Drug Reaction, Causality Assessment, Pharmacology, Pharmacovigilance, Preventability, Severity Assessment.

Introduction

Adverse drug reactions are undesirable, unintended, and harmful responses to medicines occurring at doses normally used in humans for prophylaxis, diagnosis, or treatment of disease. They are an important cause of patient morbidity and are recognized as a major public health concern worldwide. Adverse drug reactions may result in discomfort, additional treatment, hospitalization, prolonged hospital stay, disability, or death.[1]

Drug safety cannot be fully established during premarketing clinical trials because such trials are usually conducted in limited numbers of selected patients under controlled conditions. Rare, delayed, chronic, dose-related, idiosyncratic, drug-interaction-related, and population-specific reactions may become apparent only after wider clinical use. Therefore, post-marketing surveillance is essential for continuous safety evaluation of medicines.[2]

Pharmacovigilance is defined as the science and activities relating to detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. It aims to improve patient safety, promote rational drug use, identify signals, support regulatory decisions, and reduce avoidable harm associated with medicines.[3]

Adverse drug reaction monitoring is important in hospitals because hospitalized patients frequently receive multiple medications and may have comorbid illnesses, altered pharmacokinetics, organ dysfunction, and increased susceptibility to drug interactions. Older adults, pregnant women, children, patients with renal or hepatic impairment, and critically ill patients are particularly vulnerable.[4]

The clinical presentation of adverse drug reactions is highly variable. Cutaneous manifestations such as rash, itching, urticaria, fixed drug eruption, photosensitivity, Stevens-Johnson syndrome, and toxic epidermal necrolysis are frequently reported. Gastrointestinal symptoms such as nausea, vomiting, diarrhea, gastritis, and abdominal pain are also common. Other adverse reactions may involve the central nervous system, cardiovascular system, respiratory system, liver, kidneys, blood, and endocrine system.[5]

Certain drug groups are more commonly associated with adverse drug reactions because of their frequency of use and pharmacological properties. Antimicrobials, non-steroidal anti-inflammatory drugs, antiepileptic drugs, antitubercular drugs, antidiabetic drugs, antihypertensives, and anticancer drugs are commonly implicated. Irrational prescribing, self-medication, polypharmacy, and incomplete drug history increase the risk of preventable reactions.[6]

Assessment of adverse drug reactions requires structured evaluation. Causality assessment determines the probability that a suspected drug caused the reaction. The WHO-UMC scale and Naranjo algorithm are commonly used tools for causality assessment. Severity assessment classifies reactions as mild, moderate, or severe according to clinical impact. Preventability assessment identifies whether the reaction could have been avoided by appropriate prescribing, monitoring, dose adjustment, or patient counseling.[7]

Spontaneous reporting is one of the most widely used methods of pharmacovigilance. However, underreporting remains a major limitation. Healthcare professionals may not report adverse drug reactions due to lack of awareness, uncertainty regarding causality, fear of legal consequences, lack of time, or misconception that only serious reactions should be reported. Continuous sensitization of doctors, nurses, pharmacists, and students is essential to improve reporting culture.

The present study was conducted to evaluate the pattern, causality, severity, preventability, implicated drug groups, clinical manifestations, and outcome of adverse drug reactions reported in a tertiary care teaching hospital.

Materials and Methods

This prospective observational study was conducted in the Department of Pharmacology during the year 2015. A total of 200 suspected adverse drug reaction reports received from various outpatient and inpatient clinical departments were included.

All suspected adverse drug reactions reported during the study period were considered for analysis. Reports from medicine, dermatology, pediatrics, surgery, orthopedics, obstetrics and gynecology, psychiatry, tuberculosis clinic, emergency department, and intensive care areas were included. Reports with adequate information regarding patient details, suspected drug, clinical reaction, time relationship, and outcome were analyzed.

Medication errors without clinical reaction, accidental poisoning, deliberate overdose, drug abuse, vaccine reactions without adequate details, reactions due to alternative medicines without proper documentation, and incomplete reports lacking essential information were excluded.

Data were collected using a structured adverse drug reaction reporting form. The form included patient age, gender, registration details, clinical department, diagnosis, suspected drug, dose, route, frequency, indication, date of drug initiation, date of reaction onset, clinical description of reaction, relevant laboratory findings, treatment given, dechallenge information, rechallenge information if available, concomitant medications, seriousness, and outcome.

The suspected drugs were grouped into pharmacological categories such as antimicrobials, non-steroidal anti-inflammatory drugs, antiepileptics, antihypertensives, antidiabetic drugs, gastrointestinal drugs, antitubercular drugs, psychotropic drugs, and others. Clinical manifestations were classified according to organ system involvement.

Causality assessment was performed using WHO-UMC causality assessment scale. Reactions were categorized as certain, probable/likely, possible, unlikely, conditional/unclassified, or unassessable. The Naranjo adverse drug reaction probability scale was also applied and reactions were categorized as definite, probable, possible, or doubtful.

Severity assessment was done using the modified Hartwig and Siegel severity assessment scale. Reactions were classified as mild, moderate, or severe. Mild reactions required no treatment or minimal treatment and did not prolong hospitalization. Moderate reactions required treatment, drug withdrawal, dose modification, or increased hospital stay. Severe reactions were life-threatening, caused permanent harm, required intensive medical care, or contributed to death.

Preventability assessment was performed using modified Schumock and Thornton criteria. Reactions were classified as definitely preventable, probably preventable, or not preventable. Factors considered included known drug allergy, inappropriate drug choice, improper dose, drug interaction, lack of monitoring, previous history of reaction, and availability of safer alternatives.

Seriousness was recorded according to whether the reaction resulted in death, life-threatening event, hospitalization, prolongation of hospitalization, disability, congenital anomaly, or required intervention to prevent permanent impairment.

Outcome was recorded as recovered, recovering, continuing, unknown, or fatal. Management of adverse drug reactions included drug withdrawal, dose reduction, symptomatic treatment, substitution with alternative drug, hospitalization, or supportive care.

Data were entered in Microsoft Excel and analyzed using descriptive statistics. Results were expressed as frequencies and percentages.

Institutional ethical approval was obtained prior to commencement of the study. Confidentiality of patient information was maintained.

Results

A total of 200 adverse drug reaction reports were analyzed during the study period.

Table 1: Demographic Characteristics of ADR Cases

Variable	Frequency (%)
Male	92 (46.0)
Female	108 (54.0)
Age ≤18 years	22 (11.0)
Age 19–30 years	44 (22.0)
Age 31–60 years	96 (48.0)
Age >60 years	38 (19.0)

Female patients constituted 108 (54.0%) cases, while male patients constituted 92 (46.0%) cases. The most commonly affected age group was 31–60 years, accounting for 96 (48.0%) adverse drug reactions. Elderly patients above 60 years constituted 38 (19.0%) cases.

Table 2: Commonly Implicated Drug Groups

Drug Group	Frequency (%)
Antimicrobials	68 (34.0)
NSAIDs	38 (19.0)
Antiepileptics	24 (12.0)
Antihypertensives	18 (9.0)
Antidiabetic drugs	16 (8.0)
Antitubercular drugs	12 (6.0)
Gastrointestinal drugs	10 (5.0)
Others	14 (7.0)

Antimicrobials were the most commonly implicated drug group, accounting for 68 (34.0%) cases. Non-steroidal anti-inflammatory drugs were responsible for 38 (19.0%) cases. Antiepileptics, antihypertensives, antidiabetic drugs, and antitubercular drugs were also important contributors.

Table 3: Clinical Pattern of ADRs

Organ System/Clinical Pattern	Frequency (%)
Cutaneous reactions	82 (41.0)
Gastrointestinal reactions	46 (23.0)
Central nervous system reactions	26 (13.0)
Metabolic/endocrine reactions	14 (7.0)

Cardiovascular reactions	12 (6.0)
Hepatic reactions	8 (4.0)
Respiratory reactions	6 (3.0)
Others	6 (3.0)

Cutaneous reactions were the most common clinical presentation, observed in 82 (41.0%) cases. Gastrointestinal reactions were reported in 46 (23.0%) cases, followed by central nervous system reactions in 26 (13.0%) cases. Cutaneous reactions included rash, pruritus, urticaria, fixed drug eruption, and maculopapular eruption.

Table 4: Causality Assessment Using WHO-UMC Scale

Causality Category	Frequency (%)
Certain	6 (3.0)
Probable/Likely	88 (44.0)
Possible	98 (49.0)
Unlikely	6 (3.0)
Conditional/Unclassified	2 (1.0)

Most reactions were categorized as possible or probable. Possible reactions accounted for 98 (49.0%) cases, while probable reactions accounted for 88 (44.0%) cases. Certain causality was assigned in only 6 (3.0%) cases because rechallenge was rarely performed.

Table 5: Naranjo Causality Assessment

Naranjo Category	Frequency (%)
Definite	4 (2.0)
Probable	92 (46.0)
Possible	98 (49.0)
Doubtful	6 (3.0)

According to Naranjo assessment, most reactions were classified as possible or probable. Definite adverse drug reactions were uncommon because intentional rechallenge was avoided for patient safety.

Table 6: Severity Assessment

Severity	Frequency (%)
Mild	108 (54.0)
Moderate	78 (39.0)
Severe	14 (7.0)

Most adverse drug reactions were mild, accounting for 108 (54.0%) cases. Moderate reactions were observed in 78 (39.0%) cases. Severe reactions were reported in 14 (7.0%) cases and required urgent intervention or hospitalization.

Table 7: Preventability Assessment

Preventability Category	Frequency (%)
Definitely preventable	10 (5.0)
Probably preventable	42 (21.0)
Not preventable	148 (74.0)

Most adverse drug reactions were not preventable. However, 52 (26.0%) reactions were definitely or probably preventable, indicating the need for better drug history, monitoring, and rational prescribing.

Table 8: Outcome of ADRs

Outcome	Frequency (%)
Recovered	132 (66.0)
Recovering	44 (22.0)
Continuing	14 (7.0)
Unknown	10 (5.0)
Fatal	0 (0.0)

Most patients recovered completely after withdrawal of the suspected drug or appropriate management. No fatal reaction was reported during the study period.

Discussion

The present prospective observational study evaluated the pattern, causality, severity, preventability, and outcome of adverse drug reactions reported in a tertiary care teaching hospital. A total of 200 adverse drug reaction reports were analyzed. Females constituted a slightly higher proportion of cases, and the 31–60 years age group was most commonly affected. Antimicrobials and NSAIDs were the most common implicated drug groups. Cutaneous reactions were the most frequent clinical presentation.

Lazarou et al. reported that adverse drug reactions are an important cause of morbidity and mortality among hospitalized patients.[8] The present study also supports the clinical importance of ADR monitoring because many patients required drug withdrawal, symptomatic treatment, or change in therapy.

Pirmohamed et al. studied adverse drug reactions as a cause of hospital admission and observed that ADRs contribute significantly to healthcare burden.[9] In the present study, although fatal reactions were not reported, moderate and severe reactions together accounted for 46.0% cases, indicating that ADRs have meaningful clinical impact.

Edwards and Aronson emphasized the importance of clear definition, diagnosis, and management of adverse drug reactions.[10] The present study used structured reporting and standardized causality, severity, and preventability tools to improve reliability of assessment.

Davies et al. reported that hospitalized patients are at risk of ADRs due to polypharmacy, comorbidities, and complex treatment regimens.[11] The present study included reports from both outpatient and inpatient departments and showed that multiple drug groups were involved.

Arulmani et al. studied adverse drug reaction monitoring in a secondary care hospital in South India and reported that cutaneous reactions were among the most common clinical patterns.[12] The present study similarly found cutaneous reactions to be the most frequent presentation.

Ramesh et al. evaluated adverse drug reactions in a South Indian hospital and reported that antimicrobials and NSAIDs were commonly implicated.[13] The present study showed a comparable pattern, with antimicrobials accounting for 34.0% and NSAIDs for 19.0% ADRs.

Sriram et al. reported that antimicrobial agents are frequent causes of adverse drug reactions in tertiary care settings.[14] In the present study, antimicrobials were the leading drug group responsible for ADRs, reflecting their high prescription frequency and potential for hypersensitivity reactions.

Antimicrobials were the most frequently implicated drugs in the present study. This may be due to their wide use across clinical departments. Common reactions included rash, urticaria, gastrointestinal upset, and hypersensitivity reactions. Rational antibiotic prescribing and documentation of previous allergy can reduce avoidable reactions.

NSAIDs were the second most common group. These drugs are frequently used for pain, fever, and inflammation. Gastritis, abdominal pain, skin rash, urticaria, edema, and renal-related effects may occur. Unsupervised use of NSAIDs should be discouraged, particularly among elderly patients and those with renal disease or peptic ulcer history. Antiepileptic drugs accounted for 12.0% of reactions. Common adverse effects included sedation, dizziness, rash, and hypersensitivity. Serious cutaneous adverse reactions, though uncommon, require early recognition and immediate drug withdrawal. Patients should be counseled to report rash or fever during early therapy. Antihypertensive drugs and antidiabetic drugs were also implicated. Dizziness, hypotension, cough, edema, hypoglycemia, and metabolic disturbances are commonly encountered. Regular monitoring and patient counseling are important, particularly in elderly patients and those receiving multiple medications.

Cutaneous reactions were the commonest organ system involved. Skin reactions are easily visible and therefore more likely to be reported. However, mild rashes should still be documented because repeat exposure may lead to more severe hypersensitivity in some patients. Gastrointestinal reactions were the second most common group. Nausea, vomiting, diarrhea, gastritis, and abdominal pain may reduce compliance and lead to discontinuation of therapy. Taking medicines with food where appropriate and avoiding unnecessary polypharmacy can reduce such reactions.

Shamna et al. conducted a prospective study on antibiotic-related adverse drug reactions and observed that skin and gastrointestinal manifestations were common.[15] The present study also observed that cutaneous and gastrointestinal reactions formed the majority of presentations.

Most reactions were categorized as possible or probable by causality assessment. Certain causality was uncommon because rechallenge is rarely ethical or safe, especially in hypersensitivity reactions. This is a common limitation in routine pharmacovigilance.

Severity assessment showed that the majority of reactions were mild or moderate. Mild reactions required reassurance or symptomatic care, while moderate reactions required drug withdrawal or additional treatment. Severe reactions, though fewer, required urgent attention.

Preventability assessment showed that 26.0% reactions were definitely or probably preventable. Preventable reactions may be reduced by checking previous allergy, avoiding irrational combinations, adjusting dose according to renal or hepatic function, monitoring high-risk drugs, and educating patients. The absence of fatal reactions is reassuring. However, this does not reduce the importance of pharmacovigilance because serious and rare reactions may be missed unless active reporting systems are maintained.

The present study highlights the need for sensitizing healthcare workers regarding ADR reporting. Nurses, pharmacists, interns, residents, and consultants should be encouraged to report even suspected reactions. Reporting should not wait for complete proof of causality.

The present study has certain limitations. It was a single-center study, and underreporting cannot be excluded. Laboratory confirmation was not possible for all reactions. Long-term follow-up was limited. The study did not

calculate incidence because total drug exposure was not available. Future studies with active surveillance and electronic reporting may provide more comprehensive data.

Conclusion

Adverse drug reactions are an important cause of morbidity in hospital practice. In the present study, antimicrobials and NSAIDs were the most frequently implicated drug groups, and cutaneous reactions were the most common clinical presentation. Most reactions were possible or probable in causality and mild to moderate in severity. A clinically significant proportion of reactions was preventable. Strengthening pharmacovigilance systems, regular training of healthcare professionals, rational prescribing, careful medication history, patient counseling, and periodic ADR analysis are essential to improve medication safety and reduce preventable harm.

References

1. World Health Organization. International drug monitoring: the role of national centres. World Health Organ Tech Rep Ser. 1972;498:1-25.
2. World Health Organization. The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products. Geneva: World Health Organization; 2002.
3. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356(9237):1255-1259.
4. Rawlins MD, Thompson JW. Mechanisms of adverse drug reactions. In: Davies DM, editor. Textbook of Adverse Drug Reactions. 4th ed. Oxford: Oxford University Press; 1991.
5. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-245.
6. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-2232.
7. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27(6):538.
8. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients. JAMA. 1998;279(15):1200-1205.
9. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reactions as cause of admission to hospital. BMJ. 2004;329(7456):15-19.
10. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356(9237):1255-1259.
11. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients. PLoS One. 2009;4(2):e4439.
12. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol. 2008;65(2):210-216.
13. 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):687-692.

14. Sriram S, Ghasemi A, Ramasamy R, Devi M, Balasubramanian R, Ravi TK, et al. Prevalence of adverse drug reactions at a private tertiary care hospital in South India. J Res Med Sci. 2011;16(1):16-25.
15. Shamna M, Dilip C, Ajmal M, Mohan PL, Shinu C, Jafer CP, et al. A prospective study on adverse drug reactions of antibiotics in a tertiary care hospital. Saudi Pharm J. 2014;22(4):303-308.