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(11); 1910-1914

Review Article

Adverse Drug Reactions: An Overview

Dinesh[1], P. Balaji[2], Vidya Lakshmi[3], Nitish R. Jayaharan[4]

[1]MBBS, MPH, MRCPs, MBA, Medical Manager, SRM Institute of Medical Sciences
[2]MS, PhD, FRCS, FCLS, Director, Department of General Surgery and Minimal Invasive Surgery, SRM Institute of Medical Sciences
[3]MS, Consultant, Department of General Surgery and Minimal Invasive Surgery, SRM Institute of Medical Sciences
[4]MBBS, Junior Resident, Department of General Surgery and Minimal Invasive Surgery, SRM Institute of Medical Sciences

Received: 01-10-2025 / Revised: 25-10-2025 / Accepted: 15-11-2025
Corresponding Author: Dr. Dinesh
Conflict of interest: Nil

Abstract

Adverse drug reactions (ADRs) are unintended, harmful, and noxious responses to medications administered at normal therapeutic doses. ADRs remain a major global public health concern and are associated with increased morbidity, mortality, prolonged hospitalization, and rising healthcare costs. They are particularly common in general medicine departments due to polypharmacy, multiple comorbidities, advanced age, and prolonged drug exposure. According to the World Health Organization (WHO), ADRs are among the leading causes of hospitalization and are responsible for a significant proportion of preventable medical complications worldwide. Antibiotics, anticoagulants, antiepileptics, antidiabetic agents, and cardiovascular drugs are among the medications most frequently implicated.

Pharmacovigilance plays a central role in the detection, assessment, understanding, and prevention of ADRs. The increasing introduction of newer therapeutic agents and expanding use of combination therapies have emphasized the need for effective ADR monitoring systems. ADRs are broadly classified into predictable dose-dependent reactions (Type A) and unpredictable idiosyncratic or immunological reactions (Type B), with additional classifications including chronic, delayed, withdrawal-related, and therapeutic failure reactions.

This review highlights the epidemiology, classification, mechanisms, risk factors, clinical manifestations, reporting systems, and management strategies of ADRs. Particular emphasis is placed on the importance of pharmacovigilance programs, rational prescribing practices, early identification, and multidisciplinary collaboration in minimizing drug-related harm and improving patient safety outcomes.

Keywords: Adverse drug reactions, Pharmacovigilance, Drug safety, Polypharmacy, Hypersensitivity reactions, Drug toxicity, Medication safety, ADR reporting, Pharmacogenomics, Patient safety.

Introduction

Adverse drug reactions (ADRs) constitute a major challenge in modern clinical practice and significantly influence patient safety, therapeutic outcomes, and healthcare expenditure. The World Health Organization (WHO) defines an ADR as "a response to a drug that is noxious, unintended, and occurs at doses normally used in humans for prophylaxis, diagnosis, therapy, or modification of physiological function."[1,6]

In contrast, an adverse drug event (ADE) refers to any undesirable medical occurrence during treatment with a pharmaceutical product, irrespective of whether a causal relationship with the drug has been established. Therefore, all ADRs are considered ADEs, but not all ADEs qualify as ADRs. Globally, ADRs are recognized as one of the leading causes of morbidity and mortality. Studies estimate that ADRs account for approximately 5–10% of hospital admissions and occur in nearly 10–20% of hospitalized patients.[5] Severe ADRs may result in prolonged hospitalization, permanent disability, intensive care admission, or death. Elderly patients are particularly vulnerable because of altered pharmacokinetics, polypharmacy, reduced physiological reserve, and the presence of multiple comorbidities.

Pharmacovigilance is the science and activity concerned with the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems.[6] The importance of pharmacovigilance increased substantially following drug-related disasters such as thalidomide-induced congenital malformations. In India, organized pharmacovigilance activities began

in 1998 through participation in the WHO Programme for International Drug Monitoring coordinated by the Uppsala Monitoring Centre. Subsequently, the Pharmacovigilance Programme of India (PvPI) was established to strengthen ADR monitoring and reporting nationwide.

The growing availability of newer drugs, biologics, vaccines, and combination therapies has further highlighted the need for robust post-marketing surveillance systems. Pre-marketing clinical trials often involve limited patient populations and controlled conditions, which may fail to identify rare, delayed, or population-specific adverse effects. Consequently, continuous post-marketing pharmacovigilance remains essential for ensuring drug safety in real-world clinical settings.

ADRs are commonly categorized into six major types (A–F).[1] Type A reactions are dose-dependent, predictable, and related to the known pharmacological actions of the drug, whereas Type B reactions are bizarre, unpredictable, and often immunologically mediated. Types C to F include chronic, delayed, end-of-use, and therapeutic failure-related reactions. The Dose-Time-Susceptibility (DoTS) classification further enhances understanding by incorporating dose relationships, timing of occurrence, and patient susceptibility factors.

Several risk factors contribute to ADR development, including advanced age, female gender, renal or hepatic impairment, polypharmacy, genetic predisposition, drug interactions, irrational prescribing, and medication errors. Drugs frequently associated with ADRs include antibiotics, anticoagulants, nonsteroidal anti-inflammatory drugs (NSAIDs), antiepileptics, antipsychotics, and antineoplastic agents. Effective ADR management requires prompt recognition, withdrawal or dose adjustment of the offending drug, supportive care, and appropriate documentation.[1] Standardized causality assessment tools such as the WHO-UMC scale and Naranjo algorithm are commonly used to evaluate the relationship between a drug and the adverse event. Severity assessment scales, including the Hartwig and Siegel scale, aid in determining the clinical impact of ADRs. Healthcare professionals play a pivotal role in ADR reporting and prevention. Spontaneous reporting systems, cohort studies, case-control studies, electronic health records, and active surveillance programs contribute significantly to pharmacovigilance databases and regulatory decision-making.[13–15] Strengthening awareness among clinicians, pharmacists, nurses, and patients remains critical for improving ADR reporting rates and promoting rational drug use.

Classification of Adverse Drug Reactions

Type A (Augmented) Reactions: Type A reactions are predictable, dose-dependent, and related to the known pharmacological action of the drug. They account for nearly 80–90% of all ADRs and are generally preventable.[1]

Drug Overdose: Drug overdose occurs when excessive quantities of a medication are administered intentionally or unintentionally. Examples include acetaminophen-induced hepatotoxicity, warfarin-associated bleeding, and opioid-induced respiratory depression.

Side Effects: Side effects are secondary pharmacological effects that occur at therapeutic doses. Examples include NSAID-induced gastritis, aminoglycoside-associated nephrotoxicity, and antibiotic-associated diarrhea.

Drug Interactions: Drug interactions occur when one drug alters the effect of another medication, food, or disease condition. Examples include enhanced theophylline toxicity with macrolide antibiotics and increased bleeding risk when warfarin is combined with antiplatelet agents.

Type B (Bizarre) Reactions : Type B reactions are unpredictable, uncommon, and not related to the known pharmacological action of the drug.[1]

Hypersensitivity Reactions

Type I Hypersensitivity: IgE-mediated immediate reactions causing urticaria, angioedema, bronchospasm, and anaphylaxis. Common causative drugs include beta-lactam antibiotics and platinum-based chemotherapeutic agents.[3,7,9,10]

Type II Hypersensitivity: Cytotoxic antibody-mediated reactions causing hemolytic anemia, thrombocytopenia, and neutropenia.

Type III Hypersensitivity: Immune complex-mediated reactions such as serum sickness and vasculitis.

Type IV Hypersensitivity: T-cell mediated delayed hypersensitivity reactions including Stevens–Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN), DRESS syndrome, and contact dermatitis.[8,11,12]

Idiosyncratic Reactions: These reactions occur because of genetic or metabolic abnormalities. Examples include hemolysis with dapsone in patients with glucose-6-phosphate dehydrogenase deficiency. Genetic susceptibility reactions such as abacavir hypersensitivity associated with HLA-B*5701 have also been documented.[4]

Pseudoallergic Reactions: Pseudoallergic reactions clinically resemble allergic reactions but occur through non-immunologic mast cell activation. Vancomycin flushing syndrome is a classic example.

Typer C (Chronic) Reactions: Type C reactions are dose- related and time related adverse effects that

occur due to prolonged use of a medication. These reactions develop gradually during long-term therapy and are often associated with cumulative drug exposure. Examples include corticosteroid induced osteoporosis, analgesic nephropathy due to chronic NSAID use and tardive dyskinesia associated with long term antipsychotic therapy. These reactions may significantly affect quality of life and often require regular monitoring during extended treatment period.

Type D (Delayed) Reactions: Type D reactions are delayed adverse effects that become apparent after a considerable period following drug exposure, sometimes even after discontinuation of therapy. They are uncommon but may have serious long-term consequences. Examples include teratogenicity caused by thalidomide, secondary malignancies following chemotherapy or radiotherapy and carcinogenic effects associated with certain immunosuppressive agents. Because of their delayed onset, these reactions are often difficult to identify during pre-marketing clinical trials.

Typer E (End of use) Reactions: Typer E reactions occur following the sudden withdrawal or discontinuation of a drug, particularly after prolonged use. These reactions are commonly referred to as withdrawal or rebound phenomena. Examples include adrenal insufficiency after abrupt cessation of corticosteroids, rebound hypertension following sudden discontinuation of clonidine and opioid withdrawal syndrome after stopping long-term opioid therapy. Gradual tapering of medications is often necessary to prevent such reactions.

Type F (Failure of Therapy) Reactions: Typer F reactions refer to unexpected failure of a drug to produce the intended therapeutic effect. These reactions may result from drug interactions, antimicrobial resistance, incorrect dosing, poor patient adherence or genetic variations affecting drug metabolism. Examples include failure of oral contraceptives due to interaction with enzyme inducing antiepileptic drugs and antibiotic treatment failure caused by resistant microorganisms. Type F reactions may lead to disease progression and increased healthcare burden if not recognised promptly.

Risk Factors for ADRs: Multiple patient-related, drug-related, and healthcare-related factors contribute to the development of adverse drug reactions (ADRs). Advanced age is one of the most significant risk factors because physiological changes associated with aging alter drug absorption, distribution, metabolism, and excretion, thereby increasing susceptibility to toxicity. Elderly patients frequently suffer from multiple chronic illnesses such as hypertension, diabetes mellitus, chronic kidney disease, and cardiovascular disorders, necessitating the use of numerous medications simultaneously. Polypharmacy significantly increases the likelihood of drug interactions, cumulative toxicity, and medication errors.[5] Renal and hepatic dysfunction further predispose patients to ADRs because impaired elimination and metabolism may result in drug accumulation within the body. Female patients have also been reported to experience ADRs more frequently than males, possibly because of hormonal influences, differences in body composition, and pharmacokinetic variations. Genetic polymorphisms affecting drug-metabolizing enzymes, transport proteins, and receptors may alter drug responses and contribute to idiosyncratic reactions.[4] Additional contributing factors include irrational prescribing practices, inappropriate self-medication, prolonged duration of therapy, previous history of drug allergies, poor medication adherence, and inadequate monitoring during treatment. Hospitalized patients are particularly vulnerable because of the severity of illness, exposure to high-risk medications, and frequent therapeutic modifications.

Management of ADRs: The management of adverse drug reactions primarily depends on the severity of the reaction, the suspected causative agent, and the patient's overall clinical condition. Early recognition and prompt intervention are essential to prevent progression to serious complications. In most cases, the first step involves discontinuation of the offending drug or reduction of its dosage if continuation is necessary.[1] Alternative medications with safer profiles may be substituted whenever appropriate. Supportive and symptomatic treatment forms the cornerstone of management and may include intravenous fluids, antihistamines, corticosteroids, bronchodilators, or vasopressors depending on the nature and severity of the reaction.[7,10]

Severe life-threatening reactions such as anaphylaxis require immediate emergency management with intramuscular adrenaline and intensive monitoring.[7] In cases of drug toxicity or overdose, specific antidotes may be administered when available, such as N-acetylcysteine for acetaminophen poisoning or vitamin K for warfarin toxicity. Severe cutaneous adverse reactions including SJS, TEN, and DRESS syndrome often require hospitalization, withdrawal of the offending drug, intensive supportive care, and immunomodulatory therapy.[11,12]

Continuous monitoring of vital signs, renal function, hepatic parameters, and hematological indices is important during recovery. Proper documentation of ADRs in patient records and communication to the patient regarding future drug avoidance are critical preventive measures. Reporting ADRs to pharmacovigilance centers through standardized

reporting systems contributes to drug safety surveillance and helps identify emerging safety signals.[6] Preventive strategies such as rational prescribing, therapeutic drug monitoring, electronic prescribing systems, computerized surveillance, medication reconciliation, and regular healthcare professional training play a vital role in minimizing the incidence of ADRs and improving patient safety.[13–15].

Conclusion

Adverse drug reactions continue to represent a major burden on healthcare systems worldwide and remain an important cause of preventable morbidity and mortality. In general medicine departments, where patients frequently receive multiple medications for chronic illnesses and complex medical conditions, the risk of ADRs is particularly high. Elderly individuals and patients with comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, and cardiovascular disorders are especially vulnerable because of altered drug metabolism and increased exposure to polypharmacy. The present review emphasizes that antibiotics, anticoagulants, anticonvulsants, NSAIDs, and gastrointestinal medications are among the most commonly implicated drug groups. Although many ADRs are mild to moderate in severity, a substantial proportion may lead to prolonged hospitalization, increased healthcare costs, reduced quality of life, permanent disability, or even death if not recognized promptly.[5] Early identification and timely management of ADRs are essential to reduce complications and improve clinical outcomes. The use of validated causality assessment tools, severity grading scales, and standardized reporting systems significantly enhances the accuracy of ADR evaluation and facilitates evidence-based clinical decision-making. Strengthening pharmacovigilance practices within hospitals and healthcare institutions is crucial for improving medication safety. Underreporting remains one of the major barriers to effective pharmacovigilance, particularly in developing countries. Increasing awareness and training among healthcare professionals regarding ADR recognition and reporting can substantially improve surveillance systems. Active participation from physicians, pharmacists, nurses, and patients is essential for developing a strong culture of medication safety.

Advances in pharmacogenomics, electronic prescribing systems, artificial intelligence–based signal detection, and real-time surveillance technologies may further improve ADR prediction and prevention in the future.[13–15] Personalized medicine approaches have the potential to reduce drug toxicity by tailoring therapy according to individual genetic profiles and susceptibility factors. Ultimately, ADR monitoring should not be viewed merely as a regulatory requirement but as an integral component of quality healthcare delivery. Continuous pharmacovigilance, rational prescribing, patient education, and interdisciplinary collaboration remain fundamental in minimizing drug-related harm and ensuring safer therapeutic practices for patients worldwide.

Reference

1. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000 Oct 7;356(9237):1255-9. doi: 10.1016/S0140-6736(00)02799-9. PMID: 11072960.
2. Wang JG, Wang N. The present situation and management measures of adverse drug reactions in China. In: Hee T, Liu J, editors. Advances in Social Science Education and Humanities Research. Atlantis Press; 2016. pp. 311–314.
3. Faria E, Rodrigues-Cernadas J, Gaspar A, et al. Drug-induced anaphylaxis survey in Portuguese Allergy Departments. J. Investig. Allergol. Clin. Immunol. 2014;24(1):40–48.
4. Mallal S, Phillips E, Carosi G, et al. HLA-B*5701 screening for hypersensitivity to abacavir. N. Engl. J. Med. 2008;358(6):568–579. doi: 10.1056/NEJMoa0706135.
5. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. JAMA. 1998;279(15):1200–1205. doi: 10.1001/jama.279.15.1200.
6. World Health Organization. The importance of pharmacovigilance: safety monitoring of medicinal products. Geneva: WHO. 2002.
7. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Greenhawt M, Khan DA, Lang DM, Lang ES, Lieberman JA, Portnoy J, Rank MA, Stukus DR, Wang J, Collaborators. Riblet N, Bobrownicki AMP, Bontrager T, Dusin J, Foley J, Frederick B, Fregene E, Hellerstedt S, Hassan F, Hess K, Horner C, Huntington K, Kasireddy P, Keeler D, Kim B, Lieberman P, Lindhorst E, McEnany F, Milbank J, Murphy H, Pando O, Patel AK, Ratliff N, Rhodes R, Robertson K, Scott H, Snell A, Sullivan R, Trivedi V, Wickham A, Chief Editors. Shaker MS, Wallace DV, Workgroup Contributors. Shaker MS, Wallace DV, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Golden DBK, Greenhawt M, Lieberman JA, Rank MA, Stukus DR, Wang J, Joint Task Force on Practice Parameters Reviewers. Shaker MS, Wallace DV, Golden DBK, Bernstein JA, Dinakar C, Ellis A, Greenhawt M, Horner C, Khan DA, Lieberman

JA, Oppenheimer J, Rank MA, Shaker MS, Stukus DR, Wang J. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Rekommandation, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol. 2020 Apr;145(4):1082-1123.

8. Roujeau JC, Bioulac-Sage P, Bourseau C, Guillaume JC, Bernard P, Lok C, Plantin P, Claudy A, Delavierre C, Vaillant L. Acute generalized exanthematous pustulosis. Analysis of 63 cases. Arch Dermatol. 1991 Sep;127(9):1333-8.
9. Schwartz LB, Metcalfe DD, Miller JS, Earl H, Sullivan T. Tryptase levels as an indicator of mast-cell activation in systemic anaphylaxis and mastocytosis. N Engl J Med. 1987 Jun 25;316(26):1622-6.
10. Grattan C, Powell S, Humphreys F., British Association of Dermatologists. Management and diagnostic guidelines for urticaria and angio-oedema. Br J Dermatol. 2001 Apr;144(4):708-14
11. Wang CW, Yang LY, Chen CB, Ho HC, Hung SI, Yang CH, Chang CJ, Su SC, Hui RC, Chin SW, Huang LF, Lin YY, Chang WY, Fan WL, Yang CY, Ho JC, Chang YC, Lu CW, Chung WH., the Taiwan Severe Cutaneous Adverse Reaction (TSCAR) Consortium. Randomized, controlled trial of TNF-α antagonist in CTL-mediated severe cutaneous adverse reactions. J Clin Invest. 2018 Mar 01;128(3):985-996.
12. Funck-Brentano E, Duong TA, Bouvresse S, Bagot M, Wolkenstein P, Roujeau JC, Chosidow O, Valeyrie-Allanore L. Therapeutic management of DRESS: a retrospective study of 38 cases. J Am Acad Dermatol. 2015 Feb;72(2):246-52.
13. Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. JAMA. 1991 Nov 27;266(20):2847-51.
14. Hurdle JF, Weir CR, Roth B, Hoffman J, Nebeker JR. Critical gaps in the world's largest electronic medical record: Ad Hoc nursing narratives and invisible adverse drug events. AMIA Annu Symp Proc. 2003; 2003:309-12.
15. Evans RS, Pestotnik SL, Classen DC, Bass SB, Burke JP. Prevention of adverse drug events through computerized surveillance. Proc Annu Symp Comput Appl Med Care. 1992:437-41.