Review Article

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ADVERSE DRUG REACTIONS: A COMPREHENSIVE REVIEW

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ABSTRACT
Adverse drug reactions (ADRs) represent a major challenge in clinical practice and public health worldwide. They contribute significantly to patient morbidity, mortality, prolonged hospitalization, and increased healthcare costs. An ADR is defined by the World Health Organization (WHO) as a response to a medicinal product that is noxious and unintended and occurs at doses normally used in humans for prophylaxis, diagnosis, therapy, or modification of physiological function. ADRs may be predictable and dose-dependent (Type A) or unpredictable and unrelated to dose (Type B), with further modern classifications expanding to Types C, D, E, and F. Risk factors include patient-related variables (age, genetics, comorbidities), drug-related factors (polypharmacy, narrow therapeutic index), and system-related issues (medication errors, lack of monitoring). Pharmacovigilance systems play a pivotal role in detection, assessment, understanding, and prevention of ADRs. This review discusses definitions, classification, epidemiology, mechanisms, risk factors, diagnosis, prevention strategies, and reporting systems, emphasizing their clinical and regulatory importance.

Keywords: *Adverse drug reactions; Pharmacovigilance; Drug safety; Type A reactions; Drug hypersensitivity; Medication errors; Polypharmacy.*

INTRODUCTION
Medicinal products have transformed healthcare, yet their use is not without risk. Adverse drug reactions (ADRs) are among the leading causes of morbidity and mortality globally [1-2]. Studies suggest that ADRs account for approximately 5–10% of hospital admissions and occur in 10–20% of hospitalized patients [3]. With increasing polypharmacy, aging populations, and expanded therapeutic options, ADR monitoring has become a priority in modern medicine. The science of pharmacovigilance, strongly supported by the Uppsala Monitoring Centre, coordinates global ADR reporting and safety monitoring [4].

DEFINITION AND TERMINOLOGY
The WHO defines an ADR as a harmful and unintended response to a drug occurring at normal doses [1]. This definition excludes overdose, drug abuse, and therapeutic failures.
It is important to distinguish ADRs from:

- **Adverse drug events (ADEs):** Any injury related to drug use, including medication errors.
- **Side effects:** Expected pharmacological effects that may be undesirable.
- **Drug toxicity:** Dose-related harmful effects.

CLASSIFICATION OF ADRS
1. Rawlins and Thompson Classification
Type A (Augmented)

- Dose-dependent
- Predictable from pharmacology
- Common (e.g., hypoglycemia with insulin)

Type B (Bizarre)

- Dose-independent
- Unpredictable
- Often immune-mediated (e.g., anaphylaxis with penicillin)

2. Extended Classification

- **Type C (Chronic):** Dose- and time-related (e.g., adrenal suppression with corticosteroids)
- **Type D (Delayed):** Time-related (e.g., teratogenicity)
- **Type E (End-of-use):** Withdrawal reactions
- **Type F (Failure):** Unexpected therapeutic failure

EPIDEMIOLOGY
ADRs are a significant cause of hospital admissions and in-hospital complications. A meta-analysis reported serious ADRs in 6.7% of hospitalized patients, with fatal reactions in 0.32% [5]. The burden is higher in elderly populations due to comorbidities and polypharmacy.
High-risk drug classes include:

- Anticoagulants
- Antidiabetics
- Antibiotics
- Antineoplastics
- Cardiovascular drugs

PATHOPHYSIOLOGY AND MECHANISMS

Pharmacological Mechanisms

- Exaggerated therapeutic effects
- Secondary pharmacological effects
- Drug–drug interactions

Immunological Mechanisms

- Type I (IgE-mediated) hypersensitivity
- Type II cytotoxic reactions
- Type III immune complex reactions
- Type IV delayed hypersensitivity

Genetic Predisposition

Pharmacogenomic variations influence susceptibility. For example, HLA-B*1502 is associated with carbamazepine-induced Stevens–Johnson syndrome in certain populations [6].

RISK FACTORS

Patient-related

- Extremes of age
- Female gender
- Renal/hepatic impairment
- Genetic polymorphisms
- History of allergy

Drug-related

- Polypharmacy
- Narrow therapeutic index drugs
- Long duration of therapy
- Parenteral administration

Disease-related

- Multiple comorbidities
- Impaired organ function

CLINICAL MANIFESTATIONS

ADRs may affect any organ system:

- **Cutaneous:** Rash, urticaria, Stevens–Johnson syndrome
- **Gastrointestinal:** Nausea, hepatotoxicity
- **Hematological:** Agranulocytosis
- **Cardiovascular:** QT prolongation
- **Respiratory:** Bronchospasm

Severe cutaneous ADRs such as Stevens–Johnson syndrome and toxic epidermal necrolysis are life-threatening emergencies.

DIAGNOSIS OF ADRS

Diagnosis is primarily clinical and involves:

1. Detailed drug history
2. Temporal relationship assessment
3. Dechallenge and rechallenge evaluation
4. Exclusion of alternative causes

Causality assessment tools include the Naranjo algorithm and WHO-UMC scale [7].

MANAGEMENT

- Immediate withdrawal of suspected drug
- Supportive care
- Antidotes where applicable
- Documentation and patient counseling
- Reporting to pharmacovigilance centers

PREVENTION STRATEGIES

- Rational prescribing
- Therapeutic drug monitoring
- Pharmacogenetic screening
- Electronic prescribing systems
- Patient education

PHARMACOVIGILANCE AND REPORTING

Pharmacovigilance systems are essential for ADR detection. The WHO Programme for International Drug Monitoring collects global ADR reports via national centers [4]. Spontaneous reporting remains the cornerstone of signal detection.

Healthcare professionals are encouraged to report ADRs to national pharmacovigilance authorities to improve drug safety databases.

CONCLUSION

Adverse drug reactions are a significant yet preventable cause of patient harm. Early detection, appropriate management, rational prescribing, and active pharmacovigilance are critical to minimizing their impact. Integration of pharmacogenomics and digital health technologies may further enhance ADR prediction and prevention. Continuous education of healthcare professionals and patients remains fundamental to improving medication safety worldwide.

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Not Applicable

REFERENCES

1. World Health Organization. International drug monitoring: the role of national centres. Report of a

WHO meeting. World Health Organ Tech Rep Ser. 1972;498:1–25.
2. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. BMJ. 2004;329(7456):15–19.
3. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis. JAMA. 1998;279(15):1200–1205.
4. Lindquist M. VigiBase, the WHO Global ICSR database system: basic facts. Drug Inf J. 2008;42(5):409–419.
5. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis. JAMA. 1998;279(15):1200–1205.
6. Chung WH, Hung SI, Hong HS, et al. Medical genetics: a marker for Stevens–Johnson syndrome. Nature. 2004;428(6982):486.
7. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239–245.