JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Adverse Drug Reactions: Classification, Detection, Reporting, and Clinical Implications.

Usha Vaijinath kadbane, Shaikh Kadar. M, Kanhaiya rajesh lamture, Shaikh Ayesha Ayub , Krishnakant Shivprakash Birajdar
Student
Latur College of Pharmacy, Hasegaon

➢ Abstract :-

Adverse Drug Reactions (ADRs) remain a major challenge in modern healthcare, affecting patient safety, quality of life, and the overall effectiveness of treatment. Although medications are designed to heal, they can also produce harmful and sometimes life-threatening effects. Many ADRs go unnoticed or unreported, especially in busy clinical settings, leading to preventable complications. This review highlights the importance of building a strong culture of ADR reporting among healthcare and the methods user detect and evaluate It explores the history and growth of pharmacovigilance, the classification and mechanisms of ADRs, and the methods used to detect and evaluate them. Barriers to reporting—such as lack of awareness, fear, or insufficient training—are discussed along with strategies to overcome them. Case studies and global examples illustrate how timely reporting can save lives and improve therapeutic outcomes. With India emerging as a major pharmaceutical hub, strengthening ADR monitoring systems is more important than ever. By promoting awareness, encouraging transparent reporting, and integrating advanced technologies, pharmacovigilance can significantly reduce drug-related harm.This review emphasizes that ensuring drug safety is a shared responsibility and remains essential for protecting patients in an evolving healthcare landscape.

➢ Introduction :-

- Medicines are essential for improving health, but no drug is completely free from harmful effects.

- Adverse Drug Reactions (ADRs) occur when a medication causes unwanted or harmful effects during normal use.
- ADRs can range from mild symptoms to severe, life-threatening complications, affecting patient safety and overall treatment outcomes.
- With increasing use of multiple medicines (polypharmacy) and an aging population, the risk of ADRs has grown significantly.
- Many ADRs remain undetected or unreported, as they can resemble normal disease symptoms or may be overlooked in busy clinical settings.

- This creates a strong need for pharmacovigilance, the scientific system that monitors, detects, assesses, and prevents ADRs.
- Pharmacovigilance helps ensure that medicines remain safe even after they are marketed and used by large, diverse populations.
- India, known as the "pharmacy of the world," carries a major responsibility to maintain strong drug safety standards due to its large pharmaceutical output.
- The country's vast population, genetic diversity, and widespread medication use make effective ADR monitoring both essential and challenging.
- Raising awareness and improving ADR reporting can prevent harm, build trust in healthcare, and enhance the overall quality of treatment.
- This review highlights the importance of ADR reporting, barriers faced by healthcare professionals, and strategies to strengthen the pharmacovigilance system.
- Ensuring drug safety is not only a scientific requirement but also a moral responsibility to protect patients and save lives.

➢ Defination: -

- An Adverse Drug Reaction (ADR) is any harmful, unwanted, or unpleasant effect that occurs when a person takes a medicine at its normal dose. In simple words, it means the medicine causes a problem instead of helping the patient. ADRs can be mild—like a headache or stomach upset—or very serious, such as allergic reactions, skin rashes, organ damage, or even life-threatening conditions.

- Even though medicines are designed to cure or control diseases, every drug has the potential to cause side effects. These reactions may happen because the dose is too strong for someone, the body reacts unusually, or the medicine interacts with other drugs. Recognizing and reporting ADRs is important because it helps protect patients and improves the safe use of medicines.

➢ Case of Methotrexate-Induced Severe Adverse Drug Reaction Leading to Stevens–Johnson Syndrome (SJS).

- **Patient Background :-**

A 41-year-old woman with a long history of rheumatoid arthritis had been taking methotrexate irregularly for nearly ten years. She often suffered from joint stiffness and pain but never experienced major drug-related issues in the past.

- **Initial Symptoms :-**

Over a period of three months, she began experiencing severe vomiting, up to 15–20 episodes a day. Initially, the vomit was watery, but later an episode of blood-mixed vomiting occurred, signaling serious internal irritation.

- **Appearance of Skin and Mucosal Lesions :-**

About one week before hospital admission, she developed: Painful ulcers in her mouth and throat Crusting and erosions on the lips Rashes and ulcerations on the vaginal mucosa Multiple erosions on buttocks, legs, and hands. These lesions caused intense pain, making it impossible for her to eat or drink.

Figure 1 : erosion and ulcers with crusting over lips, buccal mucosa.

Figure 2 : Multiple erosion and ulcers at thigh, legs and but tock.

- **Condition on Arrival to Emergency Department :-**

She arrived weak, dehydrated, and in visible distress. Her vital signs showed:

- ✓ BP: 110/7mmHg
- ✓ Hg HR: 90 bpm
- ✓ RR: 19/min
- ✓ Temperature: 101°F

She could not speak clearly due to severe oral ulcers.

- **Diagnosis and Causality Assessment :-**

Doctors used two standard tools:

- ✓ Naranjo Scale
- ✓ WHO-UMC Causality Scale

The reaction was classified as "Probable/Likely ADR" (Score: 5) caused by methotrexate.

- **Identified Reaction – Stevens–Johnson Syndrome (SJS) :-**

The combination of:

- ✓ Widespread mucosal ulcers

- ✓ Skin erosions
- ✓ Fever

strongly indicated Stevens–Johnson Syndrome, a rare but serious adverse drug reaction.

- **Reporting and Public Health Importance :-**

The case was formally reported in VigiFlow, the national ADR reporting system under India's Pharmacovigilance Programme (PvPI).

Reporting this case helps regulatory authorities:

- ✓ Detect patterns.
- ✓ Issue warnings.
- ✓ Improve drug safety monitoring.

- **Clinical Message :-**

This case highlights the importance of close monitoring when using drugs like methotrexate. Even commonly used medications can cause severe, life-threatening ADRs if not used properly or if early symptoms are ignored.

➢ Classification of adverse drug reaction :-

Adverse Drug Reactions are commonly classified into six major types (A–F). This system helps healthcare professionals understand why a reaction occurred and how it can be prevented. The table below summarizes the classification in a clear

.Type	Name of reaction	Features	Example
A	Augmented (Dose-related)	Predictable, common, preventable with dose adjustment.	• Hypoglycemia due to excess insulin • Bleeding due to high warfarin levels • Low BP from antihypertensives.
B	Bizarre (Non–dose-related)	Unpredictable, rare, often immune-mediated.	• Anaphylaxis from penicillin • Stevens–Johnson Syndrome from sulfonamides / antiepileptics • Drug-induced lupus from hydralazine
C	Chronic (Dose & Time-related)	Related to dose + duration; appears after months/years.	• Adrenal suppression from long-term steroids • Tardive dyskinesia

			from antipsychotics • Liver damage from long-term methotrexate
D	Delayed (Time-related)	Delayed effects; often serious.	• Cancer from chemotherapy drugs • Infertility from alkylating agents • Birth defects from thalidomide
E	End-of-use (Withdrawal)	Caused by abrupt withdrawal.	• Seizures after sudden withdrawal of benzodiazepines • Hypertension rebound after stopping clonidine • Flu-like symptoms after stopping SSRIs
F	Failure of Therapy	Due to interactions, wrong dose, or resistance.	resistance. • Antibiotic failure due to bacterial resistance • Clot formation despite warfarin due to drug interactions • Contraceptive failure when enzyme-inducing drugs are used

➢ Identification of Adverse Drug Reactions :-

Identifying an Adverse Drug Reaction (ADR) can sometimes feel like solving a small medical mystery. Many ADRs look similar to common illnesses, so healthcare professionals must pay close attention to the patient's symptoms, medication history, and timing. Below is a humanized explanation of how ADRs are identified in real clinical practice.

- **Listening to the Patient's Symptoms :-**

Many ADRs are first noticed when a patient reports a new or unusual symptom after starting a medicine.
Examples:

- ✓ A patient taking antibiotics develops diarrhea.
- ✓ A person on painkillers starts feeling excessively drowsy.

These symptoms may be the first hint of an ADR.

- **Checking When the Symptoms Started :-**

Timing is very important.
If symptoms appear soon after starting a medicine, or after increasing the dose, it raises suspicion of an ADR.
Example:

- ✓ Rash appearing two days after taking a new antibiotic.

- **Reviewing the Patient's Medication List :-**

Healthcare providers look at all the medicines the patient is taking to check whether:

- ✓ The drug is known to cause the symptom
- ✓ Two or more medications are interacting
- ✓ The dose is too high

Example:

- ✓ Potassium drops suddenly in a patient taking diuretics → possible ADR.

- **Observing Physical Signs :-**

Sometimes ADRs show clear physical changes, such as:

- ✓ Rashes or skin reactions
- ✓ Unusual bruising or bleeding
- ✓ Extreme fatigue or confusion

These clues help identify serious reactions early.

Checking Lab Test Results :-

Hospital systems often flag abnormal laboratory values that may indicate an ADR.
Examples:

- ✓ Sudden drop in liver enzymes → possible drug-induced liver injury
- ✓ Low blood cell count → bone marrow suppression from medicines like methotrexate

These alerts help clinicians catch hidden ADRs.

- **Using Causality Assessment Tools :-**

To confirm whether a medicine caused the reaction, standardized tools are used, such as:

- ✓ Naranjo Scale
- ✓ WHO-UMC Causality Criteria

These tools help classify the reaction as definite, probable, possible, or unlikely.

➢ Management :-

Managing an Adverse Drug Reaction (ADR) begins with recognizing the signs early, as timely identification can prevent the reaction from becoming more severe. Once an ADR is suspected, the first step is usually to stop the offending medication, provided it is safe to do so. This helps remove the immediate cause of harm

and allows the patient's body to begin recovering. At the same time, healthcare professionals provide supportive care to relieve symptoms—such as antihistamines for itching, pain relievers for discomfort, IV fluids for dehydration, or steroids to control inflammation. In serious cases like anaphylaxis or Stevens–Johnson Syndrome, rapid emergency treatment is crucial, and may include the use of epinephrine, oxygen support, antidotes, or hospitalization for intensive monitoring.

Patients experiencing moderate to severe ADRs often require close observation through regular vital signs, blood tests, and organ function checks, ensuring their condition does not worsen. Not all ADRs require complete withdrawal of the drug; sometimes, adjusting the dose, switching to a safer alternative, or modifying the treatment schedule may effectively resolve the problem. A vital part of management is preventing the reaction from happening again. This includes documenting the ADR in the patient's medical records, clearly informing the patient and family, and ensuring that the same drug—or similar drugs—are avoided in the future.

Finally, reporting the ADR to national systems such as the Pharmacovigilance Programme of India (PvPI) or VigiFlow is essential. Reporting helps healthcare authorities identify new safety signals, update guidelines, and protect other patients from similar harm. Educating the patient about what happened, what to avoid, and when to seek help empowers them to stay safe throughout future treatments. Overall, effective ADR management is a compassionate and systematic process aimed at protecting the patient both now and in the future.

➢ Future development

The future of pharmacovigilance is moving toward a smarter, faster, and more patient-centered system. As healthcare becomes increasingly digital and technology-driven, new opportunities are emerging to detect and prevent Adverse Drug Reactions (ADRs) long before they cause harm. One of the most promising developments is the use of artificial intelligence (AI) and machine learning, which can analyze enormous amounts of data from hospitals, electronic health records, and even mobile health apps. These tools can identify early warning signs or unusual patterns of drug reactions much more quickly than traditional methods.

Another important area of progress is personalized medicine, where treatments are tailored to a person's genetic makeup. With advances in genomics, it is becoming possible to predict who may be at higher risk for certain ADRs. For example, genetic testing can help determine whether a patient is likely to experience a severe reaction to specific drugs. In the future, routine genetic screening could significantly reduce preventable drug-related harm.

Pharmacovigilance is also becoming more patient-focused. Mobile apps, online portals, and easy reporting systems allow patients to report ADRs directly, without needing to rely only on healthcare professionals. This creates a more open, inclusive system where every voice matters. As awareness grows, more people will feel empowered to report even mild symptoms, leading to richer and more accurate safety data.

In India, the pharmacovigilance system is expected to become stronger and more integrated in the coming years. The Pharmacovigilance Programme of India (PvPI) is already adopting digital tools, improving training, and working toward nationwide coverage. With better infrastructure, more ADR monitoring centers, and stronger collaboration between hospitals, pharmacies, and regulatory bodies, India is preparing for a more advanced and responsive drug safety network.

Overall, the future of pharmacovigilance is hopeful and progressive. Technology, genetics, education, and patient engagement will work hand-in-hand to create a safer healthcare environment. As systems grow smarter and more connected, the ability to prevent serious ADRs will improve, ultimately saving lives and enhancing the well-being of millions of patients worldwide.

➢ ADR Reporting Approches :-

Adverse Drug Reaction (ADR) reporting can happen in many ways, and each approach plays an important role in keeping medicines safe. The most common method is spontaneous reporting, where doctors, nurses, pharmacists, and even patients voluntarily report any side effect they notice. This simple approach helps identify unexpected or rare reactions, although many cases still go unreported because people may be busy or unaware. To improve this, hospitals and health authorities sometimes use stimulated reporting, where awareness programs and safety campaigns encourage more consistent reporting.

In addition to voluntary methods, active surveillance offers a more proactive approach. Here, healthcare professionals closely monitor patients—especially those taking high-risk medicines—through regular checkups, follow-ups, and laboratory review. Modern electronic health record systems also help by automatically flagging unusual symptoms or abnormal test results that may indicate a drug reaction. In some cases, prescription event monitoring and patient registries are used to follow large groups of people after they start a new medication, capturing side effects that might not appear during clinical trials

Today, digital tools like mobile apps and online reporting portals have made it even easier for both professionals and the public to report ADRs quickly and accurately. Together, these different approaches create a stronger and more responsive system, helping ensure that any harmful reaction is detected, studied, and prevented in the future.

➢ Conclusion :-

Adverse Drug Reactions remain an important challenge in modern healthcare, reminding us that even the most effective medicines can cause harm when the body responds in unexpected ways. As this review highlights, early identification, proper reporting, and responsible monitoring are essential to protect patient safety. A strong culture of ADR awareness not only prevents serious complications but also strengthens trust between patients and healthcare providers. Pharmacovigilance systems—especially in a country as large and diverse as India—play a vital role in collecting reports, identifying patterns, and taking action before small problems become widespread risks.

With growing use of technology, improved training, and greater patient involvement, the future of ADR monitoring looks promising. However, no system can succeed without active participation from every healthcare professional and every patient. By reporting even the smallest side effects, staying informed, and using medicines responsibly, we contribute to a safer and more reliable healthcare environment. Ultimately, the goal of pharmacovigilance is simple yet powerful: to ensure that medicines help more than they harm, and to safeguard the well-being of every individual who relies on them.

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