Abhishek Sharma *et al*, International Journal of Pharmaceutical Sciences and Medicine (IJPSM), Vol.8 Issue. 12, December- 2023, pg. 36-45

ISSN: 2519-9889
Impact Factor: 5.9

Adverse Drug Reaction (ADR) and Pharmacovigilance: A Current Prospectives

Abhishek Sharma[1]; Aditya Kumar[1]; Akanksha[1]; Ambrish Kumar[1]; Dr. Alok Kumar Shukla*[2]; Dharna Singh Rajawat[3]

Author(s) Affiliations:
[1]Research Scholar, Babu Sunder Singh College of Pharmacy, Nigohan, Lucknow
*[2]Director, Babu Sunder Singh College of Pharmacy, Nigohan, Lucknow
[3]Associate Professor, Babu Sunder Singh College of Pharmacy, Nigohan, Lucknow

Corresponding author:
Dr. Alok Kumar Shukla
*[2]Director, Babu sunder Singh College of Pharmacy. Nigohan, Lucknow

DOI: 10.47760/ijpsm.2023.v08i12.004

ABSTRACT:
Unwanted medication response is defined as "a significantly undesirable or harmful reaction; side effects typically indicate a risk from additional management and contact for prevention, special care, a change in the dosage schedule, or withdrawal of the product. Generally, ADR have been divided into two types: Type-A which is dose dependent and predictable on the basis of the pharmacology of the drug. e.g. beta blocker. Type-B which is unpredictable and not dose dependent. e.g. anticonvulsant**.** The science and activities related to the detection, assessment, understanding and prevention of adverse events or any other drug-related problem" is the definition of pharmacovigilance. Post-marketing surveillance and additional ADR monitoring techniques include prescription event monitoring, digital medical record connection, voluntary reporting by hospitals (such as the UK's Yellow Card System), cohort/case control studies, and personal case reports from physicians**.** Because preventing or reducing the risk of adverse drug reactions (ADRs) continues to be a challenge in our daily clinical practice, reaching the highest level of possible results from treatments continue to be a top priority for individual clinicians.

Keywords: Adverse drug reaction, pharmacovigilance, side effects, prevention, management.

ISSN: 2519-9889
Impact Factor: 5.9

INTRODUCTION

Unwanted medication response is defined as "a significantly undesirable or harmful reaction; side effects typically indicate a risk from additional management and contact for prevention, special care, a change in the dosage schedule, or withdrawal of the product"[1]. This can be brought on by a policy regarding the use of a medicinal product. Since 2012, the term has been broadened to cover not only the prescribed use of a pharmaceutical product at regular dosages but also possible adverse reactions to off-label or unlicensed medication as well as reactions that may result from errors, abuse, or misuse [2]. This change might affect how regulators and pharmaceutical companies report and track adverse drug responses, but it shouldn't affect how our clinical practice handles such situations. During the late 20th and early 21st centuries, significant research in the US and the UK demonstrated that adverse medical response is a common occurrence in clinical practice, frequently resulting in unanticipated hospital admissions, occurring during hospital admission, and presenting after discharge [3-6].

Despite numerous prevention efforts, research suggests that five to ten percent of patients may encounter an adverse drug reaction (ADR) during access, admission, or discharge. The incidence of ADRs has remained mostly constant throughout time. Since most ADRs do not lead to severe systemic symptoms, the frequency of events will inevitably be impacted by the methodology utilised to identify these events. However, the frequency of potential damage needs to be carefully considered due to the associated risks of morbidity and death, potential financial burden, and potential injury to the prescriber-patient relationship. Antiplatelets, anticoagulants, cytotoxic drugs, immunosuppressants, diuretics, antidiabetics, and antibiotics are among the pharmaceuticals that have been directly connected to hospital admissions because of adverse drug reactions. When adverse drug reactions do happen, bleeding is usually the cause; antithrombotic/anticoagulant medications administered with non-steroidal anti-inflammatory drugs are most often suspected of being the culprit [7].

Classification of ADR

Generally, ADR have been divided into two types:

1. **TYPE –A**: Which is dose dependent and predictable on the basis of the pharmacology of the drug. e.g. beta blocker.
2. **TYPE-B:** It is unpredictable and not dose dependent. e.g. anticonvulsant [8].

Depending on Types of Reactions-

- Type A (augmented): dose - related common in line with a recognized pharmacological effect Consistent

ISSN: 2519-9889
Impact Factor: 5.9

- Type B (Bizarre): not connected to dosage erratic Unusual Unrelated to the drug's known pharmacological action.
- Type C (Chronic): dose-related Temporal Unusual Concerning the total dosage
- Type D (Delay): Temporal frequently dose-related Unusual
- Type E (Exit): Unusual occurs following drug withdrawal
- Type F (Failure): Dosage-related Seldom possibly brought on by drug interactions

Depending On Severity-

(1) **Minor-** It occurs for short period of time and not required any type of therapy and antidote.

(2) **Moderate-** It this ADR required changes in therapy and special treatment and at least one day hospital stay.

(3) **Severe-** It can be life threatening condition so it requires intensive medical treatment.

Others-

Side Effect- It is unavailable, that occurs due to pharmacodynamic effect of the therapeutic doses. E.g.- Atropine (preanesthetic) –Dryness of mouth

Toxic Effect- It Occur due to more pharmacological action of the drug or due to prolonged use of medication. E.g.- Barbiturates- coma, Heparin- bleeding.

Intolerance- When a patient experiences an unusual reaction to the pharmacological action of a medication, or an exaggerated sensitivity, they are unable to tolerate the usual therapeutic dose of the drug, which is known as drug intolerance. E.g.- Chloroquine (single tablet) – vomiting and abdominal pain in some individual.

Idiosyncrasy- It refers to an idiosyncrasy rxn . that is an adverse effect to an agent such as a drug. which doesn't occur in patient who've used the same agent. E.g.- Barbiturates- excitement and mental confusion is some patient.

Drug Allergy- It may be occurred even with smaller doses and called drug hypersensitivity.

Teratogenicity- Teratogenicity is the ability of a medication to induce abnormalities in the foetus or deformities when it given to the pregnant mother.

Factor influencing the occurrence of ADRs

1. **Patient- related factors**

Age

ADRs are more likely to affect children and the elderly due to physiological differences. Variations in the cardiovascular, hepatic, and renal systems all raise the risk of an ADR.[13]

Sex

Some medications, such as latex and NMBs, are more likely to cause anaphylaxis in females. An ADR is nearly twice as likely to occur in females. Pharmacokinetic variations influenced by body mass, hepatic clearance, and hormones could be the cause of this.[16]

ISSN: 2519-9889
Impact Factor: 5.9

Smoking

Smokers are more likely to experience anaphylaxis to antibiotics, which may be the result of sensitization from repeated treatments for respiratory infections.[17]

Polypharmacy

This raises the possibility of an ADR resulting from a drug interaction. Pharmacokinetics can also be affected by polypharmacy, and pharmacodynamics can be impacted by the underlying illness [14-15]

Atopy

Patients with a history of atopy are more likely to experience latex allergy and contrast media anaphylaxis. Moreover, patients with fruit allergies- particularly those to avocado, banana, and chestnut- are more likely to experience them.[18]

2. **Drug related factors**

Drug dosage

- **Overdosing**: Overdosing can raise the possibility of negative side effects.
- **Underdosing**: Due to inadequate therapeutic effects, an insufficient dosage may result in treatment failure and possible adverse drug reactions.

Drug interaction

- **Drug - drug interaction:** Drug interactions can increase or decrease the effects of one or both drugs when taken together, which can result in unanticipated side effects.
- **Drug – food interaction:** Certain foods and drugs may interact, changing the food's metabolism or absorption and raising the possibility of adverse drug reactions (ADRs).

3. **Route of administration**

The way a medication is administered can have an effect on how well it is absorbed and distributed, which can change when and how severe adverse drug reactions occur.

4. **Environmental factor**

- **Climate and Temperature:** Medication stability may be impacted by environmental factors or extremely high or low temperatures. Medicine composition and potency can alter if they are stored in environments that deviate from recommended guidelines.
- **Contaminants and Pollution:** Exposure to pollutants or contaminants in the environment can interact with medications or negatively impact an individual's general health, which may have an impact on the incidence of adverse drug reactions.
- **Place of Geographical Origin:** Variations in environmental pollutants, allergens, or infectious agents across different regions can affect adverse drug reactions (ADRs).
- **Nutrition and Diet:** Dietary environmental factors can impact drug metabolism and interactions, increasing the risk of adverse drug reactions (ADRs). Examples of these factors include the availability and consumption of specific foods.

ISSN: 2519-9889
Impact Factor: 5.9

Prevention of ADR

When some ADRs are unanticipated, like anaphylaxis in a patient after a single unremarkable exposure to an antibiotic containing penicillin, many can be avoided with sufficient precautions. monitoring and insight. Avoidability or readiness to prevent typically used to describe instances where the drug treatment regimen is uneven. It is impractical when compared to current evidence-based practise considering the circumstances as they are known [9]. Statistical Studies often reveal that between one-third and fifty percent of ADRs are (at least perhaps) avoidable, notwithstanding the fact that avoidability In retrospect, the diagnosis is considerably simpler. Nevertheless, interventions that decrease the likelihood of an ADR happening can be an important method to lower the possibility of patient damage.

There are two fundamental actions that can be taken to avoid an ADR:

1- Determine the patient subgroup that is most able to change the course of treatment in response to negative effects choose appropriately.

2- Make sure the treatment strategy minimises any potential negative effects.

Plan of treatment

- ✓ Prescribe carefully and sensibly to minimize errors that can lead to adverse drug reactions. Plans for treatment should take into account and minimize any potential negative effects [10]. Eleven while methotrexate is used in conjunction with folic acid, for instance, the likelihood of folate deficiency-related side effects is decreased. Similarly, electrolyte and renal function are monitored while using diuretics or renally active medications. All of these examples can stop side effects that arise from treatment, but their applicability may be restricted because guidelines for monitoring are frequently insufficient or unclear. It's crucial to keep in mind that cautious prescribing may help prevent medication usage entirely, and conservative or nonpharmacological approaches should always be taken into account in treatment plans.
- ✓ In order to lower the likelihood of an ADR and stop those "avoidable" reactions from happening in practice, a systems approach incorporating several techniques, the patient, and all healthcare personnel is needed.
- ✓ Reducing mistakes that can lead to adverse drug reactions (ADRs) requires cautious, safe prescribing. Plans for treatment should take into account and minimize any potential negative effects. Eleven while methotrexate is used in conjunction with folic acid, for instance, the likelihood of folate deficiency-related side effects is decreased. Similarly, electrolyte and renal function are monitored while using diuretics or renally active medications. All of these examples can stop side effects that arise from treatment, but their applicability may be restricted because guidelines for monitoring are frequently insufficient or unclear. It's crucial to keep in mind that cautious prescribing may help prevent medication usage entirely, and

ISSN: 2519-9889
Impact Factor: 5.9

conservative or nonpharmacological approaches should always be taken into account in treatment plans.

- ✓ In order to lower the likelihood of an ADR and stop those "avoidable" reactions from happening in practice, a systems approach incorporating several techniques, the patient, and all healthcare personnel is needed [11].

Identifying negative medication effects

One of the worst imitators in medicine is ADRs; they frequently imitate "traditional diseases" and show up in every bodily system. Patients who are hospitalized due to drug-related issues may exhibit a variety of symptoms, such as fatigue or weakness, hemorrhagic or biochemical disturbances (such as anemia, electrolyte imbalance, or acute kidney injury), bleeding, and gastrointestinal distress, hypoglycemia, or infections linked to medical care, like Clostridium difficile. But less common signs, such as drug-induced eosinophilia, drug-induced lupus, and fixed drug eruptions or drug-induced angioedema, call for a higher degree of caution and skepticism from the doctor, who has to work really hard to find the cause. A thorough medication history is essential for determining whether a presenting complaint or later finding may be related to an adverse drug reaction (ADR) [12]. E.g.- One such instance would be organ-specific harm coupled with drug or metabolite accumulation inside cells (such as indinavir crystalluria and nephropathy)

Pharmacovigilance

"The science and activities related to the detection, assessment, understanding and prevention of adverse events or any other drug-related problem" is the definition of pharmacovigilance. The data produced by pharmacovigilance is helpful in official drug use regulations as well as in educating physicians about adverse drug reactions. It serves as the foundation for evaluating the safety of medications, which makes it crucial to the sensible use of medications.

The activities involved in pharmacovigilance are:

- Post-marketing surveillance and additional ADR monitoring techniques include prescription event monitoring, digital medical record connection, voluntary reporting by hospitals (such as the UK's Yellow Card System), cohort/case control studies, and personal case reports from physicians**.**
- Distribution of ADR information via "drug alerts," "medical letters," and instructions that pharmaceutical companies and regulatory bodies (like the FDA in the USA and the Committee on Safety of Medicines in the UK) send to physicians**.**

In order to guarantee pharmaceutical companies and medicine regulators adhere to good vigilance practices, In 2012, new laws were presented in the European Union. The roles and responsibilities of pertinent stakeholders with regard to drug safety are clearly defined in this

ISSN: 2519-9889
Impact Factor: 5.9

new guidance. A program of more thorough surveillance for newly discovered pharmaceutical Biological substances and agents with a black triangle position —that is, those needing extra observing —has been introduced by the guidelines, which is noteworthy. One of the tenets is that the risk management policy's proactive strategies take the place of the earlier reactive ones.

Reporting of ADR

For the past 50 years, the primary method of discovering potential adverse drug reactions (ADRs) has been spontaneous reporting systems, such as the UK's Yellow Card Scheme, which is managed by the Medicines and Healthcare Products Regulatory Agency (MHRA) and the Commission on Human Medicines (CHM). Following the thalidomide tragedy of the late 1950s, the plan was created in 1964.The program gathers information on suspected adverse drug reactions (ADRs) associated with both licensed and unlicensed medications and vaccines including those obtained over-the-counter or through prescription, through voluntary reporting. A report need only contain these four pieces of information in order to be deemed valid. A known patient, a reaction, a possible medication, and a reporter who is able to be identified.

Reporters are urged, nevertheless, to give assessors as much information as they can, including extra information and the context of the clinic The UK program still receives about 25,000 reports annually, which gives medicine regulators information about the prevalence of adverse drug reactions. sadly, insufficient reporting remains a serious issue; it is estimated that less than 5% of all ADRs are actually reported. This restricts the systems' capacity to provide precise incidence data. A joint alert on improving medication error incident reporting and learning was released in 2014 by NHS England and the MHRA. Included here is the automatic submission of medication errors to the National Reporting and Learning System (NRLS) and unwanted drug reactions (ADRs) to the Yellow Card Scheme.

Patients are taking an increasingly active role in their own treatment management. After a quick assessment of patient Yellow Card reporting showed the efficacy of this strategy, every patient are now strongly encouraged to report adverse drug reactions (ADRs).

Online reporting tools and using the Yellow Card app have largely replaced paper observation (on the original yellow cards). In addition, integrated reporting—which transmits ADR data straight can be added to electronic health records used in general practice and some hospitals, or they can be sent to central agencies for processing before being added to national and international databases.

ISSN: 2519-9889
Impact Factor: 5.9

Management of ADR

- ✓ In actual practice, managing adverse drug reactions (ADRs) often involves changing a dosage schedule or stopping a medication that may be the source of an ADR. But the steps taken to handle an ADR will probably differ from one clinician to the next.
- ✓ According to EU legislation, the marketing authorization holder must now submit a comprehensive risk management plan with the approval of any new medicine before it can be placed on the market. This plan may include continuous safety testing and the development of customized treatments for managing particular ADRs. Antidotes for bleeding caused by direct oral anticoagulant have demonstrated this.
- ✓ Sometimes, taking immediate action is crucial due to the seriousness of a possible negative medication reaction, such as anaphylactic shock. There are times when receiving emergency care and stopping all medication is necessary; in these situations, carefully reintroducing necessary medications should be taken into consideration. If not, clinical benefit-risk assessment is used to determine which medication or medications should be discontinued as a trial, assisted by investigations. If the patient needs one or more of the medications, a problem appears right away. A benefit-risk assessment regarding the necessity of the medication If the cause is fairly obvious, consideration must be given to the severity of the response, its potential for treatment, and whether there are comparable choices that are likely to cause the same negative drug reaction. Depending on the severity of the reaction, the non-essential medications should be stopped first, ideally one at a time, if multiple medications may be the cause. Dosage reduction should be taken into consideration if the reaction is likely to be dose-related.
- ✓ When interactions are suspected, many prescribers unnecessarily withhold a medication rather than modifying the dosage.
- ✓ Observation of the patient is necessary during withdrawal. The length of the waiting period will change based on the type of pathology and how quickly the drug is eliminated from the body. For instance, when a drug is stopped, urticaria typically goes away quickly, but Psoriatic skin reactions that are fixed can take weeks to
- ✓ As long as the patient is receiving the necessary treatment, give symptomatic relief if they are unable to function without the medication that is causing an adverse reaction. For instance, patients taking anti-cancer medications are frequently treated symptomatically for severe nausea and vomiting.
- ✓ But it's crucial to avoid using more medications than necessary when treating a negative medication reaction. Always keep the patient's needs clearly in mind, don't treat them for longer than is necessary, evaluate them frequently, and look for methods to make their care easier.

ISSN: 2519-9889
Impact Factor: 5.9

CONCLUSION

In this review, we have discussed how to identify, manage, and report adverse medication reactions. We've talked about how modern technology affects ADR prediction, prevention, detection, and management, and how we're trying to maintain these procedures getting better with new technical advancements.

The capacity to combine phenotypic and pharmacogenetic data to give prescribers patient-specific recommendations is expanding the possibilities for individualised medication. Such national and worldwide regulatory research levels can help achieve a favourable ratio of benefits to dangers throughout the lifecycle of a pharmaceutical product. Achieving the best possible outcomes from therapies remains a primary goal for individual physicians, as preventing or lowering the risk of adverse drug reactions (ADRs) remains a problem in our day-to-day clinical practice.

FUNDING SOURCE

Nil.

CONFLICT OF INTEREST

Authors declared for none conflict of interest.

REFERENCES

[1]. Aronson JK, Ferner RE . Clarification of terminology in drug safety. Drug Saf. 2005; 28 : 851 – 70 .

[2]. European Directive 2010/84/EU of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

[3]. Bates DW, Leape LL , Petrycki S . Incidence and preventability of adverse drug events in hospitalized adults . J Gen Intern Med 1993 ; 8 : 289 – 94 .

[4]. Lazarou J , Pomeranz BH , Corey PN . Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies . JAMA 1998;279:120-5.

[5]. Pirmohamed M , James S , Meakin S et al . Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients . BMJ 2004;329: 15 – 9.

[6]. Davies EC , Green CF , Taylor S et al . Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes . PLoS One 2009 ; 4 : e4439.

[7]. Wester K , Jönsson AK , Spigset O , Druid H , Hägg S . Incidence of fatal adverse drug reactions: a population based study . Br J Clin Pharmacol 2008 ;65 : 573 – 9.

[8]. KD Tripathi , Adverse drug reaction , Text book of Essential of medical pharmacology , 2019; 8th edition . 92-96.

[9]. Ferner RE , Aronson JK . Preventability of drug-related harms - part I: a systematic review . Drug Saf 2010; 33 : 985 – 94 .

[10]. Coleman JJ , Ferner RE , Evans SJ . Monitoring for adverse drug reactions . Br J Clin Pharmacol 2006 ; 61 : 371 – 8 .

[11]. Rommers MK , Teepe-Twiss IM , Guchelaar HJ . Preventing adverse drug events in hospital practice: an overview. Pharmacoepidemiol Drug Saf 2007 ; 16 : 1129 – 35.

ISSN: 2519-9889
Impact Factor: 5.9

[12]. Naranjo CA , Busto U , Sellers EM et al . A method for estimating the probability of adverse drug reactions . Clin Pharmacol Ther 1981; 30 : 239 – 45.

[13]. Petrovic M, Cammen T, Onder G. Adverse drug reactions in older people. Drugs and Aging 2012; 29: 453–62.

[14]. Scott S, Thompson J. Adverse drug reactions. Anaesthesia and Intensive Care Medicine 2011; 12: 319–23.

[15]. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. American Journal of Geriatric Pharmacotherapy 2006; 4: 36–41.

[16]. Mertes P, Laxenaire M, Alla F. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999-2000. Anesthesiology 2003; 99: 536–45.

[17]. Association of Anaesthetists of Great Britain and Ireland. Suspected anaphylactic reactions associated with anaesthesia. Anaesthesia 2009; 64: 199–211.

[18]. Kahn SL, Podjasek JO, Dimitropoulos VA, Brown CW. Natural rubber latex allergy. Disease-a-Month 2016; 62: 5–17.

