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Adverse Drug Reactions: A comprehensive Review of Mechanism, Classification and Management

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ABSTRACT:
The review delves into the existing ADR reporting systems, including the involvement of healthcare professionals and the growing role of patient-driven reporting initiatives. It examines the strengths and weaknesses of these systems and emphasizes the need for enhanced reporting practices to capture a comprehensive range of adverse reactions. Challenges in ADR reporting, such as underreporting, reporting bias, and difficulties in causality assessment, are critically analyzed. The impact of incomplete or inaccurate information on signal detection and risk assessment is also discussed. The review underscores the significance of addressing these challenges to maintain the integrity of pharmacovigilance efforts and optimize patient care. Moreover, the review highlights emerging technologies, including artificial intelligence and real-world data integration, as potential tools to streamline ADR reporting and signal detection processes. These innovations have the potential to revolutionize drug safetysurveillance and improve the overall efficiency of pharmacovigilance practices.

Keywords : Introduction, Types of Adverse Drug Reactions, Importance of ADR reporting for drug safety, Mechanism of ADR, Challenges in ADR monitoring, Classes associated with ADRs (context), Diagnosis of adverse drug reactions, Preventing adverse drug reactions.

I. INTRODUCTION

An adverse drug reaction (ADR) is any unanticipated or detrimental reaction brought on by using a drug or therapy.Adverse Drug Events (ADEs) are another name for these reactions, which can vary from minor side effects to serious, sometimes fatal complications.ADRs can be brought on by a number of things, such as individual differences in how drugs are metabolised, interactions with other drugs or substances, allergies, incorrect dosage, or underlying medical disorders. ADRs frequently include gastrointestinal issues, skin rashes, nausea, dizziness, and allergic reactions.In more extreme situations, anaphylaxis, organ damage, or even death could result from ADRs. [1]

Observation and comprehension Because they can affect therapy results and patient safety, ADRs are important in the medical field.Detecting and controlling adverse drug reactions is greatly aided by pharmacovigilance, the process of tracking and assessing medication safety.In order to evaluate drug safety profiles, update drug labels, and make well-informed decisions regarding the continued use of pharmaceuticals, regulatory bodies and healthcare professionals can gather andanalyse data on adverse drug reactions (ADRs) through pharmacovigilance.[2]

An avoidable medication error, a side effect from the medication's delivery, or an unanticipated error like an allergic response could all lead to adverse drug reactions (ADRs).[3,4]

Types of Adverse Drug Reaction:

Adverse reaction types can be categorised under two broad headings: less common ADRs, such as type C, D, and E reactions, and more common ADRs, such as type A and B reactions.[5,6]

Type A :Type A reactions can be caused by pharmacodinemic factors such as liver disease, changes in fluid and electrolyte balance, sensitivity, and long-term consequences.[7].

It has been demonstrated that hepatic diseases impact a medicine's pharmacodynamic response and result in adverse drug reactions (ADRs) because they produce clotting factors. Additionally, drugs that alter bleeding by producing ulceration or hinder clotting must be avoided. It has been observed that the effects of cardiac glycoside, such as hypokalaemia and hypercalcemia, can intensify, leading to pharmacodynamic changes and ultimately type A adverse events. Furthermore, it has been established that the pharmacological effects of the medication are connected to type A adverse effects. Nonetheless, type A effects are typically reproducible and amenable to experimental investigation. Additionally, during the initial clinical trials, spontaneous reporting of type A adverse responses revealed their presence.[8,9]

Type B: A small percentage of individuals have experienced type B side effects, which are frequently idiosyncratic or sensitive reactions.[10]

It has also been suggested that type B side effects are unforeseen and unpredictable, showing little to no relationship to dosage. However, a drug's low background frequency and association with time are frequently the primary reasons for suspecting it of having type B effects. It is also possible to categorise type B adverse drug reactions into two groups: immunological ADRs, which are unpredictable and result from immunoglobulin (Ig) E-dependent drug reactions, immune complex-dependent drug reactions, cytotoxic drug-induced reactions, and cell-mediated reactions; and non-immunological ADRs, which are further subdivided into predictable and unpredictable reactions that are brought on by teratogeneity, metabolic modification, slow toxicity, overdose, collective effects, slow toxicity, drug interaction, metabolic modification, teratogeneity, aggravation of disease, drug-induced chromosomal disturbance, and intolerance.[11,12]

Type C : Because type C adverse reactions are a major cause of chronic disease toxicity, they have been associated with both severe and widespread side effects that significantly affect public health.Furthermore, class C reactions—such as extrapyramidal symptoms or analgesic nephropathy—have been recognised as those that have long-term effects linked to chronic pharmaceutical use.These reactions have been connected to the cumulative harmful effects of a chemical, which can worsen with time.Moreover, type C reactions, which include adaptive alterations and withdrawal symptoms, have been suggested as long-term drug side effects.[13]

The production of iatrogenic hyperadrenocorticism with long-term use of prednisolone or other corticosteroids is evidence that type C adverse effects are known to be chronic in nature and linked to long-term pharmacological therapy. Furthermore, research has documented adaptation upon drug withdrawal, which is popularly known as abstinence syndrome.[14]

Type D : Type D reactions, often known as delayed adverse drug reactions, are those that become noticeable after a certain amount of treatment.Type D adverse events are best exemplified by the emergence of secondary malignancies in patients treated with alkylating drugs such as cyclophosphamide.Adrenocortical insufficiency after stopping glucocorticoid therapy and withdrawal seizures upon stopping anticonvulsant therapy are two further instances of type E ADRs that have been documented to happen when drug treatment is abruptly stopped.[15,16,17]

Importance of ADR reporting for drug safety:

Finding Unknown Adverse responses: ADR reporting makes it possible to find uncommon or yet unidentified drug-related adverse responses.Early identification of these events can result in timely intervention, protecting patients from additional injury[18]

Signal detection and risk management:

Combining ADR findings from several sources makes it easier to spot trends or warning signs that could point to possible safety issues.These signals can be analysed to help evaluate the risk-benefit profiles of medications and, if required, take the proper regulatory action.[19]

Improving drug labeling and usage guidelines:

ADR reports offer useful information that may result in changes to medication labels that include cautions, warnings, and contraindications.This guarantees that patients and medical staff are aware of any hazards and proper use. [20]

Understanding drug interactions and comorbidities:

ADR reporting offers important information for personalised medicine and treatment strategies by evaluating the effects of underlying medical problems and the interactions between several drugs. [21]

Patient Empowerment:

Patients are empowered to take an active role in their healthcare when they are encouraged to report adverse drug reactions.Better healthcare results and increased patient safety can result from patient-driven ADR reporting. [22]

Mechanism of ADR :

An unpleasant and detrimental reaction that happens after taking medication is known as an adverse drug reaction (ADR).Direct toxicity studies and hypersensitive reactions, which arise from changes in the pharmacokinetic and pharmacodynamic properties of the therapeutic products, are two categories of adverse reaction mechanisms. [23]

The toxic effects of a molecule or its metabolites, which manifest in different organ systems and cause harmful chemical reactions, physiological dysfunction, DNA damage, or harm to cellular structures and tissues, can be ascribed to direct toxicity responses. [24,25]

However, hypersensitivity reactions can be identified when a person's immune system reacts excessively to a medication or its byproducts, such as allergic or anaphylactic reactions. 15.It has been proposed that the skin, liver, lungs, bone marrow, and kidneys are among the organs where direct cytotoxicity and an overabundance of immune response are evident. [26,27]

Challenges in ADR monitoring :-

The effectiveness and completeness of ADR reporting are impacted by a number of issues. Among the major obstacles are:

Underreporting:

The underreporting of adverse medication responses is one of the biggest problems. Patients and healthcare providers might not always be aware of or record ADRs, which could result in a sizable data gap. Underreporting may postpone critical interventions by making it more difficult to identify uncommon or chronic adverse effects.

Reporting bias:

Certain adverse reactions may be over-reported or underreported as a result of a variety of variables, including media attention, public perception, or the drug's popularity. This phenomenon is known as reporting bias. A drug's actual safety profile may be distorted by this bias [28] .

Lack of knowledge:

Patients and healthcare workers may not fully comprehend the significance of reporting adverse drug reactions. Fear of consequences, confusion about cause, or ignorance of reporting procedures can all discourage reporting [29].

Workload and time restrictions:

Healthcare workers frequently deal with a lot of work and time constraints, which can deter them from setting aside time to report adverse drug reactions. Participation rates may be lowered if reporting procedures are seen as laborious and time-consuming [30].

Difficulty assessing causality:

It can be difficult to establish a drug's causal relationship with an unpleasant reaction, particularly when a patient is taking several medications or has underlying medical issues. Accurate reporting requires the establishment of a distinct cause-and-effect relationship [31].

Information that is erroneous or incomplete:

It can be challenging to evaluate the degree and veracity of a reported adverse response when ADR reports lack important information such patient demographics, drug dosage, and concurrent drugs [32].

Patient involvement:

Although there are still obstacles to overcome, such as patient awareness, the inability to distinguish ADRs from other symptoms, and restricted access to reporting channels, patient reporting of ADRs is becoming more widely accepted [33]

Reporting incentives:

Patients and healthcare providers may not have enough incentives to report adverse drug reactions. Participation rates may be raised by rewarding and encouraging ADR reporting efforts.

Data quality and signal detection:

Analyzing and detecting signals might be difficult when dealing with large amounts of ADR data. To find pertinent safety signals, it is crucial to guarantee data quality and apply efficient data mining techniques [34].

Classes associated with ADRs (context)

Nine of the 19 included studies focused on particular drug classes, including anti-tuberculosis drugs [35], anti-epileptics [36], antipsychotics, antidepressants, and mood stabilisers [37], antibiotics [38], biochemicals anticholinergic drugs, including dementia medications [39], and insulin and oral diabetic medications [40]. Other drug classes, including beta blockers, antiplatelets, analgesics, benzodiazepines, musculoskeletal pharmaceuticals, stimulants, lipid modifying agents, selective serotonin reuptake inhibitors, and skin preparations, were the subject of the remaining research. Warfarin, antipsychotic medications, opioid analgesics, diuretics, ACE inhibitors, and medications used for the cardiovascular system (beta-adrenergic blocking agents) were the pharmacological classes linked to the highest ADRs documented in the included studies [41].

Diagnosing of adverse drug reactions :-

ADRs frequently imitate “traditional diseases” and appear in many bodily systems, making them one of the great mimics in healthcare. Weakness or drowsiness, biochemical or haematological abnormalities (such as acute kidney injury, electrolyte imbalance, or anaemia), bleeding, gastrointestinal disturbances, hypoglycemia, or infections linked to healthcare, like Clostridium difficile, are just a few of the many ways that drug-related issues in hospitalized patients can manifest. Rarer symptoms, including drug-induced lupus, fixed drug eruptions, drug-induced eosinophilia, or angioedema, call for a higher level of suspicion and attention on the part of the doctor, who should make every effort to determine the cause.In order to prevent future ADRs and determine whether a presenting complaint or subsequent finding is related to an ADR, a thorough medication history is essential. A number of factors can be used to establish a drug’s causation. [42].

Certain tests can sometimes help diagnose an adverse drug reaction (ADR) by confirming a drug-induced illness and offering objective proof of the reaction. For instance, organ-specific harm combined with drug or metabolite accumulation in intracellular tissue (e.g. indinavircrystalluria and nephropathy). [43].

Preventing adverse drug reactions :

Many ADRs can be avoided with proper planning and monitoring, but some are unpredictably occurring, such as anaphylaxis in a patient following one prior unremarkable exposure to an antibiotic containing penicillin.Preventability, also known as avoidability, typically refers to situations in which the drug treatment plan is unrealistic when taking into account known circumstances or is not in line with current evidence-based practice.

Although it is considerably simpler to identify preventability in retrospect, epidemiological studies often reveal that between one-third and half of ADRs are (at least possibly) preventable.Nonetheless, one significant strategy to lower the risk of patient injury is to implement measures that lessen the likelihood that an ADR will occur.

Interventions that lower the likelihood of an adverse drug reaction (ADR) can, nevertheless, be a significant strategy to lower the risk of patient injury.

Two fundamental actions can be taken to stop an ADR from happening :

1.Determine which patient subgroup is most likely to experience the negative effect and adjust the treatment plan appropriately.

2. Make sure any potential negative effects are minimised by the treatment approach.

Identifying susceptibility:

It is possible to reduce the likelihood of adverse drug reactions and use patient susceptibilities to inform prescription decisions.By looking up any previous adverse drug reactions (ADRs) in the patient's prescription history, re-exposure to the drug is avoided.Age, gender, ethnicity, and pregnancy status are examples of susceptibility characteristics that can be used in some circumstances to predict the chance of an adverse drug reaction (ADR).

For instance, due to the possibility of ACE inhibitor-induced angioedema, the National Institute for Health and Care Excellence has recommended that patients of African or Caribbean heritage be prescribed anangiotensin-II receptor blocker rather than an ACE inhibitor for hypertension.Pharmacogenetics is beginning to provide more individualised medication options by identifying individuals who are more likely to experience a certain adverse drug reaction.

At the point of care, clinical decision support systems can alert clinicians to any patient-specific therapy warnings or extra monitoring needs to lower the risk of injury.Although a thorough analysis is outside the purview of this work, practitioners shouldn't depend on decision support because systems differ greatly in how they provide information, ranging fromthe lack of pertinent alerts to information overload that causes alert fatigue[44]

Treatment Plan:

Reducing mistakes that can lead to adverse drug reactions requires careful, safe prescribing.Plans for treatment should take into account and minimise any potential negative effects.[45]

Folic acid and methotrexate co-prescription, for instance, will lessen the likelihood of side effects linked to folate deficiency.Additionally, electrolyte and renal function monitoring is necessary when using diuretics or other renally active medications.All of these instances can stop treatment-emergent side effects, but their applicability may be restricted because monitoring guidelines are frequently vague or insufficient.

The treatment plan should always take conservative or non-pharmacological approaches into account, and it's crucial to keep in mind that wise prescribing may also prevent the usage of medications entirely.In order to lower the likelihood of an ADR and stop those "avoidable" reactions from happening in practice, a systems approach encompasses several tactics and involves the patient as well as all medical providers. [46]

II. CONCLUSION:

This narrative study concludes by highlighting the critical function that ADR reporting plays in drug safety and pharmacovigilance.Healthcare systems can make great progress towards a more reliable and patient-centered approach to ADR monitoring by recognising and resolving present issues.To improve patient outcomes by fast and accurate ADR reporting and progress the area of pharmacovigilance, stakeholders must collaborate and integrate cutting-edge technologies.

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REFERENCE:

[1]. Al Dweik R, Stacey D, Kohen D, Yaya S. Factors affecting patient reporting of adverse drug reactions: a systematic review. Br J ClinPharmacol. 2017;83(4):875-83.

[2]. Vivekanandan K, Rishi K, Prasad T, Arunabh T, Singh GN. Status of documentation grading and completeness score for Indian individual case safety reports. Indian J Pharmacol. 2015;47(3):325-7.

[3]. Nivya K, Sri Sai Kiran V, Ragoo N, Jayaprakash B, SonalSekhar M. Systemic review on drug related hospital admissions - a pubmed based search. SaudiPharmaceut J. 2015;23(1):1–8.

[4]. Jokanovic N, Wang KN, Dooley MJ, Lalic S, Tan EC, Kirkpatrick CM, Bell JS.Prioritizing interventions to manage polypharmacy in Australian aged carefacilities. Res SocAdm Pharm. 2017;13(3):564–74

[5]. Dr. Ramesh KG, Dr.Parloop AB, Dr. Mahesh DB. Elements of clinical pharmacy, 4th edn:2008-2009, B.S. Shah prakashan; page no-109-114.

[6]. Bennett PN, Brown MJ. Clinical Pharmacology. Tenth edition. Churchill Livingstone, Edinburgh, 2008

[7]. Walker R, Whittlesea C. Clinical pharmacy and therapeutics, 4th edn, Churchill Livingstone, Edinburgh 2007.

[8]. Fattahi F. Adverse drug reactions in hospitalized children in a department of infectious diseases. J ClinPharmacol 2005; 45: 1313-1318.

[9]. Aronson JK, Ferner RE. Classification of terminology in drug safety. Drug Safety 2005; 28: 851-870.

[10]. Bowman L, carlsted BC, Hancock EF, Black CD. Adverse drug reaction (ADR) occurrence and evaluation in elderly in patients. Pharmacoepidemiol Drug Safety 1996; 5: 9-18.

[11]. Bennett PN, Brown MJ. Clinical Pharmacology. Tenth edition. Churchill Livingstone, Edinburgh, 2008.

[12]. Walker R, Whittlesea C. Clinical pharmacy and therapeutics, 4th edn, Churchill Livingstone, Edinburgh 2007.

[13]. Dr. Ramesh KG, Dr.Parloop AB, Dr. Mahesh DB. Elements of clinical pharmacy, 4th edn:2008-2009, B.S. Shah prakashan; page no-109-114.

[14]. Clemerson J, Payne K. Pharmacogenetics current applications. Hospital Pharmacist 2008; 15: 167-173.

[15]. Dr. Ramesh KG, Dr.Parloop AB, Dr. Mahesh DB. Elements of clinical pharmacy, 4th edn:2008-2009, B.S. Shah prakashan; page no-109-114.

[16]. Bennett PN, Brown MJ. Clinical Pharmacology. Tenth edition. Churchill Livingstone, Edinburgh, 2008.

[17]. Walker R, Whittlesea C. Clinical pharmacy and therapeutics, 4th edn, Churchill Livingstone, Edinburgh 2007

[18]. Bodenheimer T, Berry-Millett R. Follow the money--controlling expenditures by improving care for patients needing costly

services. N Engl J Med. 2009;361(16):1521-3.
[19]. Parameswaran Nair N, Chalmers L, Bereznicki BJ, Curtain CM, Bereznicki LR. Repeat adverse drug reaction-related hospital admissions in elderly australians: a retrospective study at the royal hobart hospital. Drugs Aging. 2017;34(10):777-83.
[20]. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43(11):1130-9.
[21]. Gould AL, Lystig TC, Lu Y, Fu H, Ma H. Methods and issues to consider for detection of safety signals from spontaneous reporting databases: a report of the diabayesiansafety signal detection working group. TherInnovRegul Sci. 2015;49(1):65-75
[22]. Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of hospitalization resulting from medicine-related problems in adult patients. Br J ClinPharmacol. 2014;78(2):202-17
[23]. Dr. Ramesh KG, Dr.Parloop AB, Dr. Mahesh DB. Elements of clinical pharmacy, 4th edn:2008-2009, B.S. Shah prakashan; pageno-109-114.
[24]. Tarantino G. Drug-induced liver injury: is it somehow foreseeable? World J Gastroenterol 2009; 15: 2817-2833.
[25]. Elbe D, Savage R. How does this happen?. Part 1: mechanisms of adverse drug reactions associated with psychotropic medications.J Can Aca Child AdolPsychiat 2010; 19: 40-45.
[26]. Roujeau JC. Immune mechanisms in drug allergy. AllergolInt 2006; 55: 27-33.
[27]. Zaccara G. Idiosyncratic adverse reactions to antiepileptic drugs. Epilepsia 2007; 48: 1223-1244.
[28]. Zhang H, Du W, Gnjidic D, Chong S, Glasgow N. Trends in adverse drug reaction-Related hospitalisations over 13 years in New South Wales, Australia. Intern Med J.2019;49(1):84-93.
[29]. Rottenkolber D, Schmiedl S, Rottenkolber M, Farker K, Saljé K, Mueller S, et al. Adverse drug reactions in Germany: direct costs of internal medicine hospitalizations. Pharmacoepidemiol Drug Saf. 2011;20(6):626-34
[30]. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27(6):538.
[31]. Shepherd G, Mohorn P, Yacoub K, May DW. Adverse drug reaction deaths reported in United States vital statistics, 1999-2006. Ann Pharmacother. 2012;46(2):169-75.
[32]. Scondotto G, Pojero F, PollinaAddario S, Ferrante M, Pastorello M, Visconti M, Scondotto S, Casuccio A. The impact of polypharmacy and drug interactions among The elderly population in Western Sicily, Italy. Aging ClinExp Res. 2018;30(1):81-7.
[33]. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. Eur J ClinPharmacol. 2017;73(6):759-70.
[34]. ObreliNeto PR, Nobili A, de Lyra DP Jr, Pilger D, Guidoni CM, de Oliveira BaldoniA, et al. Incidence and predictors of adverse drug reactions caused by drug-drug Interactions in elderly outpatients: a prospective cohort study. J Pharm Pharm Sci. 2012;15(2):332-43.
[35]. Jacobs TQ, Ross A. Adverse effects profile of multidrug-resistant Tuberculosis treatment in a south African outpatient clinic. S Afr Fam Pract. 2012;54(6):531–9
[36]. Kowski AB, Weissinger F, Gaus V, Fidzinski P, Losch F, Holtkamp M. Specific Adverse effects of antiepileptic drugs—a true-to-life monotherapy study.EpilepsyBehav. 2016;54:150–7.
[37]. Lahon KI, Shetty HM, Paramel AM, Sharma GY. Adverse drug reaction Monitoring of antipsychotics, antidepressants and mood stabilizers in the Psychiatric outpatient unit of a teaching hospital–a retrospective study. Int J Pharma Bio Sci. 2012;3:470-8.
[38]. Lin HY, Liao CC, Cheng SH, Wang PC, Hsueh YS. Association of potentially AInappropriate medication use with adverse outcomes in ambulatory elderlyPatients with chronic diseases: experience in a Taiwanese medical setting.Drugs Aging. 2008;25(1):49–59 Bio Sciences 2012;3(1):P470-P8.
[39]. Wucherer D, Thyrian JR, Eichler T, Hertel J, Kilimann I, Richter S, et al. Drug-Related problems in community-dwelling primary care patients screened Positive for dementia. IntPsychogeriatr. 2017;29(11):1857–68.
[40]. Milligan F. Diabetes medication incidents in the care home setting. NursStand. 2012;26(29):38–43.
[41]. Gandhi TK, Weingart SN, Borus J, Seger AC, Peterson J, Burdick E, et al.Adverse

drug events in ambulatory care. N Engl J Med. 2003;348(16):1556–64.
[42]. Naranjo CA , Busto U , Sellers EM et al . A method for estimating The probability of adverse drug reactions . ClinPharmacolTher1981 ; 30 : 239 – 45 .
[43]. Hauben M , Aronson JK . Gold standards in pharmacovigilance: the Use of definitive anecdotal reports of adverse drug reactions as pure Gold and high-grade ore . Drug Saf 2007 ; 30 : 645 – 55 .
[44]. Ferner RE , Aronson JK . Preventability of drug-related harms –partI: a systematic review . Drug Saf 2010 ; 33 : 985 – 94 .
[45]. Coleman JJ , Ferner RE , Evans SJ . Monitoring for adverse drug reactions . Br J ClinPharmacol 2006 ; 61 : 371 – 8 .
[46]. Rommers MK , Teepe-Twiss IM , Guchelaar HJ . Preventing adverse drug events in hospital practice: an overview . Pharmacoepidemiol Drug Saf 2007 ; 16 : 1129 – 35 .