DETECTION AND MANAGEMENT OF ADRS IN TERTIARY HOSPITAL IN INDIA

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Abstract

Adverse drug reactions (ADRs) are a major cause of morbidity and hospitalizations have consistently increased, leading to economic burden to developing countries like India. Identification of ADRs and their reporting pattern can provide useful information for their management. Medicines that treat illnesses can modify, mostly in a beneficial manner, the physiological processes in the body. At the same time, drugs always carry a certain amount of risk, in the form of unintended or unwanted side effects, also known as Adverse Drug Reactions (ADRs). The utility of a medicine depends on a combination of the extent of expected benefits of the remedy and the seriousness of possible unwanted effects. Every time a community is exposed to a new medication, the risk of ADRs increases. This occurs when a new drug is introduced into the market for the first time. No drug is absolutely safe, even when prescribed in therapeutic doses. The World Health Organization (WHO) defines Pharmacovigilance (PV) as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects of drugs. An ADR is a reaction to a drug and/or a combination of drugs which is harmful and unintended and which occurs at a dose that is normally used for prophylaxis, diagnosis or treatment. This study is mainly focus on Detection and management of ADRs in Tertiary Hospital. It is suggested that the most appropriate approach of medication control to minimize the incidence of ADR is screening the total medication of the individual patient by a hospital/clinical pharmacist and by taking history of allergy as well as past medication and medical history.

Keywords: *Adverse drug reaction, medicines, physiological process, WHO, pharmacovigilance, tertiary hospital*

Introduction

Drug therapy, a major health care approach paradoxically at time poses major health problems or even death. These unwanted outcomes of drug therapy were recognised as Adverse Drug Reactions (ADRs). The term "tertiary" may be a useful way to categorize a university hospital or specialist centre, but when the term is used to describe the care given to a patient, it is a vacuous construct. When hospital administrators define some patients or medical conditions as outside the remit of tertiary care, doctors come under pressure to think in silos and to abandon their patients. In India, patients go to tertiary hospitals even on the slightest suspicion of viral fever. In an ideal healthcare setup, they should have been treated through preventive or primary healthcare systems. Unfortunately, primary healthcare systems are weak, dilapidated and untrustworthy. Thus, a lot of burden falls on tertiary hospitals which are otherwise meant for complex medical conditions such as cancers, pulmonary diseases, cardiovascular diseases and so on. Besides the issue of overcrowding in public tertiary hospitals, there is also the problem of underfunding.

An adverse drug reaction (ADR)is a damage affected by taking a medication. ADRs may happens following a single dose or prolonged administration of a medication or outcome from the combination of two or more medications. The meaning of this appearance varies from the meaning of "side effect", as this last apperence might also imply that the effects can

be beneficial. The study of ADRs is the concern of the field known as *pharmacovigilance*. An adverse drug event (ADE) refers to any damage happensring at the time a medication is used, whether or not it is identified as a cause of the damage. An ADR is a special type of ADE in which a causative relationship can be shown.

Any noxious, undesired, or unintended reaction to atherapeutic agent, which may be expecte d or unexpected, and may happens at dosages used for theprophylaxis, diagnosis, or therapy o f disease, or for modifying physiologic function. ADRs do not includetherapeutic failures, poi soning, accidental or intentional overdoses.

Clinical findings Pruritus, nausea, vomiting, rash, confusion, lethargy, etc.

Culprits ADR are most commonly affected by analgesics and narcotics, antibiotics, cardiovas cular agents, anticoagulants, and psychotherapeutics.

Regulatory process in the preapproval clinical involving with a new medicinal product or its newusages, particularly as the therapeutic dose(s) may not be established, all noxious and uni ntendedreactions to a medicinal product related to any dose should be considered adverse me dication reactions; acausal relationship between a medicinal product and an adverse event is a t least a reasonable possibility—i.e., the relationship cannot be ruled out.

There are several terms commonly used to describe adverse effects of medication therapy:

- An adverse drug reaction (ADR)is an unwanted or harmful reaction involvingd following the administration of a medication or combination of medications under normal conditions of use and is doubted to be related to the medication. An ADR will commonly need the medication to be discontinued or the dose reduced.
- An adverse event is harm that happens while a sufferer is taking a medication, irrespective of whether the medication is suspected to be the cause.
- A side-effect is any effect affected by a medication other than the intended therapeutic effect, whether beneficial, neutral or harmful. The term 'side-effect' is often used interchangeably with 'ADR' although the former commonly implies an effect that is less harmful, predictable and may not even require discontinuation of therapy (e.g. ankle oedema with vasodilators).
- Medication toxicity describes adverse effects of a medication that happens because the dose or plasma concentration has risen above the therapeutic range, either unintentionally or intentionally (medication overdose).
- Medication abuse is the misuse of recreational or therapeutic medications that may lead to addiction or dependence, serious physiological injury (such as damage to kidneys, liver, heart), psychological harm (abnormal behavior patterns, hallucinations, memory loss), or death.

Any medication that is creating of creating beneficial therapeutic effects can also cause unwanted 'adverse' effects. Adverse medication reactions (ADRs) are therefore common and constitute an important public health challenge in their own right. A important proportion of admissions to hospital are affected by ADRs and hospitalised sufferers regularly involving ADRs that complicate and prolong their stay. Many of these ADRs can be avoided if greater care is taken. All prescribers need to make a judgment about the likelihood that a sufferer will either gain from the beneficial effects or involving an ADR before prescribing. Some medications rarely cause ADRs (e.g. paracetamol) while others regularly do so (e.g. cancer chemotherapy). The decision to prescribe these 'higher risk' medications will depend on the

extent of the potential benefits. Although prescribers always face the possibility of causing an ADR the risks of doing so can be minimised by (i) recognition of sufferer and medication factors that increase the susceptibility and (ii) by counselling sufferers about early indications that an ADR may be developing.

Literature review

Verman S, Anjankar A (2022) An adverse event is any abnormal clinical finding associated with the use of a therapy. Adverse events are classified by reporting an event's seriousness, expectedness, and relatedness. Monitoring patient safety is of utmost importance as more and more data becomes available. In reality, very low numbers of adverse events are reported via the official path. Chart review, voluntary reporting, computerized surveillance, and direct observation can detect adverse drug events. Medication errors are commonly seen in hospitals and need provider and system-based interventions to prevent them. The need of the hour in India is to develop and implement medication safety best practices to avoid adverse events. The utility of artificial intelligence techniques in adverse event detection remains unexplored, and their accuracy and precision need to be studied in a controlled setting. There is a need to develop predictive models to assess the likelihood of adverse reactions while testing novel pharmaceutical drugs.

Shukla (2021) The Pharmacovigilance Program of India recommends the use of the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) scale, while many clinicians prefer the Naranjo algorithm for its simplicity. In the present study, we assessed agreement between the two widely used causality assessment scales, that is, the WHO-UMC criteria and the Naranjo algorithm. In this study, 842 individual case safety reports were randomly selected from 1000 spontaneously reported forms submitted to the ADR Monitoring Center at a tertiary healthcare Institute in Central India between 2016 and 2018. Two well-trained independent groups performed the causality assessment. One group performed a causality assessment of the 842 ADRs using the WHO-UMC criteria and the other group performed the same using the Naranjo algorithm. The agreement between two ADR causality scales was assessed using the weighted kappa (κ) test.

Basics of adverse drug reactions

An adverse drug reaction (ADR) can be defined as 'an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product'.Since 2012, the definition has included reactions occurring as a result of error, misuse or abuse, and to suspected reactions to medicines that are unlicensed or being used off-label in addition to the authorised use of a medicinal product in normal doses. While this change potentially alters the reporting and surveillance carried out by manufactures and medicines regulators, in clinical practice it should not affect our approach to managing ADRs. Seminal research undertaken in the late 20th and early 21st century in the USA and the UK demonstrated that ADRs are a common manifestation in clinical practice, including as a cause of unscheduled hospital admissions, occurring during hospital admission and manifesting after discharge. The incidence of ADRs has remained relatively unchanged over time, with research suggesting that between 5% and 10% of patients may suffer from an ADR at admission, during admission or at discharge, despite various preventative efforts. Inevitably, the event

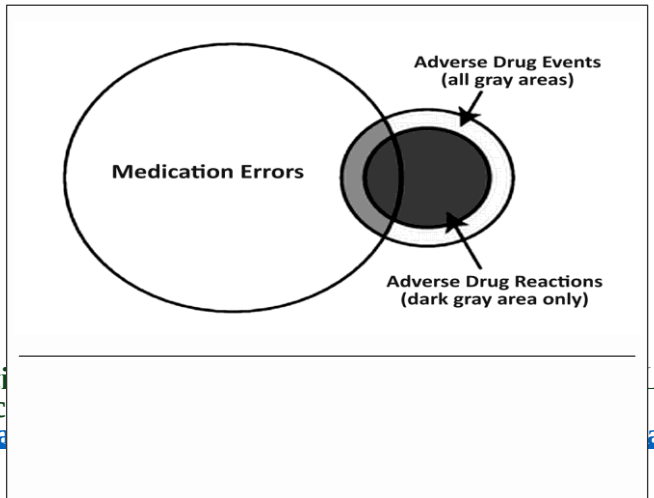
frequency is associated with the method used to identify such events and the majority of ADRs do not cause serious systemic manifestations. Nevertheless, this frequency of potential harm needs to be considered carefully because it has associated morbidity and mortality, can be financially costly and has a potentially negative effect on the prescriber-patient relationship. Medicines that have been particularly implicated in ADR-related hospital admissions include antiplatelets, anticoagulants, cytotoxics, immunosuppressants, diuretics, antidiabetics and antibiotics. Fatal ADRs, when they occur, are often attributable to haemorrhage, the most common suspected cause being an antithrombotic/anticoagulant co-administered with a non-steroidal anti-inflammatory drug (NSAID).

Detection of ADRs

Defining ADRs

The definition of an ADR is often confused with that of an adverse medication event (ADE). The World Health Organization (WHO) defines an ADE as "any untoward medical happensrence that may present in the course of managment with a pharmaceutical product but which does not nec- essarily have a causal relationship with this managment" (WHO 2005). The WHO defines an ADR as "a reaction to a medication which is noxious and unintended and which happenss at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function." An ADR is a type of ADE whose cause can be directly attributed to a medication and its physiologic properties. A main distinction between ADRs and ADEs is that ADRs happens despite appropriate prescribing and dosing, whereas ADEs may also be associated with inappropriate use of the medication or other confounders that happens in the course of medication therapy but are not necessarily affected by the pharmacology of the medication itself. A causal relationship is suspected for an ADR but is not required for an ADE. Adverse medication events may also be affected by medication faults, which the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) defines as "any preventable event that may cause or lead to inappropriate medication use or sufferer harm while the medication is in the con- trol of the health care professional, sufferer, or consumer." Figure shows the relationship between ADRs, ADEs, and medication faults.

Published studies of ADRs, ADEs, and medication faults often use these terms interchangeably, leading to inconsistency in the reported prevalence of each. Definitions are often subject to the individual researcher's preference, making the interpretation of outcomes and reproducibility difficult. Standardizing and using terminology such as that defined by the Medical Dictionary for Regulatory Activities can improve the quality and consistency of research in this realm. Other publication authors and governing bodies that have proposed alternative



Methodology

Methods of detecting an ADR

The first step in detection of ADRs is collection of data. The data to be collected includes patient's demographic data; presenting complaints; past medication history; drug therapy details including over- the- counter drugs, current medications and medication on admission; and lab data such as hematological, liver and renal function tests. Details of the suspected adverse drug reaction such as time of onset and duration of reaction, nature and severity of reaction; details of the suspected drug including dose, frequency, time of administration, duration of treatment, plasma concentration of drug; previous reports on reported reactions; data on any other causes including risk factors and predisposing factors are useful. Every healthcare practitioner should see it as a part if his/her professional duty to report any suspicion of a drug unexpectedly causing a risk situation for a patient under his/her cares.

MANAGEMENT OF ADR:

First and foremost step is withdrawal of suspected drug(s), if the reaction is likely to be dose related, dose reduction should be considered, and treatment for suspected reaction. While managing an ADR, always have a clear therapeutic objective in mind, do not treat for longer than necessary, review the patient regularly and simplify management.

The study population consisted of 3 groups -

1) Medical practitioners,

2)patients and

3) experts

in the field of PV I ADR monitoring and coordinators of PV I ADR monitoring centers.

After completing analysis of these surveys I information sharing sessions, a list of suspected factors I variables responsible for underreporting were identified. The list of MPs was prepared who provided us the data on number of ADRs observed and the numbers of ADRs reported to regulatory bodies. Then data available from this subset of MPs was analyzed using Logistic Regression Analysis (LRA) model to isolate statistically valid and significant factors responsible for underreporting of ADRs.

Results

A total of 164 documented ADRs were identified in 2126 General Medicine ward admissions during the study period. The results of the age categorization revealed that the patients of 60 years and above age group experienced maximum ADRs which were about 52%, followed by 32% in age group between 30-59 years old and 16% in 18-29 years age group.

Table : Age Categorization of patients

Age group	No.of Patients	Percentage
18-29	26	16
30-59	53	32
60 and above	85	52

Graph : Age Categorization of patients

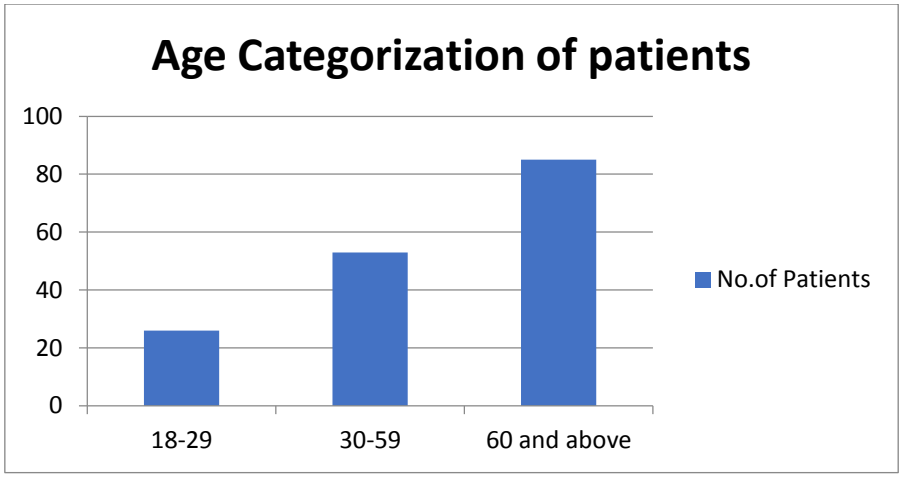


Table : Causality assessment of suspected Adverse Drug Reactions (WHO scale)

Causality Assessment scale	No.of patients	Percentage
Certain	52	32
Probable	34	21
Possible	66	40
Unclassified	7	4
Unclassifiable	5	3

Graph : Causality assessment of suspected Adverse Drug Reactions

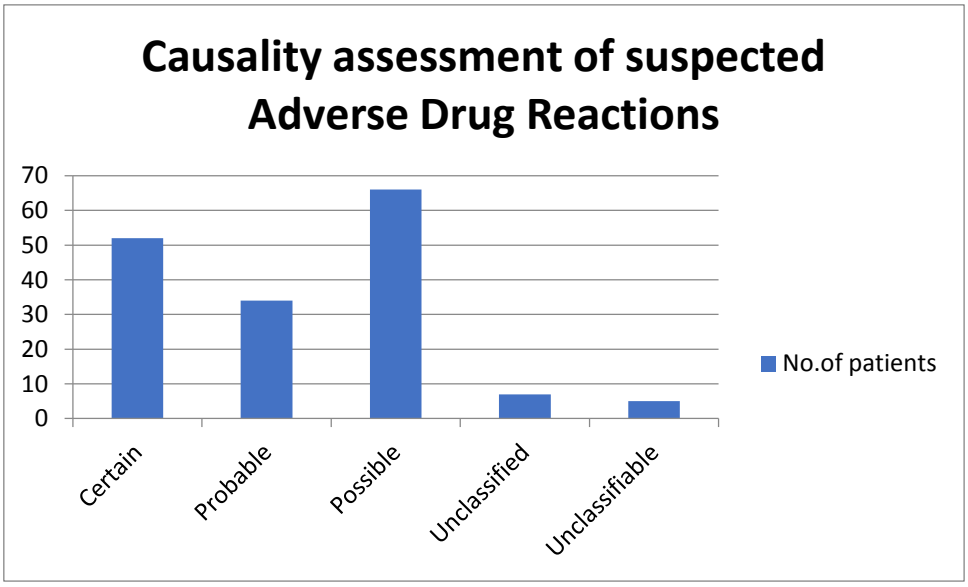
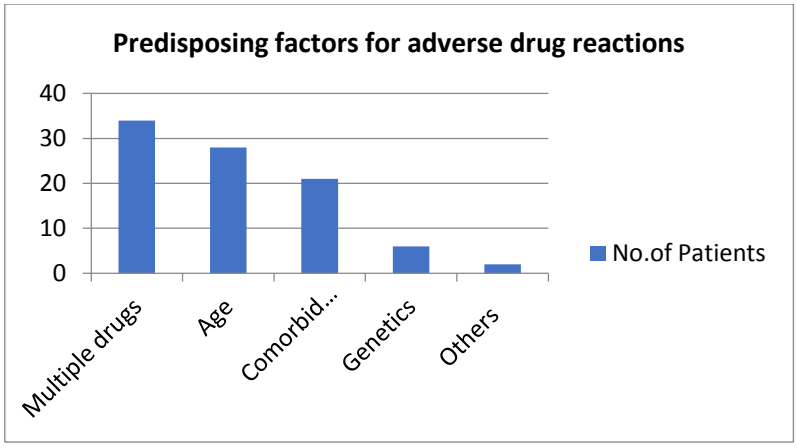


Table :Predisposing factors for adverse drug reactions

Factors	No.of Patients	Percentage
Multiple drugs	57	35
Age	46	28
Comorbid disease	32	20
Genetics	21	12
Others	8	5

Graph : Table 3:Predisposing factors for adverse drug reactions



Conclusion

This study strongly suggests there is a need for streamlining hospital-based ADR reporting and monitoring system in order to create awareness and to promote the reporting of ADR among HCPs. The present study concludes pharmacist's involvement greatly increases the reporting rate as well as quality of reporting. This study there is greater need for streamlining of hospital-based ADR reporting and monitoring system to create awareness; and to promote the reporting of ADR among healthcare professionals of the country. Measures to improve detection and reporting of ADR by all health care professionals should be undertaken, to ensure patient's safety. The present study hints that pharmacists' involvement may not only greatly increase the reporting rate but also quality of reporting. It is suggested that the most appropriate approach of medication control to minimize the incidence of ADR is screening the total medication of the individual patient by a hospital/clinical pharmacist and by taking history of allergy as well as past medication and medical history. Hospital/clinical pharmacists have also a greater role to play in the area of pharmacovigilance to strengthen the national pharmacovigilance program.

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