A STUDY TO ESTIMATE THE PREVALENCE OF ADVERSE DRUG REACTIONS AT A PRIVATE DELECT HOSPITAL

S. R. Rahul
Research Scholar
Department of Pharmacy
SunRise University

Dr.Balla Ramakrishna
Research Supervisor
Department of Pharmacy
SunRise University

Abstract

An adverse drug reaction (ADR)is an 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 appearance might also imply that the effects can be beneficial. Adverse drug reactions (ADRs) remain a challenge in modern healthcare, particularly given the increasing complexity of therapeutics, an ageing population and rising multimorbidity. This article summarises some of the key facts about ADRs and explores aspects relating to their prevention, diagnosis, reporting and management in current clinical practice. 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.[1] An ADR is a special type of ADE in which a causative relationship can be shown.

Keywords:ADR, Drug, Side Effects, Reactions.

Introduction

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.2 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).

Traditionally, ADRs have been classified into two types:

Type A reactions – sometimes referred to as augmented reactions – which are 'dose-dependent' and predictable on the basis of the pharmacology of the drug

Type B reactions – bizarre reactions – which are idiosyncratic and not predictable on the basis of the pharmacology.

Although still widely quoted, this basic classification does not work for all ADRs, such as with chronic adverse effects associated with cumulative drug exposure (eg osteoporosis with long-term corticosteroid treatment) or withdrawal reactions (eg rebound hypertension with centrally-acting antihypertensive cessation). An alternative and perhaps more comprehensive classification scheme is 'DoTS', which classifies reactions dependent on the Dose of the drug, the Time course of the reaction and relevant Susceptibility factors (such as genetic, pathological and other biological differences). As well as classifying reactions, DoTS has the advantage of being helpful to consider the diagnosis and prevention of ADRs in practice.

Preventing adverse drug reactions

While some ADRs are unpredictable – such as anaphylaxis in a patient after one previous uneventful exposure to a penicillin-containing antibiotic – many are preventable with adequate foresight and monitoring. Preventability (or avoidability) usually refers to when the drug treatment plan is inconsistent with current evidence-based practice or is unrealistic when taking known circumstances into account.10 Epidemiological studies tend to find that between a third and a half of ADRs are (at least potentially) preventable although preventability is much easier to diagnose in hindsight. However, interventions that reduce the probability of an ADR occurring can be an important way to reduce the risk of patient harm.

There are two basic steps that can be followed to prevent an ADR occurring:

- Identify the subgroup of patients who are likely to be susceptible to the adverse effect and modify the treatment choice accordingly.
- Ensure the treatment plan mitigates any possible adverse effects.

Research Methodology

Study design : Prospective observational study.

Study period : Study was carried out for a period of six months.

Source of data : Data was collected from - Case files of patient who was admitted for more than 24 hours in the hospital (tertiary care hospital).

Inclusion criteria:

- All patients admitted to the hospital
- Both gender

Exclusion criteria:

- Clinical trial patients
- Pregnant patients
- Neonates

Method of data collection:

- Case series study
- Spontaneous reporting

Analysis:

- Microsoft Excel

Results and discussion

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 1: Age Categorization of patients

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

Graph 1: Age Categorization of patients

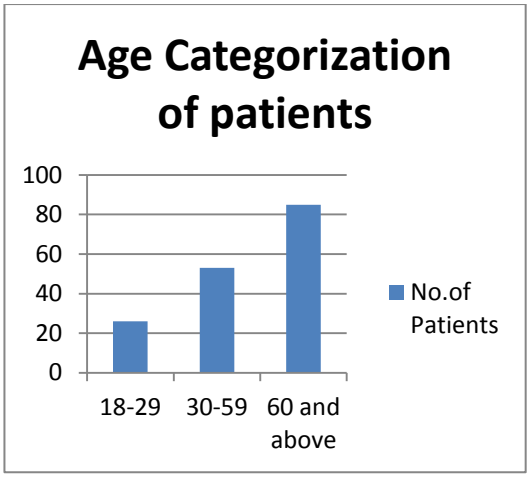


Table 2: Causality assessment of suspected Adverse Drug Reactions (WHO scale)

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

Graph 2: Causality assessment of suspected Adverse Drug Reactions

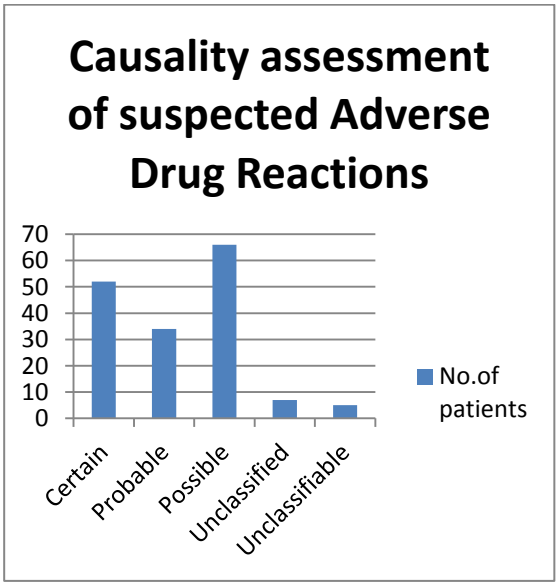


Table 3:Predisposing factors for adverse drug reactions

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

Graph 3: Table 3:Predisposing factors for adverse drug reactions

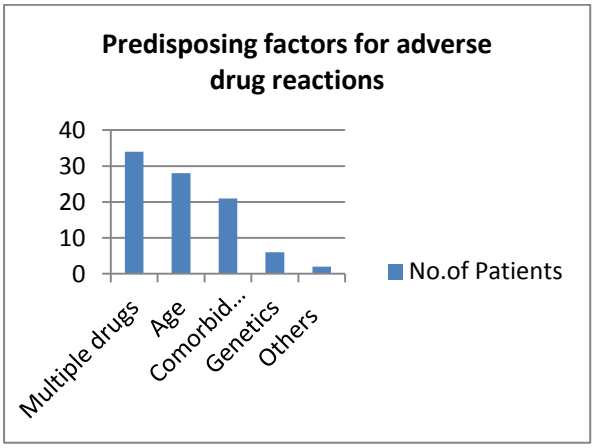
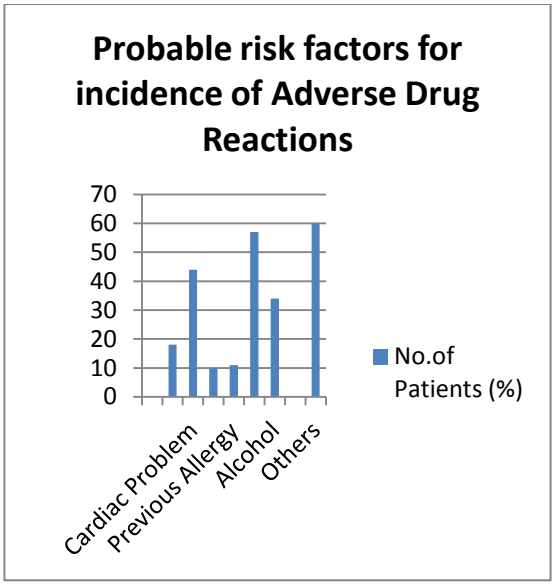


Table 4: Probable risk factors for incidence of Adverse Drug Reactions

Risk Factors	No.of Patients (%)
Renal Insufficiency	18(11)
Cardiac Problem	44(27)
Hepatic Problem	10(6)
Previous Allergy	11(7)
Smoking	57(35)
Alcohol	34(21)
Drug addiction	00(00)
Others	60(37)

Graph 4: Probable risk factors for incidence of Adverse Drug Reactions



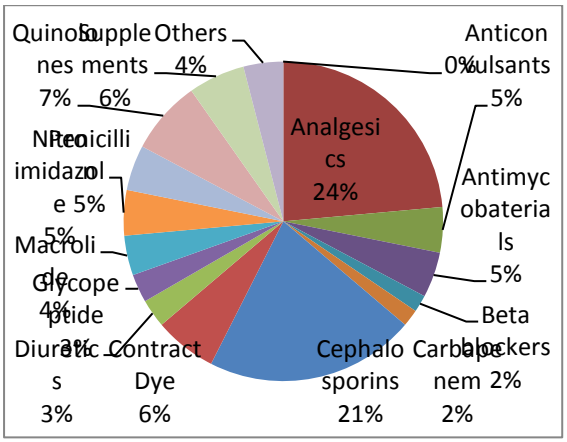
Of the patients who experienced ADR during the study period 61% were male and 39% were female. Causality assessment through WHO scale indicated that 42% of them were possible . Causality assessment of suspected ADRs using Naranjo's scale showed that 63% of them were probable and the rest of them categorized as possible. The severity of 45% of reactions (using Hartwig scale) was reported as moderate and 14% considered as severe. On the basis of Modified Schumock and Thornton scale, 46 (28%) and 13 (8%) reactions of the suspected ADRs were definitely and probably preventable, respectively. In 57 (35%) of cases the ADR was managed by withdrawal of drug and in 41 (25%) patients the dose of drug was altered. While in 41 (25%) of cases the severity of ADR was safely decreased, 118 (72%) patients recovered from the reaction. No fatal cases were reported. Dechallange was done in 52 (32%) and the affected patients were not subjected to rechallenge. Multiple drug therapy, age and comorbid diseases were identified as the major predisposing factors for occurrence of ADRs. The major risk factors for causing ADRs were

identified as cardiac problems, smoking, alcohol intake, etc.

Table 5:Class of Drugs Associated with ADRs

Class of Drug	No.of Patients (%)
Analgesics	41(25)
Anticonvulsants	8(5)
Antimycobaterials	8(5)
Beta blockers	3(2)
Carbapenem	3(2)
Cephalosporins	37(23)
Contract Dye	11(7)
Diuretics	5(3)
Glycopeptide	5(3)
Macrolide	7(4)
Nitro imidazole	8(5)
Penicillin	8(5)
Quinolones	13(8)
Supplements	10(6)
Others	7(4)

Graph 5:Class of Drugs Associated with ADRs

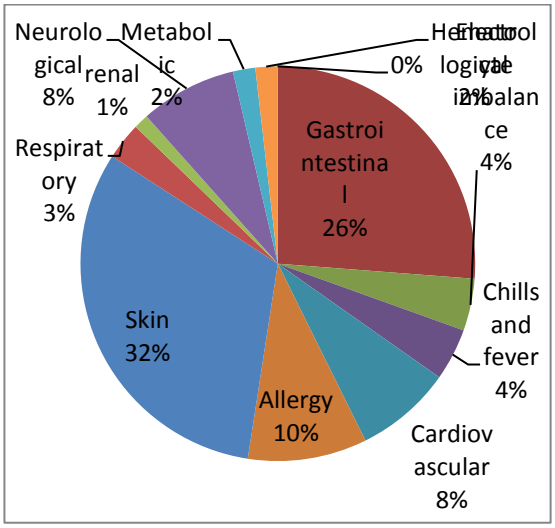


In our retrospective study ADRs were commonly associated with Analgesic (25%) followed by Cephalosporins (23%), Quinolones (7%) and Contrast Dye (6%). Our prospective study shows that ADRs were most common in Chemotherapy (33.3%) followed by Fluroquinolones and Sympatholytics (11.1%).

Table 6: Organ Systems Affected by ADRs & commonly Occurring Reactions.

Organ System Affection	No.of Patients (%)
Gastrointestinal	43(26)
Electrolyte imbalance	7(4)
Chills and fever	7(4)
Cardiovascular	13(8)
Allergy	16(10)
Skin	52(32)
Respiratory	5(3)
renal	2(1)
Neurological	13(8)
Metabolic	3(2)
Hematological	3(2)

Graph 6: Organ Systems Affected by ADRs & commonly Occurring Reactions.



Our retrospective data shows the organ systems most commonly affected by ADRs were Skin (32%) followed by Gastrointestinal System (26%), Allergies (10%) and Neurological (8%). Our prospective analysis shows that Skin

(11%) and Gastrointestinal system (7%) predominance.

DISSCUSION

The incidence of suspected ADRs was found to be 1.82% and is comparable with the study done by Rao et al,[3] which evaluated the reports of ADRs in the inpatients at a south Indian hospital for their incidence and pattern and found that the incidence of ADRs was 2.8% in hospitalized patients. Pirmohamed et al[12] concluded from a prospective analysis of about 18,820 patients in UK in which about 1225 admissions were related to ADRs giving a prevalence of 6.5%. This is consistent with the findings of Arulmani et al.[13]

Pirmohamed et al have shown a greater percentage of geriatric population suffering from adverse reactions which is consistent with the present results that mentioned before.[12]

According to the present findings the ADRs in the hospital patients were more documented in males which is consistent with the earlier report by Gupta et al.[14] Sex ratio in admitted patients might be an intervening factor but does not seem to be a major determinant.

Causality assessment was done by using WHO and Naranjo scale. The assessment done by using WHO scale reveals that 42% of ADRs were possibly drugrelated, 23% of ADRs were probably drug-related, whereas 30% were classified as certainly related to drug. Assessment by Naranjo scale showed that 63% of ADRs were possibly drug-related, whereas 37% were classified as probably or definitely related to the drug. These results matches with Davies et al[15] study which had assessed the feasibility and established the methodology for conducting a large prospective study to fully assess the impact of ADRs on inpatients. Causality assessment showed that 62% of ADR were possibly drug-related whereas 32% were classified as probably or definitely related to the drug and almost two-thirds of reactions were potentially avoidable.

Severity of the suspected ADRs assessed using Modified Hartwig and Siegel Scale, revealed that 12% of suspected ADRs were severe, 49% of ADRs were moderate and 39% of ADRs were mild in severity. These were comparable with the review conducted by Shuster[16] in reporting ADR from the Institute of Safe Medication Practices (ISMP) in cooperation with the FDA's MEDWATCH program during the month of June 2005 in a 200-bedded community hospital which reported 36 distinct admissions due to ADRs, with 9% of the cases categorized as severe, and 76% of the events were regarded as moderate.

Systems most commonly affected were gastrointestinal in 37% of patients, dermatological in 25% of patients, central nervous system in 14% of patients, followed by cardiovascular in 12% of patients. The results were comparable with an international study conducted by Suh et al, which revealed that the system most badly affected was the dermatological and gastrointestinal system.[17] The drug class mostly associated with ADR was antibiotics in 23% of cases, followed by NSAIDs in 19% in the present study. Murphy and Frigo developed and implemented an ADR reporting program in Loyola University Medical Center, a 563-bed tertiary care teaching hospital located in the western suburbs of Chicago.

This study revealed that the most common adverse reactions were rash; and antibiotics were the most commonly implicated drug class.[18] The results were also comparable with other studies like one done by Classen et al[19] which indicated that NSAIDs have caused extensive damage to human health.

Preventability of suspected ADRs were assessed by using Modified Schumock and Thornton scale, revealed that 28% of ADRs were definitely preventable while 7% of ADRs were probably preventable. This study revealed that an increased risk of ADRs is suspected in elderly patients, and that almost one-thirds of reactions were preventable. Knowledge of pharmacological principles and how aging affects drug kinetics and response were essential if we are to promote safe prescribing practices.[20]

The provision of "alert card" was aimed at preventing the occurrence of the similar ADR to the same drug and/or other drug(s) belonging to similar class or other classes of drugs which shows cross sensitivity reaction with suspected drug(s) in the same patient in the future.

Under-reporting is a major problem even in western countries where the pharmacovigilance system is well established. In India the major problem is a lack of proper system of pharmacovigilance. Our ability to anticipate and prevent such ADRs can be facilitated by the establishment of standardized approaches and active reporting of suspected ADRs by all healthcare professionals including physicians, dentists, nurses and pharmacists. This could be further improved by pharmacist involvement for encouraging them through conducting educational programs on pharmacovigilance, lectures, newsletters, personalized letters, etc to aid and increase reporting of ADR.

A study by S Sriram et al on Prevalence of adverse drug reactions in a private tertiary care hospital in South India associated Antibiotics as 23% followed by NSAIDs as 19% of drug classes causing ADR.
Study by S Sriram et al showed organ systems most commonly affected by ADRs were Gastrointestinal in 37% of patients, Dermatological in 25% of patients, Central Nervous System in 14% of patients, followed by Cardiovascular in 12% of patients [20]. Our results were comparable with an international study conducted by Suh et al, which revealed that the system most badly affected was the dermatological and gastrointestinal system [25].

Conclusion

This study strongly suggests that 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. Developing and maintaining electronic documentation of patients' medical records may serve as a valuable tool to detect early signals of potential ADRs. In addition, creating intranet facilities within a hospital may help in easy access for healthcare professionals to updated patients' medical records resulting in possible detection and prevention of ADRs. Also, the implementation of a computerized reporting system in hospital setup may hasten reporting of ADRs and is suggested.

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