

A study of pattern of adverse drug reactions in inpatients department of medicine of tertiary care hospital in Madhya Pradesh, India**Pradeep Phadnis, Shashi Marko***

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ABSTRACT

Background: Adverse Drug Reactions are the recognized hazards of drug therapy and they can occur with any class of drugs. The main aim of the study was to detect and analyze Adverse Drug Reactions in inpatients of medicine department in tertiary care hospital. The study assesses the incidence and pattern of ADRs, identifying co-morbidities, past and present illness, assess causality and the offending drugs, monitoring and documenting suspected adverse drug reactions.

Methods: A prospective study was conducted over a period of 6 months. The WHO definition of an ADR was adopted. Each ADR was assessed for its causality by using WHO probability scale. The severity of each ADR was assessed by using modified Hartwig et al, and Siegel scale.

Results: A total 58 ADR were reported during study period out of which 28 (48.27%) were male and 30 (51.72%) were female patients. The assessment by WHO probability scale showed that out of 58 ADR 22 (37.93%) were probable and 17 (29.31%) were possible and 6 (10.34%) were certain. Most commonly involved system was gastrointestinal system with 24 (41.37%) ADRs. Severity assessment by modified Hartwig and Siegel scale showed that 22 (37.93%) were moderate, 32 (55.17%) were mild and 4 (6.89%) were severe ADRs. No lethal effects were observed or produced.

Conclusions: The study concluded that Adverse Drug Reactions are common and some of them resulted in increased health care cost due to need of some interventions and increased length of hospital stay. The health system should promote the reporting of Adverse Drug Reactions, proper documentation and periodic reporting to regional pharmacovigilance centers to ensure drug safety.

Keywords: Adverse drug reactions, World Health Organization probability scale

INTRODUCTION

According to WHO's definition on Adverse Drug Reaction (ADR) is a response to a drug that is noxious and unintended and occurs at doses normally used in human for the prophylaxis, diagnosis and treatment of disease or for modification of physiological function.^{1,2}

Adverse drug reactions (ADR) are common occurrences in a hospital setting, attributed to the severity and complexity of the disease Process, the use of multiple drugs, drug interactions and possible negligence.³ ADR could be

observed in 10-20% of hospitalized patients and may be responsible for prolonged hospital stay.⁴

The female gender, elderly age group, and the recent introduction of new drugs are important risk factors for ADRs.⁵ Other important factors for their occurrence are race, pregnancy, breastfeeding, alcohol intake, and state of liver and kidney functions.⁶

ADR monitoring and reporting helps in detection and prevention of recurrence of ADRs. The detection of adverse drug reactions (ADRs) has become increasingly significant because of introduction of a large number of potent toxic chemicals as drugs in the last two or three

decades. WHO has intervened seriously in this matter and established an international adverse drug reaction monitoring centre at Uppsala, Sweden, which is collaborating with national monitoring centers in around 70 countries.

The Pharmacovigilance Programme of India was initiated by the Government of India on 14.07.2010 with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Co-Ordination Centre for monitoring Adverse Drug Reactions (ADR) in the country for safe guarding public health. To ensure implementation of this programme in a more effective way, the National Coordination Centre has been shifted to the Indian Pharmacopoeia Commission, Ghaziabad, (UP) on 15.04.2011. The national Coordination Centre is operating under the supervision of Steering Committee to recommend procedures and guidelines for regulatory intervention.

Aims and objectives

- To detect adverse drug reactions (ADRs) to drugs used in admitted patient of medicine department in BMC Hospital.
- Find out the incidence, type and nature of ADR, causality drugs causing the same and their outcome amongst the hospitalized patients in the medicine ward of Bundelkhand Medical college tertiary care teaching hospital located in Sagar Madhya Pradesh.

METHODS

A prospective study of 6 month's duration, from Dec 2016-May 2017, was carried out in the Bundelkhand Medical College, Sagar in indoor patients of medicine department with the help of Department of Pharmacology in Bundelkhand Medical College, Sagar, Madhya Pradesh.

Appropriate study protocol and protocol and proforma for monitoring ADR were developed.

Inclusion criteria

Patients of either sex of any age admitted in medicine ward who developed an ADR.

Exclusion criteria

Patient's presenting difficulties in communication and accidental or intentional poisoning or known allergic reaction due to drugs will be excluded from the study.

On receiving the report, investigator visited the respective ward and collected the necessary details. When an ADR was suspected, the data from the patient profile form such as patient details, patient medication details including non-prescription drugs, alternative treatments and recently ceased medications, comprehensive adverse reaction details including description of the reaction, time of onset

and duration of the reaction and treatment given with relevant investigation reports were collected.

The causality was assessed by using WHO probability scale and the severity was assessed by using the Hartwig and Siegel severity assessment scale according to the recommendation by the WHO Uppsala Monitoring Center.⁷

Statistical method

From pooled data we calculated mean, standard deviation, percentage, and as required the Chi-squared test were applied to find the association between outcome and parameters and P-values less than 0.05 were considered as significant.

RESULTS

During the 6 months study period, a total 2780 patients studied prospectively. A total of 58 ADRs were reported in 2780 patients. Among 2780 patients, 1820 were in the age group of less than 40 years and 960 in age group of more than 40 years and they had 32 patients (55.17%) and 26 patients 44.82% with ADRs respectively.

The gender distribution among the patients, who experienced ADRs were 28 (48.27%) males and 30 (51.72%) females. Taking the whole study population 2780 females (1080) have experienced more number of ADRs as compared to the male (1700) population (Table 1).

Table 1: Demographic data of patients who had adverse drug reactions.

Demographic parameter	No of ADRs (%)	
Age wise	<40 years	32(54.5%)
	>40years	26(44.82%)
Gender wise	Male	28(48.27%)
	Female	30(51.72%)
Total	58	

As expected, polypharmacy had a major influence on the occurrence of ADRs with a total of 36(62.06%) ADRs observed in patients receiving 4 or more medications concurrently.

Conversely, 22 (37.93%) ADRs were detected in patients on 3 or less medications (Table 2).

The frequency of ADRs associated with different routes of administration was as follows- oral (n=50), parenteral (n=6) and topical (n=2) (Table 3).

The gastrointestinal side effects (e.g. gastritis, dysphasia,) were at the top with 41% followed by skin and subcutaneous disorders (29%), other main group were respiratory (12%) CNS and neurological disorders (6%).

The detailed description of organ system affected by ADRs is shown in Table 4.

Table 2: Number of drugs and adverse drug reactions (%).

Number of drugs	No of ADRs (%)	(%)
1	4(6.89%)	
2	6(10.34%)	22(37.93%)
3	12(20.68%)	
4	8(13.79%)	
5	10(17.24%)	
6	9(15.51%)	36(62.06%)
7	9(15.51%)	
Total	58	

Table 3: Adverse drug reactions related to route of drug administration.

Route	ADRs (%)
Oral	50(86.20%)
Parenteral	6(10.34%)
Topical	2(3.4%)
Total	58

Table 4: Adverse drug reactions and organ system involved.

Organ system involved	No of ADRs (%)
Gastrointestinal disorders	24(41.37%)
Skin and mucous membranes	17(29.31%)
Respiratory disorders	7(12.06%)
CNS and neurological disorder	4(6.89%)
Hepatobiliary disorders	2(3.44%)
Others	4(6.89%)
Total	58

Table 5: Causality assessment of adverse drug reactions by WHO probability scale.

Probability scale	No of ADRs
Certain	6(10.34%)
Probable	22(37.93%)
Possible	17(29.31)
Unlikely	3(5.17%)
Conditional	4(6.89%)
Un-assessable	6(10.34%)
Total	58

Out of total number of 58 ADRs, 6 (10.34%) were classified as certain, e.g. hypersensitivity reaction with intravenous contrast medium, skin reactions with cefotaxime injection, itching and dermatitis with etophylline tablets, and hypoglycemia with glibenclamide tablets. 22 ADRs (37.93%) were considered Probable e.g. dry cough with enalapril and dysphasia with furosemide tablets 17 (29.31%) were classified as possible 6 (8.62%)

could not be categorized and were placed under unassessable category Table 5.

Out of 58 ADRs, 28 (48.27%) were found to be mild e.g. cold extremities with atenolol, 22 (37.93%) moderate e.g. dry cough with ramipril, and 8 (13.79%) severe Table 6.

Table 6: Classification of adverse drug reactions on the basis of severity.

Severity	No of ADRs (%)
Mild	28(49%)
Moderate	22(37.93%)
Severe	8(13.79%)
Total	58

Most of the severe ADRs were associated with oral hypoglycemic drugs, insulin and heparin. These were reported more commonly with injectable as compared to oral medications.

Distribution of ADRs according to therapeutic classes: antimicrobial 19 (32.75%), antihypertensive 15 (25.86%), antidiabetics 8 (13.79) and NSAIDs 7 (12.06%). Among the individual drugs ramipril was associated with maximum cases of ADRs 4 (6.8%) followed by atenolol 3 (5.17%) and amlodipine 2 (3.44%) Table 7.

Table 7: Pharmacological classes of drugs implicated to cause adverse drug reactions.

Drug classes	No of ADRs (%)
Antimicrobials	19(32.75%)
Antihypertensive	15(25.86%)
Antidiabetic	8(13.79%)
NSAIDs	7(12.06%)
CNS drugs	4(6.8%)
Anticoagulants	3(5.17%)
Others	2(3.44%)
Total	58

DISCUSSION

In this study, the overall incidence of ADRs was 2%. Jose and Rao based on the data of spontaneous reporting observed the incidence of 1.14% for inpatients and 0.012% for the out patients.⁸

In this study, demographic data showed slightly high incidence of ADRs in females. Female gender is considered important risk factors for ADRs.^{5,6} Other Indian spontaneous reporting studies had also observed high percentage ADRs in females.^{9,10} This finding may be because of differences in weight and body mass index, hormonal changes unique to females (during puberty, menstrual cycles, menopause), and the effect of these changes on drug metabolism. Other possible factors include differences in fat composition (with respect to impact on drug distribution) and genomic constitutional

differences influencing the levels of various enzymes involved in drug metabolism.^{11,12}

In present study the elderly showed high frequency of reactions, which is in concurrent with the studies by Ramesh et al⁹ and Arulmani et al.¹⁰ The reasons that could be attributed are that the patients of this age group suffered from hypertension and diabetes. So, this age group used more number of medicines and complained about drug-related adverse events, though most of these adverse events were mild and easily tolerated. whereas in other studies by Venkatesan et al, Rajkannan et al, showed high frequency of reactions in adults.^{13,14}

A majority of the ADRs were associated with oral administration of medicines followed by parenteral route. Most of ADRs with injectable medications were severe. The two topical reactions observed was erythema (localized skin redness) on application of heparin sodium. Gastrointestinal ADRs were most commonly observed with oral medications.

In the present study, most commonly involved system was gastrointestinal tract followed by skin and subcutaneous disorders. Next main groups are respiratory, neurological and hepatobiliary disorders however in previous studies 6,8,10 the most commonly involved system was skin cream.

The incidence of adverse drug events is directly proportional to the number of drugs being taken and increases remarkably as number of drugs rises. Many epidemiological studies of risk factors for adverse drug reactions have shown that the number of concurrently used drugs is the most important predictor of these complications.¹⁵ Polypharmacy needs to be discouraged as a good number of ADRs results from drug drug interaction.

The major causative drug class was antimicrobial. This finding is concurrent with many epidemiological studies.^{10,14} In this study, antimicrobials were most commonly reported class for the drug allergies as observed earlier.¹⁶ They are reported as most frequent cause of serious cutaneous reactions like SJS in India.¹⁷ In concurrently with the previous study, commonly observed antimicrobial group were beta lactam antibiotics and fluoroquinolones.¹⁸

In causality assessment, almost 38% reactions belonged to probable category and 30% cases belonged to possible category. In most cases, it was because of multiple drug suspects. This may be because of high frequency of polypharmacy. The study strongly suggest 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.

CONCLUSION

This study has the limitation of being a short term study, which yielded 58 ADR's other limitations were the fact that the time of onset and rechallange was not possible or performed. Pharmacovigilance may be enforced in this country for better and safe use of drugs. Our ability to anticipate and present such ADR's can be facilitated by the standardized approaches and active reporting of suspected ADR's by all healthcare professionals including clinical pharmacist. In this study, around 2% of the hospital patients develop ADRs and a significant number of these ADRs were preventable (a lot can be saved in terms of financial resources and human suffering). Our study has generated a useful data particularly in the Indian context. In any case, our study is no more effort in making the drug use much more rational and safe.

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