

## Causality assessment and pattern of adverse drug reactions in a tertiary care hospital

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### ABSTRACT

**Background:** Adverse drug reactions (ADRs) have become frequent cause for hospitalization and are coming up as an economic burden on health systems. Identification of ADRs and their reporting pattern can provide useful information for their management. Hence, this study was planned to evaluate causality and pattern of ADRs in a tertiary care hospital.

**Methods:** The present study was undertaken in a tertiary care teaching hospital. A total of 200 ADRs reports collected in the ADR monitoring centre were analysed. The WHO definition of an ADR was adopted as well as WHO scale for causality assessment was used. Evaluation of the data was done for various parameters which included drug groups causing ADRs, body systems affected in ADRs, reporters and seriousness of reactions.

**Results:** Overall occurrence of ADRs was slightly more in males (58%). Skin (72%) was the most commonly affected organ system. Antimicrobials (47%) were the drug group most commonly involved in ADRs. The causative drug was withdrawn for the management of the ADR in the majority (86%) of the patients. Upon causality assessment, majority of the ADRs were rated as probable (83.5%). Almost all of the reports were contributed by clinicians (99%).

**Conclusions:** The causality assessment and pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere, although there are few differences. The study results revealed opportunities for interventions in ADR management especially for the preventable ADRs to ensure safer drug use.

**Keywords:** ADR monitoring, Causality assessment, India, Tertiary hospital

### INTRODUCTION

The safety concerns with drugs have assumed more relevance in the last decade. The present-day physician has at his disposal a large number of potent drugs and hence it is very probable that these drugs can cause undesirable reactions/actions which have to be considered. In fact, these undesirable actions/reactions play a very important role in clinical practice today. The morbidity and mortality due to adverse drug reactions (ADRs) is coming up as one of the major health problems being recognized by health professionals and the public. ADRs are being reported to be the 4th to 6th largest cause for mortality in the USA.<sup>1,2</sup>

The incidence of ADR varies from as low as 0.15% to as high as 30% in various studies.<sup>1,3</sup> More than half of these ADRs are not recognized by the physicians on admission and ADRs may be responsible for death of 15 of 1000 patients admitted.<sup>4</sup> These figures represent a serious concern related to drug safety even in countries having a reasonable ADR monitoring system.<sup>4,5</sup> The earlier recognition of association of the ADR with a suspected medication by health care professionals can help a lot in preventing ADR related morbidity and mortality. There are a number of tools available to evaluate the causality or association of adverse event with drug. The causality assessment is an important parameter for establishing the relationship of the drug with the reported adverse event.

When the relationship is established then adverse event is labelled as ADR. There are a number of tools available to establish the causality. The world health organization (WHO) scale for causality assessment is a convenient tool to evaluate the causality and is being used in the ADR reporting form used in the India.<sup>5-7</sup>

ADR monitoring plays a major role in pharmacotherapy decision making in individual reports, regional, national and international programs. ADR monitoring can help to ensure that patients obtain safe and efficacious products.<sup>5</sup> The pattern of ADR reporting has an important educational and practical value. The information about the various aspects of ADRs and their causality assessment can provide useful information to manage ADRs. Hence, this study was designed to evaluate the causality assessment and pattern of ADRs in a tertiary care hospital.

**METHODS**

A total of 200 ADR reporting forms of patients submitted to ADR monitoring centre of the institute were evaluated. These ADR forms were of the patients visiting the outpatient and inpatient departments in the various departments in the institute.

**Inclusion criteria**

- ADR reports of patients of all ages and both genders
- ADR reports of patients having definite history of consumption of drugs and reporting with adverse drug reactions

**Exclusion criteria**

- ADR reports of patients with incomplete data

**Study procedure**

The ADR reporting form of Central Drugs Standard Control Organization (CDSCO), New Delhi, India was used to collect information on ADRs.<sup>8</sup> The form was distributed to all the departments. The health care providers were briefed about how to collect and record information on the ADR form. Health care providers reported ADRs to ADR monitoring centre of the Pharmacovigilance Program of India (PvPI) in the institute. The ADR monitoring centre personnel also went to all departments regularly to observe the ADRs and collect data.

Information on all the patients including relevant history, examination details, investigations and drug therapy. This information was collected and recorded in the form by visiting them daily till they were discharged from the hospital. When any other relevant information about ADR was required, the treating physicians were also contacted. Any untoward event was labeled as ADR as per WHO definition.<sup>9</sup>

WHO causality assessment scale was used for the ADR causality assessment.<sup>7</sup> After analysis all the ADR were entered online into vigiflow at the centre. This contributed ADRs to the National database of ADRs. Evaluation of the data was done for various parameters which included patient demographics, drug and reaction characteristics and outcome of the reactions. Assessment was also done for causality, duration of ADR and seriousness. The reasons for seriousness were also recorded. The serious ADRs and drug causing these were sorted out. Data was analysed using descriptive statistics and expresses in percentages.

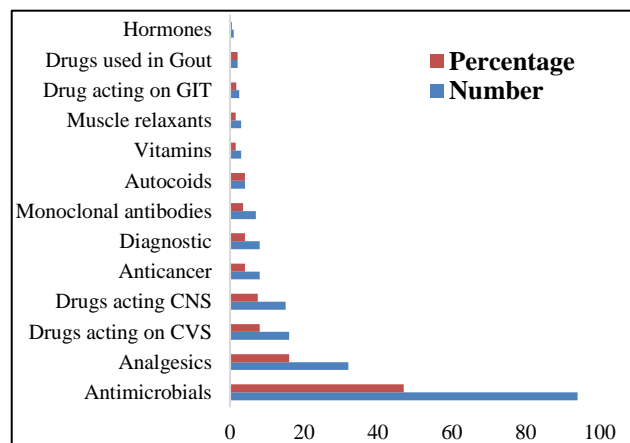
**RESULTS**

The mean age was of patients reported with ADRs was 42 years. ADRs were reported more in males (58%) as compared to females. Various ADRs reported as per gender (Table 1). The commonest drug group responsible for ADRs was antimicrobials (47%) followed by analgesics (16%), drugs acting on central nervous system (CNS) (8%) and drugs acting on cardiovascular system (CVS) (8%) in present study (Figure 1). The most adverse reactions with a single drug were attributed to morphine (n=10; 5%), followed by vancomycin (n=7; 3.5%), meropenem (n=7; 3.5%) and imipenem (n=7; 3.5%). The use of cephalosporins was also more (n=16; 8%).

**Table 1. Gender wise distribution of ADRs.**

Gender	Number	Percentage
Male	116	58
Female	84	42

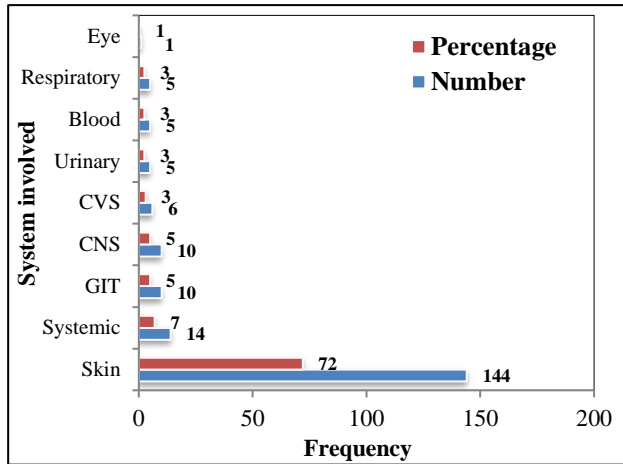
ADR: Adverse drug reactions



**Figure 1: Distribution of ADRs according to drug group involved (n=200).**

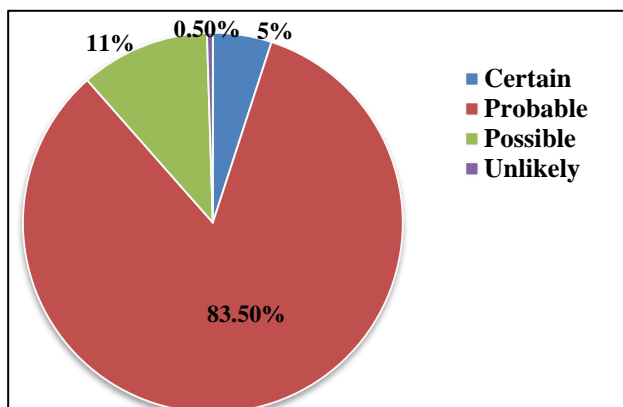
Only 15% of reports mentioned the brand name of the drug used. Diagnostic agents were also reported to cause ADRs (4%). Figure 2 depicts the distribution of ADRs according to body system involved. Skin was the most commonly affected organ system with ADRs (72%) followed by systemic reactions involving whole body (7%), GIT (5%)

and CNS (5%). Most of the ADRs related to skin were erythematous rash type reactions. Almost all of the reports were contributed by clinicians (99%).



**Figure 2: Distribution of ADRs according to body system involved (n=200).**

Causality assessment as per WHO scale (Figure 3). The causality of most ADRs was “probable/likely in nature” with all drugs (83.5%) followed by possible in 11% reports. Less than half of the ADRs were serious (41.5%). The major cause for seriousness was prolongation of hospitalization in these patients (82%). Anaphylaxis was reported in seven reports with albumin, carboplatin, cisplatin, a dye, L-asparaginase, meropenem and piperacillin. Steven Johnsons Syndrome was reported in 5 reports with allopurinol, amoxicillin, clindamycin, ofloxacin and aceclofenac. Hematuria was reported in 4 reports with amoxicillin, nimesulide and 2 with heparin.



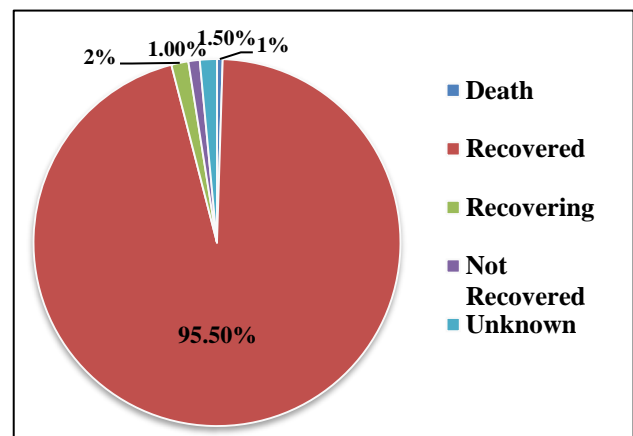
**Figure 3: Causality assessment of adverse events.**

Two patients reported with gum hypertrophy with phenytoin and valproic acid. Most of the patients recovered (95.5%) after ADR occurrence (Figure 4).

**DISCUSSION**

Author collected ADR reports of 200 patients in this study. ADRs were reported more in males (62%) as compared to

females. Earlier studies have also shown similar results in ADRs differences in genders for occurrence of ADRs.<sup>11,12</sup> Although few studies have shown almost similar distribution of ADRs in both sexes.<sup>13</sup> In present study antimicrobials were the most common drug group involved in ADRs. In most of the earlier studies also antimicrobials were reported to be the commonest drug group involved in ADRs.<sup>12,14</sup> The common antimicrobials which were associated with ADRs in present study belonged to carbapenems. This trend is a shift from earlier reports where penicillins were the main antimicrobials used. This might be because of the reason that uses of carbapenems have become quite extensive but at the same time irrational too. The cephalosporins were associated with a number of ADRs in present study. These trends indicate more use of newer antimicrobials like carbapenems and newer cephalosporins.



**Figure 4: Outcome of adverse drug reactions.**

ADR related to skin were most frequent followed by systemic reactions, gastrointestinal tract (GIT) and CNS. As skin is the largest organ of the body, it was reported to be the common organ system affected in other studies also.<sup>12</sup> Serious ADRs were 41.5% which is higher than other studies.<sup>5,12</sup> This might be due to the fact that reporters mainly tend to report when ADR is serious. It is important for healthcare professionals to differentiate severe from serious ADRs.

Serious ADRs are defined as ADRs that lead to death, congenital anomaly, disability, are life threatening, needs intervention to prevent permanent disability and prolongation of hospitalization. In present study most of the serious ADRs were due to the prolongation of hospitalization (82%). There were 5 reports of Steven Johnson Syndrome (SJS) and 7 reports of anaphylaxis. SJS was associated with commonly used drugs like clindamycin, ofloxacin, amoxicillin, allopurinol and aceclofenac.

Anaphylaxis was reported with albumin, cisplatin, piperacillin and meropenem. Both of these serious ADRs were related mainly to antimicrobials and anticancer drugs. Out of above mentioned drugs, a number of these

are commonly used. Hence, the clinicians should be more careful in observing these serious ADRs with these drugs.

Almost all ADRs were reported by doctors in present study. Health care providers are in the best position to report on suspected ADRs observed in their everyday patient care. All healthcare providers including nurses, pharmacist and dentists should report ADRs as part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication.

The causality assessment shows that the relatedness was “probable” with most of the ADRs. Earlier studies also show similar trend in relatedness.<sup>12</sup> Earlier studies have reported probable to be a common causal relationship.<sup>12</sup> The main reason for this trend can be polypharmacy in these cases. The “certain” relatedness is rare these days as it is not ethical to rechallenge the patient with the same causative drug, hence the assessment infrequently goes to probable category. Due to causality assessment, ADRs have today assumed a differential diagnostic role in clinical medicine. Since these scales are subjective in nature as well as the rechallenge part has become redundant, we should be exploring and designing better causality assessment scales.

While managing the patients of ADR, the first basic principle which should be followed is to discontinue the suspected drug and substitute the same by another drug if required. In present study, the suspected drugs were discontinued in 86% patients. These findings are in accordance with earlier studies.<sup>3,15</sup>

All the patients except three (98.5%) recovered fully after discontinuing the offending drug. This fact highlights the proper management of ADRs in a tertiary care hospital. The reporting of ADRs in this study added to the national database. The study also exposed health care providers to the methodology of ADR monitoring and they got familiar with the importance and methodology of ADR monitoring in the institution. Overall, the study is a step towards fostering a culture of ADR reporting in the institute.

## CONCLUSION

In conclusion, the pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital set up elsewhere. Present study results indicate the possible opportunities for interventions especially for the preventable ADRs to ensure safer drug use.

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## REFERENCES

1. Lazarou J, Pomeranz BH, Corey PN. Incidence of ADR in hospitalized patients: A Meta-analysis of prospective studies. *JAMA.* 1998;279:1000-5.
2. Badyal DK, Bhatia RS. Adverse drug reactions. Peepee publishers, New Delhi; 2006:2-8.
3. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res.* 2006;54:226-33.
4. Lazarou J, Pomeranz B, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *JAMA.* 1998;279:1200-05.
5. Muraraiiah S, Rajarathna K, Sreedhar D, Basavalingu D, Jayanthi CR. A questionnaire study to assess the knowledge, attitude and practice of pharmacovigilance in a paediatric tertiary care centre. *J Chem Pharm Res.* 2011;6:416-22.
6. Joseph SG, Badyal DK. Spontaneous adverse drug reaction monitoring in a tertiary care hospital in Northern India. *JK Sci.* 2016;18:103-6.
7. World health organization. Safety of medicines: a guide to detecting and reporting adverse drug reactions; WHO Geneva 2002. Available at: [http://whqlibdoc.who.int/hq/2002/WHO\\_EDM\\_QSM\\_2002.2.pdf](http://whqlibdoc.who.int/hq/2002/WHO_EDM_QSM_2002.2.pdf). Accessed 9 November 2017.
8. Pharmacovigilance program of India. CDSCO. Ministry of Health and Family Welfare, Government of India; 2010. Available at: <http://cdsco.nic.in/pharmacovigilance.htm>. Accessed 9 November 2017.
9. World Health Organization. International drug monitoring: The role of the hospital. Geneva, Switzerland: World Health Organization; 1966.
10. Guideline for post marketing reporting of adverse drug experiences. Rockville, MD: US Department of Health and human services, Food and Drug Administration, 1992. Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM299138.pdf>. Accessed 9 November 2017.
11. Subish P, Mishra P, Shankar PR. Systemic adverse drug reactions: a preliminary report from the regional pharmacovigilance center, western Nepal. *Pakistan journal of pharmaceutical sciences.* 2008 Oct 1;21(4).
12. Rajeshreddy SGSV, Patil LV. Causality assessment and the severity of the adverse drug reactions in tertiary care hospital: a pharmacovigilance study. *Int J Basic Clin Pharmacol.* 2017;6:2800-3.
13. Jose J, Rao Padma GM. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res.* 2006; 54:226-33.

14. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. *Br J Clin Pharmacol.* 2008;65:210-6.
15. Gupta A, Kaur A, Shukla P, Chhabra H. Adverse drug reactions pattern in a tertiary level teaching hospital: a retrospective study. *Indian J Pharmacy Pract.* 2017;10:27-31.

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