Original Article

Preventability, predictability, severity and causality assessment of adverse drug reactions reported from a teaching hospital in chhattisgarh: A retrospective analysis

Yogendra Keche, Nitin Gaikwad, Suryaprakash Dhaneria

Department of Pharmacology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

Abstract

Background and Objectives: Adverse Drug Reactions (ADRs) can lead to significant morbidity, rarely mortality and financial burden over the patient. ADRs that can be prevented can be considered as form of medication error sometimes. This study assessed the preventability, predictability and severity of ADRs using different assessment scales. **Methods:** ADR Monitoring Centre under newly established teaching hospital in Chhattisgarh collected ADR reports from different healthcare professionals during the period from November 2016 to November 2018. Analysis of the reported ADRs was done for their causality assessment, demographic details of patients, most common drug class responsible for the ADR. Seriousness and preventability of ADRs were analysed by using WHO Causality Scale and Modified Schumock and Thornton Scale respectively. Severity of ADRs was assessed by Modified Hartwig and Siegel Scale. **Results:** Totally 288 ADRs were reported in a 2-year period. 92.01% ADRs were non serious. 44.8% were mild, 53.81% moderate and 1.39% were severe ADRs. Causality assessment showed: 5.21% certain, 54.86% probable, 39.24% possible and 0.69% unlikely ADRs. Around 26% ADRs were definitely and probably preventable and 27.78% ADRs were predictable. The highest number (32.29%) of ADRs were reported to antimicrobials. 11.15% ADRs were reported to NSAIDs, in that 37.5% ADRs were due to NSAIDs combination. **Conclusion:** Many ADRs in this study are non-serious, preventable and predictable. Management of such ADRs through therapeutic interventions would be beneficial in a better patient outcome. Multidisciplinary strategies involving physicians, pharmacists, other healthcare professionals and patient education and awareness about ADRs are needed for prevention of ADRs.

Keywords: Pharmacovigilance, Preventability of ADRs, Severity of ADRs

Introduction

Drugs can produce therapeutic benefit as well as harmful effects. These harmful effects are called as Adverse Drug Reactions (ADRs). According to WHO, an ADR can be defined as "A response to a drug that is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function".[1] When a drug is released into the market, it has been rarely exposed to more than 5000 individuals, less than 0.1% of the global population.[2]

ADRs are one of the causes for hospital admission. More than 10% ADRs lead to hospitalization.[3] A study showed that more than 50% of the drugs approved for human use in the United States were associated with some type of adverse effect in the general population which was not detected prior to approval.[4]

Address for correspondence: Dr. Yogendra Keche, Department of Pharmacology, Room No. 2215, 2nd Floor, College Building, All India Institute of Medical Sciences, Raipur – 492 099, Chhattisgarh, India.
E-mail: drynkeche@aiimsraipur.edu.in

Received: 03-12-2020 **Revised:** 20-02-2021
Accepted: 10-04-2021 **Published:** 30-07-2021

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_2374_20

How to cite this article: Keche Y, Gaikwad N, Dhaneria S. Preventability, predictability, severity and causality assessment of adverse drug reactions reported from a teaching hospital in chhattisgarh: A retrospective analysis. J Family Med Prim Care 2021;10:2541-5.

ADRs can lead to significant morbidity, rare mortality and financial burden over the patient. ADRs are estimated to be the 4th and 6th leading cause of death in USA.[4] ADRs that can be prevented can be considered as form of medication error sometimes.[5] In a meta-analysis carried out by Hakkarainen *et al.* (2012)[6] observed that preventable ADRs are significant cause of morbidity in outpatients. Approximately half of the ADRs occurring in both inpatients and outpatients may be prevented. ADRs were considered preventable when they occurred due to contraindication, inappropriate dose or lack of monitoring, interactions, ignoring toxic serum drug concentration, allergic reactions or noncompliance. ADRs due to these reasons need definite strategies for prevention to reduce the burden of the ADRs as well as for reducing costs for the treatment of ADRs.

WHO started the pharmacovigilance programme for ADR monitoring with the aim to improve patient care and safety with the use of any kind of medication, improve public health and safety in relation to medication use, contribute to the assessment of benefits, harm, effectiveness and risks of medicines and encourage safe, rational, more effective and cost effective use of drugs in 65 countries.[7] In our tertiary healthcare, we had an ADR monitoring center where ADRs are reported to and also the data is collected by this center. As the aim of pharmacovigilance there is greater, there is an urgent need to create and increase awareness about detection, reporting, management and prevention of ADRs among healthcare providers as well as in the general population.

Primary Objectives

1. To assess the severity of ADRs by Modified Hartwig and Siegel Scale.
2. To assess the preventability of ADRs with the help of Modified Schumock and Thornton Scale.

Secondary Objectives

1. To assess the causality of ADRs as per WHO-UMC Scale.
2. To assess the predictability of ADRs according to the types of ADRs.

Material and Methods

Study design

Retrospective secondary data analysis.

Study procedure

Data for this study was collected under the Pharmacovigilance Programme of India (PvPI). Confidentiality regarding data was maintained as patient and reporter's identity was not revealed under this Programme. Secondary analysis of data collected at the tertiary care centre and teaching hospital was carried out. As no ethical issues were involved in this study, no ethical clearance was obtained for this study. Permission from PvPI Coordinator of this tertiary healthcare center was obtained to carry out this secondary analysis. ADR Monitoring Centre under this tertiary healthcare teaching hospital in Chhattisgarh, collected ADR reports from different healthcare professionals during period of November 2016 to November 2018. Demographic details of patients, detailed clinical history including pre-existing medical conditions if any and relevant laboratory data was noted in ADR Reporting Form. Other drugs used for treatment of patient as well as treatment of ADRs was noted in ADR reporting form at the time of collection of ADR. Suspected drug as well as concomitant drug history was taken in terms of dosage, route of administration, purpose for taking drug, improvement after discontinuation of drug, whether over the counter formulation or prescribed drug, past history of drug allergy family history of drug allergy and history of skin diseases was noted in ADR reporting form used for collection of ADR data. All the collected ADRs during above mentioned period were analysed in Department of Pharmacology with the help of different scales.

Causality analysis of ADRs was done per WHO UMC scale which classifies ADRs as certain, probable, possible or unlikely.[8]

Seriousness of ADRs was analysed by WHO UMC scale which classifies ADRs as Non serious or Serious as per criteria for reporting of ADRs in India.[9,10]

Preventability of ADRs was analysed by Modified Schumock and Thornton scale by using nine point scale based on history of allergy, appropriateness of drug for clinical condition, dose, frequency, route of administration as per patient's age, weight and disease state, laboratory levels for toxic serum concentration and based known treatment of ADR, Drug interactions, poor compliance and preventive measure for ADR prevention was also taken into account.[11]

Severity of ADRs was assessed by Modified Hartwig and Siegel Scale which contain seven levels and classify the ADR as Mild/Moderate/Severe.[12] Mild ADR is an ADR which requires no change in treatment with the suspected drug and/or requires treatment with the suspected drug be held, discontinued, or otherwise changed and in addition no antidote or other treatment was required, without increase in length of stay. Moderate ADR is that requires treatment with the suspected drug be held, discontinued or otherwise changed and antidote or other treatment was required without increase in length of stay/ADR which increases length of stay by at least a day/ADR was the reason for hospitalization. Severe ADR is the ADR which requires intensive medical care/cause permanent harm to the patient/directly or indirectly led to death of the patient.[12]

Predictability of ADRs was assessed as per types of ADR i.e., Type A/Type B/Type C/Type D.[12]

Most common drug/drug class responsible for ADR and common ADRs reported in a tertiary care teaching hospital in Raipur, Chhattisgarh were calculated from the collected data.

Results

288 ADRs were reported in the period from November 2016 to November 2018. Of 288 ADRs, 23 (7.99%) were serious ADRs. Around 170 (59%) ADRs appeared in the age group of 16-45 years that is in the younger population and more ADRs were seen in females 180 (63%) [Table 1]

129 (44.8%) ADRs as mild, 155 (53.81%) as moderate and 4 (1.39%) as severe are classified as per Modified Hartwig and Siegel Severity Scale for analysis of ADRs. [Table 2]

The categorization of ADRs based on causality assessment was observed as 15 (5.21%) certain, 158 (54.86%) probable, 113 (39.24%) possible and 2 (0.69%) unlikely ADRs. [Table 3]

As per Schumock and Thornton Scale, 212 (73.61%) ADRs were not preventable, 30 (10.42%) and 46 (15.97%) were definitely and probably preventable respectively. [Table 2]

80 (27.78%) ADRs were predictable in this study as per types of ADRs [Table 2]. Most of the predictable ADRs were Type A (77.5%) like Hyperkalaemia with Enalpril, Vomiting due to anticancer drugs. Type C (22.5%) like weight gain/moon face with Glucocorticoid tablet, Pedal Oedema with Amlodipine, EPS with antipsychotics 8% Serious ADRs were caused in this study [Table 2]. Seriousness was labelled to these ADR due to hospitalization. Common drugs responsible for serious ADRs were Mefenamic acid plus Paracetamol combination, Zoledronic acid, Phenytoin causing Steven Johnson's (SJ) syndrome. The other drugs that led to serious ADRs in this study were Cephalosprins and Piperacillin like antimicrobials.

Table 1: Demographic characteristics of ADRs

	No of persons (%)
Age group of population under study	
<1	6 (2.08)
1-15	24 (8.33)
16-30	93 (32.29)
31-45	77 (26.74)
46-60	49 (17.01)
>60	39 (13.54)
Sex	
Male	108 (37.50)
Female	180 (62.50)

The highest number (32.29%) of ADRs were reported to antimicrobials. Next to antimicrobials, more ADRs were reported NSAIDs and 37.5% ADRs were due to NSAIDs combination (like Aceclofenac and Rabeprazole or others).

Rash 110 (38.09%) was the most common ADR reported in this study. This ADR was observed more with antimicrobials 49 (17.01%).

Discussion

Around 59% ADRs were observed in the age group of 16-45 years and were more in the younger population. Similarly, more ADRs were observed at a young age in previous studies also.[13,14] In a study carried out by Basavaraj *et al.* (2017),[15] more ADRs were observed in the age group of 45-60 years. In this study, more ADRs were seen in females (63%). Similarly, 56% ADRs were observed in females in a study carried out by Verma *et al.* (2014).[16] This study was carried out in a paediatric population, but another study shows equal distribution of ADRs in males and females.[13]

Severe ADRs observed were 1-3% in previous different studies.[13,16] Moderate ADRs were found in different studies as (29.44%),[14] (58.5%),[13] (81%)[16] and (86.3%)[17] respectively, suggesting severity of ADRs differs with analysis of ADRs with different scales. In this study, 53.81% moderate and 1.39% severe were observed ADRs as per Modified Hartwig and Siegel Severity Scale. Similar findings were also observed in a study carried out by Palappallil *et al.* (2016).[18] Most of the moderate ADRs required that treatment with the suspected drug be held, discontinued or changed and other treatment was required without increase in hospital stay.

As treatment required for the ADRs in the moderate category, there is an increase in the financial burden over patients for treatment of ADRs. 50% moderate were either definitely or probably preventable and of these 23% were predictable. Modified Hartwig and Siegel Severity Scale is more objective hence more useful for taking preventive measures against the ADRs due to the drugs.

As per Schumock and Thornton Scale, 73.61% ADRs were not preventable, 10.42% and 15.97% were definitely and probably

Table 2: Preventability, Severity, Predictability and Seriousness Analysis of Different ADRs

Analysis of ADRs	Definitely Preventable No. (%)	Probably Preventable No. (%)	Not Preventable No. (%)
Preventability by Modified Schumock and Thorton Scale	30 (10.42)	46 (15.97)	212 (73.61)
	Mild	**Moderate**	**Severe**
Severity Modified Hartwig and Siegel Scale	129 (44.8)	155 (53.81)	4 (1.39)
	Predictable	**Not Predictable**	
Predictability as per types of ADRs	80 (27.78)	208 (72.22)	
	Serious	**Not Serious**	
Seriousness as per WHO UMC Scale	23 (7.99)	265 (92.01)	

Table 3: Causality Analysis of ADRs According to WHO UMC Scale

Causality Analysis	No. (%) of ADRs
Certain	15 (5.21)
Probable	158 (54.86)
Possible	113 (39.24)
Unlikely	2 (0.69)

preventable respectively. Approximately 26% ADRs were preventable in our study. Different studies' observation had shown preventable ADRs in the range from 55% to 79%.[5,11,14,16] In a Meta-analysis, 2% ADRs were preventable in OPD settings and 52% ADRs were preventable at the time of hospitalization or emergency care.[6] In the same study, 71% ADRs were preventable in the elderly.[6] Gholami *et al.* (1996)[17] observed increase in incidence of preventable ADRs with increase in patient's age and appropriate preventive measures in the form of patient education about the drug ADRs can be given. In another study, it was observed that 55.3% ADRs were unpreventable. Insufficient monitoring was seen in about 30% preventable adverse reactions and inappropriate dosing and drug–drug interactions were cause for about 18% of the preventable adverse reactions.[19]

In our study, association of preventability was seen with drug allergy, inappropriate drug therapy, lack of lab monitoring, drug-drug interactions and no administration of preventive measures for ADRs. In previous studies, characteristic association was observed with toxic drug concentration, abnormal laboratory value, inadequate monitoring of patient drug therapy, inappropriate dose, patient noncompliance, drug-drug interaction, contraindication to the therapy and documented allergy.[5,10,19,20]

Totally 26% ADRs were predictable in this study as per types of ADRs. Out of these, 27% ADRs were preventable. Previous studies had found 96.1%, 69%, 53% and 7.4% predictable ADRs respectively.[4,6,10,11] Predictable ADRs can be prevented by taking appropriate measures like dose modification or education of patient about symptoms of ADR and training of healthcare professionals.

In most of the previous studies, possible was the causality assessment for the ADRs.[6-8] But in our analysis, probable (54.86%) was the causality assessment as per WHO UMC Scale had been observed. This was observed because we had followed up each and every case for a sufficient time period.

The highest number (32.29%) of ADRs were reported to antimicrobials. In different studies, anti-infective caused ADRs ranging from 35% to 68%.[6,8,9,21] Antibiotics had caused ADRs in 33% of patients in a study carried out by Palappallil *et al.* (2016).[18]

Next to antimicrobials, more ADRs were reported to NSAIDs, in that, 37.5% ADRs were due to NSAIDs combination (Aceclofenac and Rabeprazole or other drugs). A similar finding, 22.5% ADRs were observed with NSAIDs in a study carried out by Basavaraj *et al.* (2017).[8]

Rash (38.09%) was the most common ADR reported in this study. This ADR was observed more with antimicrobials 49 (17.01%). Rash was the most commonly reported ADR as observed in the previous studies also.[9,8,21]

Our study had certain limitations as we were not able to test the knowledge of the patient about ADRs to the drugs. Improving knowledge about ADRs is the most important intervention for the prevention of ADRs and this can be achieved by patient education about the ADRs. In fifteen cases, accidental re-challenge was done. Re-challenge test was not done due to concern regarding patient safety and ethical issues.

Conclusions

More number of ADRs were observed with antimicrobials and rash was the common ADR observed with antimicrobials. Next to antimicrobials, more ADRs were reported NSAIDs and out of which one third ADRs were due to NSAIDs combination. As many ADRs in this study are non-serious, preventable and predictable, management of such ADRs through therapeutic interventions would be beneficial in better patient outcome. Modified Hartwig and Siegel Scale of severity of analysis had shown around half the ADRs were moderate and half the moderate ADRs were preventable. Treatment was required for moderate ADRs and there is an increase in the financial burden on patients for treatment of ADRs. Hence, multidisciplinary strategies involving physicians, pharmacists, other healthcare professionals, education and awareness in patients about ADRs are needed. Hence, in addition to causality assessment, ADRs shall also be analysed for preventability, predictability and severity assessment for better patient care and remedial action for prevention of ADRs in future.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Quality Assurance and Safety of Medicines Team. (2002). Safety of medicines: A guide to detecting and reporting adverse drug reactions : why health professionals need to take action. World Health Organization, Geneva. Available from: https://apps.who.int/iris/handle/10665/67378. [Last accessed on 2021 May 06].
2. WHO Policy Perspectives on Medicines — Pharmacovigilance: ensuring the safe use of medicines (Ensuring The Safe Use Medicines.; 2004). World Health Organization, Geneva. Available from: https://apps.who.int/iris/bitstream/handle/10665/68782/WHO_EDM_2004.8.pdf;sequence=1. [Last accessed on 2021 May 06].

3. Lazaru J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patient: A meta-analysis of prospective studies. JAMA 1998;279:1200-5.
4. Rabbur RSM, Emmerton L. An introduction to adverse drug reaction reporting system in different countries. Int J Pharm Prac 2005;13:91-100.
5. McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. Ann Pharmacother 2002;36:1331-6.
6. Hakkarainen KM, Hedna K, Petzold M, Hägg S. Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions – A meta-analysis. PLoS One 2012;7:e33236.
7. World Health Organization. (2002). The importance of pharmacovigilance. World Health Organization, Geneva. https://apps.who.int/iris/handle/10665/42493. [Last accessed on 2021 May 06].
8. Zaki SA. Adverse drug reaction and causality assessment scales. Lung India 2011;28:152-3.
9. Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: A clinician's guide to terminology, documentation, and reporting. Ann Intern Med 2004;140:795-801.
10. Du Y, Lin J, Shen J, Ding S, Ye M, Wang L, *et al.* Adverse drug reactions associated with six commonly used antiepileptic drugs in southern China from 2003 to 2015. BMC Pharmacol Toxicol 2019;20:7.
11. Raut AL, Patel P, Patel C, Pawar A. Preventability, predictability and seriousness of adverse drug reactions amongst medicine inpatients in a teaching hospital: A prospective observational study. Int J Pharm Chem Sci 2012;1;1293-9.
12. Srinivasan R, Ramya G. Adverse drug reaction-causality assessment. Int J Res Pharm Chem 2011;1:606-12.
13. Padmavathi S, Manimekalai K, Ambujam S. Causality, severity and preventability assessment of adverse cutaneous drug reaction: A prospective observational study in a Tertiary care hospital. J Clin Diagn Res 2013;7:2765-7.
14. Kumar A, Majhee L, Gari M. Causality, severity and preventability assessment of adverse drug reactions in patients received anti-retroviral therapy in a Tertiary care hospital: A retrospective study. Natl J Physiol Pharm Pharmacol 2017;7:178-82.
15. Basavaraj B, Shabeer D, Satyanarayana V. A study on adverse drug reactions in a Tertiary care hospital in Bangalore. Indian J Pharm Pharmaco 2017;4:49-54.
16. Verma R, Verma J, Verma N, Sharma P, Rai N. Study of adverse drug reactions in paediatric age group with assessment of causality, severity and preventabilty in a Tertiary care hospital. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) IOSR J Dent Med Sci 2014;13:42-8.
17. Gholami K, Shalviri G. Factors associated with preventability, predictability, and severity of adverse drug reactions. Ann Pharmacother 1999;33:236-40.
18. Palappallil DS, Ramnath SN, Gangadhar R. Adverse drug reactions: Two years' experience from a tertiary teaching hospital in Kerala. Natl J Physiol Pharm Pharmacol 2017;7:403-11.
19. Damen LA, Basheti I. Preventability analysis of adverse drug reactions in a Jordanian hospital: A prospective observational study. Int J Clin Pharm 2019;41:1599-610.
20. Ducharme MM, Boothby LA. Analysis of adverse drug reactions for preventability. Int J Clin Pract 2007;61:157-61.
21. Belhekar MN, Tondare SB, Pandit PR, Bhave KA, Patel TC, Pandey K, *et al.* A prospective study on causality, severity and preventability assessment of adverse drug reactions in a Tertiary care hospital in India. Int J Basic Clin Pharmacol 2019;8:104-10.