

An evaluation of adverse drug reactions monitoring at a pharmacovigilance unit under pharmacovigilance program of India in a tertiary care hospital of Haryana

Preeti Kharb*, Niti Mittal, Mahesh C. Gupta

Department of Pharmacology,
Pt BD Sharma University
of Health Sciences, Rohtak,
Haryana, India

Received: 29 April 2015

Accepted: 11 May 2015

***Correspondence to:**

Ms. Preeti Kharb,
Email: preetikharb88@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Adverse drug reactions (ADRs) are among top 10 causes of mortality in patients. Pharmacovigilance programme of India (PvPI) is a step towards participation in the WHO programme for International Drug Safety Monitoring. The present article is an evaluation of the incidence and the patterns of ADRs from the reports collected from various clinical departments of this hospital.

Methods: A total of 859 suspected ADR reports submitted to the pharmacovigilance unit at Department of Pharmacology under PvPI were evaluated for 6 months with respect to demographics, causative drug, organ system involvement, severity and seriousness of ADRs. The causality assessment was carried out by using WHO assessment method and Naranjo's scale.

Results: Males experienced more (66.33%) ADRs. The highest percentage (45.83%) of ADRs was seen in the age group of 46-60 years (35.33%), followed by 16-30 years (25.5%). The most common drug group causing ADRs was antimicrobials (43.37%), followed by anticancer and immunosuppressive agents (29.02%). The gastrointestinal system (31.43%) was most prone system, followed by generalized body reactions (22.93%) and cutaneous reactions (17.11%). 662 (77%) ADRs were non-serious, 197 (22.9%) were serious. On severity scale, 682 (79.39%) were mild, 168 (19.65%) moderate and only 9 (1.05%) ADRs were severe out of which three were fatal. As per WHO assessment method 66.94% ADRs were probable and 33.06% possible. The probability was comparable with Naranjo's scale.

Conclusion: ADRs to drugs happen commonly, and their reporting is important for the early recognition and prevention of ADRs and will also help in generating signals. ADR monitoring not only acts as an alerting mechanism for physicians, but helps the regulatory authorities in making the policy decision.

Keywords: Adverse drug reaction, Causality assessment, Pharmacovigilance

INTRODUCTION

Medicines are the most common medical interventions to relieve sufferings but as said rightly "drugs are double edged weapons" with a potential to cause benefit, as well as harm.¹ The most crucial step toward making drugs safer for human use is to prevent the occurrence of an adverse drug reaction (ADR). ADR is defined as "any response to a drug, which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function."² ADRs are among top 10 causes of mortality and morbidity in both hospitalized and ambulatory patients worldwide. The incidence of ADRs varies from as low as 0.15% to as high as 30%.³ They are a major clinical problem, accounting for 2-6% of all

the hospital admissions.⁴ ADRs adversely affect patient's recovery as well as increase the health care expenses. Therefore, to reduce harm to patients and improve public health; early detection, evaluation and monitoring of ADRs is essential.

India is a developing country with a large drug consuming population and 4th leading pharmaceutical sector. The Ministry of Health and Family Welfare had initiated the National Pharmacovigilance Program on 1st January 2005, which was further revised in July 2010 as Pharmacovigilance programme of India (PvPI) with the goal, that the benefits of use of medicine should outweigh the risks.⁵ This program is overseen by the Central Drugs Standard Control Organization (CDSCO), New Delhi.⁶ Spontaneous reporting has contributed significantly to successful pharmacovigilance.

India stands at 7th position among 117 countries participating in the WHO programme for International Drug Monitoring with a worldwide contribution of 2% reports for the year 2013.⁷ Currently there are 150 ADR Monitoring Centres (AMC) operational under PvPI. The present study is an evaluation and analysis of the incidence and the patterns of ADRs from the reports collected from various inpatient and outpatient departments.

METHODS

The Department of Pharmacology, Pt. BDS. PGIMS, Rohtak is the regional AMC for Haryana under PvPI, which is a government teaching hospital, providing health facilities to more than 1.5 million patients in a year. The reports are collected from both inpatient and outpatient departments of hospital for suspected ADRs. Data is collected using structured format as per CDSCO ADR reporting form.⁸ Causality assessment is performed using WHO Uppsala Monitoring Centre (UMC) Global introspection method. The reports are then uploaded in Vigiflow software and sent to National Coordinating Centre, Indian Pharmacopoeia Commission, Ghaziabad, which then transmits the reports to the Uppsala Monitoring Center's ADR database where signal processing is carried out.

The 859 suspected ADR reports received by Pharmacovigilance unit at the Department of Pharmacology between September 2013 and February 2014 were evaluated and analyzed for the incidence and the patterns of ADRs by well-trained clinical pharmacologist on each ADR proforma. Data on demographic details for patient profile (age and sex), prescribed medications (generic name of the medicine, dose frequency, strength, date of start and stop) were evaluated. ADRs were evaluated w.r.t description of the adverse event, onset and end of the adverse event, seriousness, information on de-challenge, rechallenge. Causality assessment was carried out using WHO-UMC global introspection method⁹ and "Naranjo algorithm or ADR Probability Scale" respectively.¹⁰

International Classification of Disease (ICD-10) was used for coding the medications in the range Y40-59, which are known as "external cause" codes. The subgroups were also classified based on this coding to identify the drug classes.¹¹

Seriousness of reaction was categorized as "serious" and "non-serious" according to WHO criteria.⁹ The severity of ADRs was assessed by modified Hartwig and Siegel scale which classifies the severity of ADR as mild, moderate or severe with seven severity levels. According to factors like requirements for change in treatment, duration of hospital stay, and the disability produced by the ADR severity of the identified ADRs was assessed at different levels, ranging between 1 and 7. Levels 1 and 2 indicated mild, 3 and 4 considered as moderate and level 5 and above, as severe ADRs.¹²

Data analysis

Data were entered in Microsoft Excel 2007. Descriptive analysis was done to assess mean \pm standard error of mean, median, frequencies and the percentages as applicable for age group, gender, causative drug, seriousness, severity, and causality.

RESULTS

A total of 600 ADR reports were received which comprised of 859 ADRs. There was a predominance of males (66.33%) as compared to females (33.22%) (Figure 1).

Mean age of the patients was 42.3 years \pm 16.4 years (standard deviation) with maximum number of patients in the age group of 46-60 years (35.33%) (Table 1).

The leading causal therapeutic class of medicines as per ICD-10 classification implicated were antimicrobials, including β -lactam antibiotics, fluoroquinolones, macrolides, aminoglycosides, antifungals, antitubercular, antiprotozoals (43.43%), followed by anticancer drugs (29.06%), and analgesics (6.19%) (Table 2).

The oral route was responsible for the ADR causation in 46.72% cases as compared to the parenteral route (44.44%) and only 8.86% cases were due to the topical route of drug administration.

The most commonly affected organ system was gastrointestinal (GIT) system (31.43%) followed by general body reactions such as asthenia, fatigue, weakness, lethargy, fever (22.93%), and cutaneous reactions (17.11%) (Figure 2).

Table 1: Age distribution.

Age group (years)	Number of patients (%)
0-15	25 (4.33)
16-30	153 (25.50)
31-45	122 (20.33)
46-60	212 (35.33)
>60	88 (14.66)

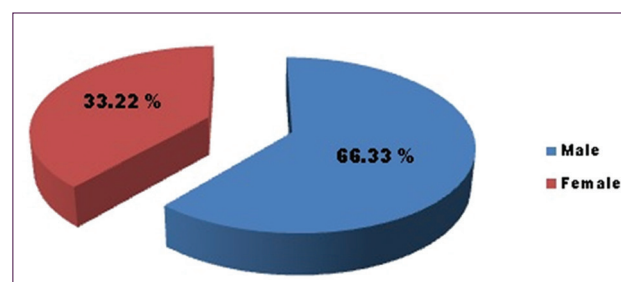


Figure 1: Gender distribution of adverse drug reactions.

The majority of reactions were non-serious 662 (77.1%) and 197 reactions (22.9%) were serious. Based on modified Hartwig severity scale, most of the reactions were categorized as mild 79.39% (682 of 859), 168 ADRs were moderate type (19.56%) and only nine ADRs (1.05%) were “severe” in nature out of which 3 were fatal (Figure 3).

The causality was almost consistent with both Naranjo’s and WHO probability scale. On causality assessment using WHO

Probability Scale, 575 (66.94%) ADRs were categorized as probable and 284 (33.06%) were categorized as possible. Naranjo’s Probability Scale showed 2 (0.23%) ADRs as definite (score >8), 536 (62.34%) ADRs were categorized as probable (score ranging from 5 to 8) and 321 (37.43%) were categorized as possible (scores ranging from 1 to 4) (Figure 4).

DISCUSSION

Safety of drugs should be of paramount importance as it affects drug regulation and a far number of tools such as pharmacoepidemiological tools, prescription event monitoring, vital statistics and observational studies (case-control studies, cohort studies) have been developed to assess the same. In recent times, spontaneous reporting of ADRs has become the most favored method for practicing pharmacovigilance by the healthcare professionals. ADR reporting adds to increased vigilance and influence recommendations of drug use, which has now become a National Programme in the Indian context.

The present study is an attempt to carry out an appraisal of spontaneous reported suspected ADRs in a tertiary care center and included 859 reports in 6 months period. These reports were collected on an average rate of 100 ADR, which is a better rate than many of the AMCs in India^{13,14} and from other countries.¹⁵ Improved reporting is possibly an outcome of the pharmacovigilance workshops, regular continuing medical education programmes and other such activities organized for the clinicians about the importance of pharmacovigilance activities.

Table 2: Drug categorization according to ICD-10.

ICD category	Class of the drug	Number of drugs (% age)
40	Systemic antibiotics	254 (28.03)
41	Other systemic antibiotics and antiparasitics	139 (15.34)
40+41	Antimicrobial agents	43.47
42	Hormones and substitutes	8 (0.88)
43	Systemic agents	263 (29.02)
44	Blood constituents	6 (0.66)
45	Analgesics, antipyretics and anti-inflammatory	56 (6.18)
46	Antiepileptics and antiparkinson’s	28 (3.09)
47	Sedatives, hypnotics and anti-anxiety	8 (0.88)
48	Anesthetics	10 (1.10)
49	Psychotropic drugs	9 (0.99)
50	CNS stimulants	4 (0.44)
51	ANS drugs	5 (0.55)
52	CVS drugs	17 (1.88)
53	GIT agents	5 (0.55)
54	Acid-base and mineral balancing drugs	5 (0.55)
55	Smooth muscles and respiratory system	12 (1.32)
56	Topical agents	29 (3.26)
57	Other unspecified drugs	48 (5.30)
	Total	906 (99.997)

ICD: International classification of disease, ANS: Autonomic nervous system, CVS: Cardiovascular disease, GIT: Gastrointestinal

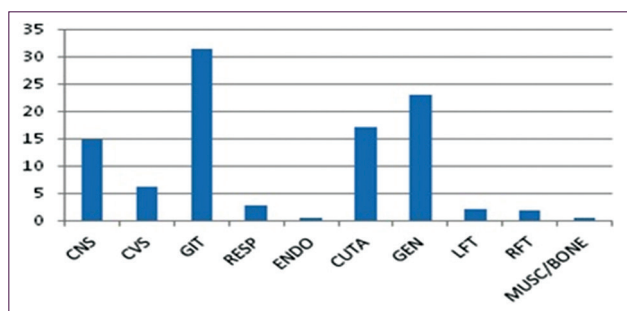


Figure 2: Various organ systems involved in reported adverse drug reactions.

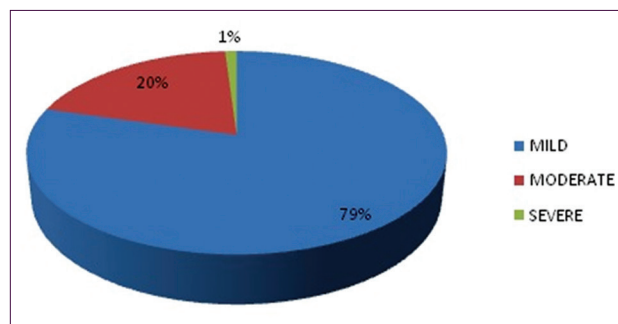


Figure 3: Severity of reaction.

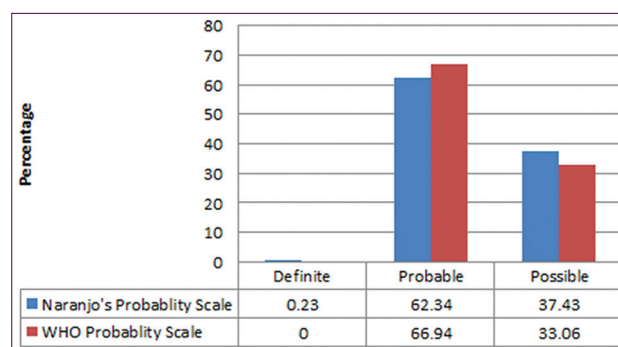


Figure 4: Causality assessment.

The demographic details of the present analysis showed male gender predominance over females w.r.t ADRs, which was similar to the findings of some other studies.^{16,17} Several other studies have found that ADRs are more common in females than in males.^{18,19} However, another study showed no difference in the occurrence of ADRs in male and female patients²⁰ showing thereby that the influence of gender may be incidental only and have no influence on the number of ADRs reported.

In the present evaluation, a higher percentage of ADRs reported occurred in the adult population (16-60 years), the mean age being >42 years, which is similar to that reported by the other studies.^{21,22} This possibly may be incidental again, but it may also be possible because of under-reporting of ADRs by elderly and pediatric population due to inability to frequently visit the hospital, unidentification of the ADRs and non-reporting by these age groups.

The most frequently implicated group of medicines in the ADRs was antimicrobial agents, this finding is consistent with other studies.^{23,24} β lactam antibiotics accounted for the highest number of the ADR reports^{25,26} and the other important ones included anti-neoplastic drugs, analgesics and non-steroidal anti-inflammatory drugs. The other studies have implicated same drugs.^{27,28} The association might be because the antimicrobials and analgesics are most frequently and irrationally prescribed group of drugs.

The organ system most often affected by ADRs in this evaluation was GIT system, which was also most commonly involved in the other published data²⁹ followed by generalized body reactions such as asthenia, fatigue, weakness, lethargy, fever and then followed by cutaneous ADRs. The pattern was consistent with many studies, which have reported a higher percentage of dermatological manifestations.³⁰⁻³² One of the reasons may be that these ADRs are visible and easily identified by patient themselves using symptoms only where as other reactions need necessary laboratory evaluation.

The majority of reactions were non-serious 662 (77.1%) and 197 reactions (22.9%) were serious. Most of the ADRs reported were mild and thus were managed by withdrawing the offending drug and by providing the symptomatic treatment to manage the ADRs; as done in few other studies.^{33,34} In severe cases hospitalization was done, and most of them recovered; however, three ADRs were fatal.

The causal relation was assessed with both WHO global introspection method and Naranjo's probability scale. WHO global introspection method showed probable causality association for 66.94% ADRs with the drug, followed by 33.06% categorized as possible; consistent with other results showing a majority of reactions as probable.^{35,36} However, a few other studies have reported vice versa also.^{37,38} The causality was almost consistent with both Naranjo's probability scale and WHO global introspection method.

The Naranjo's probability scale showed 0.23% reactions having a definite association with the drug.

The study has the limitation that the data evaluated is for a short duration i.e., only for 6 months and also it is based on spontaneous reporting system because of which exact calculation of incidence and prevalence of ADRs could not be assessed. However, it was aimed to represent the pattern and trends of ADRs at the hospital.

Early identification and management of ADRs are essential to imply the safe and rational use of drugs as the impact on patient's quality of life is major. The current Indian scenario of PvPI is upholding well and the combined effort of regulatory authorities and healthcare professionals is raising the data contribution but still there are many healthcare professionals totally unaware of the Pharmacovigilance programme and the need of reporting and monitoring of ADRs.

CONCLUSION

The monitoring and reporting of suspected ADRs by healthcare professionals aids in improved patient welfare. This also acts as an alerting mechanism for physicians. ADRs to drugs happen commonly, and their reporting is important for the early recognition and prevention of ADRs. It not only help in generating signals but also helps the regulatory authorities in making the policy decision. Furthermore, the awareness about risk factors and in-depth knowledge of the literature of ADRs can help physicians to identify patients with greater risk of ADRs.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Fitzgerald P. Pharmacovigilance inspections. *Indian J Pharmacol.* 2008;40 Suppl 1:S21-3.
2. Medicines: safety of Medicines– Adverse Drug Reactions, Fact sheet; Updated October 2008 Geneva: WHO. Available at: <http://www.who.int/mediacentre/factsheets/fs293/en/index.html>. Accessed 29 February 2015.
3. Einarson TR. Drug-related hospital admissions. *Ann Pharmacother.* 1993;27(7-8):832-40.
4. Pirmohamed M, Breckenridge AM, Kitteringham NR, Park BK. Adverse drug reactions. *BMJ.* 1998;316(7140):1295-8.
5. Gupta YK. Ensuring patient safety - launching the new pharmacovigilance programme of India. *Pharma Times.* 2010;42:21-6.
6. Vikas D, Sindhu S, Anand KS. Adverse drug reaction monitoring in India. *J Indian Acad Clin Med.* 2004;5:27-33.
7. The Pharmacovigilance News-National Drug Authority. April 2014. Available at: <http://www.nda.or.ug/docs/bulletin%20issue%20No.1.pdf>. Accessed 29 February 2015.
8. Pharmacovigilance Programme of India. Available at: <http://>

- www.cdsc.nic.in/pharmacovigilance_intro.htm. Accessed 29 February 2015.
9. WHO-UMC Causality Assessment System. Available at: <http://www.who-umc.org/pdfs/Causality.pdf>. Cited July 2014. [Last Accessed on 29 February 2015].
 10. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-45.
 11. Classification World Health Organization. International Statistical Classification of Diseases and Related Health Problems. 10th Revision (ICD-10). Geneva: WHO; 2010.
 12. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm*. 1992;49(9):2229-32.
 13. Dikshit RK, Desai C, Desai MK. Pleasures and pains of running a pharmacovigilance center. *Indian J Pharmacol*. 2008;40 Suppl 1:S31-4.
 14. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res*. 2006;54(3):226-33.
 15. Baniasadi S, Fahimi F, Shalviri G. Developing an adverse drug reaction reporting system at a teaching hospital. *Basic Clin Pharmacol Toxicol*. 2008;102(4):408-11.
 16. Piparva KG, Buch JG, Chandrani KV. Analysis of adverse drug reactions of atypical antipsychotic drugs in psychiatry OPD. *Indian J Psychol Med*. 2011;33(2):153-7.
 17. Subbanna PK, Chandy SJ. The role of active surveillance in improving the hospital adverse drug event reporting. *Indian J Pharmacol*. 2006;38:363-4.
 18. Miller MA. Gender-based differences in the toxicity of pharmaceuticals – the food and drug Administration’s perspective. *Int J Toxicol*. 2001;20(3):149-52.
 19. Ramesh M, Pandit J, Parthasarathi G. Adverse drug reactions in a south Indian hospital – their severity and cost involved. *Pharmacoepidemiol Drug Saf*. 2003;12(8):687-92.
 20. Patel H, Bell D, Molokhia M, Srishanmuganathan J, Patel M, Car J, et al. Trends in hospital admissions for adverse drug reactions in England: analysis of national hospital episode statistics 1998-2005. *BMC Clin Pharmacol*. 2007;7:9.
 21. Harris RZ, Benet LZ, Schwartz JB. Gender effects in pharmacokinetics and pharmacodynamics. *Drugs*. 1995;50(2):222-39.
 22. Patel KJ, Kedia MS, Bajpai D, Mehta SS, Kshirsagar NA, Gogtay NJ. Evaluation of the prevalence and economic burden of adverse drug reactions presenting to the medical emergency department of a tertiary referral centre: a prospective study. *BMC Clin Pharmacol*. 2007;7:8.
 23. Ciorciaro C, Hartmann K, Kuhn M. Differences in the relative incidence of adverse drug reactions in relation to age? An evaluation of the spontaneous reporting system of SANZ Swiss Drug Monitoring Center. *Schweiz Med Wochenschr*. 1998;128(7):254-8.
 24. Suh DC, Woodall BS, Shin SK, Hermes-De Santis ER. Clinical and economic impact of adverse drug reactions in hospitalized patients. *Ann Pharmacother*. 2000;34(12):1373-9.
 25. Palanisamy S, Arul Kumaran SG, Rajasekaran A. A study on assessment, monitoring, documentation and reporting of adverse drug reactions at a multi-specialty tertiary care teaching hospital in South India. *Int J Pharmtech Res*. 2009;1:1519-22.
 26. Baniasadi S, Fahimi F, Shalviri G. Developing an adverse drug reaction reporting system at a teaching hospital. *Basic Clin Pharmacol Toxicol*. 2008;102(4):408-11.
 27. Olivier P, Boulbès O, Tubery M, Carles P, Montastruc JL, Lapeyre-Mestre M. Preventability of adverse effects in a medical emergency service. *Therapie*. 2001;56(3):275-8.
 28. Polimeni G, Salvo F, Cutroneo P, Morreale I, Patrizio Caputi A. Adverse reactions induced by NSAIDs and antibacterials: analysis of spontaneous reports from the Sicilian regional database. *Drug Saf*. 2006;29(5):449-59.
 29. Gor AP, Desai SV. Adverse drug reactions (ADR) in the in patients of medicine department of a rural tertiary care teaching hospital and influence of pharmacovigilance in reporting ADR. *Indian J Pharmacol*. 2008;40(1):37-40.
 30. Suh DC, Woodall BS, Shin SK, Hermes-De Santis ER. Clinical and economic impact of adverse drug reactions in hospitalized patients. *Ann Pharmacother*. 2000;34(12):1373-9.
 31. Jha N, Bajracharya O, Namgyal T. Prevalence of adverse drug reactions with commonly prescribed drugs in different hospitals of Kathmandu valley. *Kathmandu Univ Med J (KUMJ)*. 2007;5(4):504-10.
 32. Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. *JAMA*. 1991;266(20):2847-51.
 33. Kurokawa T, Correa-Nunes AM, Czarnecki A. Guidelines for setting up and running a Pharmacovigilance Centre. Uppsala Monitoring Centre. Sweden: WHO Collaborating Centre for International Drug Monitoring; 2000: 4-10.
 34. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. *JAMA*. 1995;274:29-34.
 35. Davies EC, Green CF, Mottram DR, Pirmohamed M. Adverse drug reactions in hospitals: a narrative review. *Curr Drug Saf*. 2007;2(1):79-87.
 36. Palanisamy SN, Raghavendra Y, Ramarao N. Monitoring and reporting of adverse drug reactions with cardiovascular drugs in a tertiary care hospital in South India. *Int J Pharm Ther*. 2014;5(1):14-8.
 37. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. *Br J Clin Pharmacol*. 2008;65(2):210-6.
 38. Rao PG, Archana B, Jose J. Implementation and results of an adverse drug reaction reporting programme at an Indian teaching hospital. *Indian J Pharmacol*. 2006;38:293-4.

doi: 10.18203/2319-2003.ijbcp20150039

Cite this article as: Kharb P, Mittal N, Gupta MC. An evaluation of adverse drug reactions monitoring at a pharmacovigilance unit under pharmacovigilance programme of India in a tertiary care hospital of Haryana. *Int J Basic Clin Pharmacol* 2015;4:556-60.