International Journal of Pharmacy and Biological Sciences-IJPBS™ (2019) 9 (2): 231-235
Online ISSN: 2230-7605, Print ISSN: 2321-3272
Research Article | Pharmaceutical Sciences | Open Access | MCI Approved
UGC Approved Journal

# A Prospective Observational Study on Causality and Severity Assessment of Adverse Drug Reactions in A Tertiary Care Teaching Hospital

**A V Kishore Babu*[1] and A Srinivasa Rao[1]**
**Department of Pharmacy Practice, Bhaskar Pharmacy College, Hyderabad- 500075.**

Received: 14 Jan 2019 / Accepted: 12 Mar 2019 / Published online: 1 Apr 2019
**Corresponding Author Email:** kishorebabu.pharma@gmail.com

## Abstract

**Objective:** Adverse drug reactions accounts for major hospital admission and relatively increased health care costs in the present days. The main purpose of the study is to assess the causality and severity of adverse drug reactions from various departments of tertiary care teaching hospital. **Method:** A prospective observational study was carried out in a tertiary care teaching hospital at Hyderabad, India, for a period of 12 months. Patients of all age and both genders were included in the study. Adverse drug reactions reported from various departments by physicians were analyzed by Naranjo's and Hartwig's Siegel's scale respectively. Descriptive statistics were used for data analysis. **Results:** A total of 86 ADRs were reported over 12 month's period. Of these, 57% in female and 43% in male category. Highest ADRs were reported from 21- 30 (31%) years of age followed by 31-40 (23%) years. Maximum numbers of cases were reported from general medicine department (37%). Among all the suspected drugs, antimicrobial agents accounted for 46% of total ADR cases. Most of the ADRs were involved on the skin (51%). Naranjo's ADR probability scale showed that 55% of ADRs were probable. Hartwig's and Siegel's the severity assessment scales shown that 63% ADRs are moderate followed by 8% severe ADR cases. **Conclusion:** This study provides a database of ADRs due to commonly used drugs. Hence our study advises that there is a need of spontaneous ADR reporting from physicians. This study also suggests further research in India for the improvement of possible intervention strategies to reduce burden and cost of ADRs.

**Keywords**
Adverse drug reactions, Spontaneous reporting, Naranjo's and Hartwig's Siegel's Severity assessment.

*****

## INTRODUCTION

The history of Pharmacovigilance started 170 years ago, on Jan 29, 1848, when a young girl (Hannah Greener) from the north of England died after receiving chloroform anesthesia before removal of an infected toenail.[1]

According to WHO Pharmacovigilance (PV) is defined as the science and activities relating to the detection,

assessment, understanding and prevention of adverse effects or any other drug-related problem. WHO established its Programme for International Drug Monitoring in response to the thalidomide disaster detected in 1962.[2] Drugs prescribed for disease are often themselves the cause of serious amount of adverse drug reactions ranging from mere inconvenience to permanent disability and death.

ADRs are responsible for 5-11% of hospital admissions of which 60-70% are preventable.[3] The recent epidemiological studies have estimated that adverse drug reactions are the fourth to sixth leading causes of death.[4] There are several factors involve in rising the number of adverse drug reactions. These include: 1) The number of drugs prescribed are high (polypharmacy); 2) The ever-increasing number of new drugs in the market; and, 3) The lack of a formal system for monitoring adverse drug reactions.[5]

**Classification of Adverse drug reactions[6]**

**Type-A (Augmented):** Commonest (up to 70%) – Dose dependent, severity increases with dose. Preventable in most part by slow introduction of low dosages. Predictable by the pharmacological mechanisms, e.g., hypotension by beta-blockers, hypoglycaemia caused by insulins or oral hypoglycaemics, or NSAID induced gastric ulcers.

**Type-B (Bizarre):** Rare, idiosyncratic, genetically determined, unpredictable, mechanisms are unknown, serious, can be fatal; unrelated to the dose, e.g., hepatitis caused by halothane, aplastic anaemia caused by chloramphenicol, neuroleptic malignant syndrome caused by some anaesthetics and antipsychotics.

**Type-C (Continuous drug use):** Occurs as a result of continuous drug use. May be irreversible, unexpected, unpredictable, e.g., Tardive dyskinesia's by antipsychotics, dementia by anticholinergic medications.

**Type-D (Delayed):** Delayed occurrence of ADRs, even after the cessation of treatment, e.g., corneal opacities after thioridazine, ophthalmopathy after chloroquine, or pulmonary/peritoneal fibrosis by methyserzide.

**Type-E (End of dose):** Withdrawal reactions. Occurs typically with the depressant drugs, e.g., hypertension and restlessness in opiate abstainer, seizures on alcohol or benzodiazepines withdrawal, first dose hypotension caused by alpha-blockers (Prazosin) or ACE inhibitors.

**Type-F (Failure of therapy):** Results from the ineffective treatment (previously excluded from analysis according to WHO definition), e.g., Accelerated hypertension because of inefficient control.

METHODOLOGY

A prospective observational study was conducted for a period of 12 months from January 2018 to December 2018 in Bhaskar Medical College and Bhaskar General Hospital, Hyderabad at outpatient and inpatient departments. Prior approval from Hospital Institutional Ethical Committee was obtained to conduct the study. Adverse Drug reactions were reported from various departments of hospital include; DVL, General medicine, Gynaecology, Pulmonology and Psychiatry.

**Study Procedure**

The suspected adverse drug reactions from various departments of hospital were collected and filled into CDSCO, Spontaneous ADR reporting forms. Causality assessment was performed by using Naranjo's probability assessment scale[7] and severity assessment was performed by using Hartwig's Siegel's scale.[8]

STATISTICAL ANALYSIS

Descriptive statistics were used for data analysis. All values were expressed in percentages and depicted using tables and charts. Data were subdivided based on age, gender, drugs class, and body systems/organs involved.

**Inclusion Criteria:**

- Both males and females of all age group were enrolled in the study.
- Any suspected ADRs of prescription and OTC medication were included in the study.
- Both inpatient and outpatient ADRs were ultimately noted.

**Exclusion Criteria**:

- The use of alternative medicines like Homeopathy, Ayurvedic and Unani etc. as well as prescription containing more than 6 drugs were excluded.
- All psychiatry, alcoholic, drug abuse and unconscious patients were not included in the study.

**Causality assessment by Naranjo's ADR probability scale[7]**

**Naranjo's Adverse Drug Reaction Probability Scale**

| Question | Yes | No | Do Not Know | Score |
|---|---|---|---|---|
| 1. Are there previous conclusive reports on this reaction? | +1 | 0 | 0 | |
| 2. Did the adverse event appear after the suspected drug was administered? | +2 | -1 | 0 | |
| 3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered? | +1 | 0 | 0 | |
| 4. Did the adverse event reappear when the drug was re-administered? | +2 | -1 | 0 | |
| 5. Are there alternative causes (other than the drug) that could on their own have caused the reaction? | -1 | +2 | 0 | |
| 6. Did the reaction reappear when a placebo was given? | -1 | +1 | 0 | |
| 7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic? | +1 | 0 | 0 | |
| 8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 | |
| 9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure? | +1 | 0 | 0 | |
| 10. Was the adverse event confirmed by any objective evidence? | +1 | 0 | 0 | |
| **TOTAL SCORE:** | | | | |

***Scoring for Naranjo's algorithm*: > 9 = definite ADR; 5-8 = probable ADR; 1-4 = possible ADR; 0 = doubtful ADR.**

**Hartwig's and Siegel's Severity Assessment Scale[8]**

| | |
|---|---|
| Level 1 | An ADR occurred but required no change in treatment with the suspected drug |
| Level 2 | The ADR required that the treatment with the suspected drug be held, discontinued or otherwise changed. No antidote or need of other treatment was required. No increase in length of stay (LOS). |
| Level 3 | The ADR required that treatment with the suspected drug be held, discontinued or otherwise changed.<br>AND/OR<br>An Antidote or other treatment was required. No increase in length of stay (LOS)<br>Any level 3 ADR which increases length of stay by at least 1 day. |
| Level 4 | OR<br>The ADR was the reason for the admission |
| Level 5 | Any level 4 ADR which requires intensive medical care |
| Level 6 | The adverse reaction caused permanent harm to the patient. |
| Level 7 | The adverse reaction either directly or indirectly led to the death of the patient |

**Mild= level 1 and 2, moderate= level 3 and 4, severe= 5, 6 and 7**

## RESULTS

A total of 86 ADRs were reported over 12 month's period. Out of these, 57% were in female and 43% were in male category. Highest numbers of ADRs were reported in the age group of 21- 30 (31%) years of age followed by 31-40 (23%) years of age group (Table 1). Maximum number of cases were reported from the department of general medicine (37%) followed by pulmonology (31%) and department of DVL (16%). (Table 2).

Among all the suspected drugs causing ADRs, antimicrobial agents (AMAs) accounted for 46% of the total cases followed by CNS drugs 21%, analgesics 15%, vitamins 10% and other drugs were implicated in 8% of cases (Figure 1).

Most of the adverse drug reactions are involved on the skin (51%) followed by GIT (17%) (Figure 2).

Assessment of all ADRs using Naranjo's ADR probability scale showed that 55% of ADRs were probable, 24% were classified as possible, 15% of ADRs are doubtful and 6% were definite to have occurred due to drug administration (Figure 3).

According to Hartwig's and Siegel's the severity assessment scale shown that 63% ADRs are moderate and 29% ADRs were mild followed by 8% severe ADR cases (Figure 4).

## DISCUSSION

In our study majority of ADRs were reported from female patients than from male which showed similar trend as in the study done by Ratan J. Lihite

et al.[9] Majority of the patients were in the age group of 21-30 years followed by 31- 40 years due to changes in present lifestyle, food habits, work stress and family responsibility in this time period. The maximum number of cases reported from general medicine department similar with the study done by S. G. S. Rajeshreddy V et al and Murphy B et al.[10, 11] The highest numbers of reports were recorded by the use of antimicrobial agents (AMAs) which is in accordance with the result of studies done by Murphy B et. al and Lukshmy M Hettihewa et al.[11, 12] The most usually effected organ system was skin and gastrointestinal tract which is in accordance with studies done by Shrivastava M et al, and Chan AL et al.[13, 14] Skin rashes, gastritis, urticaria, nausea and vomiting are the most common adverse effects and it leads to increase the total cost of health system and prolongs the hospital visit.

Analysis of the ADRs using Naranjo's probability scale showed that 55% of cases were classified as probable, 24% were possible, 15% of cases were in doubtful and 6% were definite. Severity Assessment by Hartwig's and Siegel's scale shown that 63% ADRs are moderate and 29% ADRs were mild followed by 8% severe ADR cases. No lethal effects were produced. Our study provided the database of ADRs due to commonly used drugs and monitoring and detection of such known ADRs by effective implementation of pharmacovigilance and would lead to prevention and better management of ADRs on outpatient basis.[15, 16]

## CONCLUSION

This study provides a database of ADRs due to common used drugs in hospital, which will help the clinicians for favorable and safe use of medicines. In our study antimicrobials for the treatment of tuberculosis was reported to cause majority of ADRs. The commonly reported ADR in our study was skin rashes. Hence our study advises that there is a need of spontaneous ADR reporting from all the departments of tertiary care teaching hospital for monitoring and assessment of ADRs. This study also suggests further research in different parts of teaching hospitals in India for the improvement of possible intervention strategies to reduce burden and cost of ADRs.

## ACKNOWLEDGEMENTS

Authors would like to acknowledge ADR Monitoring Centre, Bhaskar Medical College and Bhaskar General Hospital, Hyderabad, Telangana for their kind support to conduct this study.

## REFERENCES

1. Routledge P. 150 years of pharmacovigilance. Lancet. 1998; 351:1200–1.
2. WHO. https://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/
3. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): A meta-analysis of observational studies. Pharm World Sci. 2002; 24:46-54.
4. Srinivasan R, Ramya G. Adverse drug reaction causality assessment. Int J Res Pharm Chem 2011;1(3):606–11.
5. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, Small SD, Sweitzer BJ, Leape LL. The costs of adverse drug reactions in hospitalised patients. JAMA 1997; 277: 301-07.
6. Bhatt AD. Drug related problems and adverse drug events: Negligence, litigation and prevention. JAPI 1999; 47: 715-20.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;80: 289–95.
8. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992;49: 2229–32.
9. Ratan J. Lihite, Mangala Lahkar, Sukirti Das, Debeeka Hazarika, Murali Kotni, Mudasir Maqbool, Swapna Phukan. A study on adverse drug reactions in a tertiary care hospital of Northeast India. Alexandria Journal of Medicine. 2017 53, 151–156.
10. S. G. S. Rajeshreddy V., Lokesh V. Patil. Causality assessment and the severity of the adverse drug reactions in tertiary care hospital: a pharmacovigilance study, Int J Basic Clin Pharmacol. 2017 Dec;6(12):2800-2803
11. Murphy BM, Frigo LC. Development, implementation, and results of a successful multidisciplinary adverse drug reaction reporting program in a university teaching hospital, Hosp Pharm. 1993;28(12):1199-204.
12. Hettihewa LM, Sirisena B. Casualty assessment and the severity of the adverse drug reactions (ADR) actively detected in hospital-in patients in tertiary care hospital Sri Lanka: Prospective observational survey. Asian Journal of Research in Biological and Pharmaceutical Sciences. 2014;2(1):1-10.
13. Shrivastava M, Uchit G, Chakravarti A, Joshi G, Mahatme M, Chaudhari H. Adverse Drug Reactions Reported in Indira Gandhi Government Medical College and Hospital, Nagpur. JAPI. 2011; 59:1-4.

14. Chan AL, Lee HY, Ho CH, Cham TM, Lin SJ. Cost evaluation of adverse drug reactions in hospitalized patients in Taiwan: A prospective, descriptive, observational study. Curr Ther Res Clin Exp. 2008; 69:118-29.
15. Meyboom RH, Linquist M, Egberts AC, Edward IR. Signal selection and follow-up in pharmacovigilance. Drug Saf. 2002; 25:459-65.
16. Pirmohamed M, Breckenridge AM, Kitterinham NR, Park BK. Fortnightly review: adverse drug reactions. Brit Med J. 1998; 316:1295-8.