IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
December 2021 Vol.:23, Issue:1

Identifying, Assessing and Reporting Adverse Drug Reactions in Government General Hospital: A Prospective Observational Study

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Submitted: 22 November 2021
Accepted: 27 November 2021
Published: 30 December 2021

Keywords: Adverse drug reactions, prospective observational study, Pharmacovigilance, causality, and side effects

ABSTRACT

Background: Adverse drug reactions are posing a major challenge to the health care system as they compromise the safety of drug therapy. Adverse drug reactions are not only the cause of mortality and morbidity but also a significant increase in the health care cost. **Aim:** To detect, document, assess, collect and report the suspected adverse drug reactions in a tertiary care hospital. **Methodology:** A prospective observational study was conducted at Government General Hospital, Guntur for 6 months. **Objectives: -** To detect the nature and frequency of adverse drug reactions being reported from different departments. - To assess the severity of ADRs. - To assess the causality of reaction. **Results:** ADRs were mostly seen in the age group of 19-59. The gastrointestinal system was found to be the most commonly affected organ system. **Conclusion:** By improving the knowledge and awareness of ADR reporting among health care professionals it would increase the practice of drug safety which in turn will reduce the mortality and morbidity of ADRs.

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INTRODUCTION:

WHO defines adverse drug reactions as "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or modification of physiological function".[1]Adverse drug reactions are posing a major challenge to the health care system as they compromise the safety of drug therapy. Adverse drug reactions are not only the cause of mortality and morbidity but also a significant increase in the health care cost.[2] Several contributing factors for adverse drug reactions include age, sex, polypharmacy, concurrent diseases, race, and genetic polymorphism.[3] The other predisposing factors that would increase the risk of developing adverse drug reactions include drug-related factors, patient-related factors, disease-related factors, patient-related factors, disease-related factors, and social factors.[4]

WHO defines Pharmacovigilance as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems".[5] Pharmacovigilance plays a key role in ensuring that patients receive safe drugs. It is the process of being alert to the possible unwanted or harmful effects of therapeutic medications so that they could be detected early and remedial measures instituted.[6-7] Benefits of adverse drug reaction reporting includes:

I. Provide information regarding the risk profile of the drug.

II. Harmonizes the risk-management activities and efforts to minimize drug-related problems.

III. Assess the safety profile of drugs, especially recently approved drugs.

IV. Quantify the adverse drug reactions incidence rate.

V. Awareness development in health care professionals and patients about potential drug-related problems

VI. Assessment of economic impact due to adverse drug reactions and strategies to minimize the same by assessing severity and preventability.[4]

Aim: To detect, document, assess, collect and report the suspected adverse drug reactions, in a tertiary care hospital.

REVIEW OF LITERATURE:

Lobo et al., [2013] conducted a prospective study on "Adverse drug reaction monitoring: support of Pharmacovigilance at a tertiary care hospital" in northern brazil over 8 months from January 2009 to August 2009, and about 95 adverse drug reactions were confirmed and reported among 81 inpatients in a total of 2995 admissions. The overall incidence of adverse drug reactions was 3.1%. They concluded that the results obtained will contribute to the development of strategies for the Pharmacovigilance service at HGP and other hospitals throughout the country which will improve the quality of Adverse Drug Reaction Reporting and ensure safer drug use.[8]

Dindayal Patidar et al., [2013] conducted a prospective study on "Implementation and Evaluation of Adverse Drug Reaction Monitoring System in a Tertiary Care Teaching Hospital" in Mumbai over 7 months and reported about 32 adverse drug reactions out of 254 admissions. Dermatological adverse drug reactions were found to be the most frequent. The potent management of adverse drug reactions was found to be drug withdrawal. They concluded that monitoring of adverse drug reactions is an ongoing, Ceaseless and continuing process as newer and newer drugs hit the market the need for Pharmacovigilance grows more than even before. On balance, this study suggests that hospital-based monitoring is a good method to detect known and unknown links between drug exposure and ADRs.[2]

Harsha Ramakrishnaiah et al., [2015] conducted a "Prospective study on adverse drug reactions in outpatients and inpatients of medicine department in a tertiary care hospital." A total of 195 adverse drug reactions were reported from 111 patients. The majority of adverse drug reactions were probable in causality assessment, moderate in severity, and probably preventable. They concluded that a wide range of ADRs is possible in the medicine department and adequate awareness of ADR Reporting and precautions while prescribing drugs is essential.[9]

Ratan J Lihite et al., [2016] conducted "A study on Adverse Drug Reactions in a Tertiary Care Hospital of North East India" for 7 months. A total of 255 ADRs were reported by the physicians and their causality and severity assessments were performed as per Naranjo and Hartwig's assessment criteria respectively. The skin was commonly affected organ system and most of the ADRs were possible and mild in nature. They concluded that the topical steroid was reported to induce adverse drug reactions in majority of the patients. The commonly reported reaction was acne.[10]

Objectives:

- To detect the nature and frequency of adverse drug reaction being reported from 5 different departments.
- To understand the severity of adverse drug reactions.
- To assess the causality of adverse drug reactions.

MATERIALS AND METHODS:

Materials used:

- Suspected adverse drug reaction reporting form
- WHO causality assessment scale
- Hartwig's severity assessment scale
- Alert cards

Methodology: A prospective observational study was conducted in Government General Hospital, Guntur, which is a 1400 bedded tertiary care teaching hospital to which patients come from 4 districts. The study was conducted in a period of 6 months i.e. from October 2020 to March 2021 in patients who developed an adverse drug reaction in both inpatients and outpatients in specified departments.

Inclusion criteria: Patients of all ages and both genders who have suspected adverse drug reactions after the drug treatment from selective departments [general medicine, neurology, cardiology, psychiatry, gynecology].

Exclusion criteria: Adverse effects due to Drug-drug interactions, overdosing or excess consumption, medication errors, Drug-food interactions.

Statistical analysis: Description statistics were used for data analysis.

Ethical approval: The study was approved by the Institutional Human Ethics Committee of Guntur Medical College and Government General Hospital, Guntur, Andhra Pradesh, filed under number GMC/IEC/390/2020, and was conducted by the ethical guidelines of the Declaration of Helenski (created in 1964 and revised in 2002). An informed consent form

was taken from all the subjects before the study which was mentioned in the local language (Telugu).

RESULT AND DISCUSSION:

All patients enrolled in this study fulfilled the inclusion criteria and were completely compliant with the study procedures and instructions. A total of 70 ADRs were identified among patients in a study period of 6 months from October 2020 to March 2021. These collected ADRs were categorized according to patient's demographics such as age, gender; departments from which ADRs were collected, organ system involved, management for the ADRs, and causality assessment was done using WHO-UMC causality scale, and severity was assessed using Hartwig's severity assessment scale and category of drugs.

Out of 70 ADRs reported and assessed, 91.43% of ADRs were in the age group of 19 to 59 years which was followed by the age group of ≥ 60 years with 5.51% of ADRs and then 0 to 18 years of age with 2.86% of ADRs (Table-1) which was consistent with the Lobo et al.[8]. The reasons might be due to the patients at this age group suffering from many comorbidities such as diabetes, hypertension, etc., for which they require more medications which can increase the risk of adverse drug reactions.

Table-1: Prevalence of ADRs among various age groups and gender distribution of ADRs

S.No	Age	Number of ADRs (n=70)
1.	0-18	2(2.85%)
2.	19-59	64(91.4%)
3.	>60	4(5.71%)
S.No	**Gender**	**Number of ADRs (n=70)**
1.	Male	38(54.2%)
2.	Female	32(45.7%)

Male predominance was noted over females in the case of ADRs [Table-1]. Out of 70 ADRs, 38(54.2%) were men and 32(45.7%) were women. The male to female ratio was 1.1875. Harsha Ramakrishnaiah et al.[9] in his study conducted in Karnataka, had also observed a greater incidence of ADRs among males.

The most commonly affected organ system was found to be the gastrointestinal system (25.7%) followed by the central nervous system (24.2%) and integumentary system (17.1%) which was depicted in (Table-2). Our findings are consistent with Farhan Ahmad Khan et al. [11].

Table-2: Number of adverse drug reactions from different departments and Organ systems affected by adverse drug reactions

S.no	Departments	Number of ADRs (n=70)
1.	General medicine	35(50%)
2.	Neurology	8(11.4%)
3.	Psychiatry	9(12.8%)
4.	Cardiology	6(8.6%)
5.	Gynaecology	12(17.1%)
S.no	**Organ systems involved**	**Number of ADRs (n=70)**
1.	CNS	17(24.2%)
2.	CVS	0(0)
3.	ENT	0(0)
4.	Ocular	2(2.9%)
5.	GI	18(25.7%)
6.	Metabolic	7(10%)
7.	Haematological	2(2.9%)
8.	Integumentary	12(17.1%)
9.	Musculoskeletal system	3(4.3%)
1O.	Renal	6(8.5%)
11.	Respiratory	2(2.9%)
12.	Reproductive	0(0%)
13.	Endocrine	1(1.4%)

To strengthen and further emphasize the validity of the findings of the study, causality assessment was done using the WHO-UMC causality assessment scale. Out of 70 ADRs reported, 84.2% were possible and 15.8% were probable [Table-3] and it is consistent with the study conducted by Ratan J.Lihite et al. [10]. None of the reactions was categorized into

certain as rechallenging of the drugs was not attempted in any patient as it may worsen the patient's condition.

Table-3: Causality assessment of reported adverse drug reactions by WHO probability scale and severity of the reported adverse drug reactions using Hartwig's severity assessment scale.

S.NO	WHO causality assessment	Number of ADRs (n=70)
1.	Certain	0(0%)
2.	Probable / likely	11(15.7%)
3.	Possible	59(84.2%)
4.	Unlikely	0(0%)
5.	Unclassified/conditional	0(0%)
6.	Unassessable/unclassifiable	0(0%)
S.no	**Hartwig severity assessment**	**Number of ADRs(N=70)**
1.	Mild	51(72.8%)
2.	Moderate	19(27.1%)
3.	Severe	0(%)

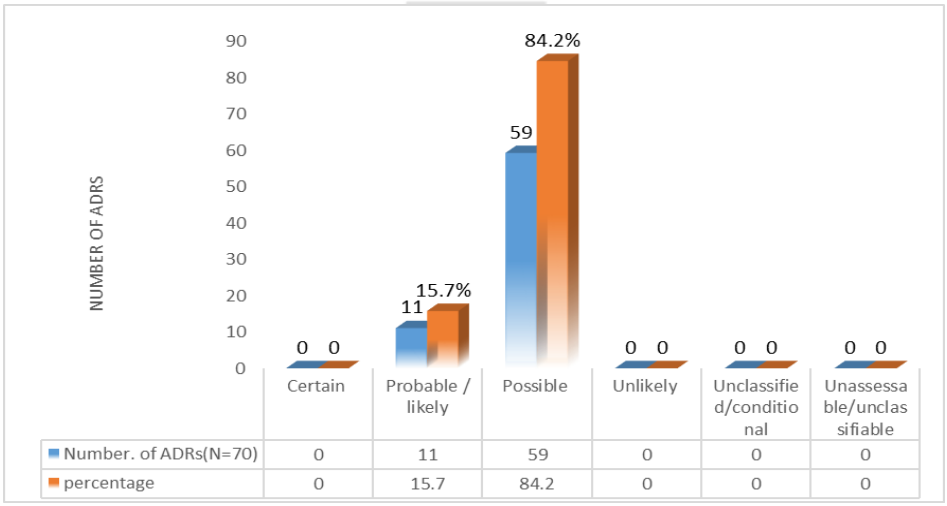

Figure-1: Causality assessment of reported adverse drug reactions by WHO probability scale

The severity assessment was done by using Hartwig's severity assessment scale[12]. According to this ADR severity assessment scale, the level of severity of ADR is classified on a scale ranging from 1 to 7. Level 1 and 2 indicates mild, level 3, 4(a) and 4(b) are

moderate and level 5, 6 and 7 are severe. On the evaluation of the severity of ADRs by Hartwig's severity assessment scale, it was evident that most of the ADRs reported in the study were of mild severity (12.8%) followed by moderate (27.1%). Similar findings were reported in Patidar et al.[2].

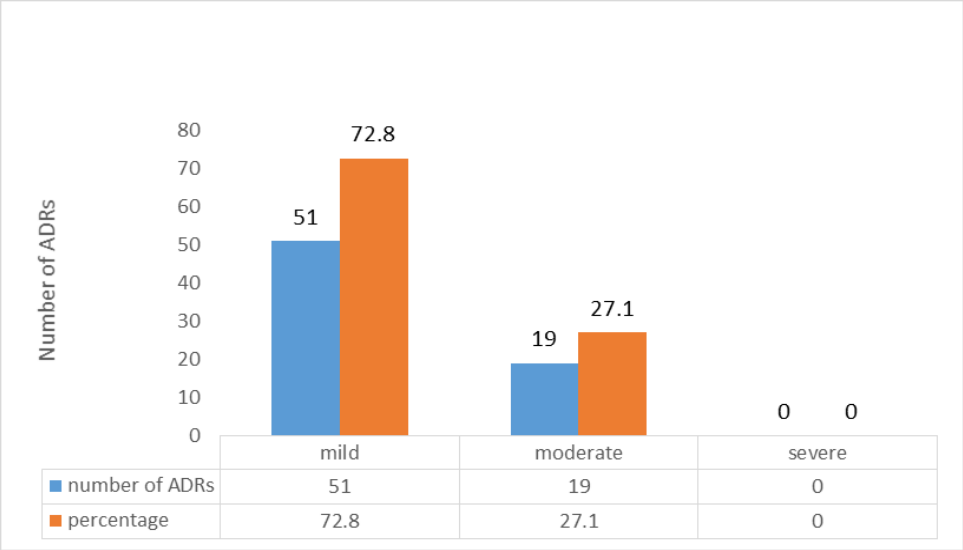

Figure-2: Severity of the reported adverse drug reactions using Hartwig's severity assessment scale

In 29(41.4%) cases, the suspected drug was continued without any changes as they are self-limiting and very mild while the suspected drug was withdrawn in 26(37.1%) cases and in 5 (7.1%) cases. Symptomatic treatments such as oral anti-histamines and anti-emetics were given. The dose of suspected was reduced in 4 (5.7%) and the suspected drug was substituted with another drug in 6 ADRs (8.5%) (Table:4).

Table-4: Seriousness, outcomes, and management of adverse drug reactions

S.no	Seriousness	Number of ADRs(N=70)
1.	Not serious	55(78.6%)
2.	Death	0(0)
3.	Congenital – anomaly	0(0)
4.	Life threatening	0(0)
5.	Disability	0(%)
6.	Hospitalization\prolonged	8(12.8%)
7.	Other medically important	6(8.6%)
S.no	**Outcomes**	**Number of ADRs(N=70)**
1.	Fatal	0(0)
2.	Not recovered	2(2.8%)
3.	Recovering	23(32.8%)
4.	Recovered	45(64.2%)
5.	Recovered with squeal	0(0)
S.no	**Management**	**Number of ADRs(N=70)**
1.	Stopped the medication	26(37.1%)
2.	Continue the same	29(41.4%)
3.	Added another drug to treat ADR	5(7.1%)
4.	Reduce the dose	4(5.7%)
5.	Substituted another drug	6(8.5%)

The drug class most commonly implicated with ADRs was antihypertensive agent 12 (17.1%) followed by anti–epileptics 11 (15.7%), mineral and vitamin supplement 11 (15.7%), antibiotics 7 (10 %). The drug classes least affected are anticoagulant 1 (1.4%), bronchodilators 1 (1.4%), antidiarrheals 1 (1.4%), antihistamines 1 (1.4%) and antispasmodic 1 (1.4%).

Table-5: Drug classes and individual drugs most commonly associated with ADRs

Category	Drug	ADR	Number of ADRs	Percentage
Anti-hypertensive	Amlodipine	Pedal oedema (5)	12	17.1
	Enalapril	Dry cough (3)		
	Furosemide	Hypokalaemia		
	Metoprolol	Pedal edema		
	Lasilactone	Gynecomastia		
	Losartan	Anemia		
Antiepileptics	Sodium valproate	Tremors (5) Vomiting	11	15.7
	Phenytoin	Ataxia (2) Blurred vision		
	Carbamazepine	Rashes (2)		
Anti–biotic	Piperacillin-tazobactam	Diarrhoea	7	10
	Amikacin	Diarrhea		
	Norfloxacin	Pruritis		
	Ciprofloxacin	Vomiting		
	Metronidazole	Vaginal irritation		
	Azithromycin	Abdominal pain		
	Amoxicillin	Urticaria		
NSAIDs	Ibuprofen	Urticaria	2	2.8
	Aspirin	Dyspnoea		
Opioid analgesic	Tramadol	Shortness of breath Nausea Chills	5	7.1

		Vomiting Epigastric pain		
Anti – cholinergic	Trihexyphenidyl	Blurred vision	3	4.3
	Amitriptyline	Dry mouth Urinary retention		
Anti – psychotics	Haloperidol	Dystonia Rigidity	5	7.1
	Olanzapine	weight gain Delusions Hyperglycaemia		
Anti-viral	Acyclovir	Rashes	2	2.8
	TLE regimen	Rashes		
Hypoglycaemic	H. actrapid	Hypoglycaemia (3)	3	4.3
Corticosteroids	Prednisolone	Urticaria Hyper pigmentation	2	2.8
Anti – coagulant	Heparin	Haematuria	1	1.4
Mineral and vitamin supplement	Calcium and vitamin D3	Vertigo (5) Headache (3) Constipation (2) Diarrhoea	11	15.7
Bronchodilators	Asthalin	Tremors	1	1.4
Anti – diarrheal	Loperamide	Constipation	1	1.4
Anti – histamine	Chlorpheneramine maleate	constipation	1	1.4
Anti – spasmodic	Buscopan	Rash	1	1.4
Anti – malaria	Chloroquine	Vomiting Rash	2	2.8

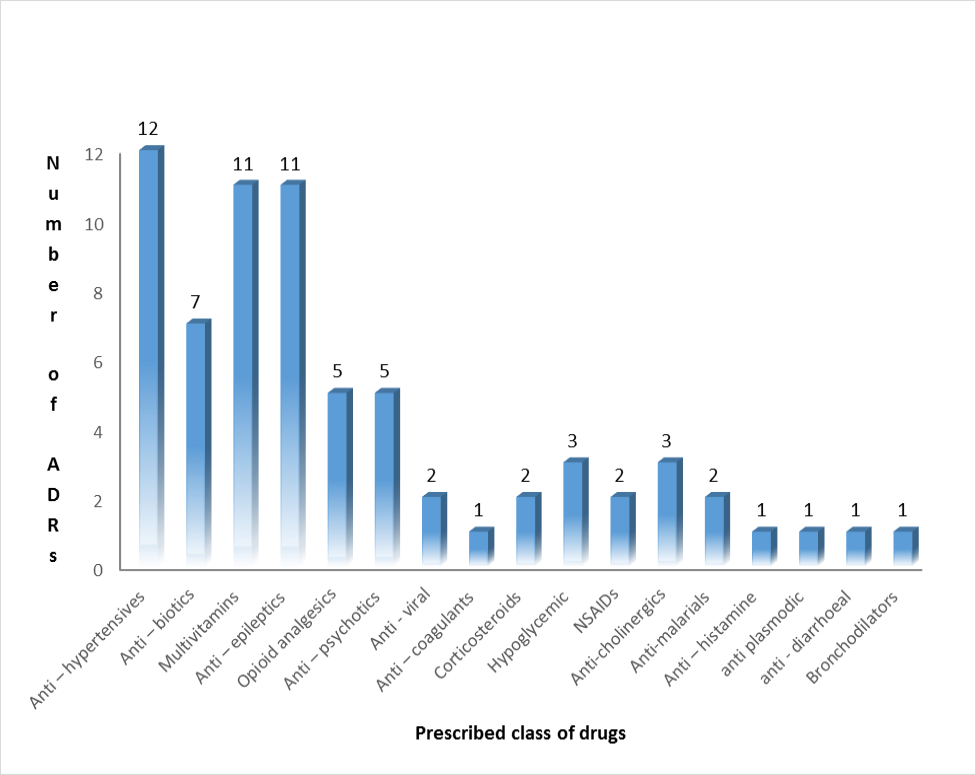

Figure-3: Drug classes in reported adverse drug reactions

CONCLUSION:

Underreporting is a major limitation of the spontaneous reporting system in pharmacovigilance and should take care of while analyzing the data. Since only one hospital data was taken into consideration and the results may not apply to the general population. But definitely, healthcare providers should be enlightened with the present data.

By observing the results of this study, it indicates the baseline information on incidence and pattern of ADRs and their distribution among the various age groups, gender, organ systems affected, and a therapeutic class of drugs. This study suggests that there is a need of spontaneous ADR reporting from all the departments for monitoring and assessment of ADRs. As ADRs are an important cause of morbidity and mortality which imparts a negative impact on the treatment and exerts a greater economic burden on the patients when it results in hospitalization or other comorbidities.

We conclude that monitoring ADRs is an ongoing, ceaseless, and continuing process. Imparting knowledge and awareness on ADR reporting among health care professionals will improve the reporting rates of reactions. Careful consideration involved in planning and

monitoring of drug therapy will improve drug safety and rational use of drugs thereby it will lead to the prevention of ADRs.

ACKNOWLEDGMENT:

We would like to acknowledge the Adverse drug reaction Monitoring Center, GMC, GGH, Guntur, NCC-PvPI, IPC, MoHFW, GOI, Ghaziabad for their kind support to conduct this study. We wish to thank Dr. K Chandrakala, Professor Ramarao Nadendla, Dr. N V Ramarao, Dr. Sravani for their constant guidance, support, and encouragement.

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