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IDENTIFICATION, ASSESSMENT AND REPORTING OF ADVERSE DRUG REACTIONS (ADRs) IN LARGE TERTIARY CARE HOSPITAL USING SPONTANEOUS REPORTING SYSTEM (SRS): A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract:

Background:

Detection, assessment and reporting of Adverse drug reactions (ADRs) is the need of the hour. Under-reporting of ADRs has been a major problem and Health care professionals (HCPs) must be encouraged to identify and report ADRs.

Objective: *The present study is aimed to Identify, assess and report ADRs in a large tertiary care Government teaching Hospital in South India, Andhra Pradesh.*

Methods: *A Prospective, observational study was carried out in the General Medicine unit. The identified ADRs were analyzed (Causality assessment) and reported through Spontaneous reporting system (SRS) to the ADR Monitoring center located at the study site.*

Results:

A total of 103 ADRs were identified, analyzed and reported in 85 patients. The gender-wise distribution of the study population included both Males (n=42, 49.4%) and females (n=43, 50.6%) with no significant difference in ADR occurrence. Majority of patients who experienced ADRs belong to the age group of 46-55 years (n=25, 29.4%) indicating that ADRs are more prevalent in the middle aged group. Digestive system is the most affected organ system (n=46, 47.4%) and the drug class under which most ADRs were identified was ACE Inhibitors (n=11,10.7%).

Conclusion: *This study provides a clear understanding on the patterns of occurrence of ADRs in patients admitted in the Department of General Medicine. To determine the precise frequency and incidence of ADRs in the Indian population, more research with larger sample size and duration must be conducted.*

Keywords: *Adverse Drug Reactions, Causality Assessment, Spontaneous Reporting System, ADR Monitoring center.*

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INTRODUCTION:

The creation of newer medications has greatly benefited patients,and have grown to be an essential component of the global health care system. However, it has also resulted in the rise of negative drug side effects, commonly known as Adverse Drug Reaction (ADR) and even death of the patients.[1]

ADR is normally defined as "any response to a drug that is noxious and undesired which develops at doses that are commonly used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological functions".[2,3]Each instance of a putative link between an observed adverse reaction and the use of a medication is considered a suspected adverse drug reaction. It is serious if, at any dose, the medication use results in mortality, poses a life-threatening risk, necessitates inpatient hospitalization or extends a current hospitalization, causes permanent or substantial disability or incapacity, or is the cause of a congenital anomaly or birth defect.[4] As a result, ADR reporting is crucial for tracking and assessing medication activity in the healthcare industry. [5]

Based on a WHO assessment, around 60% of ADRs can be avoided. Interactions among drugs such as drug-drug interactions (DDIs) are a major contributor to avoidable adverse medication reactions. Widespread polypharmacy may be a contributing factor to the rise in potential DDIs (pDDIs), particularly in the elderly, as a result of the expanding complexity of therapeutics and the rising number of patients with multimorbidity.[6] According to a recent study, ADRs were responsible for 3.5% of hospital admissions. ADRs also contributed to 197,000 fatalities in Europe each year.[7] About 43.3% to 80% of all adverse events that result in emergency room visits and inpatient stays and are cited as a factor in rising healthcare costs are preventable adverse consequences.[5] In India, under-reporting is a significant problem. Therefore, there is a need to increase the attentiveness of healthcare personnel to the identification, prevention, and reporting of ADRs. [8]

Classification of ADRs:

Type A augmented pharmaceutical effects are predictable and dose-dependent (PK and PD-enhanced pharmaceutical effects).
Type B bizarre effects, typically mediated by the immune system, unrelated to PK/PD characteristics, unexpected.
Type C Effects of dosage and time of administration over the long term.
Type D effects over a long period of time that cause chronic organ damage, teratogenesis, or carcinogenesis.
Type E Effects of withdrawal.
Type F failure or negative therapeutic effects caused by medication interactions. [2,9]

Casualty Assessment of Suspected ADRs:

The process of determining the connection between a drug and a suspected adverse event is known as causality assessments. Numerous causative assessment methods are employed, including the algorithm-based Naranjo scale, the WHO-UMC system, Bayesian method etc. The world's largest dataset on random ADR reports is called VigiBase. [2] ADRs must be reported by healthcare providers, however many reactions are undoubtedly not recorded owing to a lack of desire, time, knowledge, or attitude. [1]

The detection and analysis of the signals form the basis for risk assessment and adjustments to the medication safety profile. In this process, it is crucial to effectively communicate reports of adverse reactions and keep an eye out for emerging trends. [6]

In our study we have adopted Spontaneous Reporting System (SRS) for reporting the ADRs. All ADRs were reported to the ADR monitoring center located at the department of pharmacology near the study site. All ADRs were documented in a well-designed ADR form in a prescribed format, provided by Indian Pharmacopoeia Commission (IPC), under the National Coordination Centre Pharmacovigilance Programme of India (NCC-PvPi) and reported.

As there is under reporting of ADRs and very less research was conducted especially in south India, our present study was carried out with an aim to detect, assess (establishing causality relationship using WHO Scale), reporting (Using Spontaneous Reporting System) and documentation of various Adverse Drug Reactions that occur in a large tertiary care teaching hospital at Visakhapatnam.

MATERIALS AND METHODS:

Study Site:

The present study was planned to be carried out in the in-patient wards of the General Medicine department of King George Hospital (KGH), a large tertiary care teaching hospital at Visakhapatnam, Andhra Pradesh, India. It is a 1300 bedded hospital with an occupancy rate of 100%. On an average about 60-70 patients are admitted to the in-patient ward of the General Medicine unit of our study site, and this study site was selected to carry out our present work.

Study Design and Duration:

The present study is a Prospective, Observational study carried out for a period of FOUR (4) months i.e, From September-2018 to December-2018.

Study Approval:

Prior approval for the study was obtained from the Institutional Ethics Committee (IEC), M/S. King George Hospital (KGH), Visakhapatnam, Andhra Pradesh.

***Study Objectives*:**

- To identify, analyze and report the Adverse drug reactions occurring in the in-patients admitted to the general medicine department of KGH.
- To identify the most affected organ system and the drug class commonly responsible for ADRs.

Inclusion Criteria:

1. Patients of either sex, who are admitted to the In-Patient wards of the department of General Medicine were enrolled into our study.
2. Patients with age >14 years were enrolled into our study.
3. Patients who submitted Informed Consent Form (ICF) and participated voluntarily in our study were included.

Exclusion criteria:

1. Patients who do not meet the Inclusion Criteria were excluded from our study.
2. Women who are pregnant and lactating, and patients who are below 14 years of age were excluded from the study as most of them were referred to the Pediatric unit and likelihood of loss to follow-up is more with them.
3. Adverse events resulting from blood transfusion and its products or IV fluids were not considered as ADRs as they are studied as a separate entity known as Hemovigilance.
4. Patients who are referred to General Medicine units from other units or shifted to other units from General Medicine were excluded.
5. Subjects who are discharged within one day are excluded from our study.

STUDY PROCEDURE:

1. After obtaining the approval from the IEC of the study site, the data pertaining to the patient including the patient's demographics, presenting complaints, past medication history, drug therapy, other details including over-the-counter drugs, current medications, laboratory investigations were collected in a well-designed ADR data collection and documentation form.
2. The study procedure was carried out by a team of 3 student researchers under the supervision of one faculty researcher, where we have split and collected the data from different units of the Department of General Medicine of our study site.
3. The data pertaining to the patient was obtained from the sources like patient medical records or case sheets, patient's medical reports and by interviewing the patients or their caretakers (if necessary) regarding the side effects experienced by them.
4. The collected data was then analyzed for identification of ADRs using Spontaneous Reporting System (SRS) and causality assessment for each and every ADR was established using WHO Probability Scale.
5. Finally the ADRs identified were reported to the ADR monitoring center using Spontaneous Reporting system (SRS)which is the regional Pharmacovigilance Centre located in the

Pharmacology department of Andhra Medical College (AMC), located at our study site and are documented in ADR documented file.

***Termination of the Study*:**

- The investigators are determined to terminate the study for safety reasons at any time and the reasons for this termination was planned to be provided to IEC and the subjects.
- In our study, there were no subjects identified with serious health hazards and no subject was terminated while the study was being carried out.

RESULTS AND DISCUSSION:

- The present study was aimed to Identify, Assess, Report and Document the suspected Adverse Drug Reactions using Spontaneous Reporting System.
- The demographic details of each and every patient i.e. age, gender and weight were collected along with the current medical condition, treatment given, the type of adverse reaction identified, the organ systems affected, drugs which are implicated in the ADRs , causality assessment using WHO causality assessment scale.
- The outcomes of each and every ADR were then assessed and reported to the ADR monitoring center at the study site and were finally documented by the Pharmacovigilance Technical associate in the Vigiflow WHO database for future reference.

Patient Demographics:

Table 1. Gender distribution with respect to occurrence of ADRs in the study population.

S. no	Gender	No. of patients	Percentage (%)
1	Male	42	49.4
2	Female	43	50.6
3	Total (n)	85	100

Age Distribution:

Patients of different age groups between 16-72 years were enrolled into our study and the mean age was found to be 44.6 years. The youngest patient enrolled in our study was 16 years of age and the patient with the oldest age was found to be 72 years. ADRs are more prevalent in the majority of patients who belong to the age group of 46-55 years.

Commonly occurred ADRs:

About 24 different reactions have been observed in patients, among which the most common ADR reported was drowsiness (n=6;5.9%).

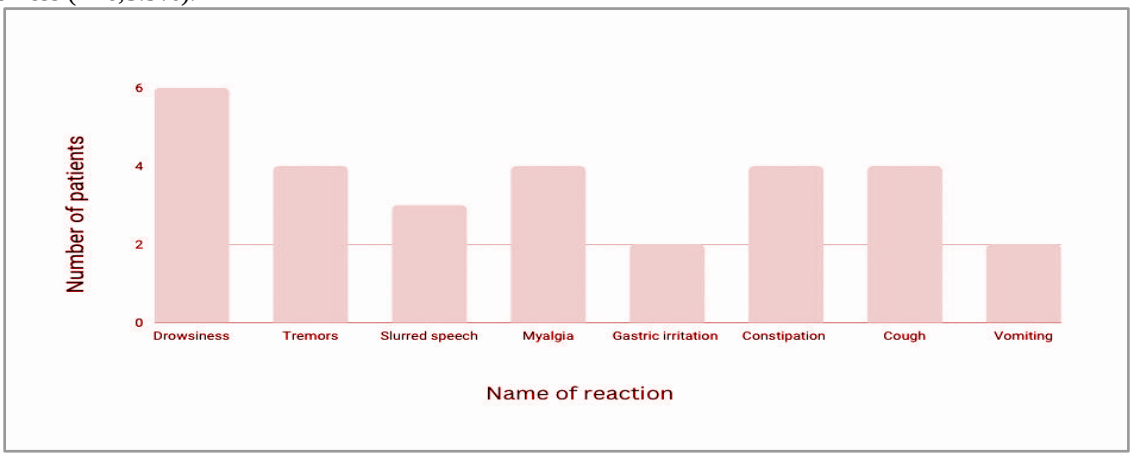

Fig. 1. Graphical representation of commonly occurred ADRs.

The most frequent drug classes associated with ADRs are **ACE inhibitors 11 (10.4%)**, Atypical anticonvulsants 10 (9.5%), Antihistamines 9 (8.5%), salicylates 7 (6.6%), HMG-coA enzyme reductase inhibitors 6 (6.6%), PPI inhibitors 6 (6.6%).

Table 2. Classes of drugs involved in ADRs.

Class of drugs Percentage (%)	No. of ADRs	Percentage (%)	Class of drugs	No. of ADRs	
Sulfonylureas	2	1.9	Beta blocker	2	1.9
5-HT3 antagonist	2	1.9	Biguanide	3	2.9
ACE inhibitors	**11**	**10.7**	Butyrophenone	1	1
Adrenal	1	1	Ca^{+2} channel blocker	2	1.9
Aminopenicillins	1	1	Cobalamin	1	1
Anti-tubercular	3	2.9	Diuretics	1	1
Anti-coagulants	5	4.9	Dopamine antagonist	1	1
Anticonvulsants	9	8.7	DPPA-4 inhibitor	3	2.9
Antihistamines	9	8.7	HMG CO-A	6	5.8
Antiepileptics	4	3.9	Insulin	1	1
Antipyretic	1	1	Loop diuretics	2	1.9
Antibiotics	3	2.9	Phenothiazine	2	1.9
PPIs	6	5.8	Protectant	1	1
Antimaniac agents	1	1	NSAIDs	1	1
Atypical antipsychotics	10	8.7	Quinolones	1	1
Azoles	1	1	Salicylates	7	6.8

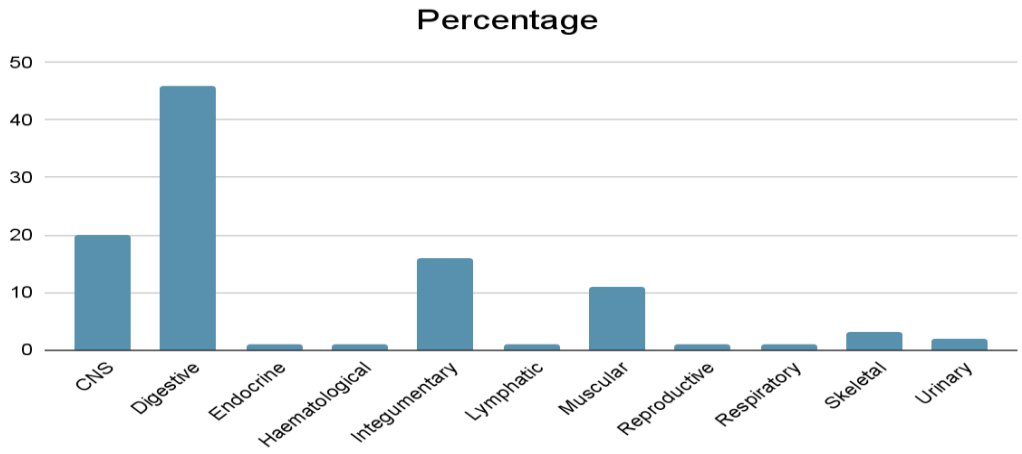

Fig. 2. Graphical representation of organ systems affected due to ADR.

The reported ADRs affected various organ systems in the body, which includes Digestive system, CNS, Endocrine system, Integumentary system, etc,.

WHO causality assessment scale

The assessment done by using WHO scale revealed that out of 103 ADR'S 81 (78.64%) were probably drug related, 21 (20.38%) ADR'S were possibly drug related and 1 (0.97%) are found to be certain

Table 3. Results of WHO-UMC causality assessment scale.[10]

S.No	Causality term	ADR's (%)	Male	Female
1	Certain	1(1)	1(2.4)	0(%)
2	Probable/likely	81(78.6)	32(76.2)	30(69.8)
3	Possible	21(20.4)	9(21.4)	13(30.2)
4	Unlikely	0(%)	0(%)	0(%)
5	Unassessable/Unclassifiable	0(%)	0(%)	0(%)
6	Conditional/Unclassified	0(%)	0(%)	0(%)

CONCLUSION:

- In our study we have screened 196 patients, out of which 103 ADRs were observed in 85 patients during our study period.
- Female patients developed more ADRs than male patients but the difference is significant which suggests that the incidence of ADRs is same in both the genders.
- Middle aged patients are the most affected age group (46-55)who are found to be having co morbidities and are receiving multiple therapies (polypharmacy).
- Digestive system is the most affected organ system followed by CNS and Integumentary.
- Early identification and management of ADRs is essential and special attention is to be taken in case of polypharmacy.
- Drug withdrawal and dose reduction is the first step employed in the management of ADRs.
- Under-reporting of ADRs and lack of awareness of reporting of ADRs among the HCPs is still a major issue to be achieved.
- Patient safety can be enhanced by conducting awareness programs and encouraging HCP's in reporting suspected ADRs.

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Conflict of interest

The authors affirm that the research was undertaken without any commercial or financial associations that could be interpreted as potential conflicts of interest. This declaration underscores the independence and objectivity of the research findings presented in the article. By maintaining a clear separation from any affiliations that could sway the outcomes, the authors uphold the credibility and integrity of their work.

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