INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY MEDICINE AND BIOALLIED SCIENCES
An International, Multi-Disciplinary, Peer-Reviewed, Open Access, Indexed Journal
|www.biomedjournal.com|
ISSN 2348-2109

# A prospective observational study of adverse drug reactions in patients at a tertiary care teaching hospital

Mohammed Shareefuddin[1], Mariya Ahmed[1*], Aijaz Fathima[1], Mohd Nishad[1], V. Rajesh Babu[1], U. Ramchander Rao[2], Mohd Faqruddin[1], Javed Akhtar Ansari[1].

[1]*Department of Pharmacy Practice (PharmD), MESCO College of Pharmacy, (Osmania University), Hyderabad, India.*
[2]*Department of General Medicine, Osmania General Hospital (OGH), Afzal Gunj, Hyderabad, India.*

ORIGINAL RESEARCH ARTICLE

## ABSTRACT

**Background:** The aim of this study was to evaluate prevalence, causality, severity, classes of drugs involved in ADRs, organ system affected, underlying cause and management of Adverse drug reactions.

**Subjects and Methods:** An observational prospective study was conducted over a 6 months period in Department of General Medicine using stimulated spontaneous reporting system for identifying ADRs. A questionnaire modified from previous studies and CDSCO-ADR reporting form was used as a data collection tool for this study keeping in mind.

**Results:** The present study was initiated in order to study prevalence, causality, severity, classes of drugs involved in ADRs, organ system affected, underlying cause and management. In this study, 181 patients were identified with ADRs. This includes (36) (20%) ADRs after Hospital admissions (Group-1) and 145 (80%), ADR causing hospital admissions (Group-2). The incidence of total ADRs was 5.6% (Group-1 (1.1%), Group-2 (4.53 %). Inter-individual variations were found to be the underlying cause for ADRs in the majority of the patients. Drug withdrawal followed by symptomatic treatment was found to be the most potent management. The occurrence of life-threatening reactions was found to be (8.9%), following three deaths due to adverse drug reactions.

**Conclusions:** The result showed that the ADRs in patients are a significant public health issue, impose a significant burden on patients through prolongation of hospital stay, increase in the admission rate, health care cost, morbidity, and mortality. Since there are considerable social and economic consequences of ADRs and the majority of these ADRs are predictable and often preventable, hence there is a need for greater awareness among the patients & health care professionals and also there is a need to improve the pharmacovigilance system in order to protect the Indian population from potential harm.

***Keywords:*** Adverse Drug Reactions, Prevalence, Causality, Severity, Pharmacovigilance.



*Author for correspondence
E-mail:
drmariya.clinicalpharmacist@gmail.com

Article ID 104

## INTRODUCTION

The WHO defines an Adverse Drug Reaction (ADRs) 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 a physiological function. Thus, this definition excludes over dose (accidental or intentional), drug abuse, and treatment failure and drug administration errors (Parthasarathi, 2011). Often the terms 'Adverse drug Reaction' and 'Adverse event' are used synonymously, although they are not. All medical products, whether drugs, biological, diagnostics (eg: radio contrast dye) natural products or nutritional agents can cause ADR (Robert, 2006).

It was also described ADRs to be the 4th-6th cause of death in US, And ADRs are estimated to cause 3-7% of all hospital admissions (Lazarou et al., 1998). A Swedish study has also implicated ADRs as 7$^{th}$ most common cause of death (Wester et al., 2008). ADRs are the 4$^{th}$ leading cause of death, ahead of pulmonary disease, DM, AIDS, pneumonia (Lazarou et al., 1998). The incidence of ADRs varies with studies from as low as 0.15% to as high as 30% depending on various criteria and methodologies used (Lazarou et al., 1998).

Risk factors for ADRs include age, gender, concurrent illness, polypharmacy, narrow therapeutic index drugs and genetics. Elderly and hospitalized patients are reported to be more susceptible to ADRs than the adult population (16% Vs 4.1%) (Beijer et al., 2002). The largest frequency of ADRs was very common in the females and has been described in various reports (Passarelli et al., 2005; Mitchell et al., 2009). Gender is one of the risk factors for development of ADR (Wiffen et al., 2002) and women are more susceptible to ADRs than men possibly by an association of factors such as greater concentration of adipose tissue and hormonal determinants that can affect metabolism, leading to the development of ADR (Edwards et al., 2000).

Early recognition of these factors is important and ultimately leading to their prevention. The presence of ADRs may be underestimated in part because treating physicians fail to recognize ADRs, as they tend to mimic any naturally occurring disease process, by acting through the same physiological and pathological pathways (Gustafson and Bennett, 1982). ADRs may also result in diminished quality of life, increasing physician visits, hospitalizations, and even death.

The world health organization (WHO) initiated a program for reporting all adverse reactions possessed by drugs. Further awareness about adverse drug reactions has resulted in the emergence of the practice and science of pharmacovigilance (WHO, 2006). The Pharmacovigilance Program of India (PvPI) was started by the Government of India Although, India is participating in this program, its contribution to this database is relatively small. This problem is essentially due to the absence of a robust adverse drug reaction monitoring system and also the lack of awareness of reporting concepts among Indian health care professionals. In India, it is very important to focus the attention of the medical community on the importance of adverse drug reporting to ensure maximum benefits for public health and safety. However ADR reporting and monitoring is yet to catch up in India (Padmaja, 2009).

Pharmacovigilance methods must be capable to designate which patients are at risk from medication use. A suitably working pharmacovigilance system is important if medicines are to be used prudently. It will be advantageous for healthcare professionals, regulatory authorities, pharmaceutical companies and consumers to monitor medicines for risk. Hence a study was undertaken to record and analyze all ADRs leading to hospitalization and ADRs among hospitalized patients in the medical wards of a tertiary care hospital in Hyderabad, India.

## SUBJECTS AND METHODS

A hospital based observational study was carried out on 181 patients in Department of General Medicine, Osmania General Hospital, Hyderabad, T.S., India. This involved both active and passive methods. Active methods include physician, clinical pharmacists (student investigators) actively looking for suspected ADRs and passive methods include stimulating prescribers to report suspected ADRs. The study was conducted in the Department of General Medicine, Osmania General Hospital, Hyderabad, Telangana, India, over a period of 6 consecutive months, starting from January 2015 to June 2015.

**Study design**

The study was reviewed and approved by the Institutional Ethics Committee (IEC). All the physicians in the wards were informed about the study, outlining the ADRs' negative impact and were asked to report all observed adverse events. In order to ensure that the rate of notifications remains constant during the whole study period, the physicians were regularly reminded about the study taking place.

In this study, patients of either sex included and they were divided into two groups. Group-1: Patients who develop ADRs after hospital admission and Gropup 2: Patients who were admitted to hospital primarily due to ADRs. A total of 181 ADRs were reported during 6 months duration of study.

Both the male and female patients of all ages were included (Figure-1)According to WHO's ADR definition, exclusion criteria was adopted i.e. exclusion of patients with accidental or intentional, drug abuse, treatment failure and drug administration errors.

The clinical pharmacist (student investigators) participated in ward rounds conducted by the Department of Pharmacy Practice. A questionnaire modified from previous studies and CDSCO-ADR reporting form was used as a data collection tool for this study keeping in mind the objectives the study.

a) The medication chart of the patient who experienced ADRs were reviewed and complete medication history was collected.

b) Personal interview with patient/ or relatives was also be done. Patients present complain were correlated with past medication history and present medications to evaluate any ADR if present the data collected was then analyzed for causality using Naranjo Causality Assessment Scale and finally documented. Then the severity was assessed using Modified Hartwig Scale.

We prepared aquestionnaire with reference to the ADR reporting form of the Central Drug Standard Control Organization (CDSCO) and previous studies which includes patient demographics like name, age, sex, medication history, diagnosis history, name of the suspected drug along with batch number. The route of drug administration, frequency and dose duration, nature of the reaction was also mentioned in the form. Basic information of adverse reaction caused by the suspected drug was also included. In addition patient's medication chart review and patients who developed ADR were interviewed to collect patient's information

such as Patient's complaints, history of present illness, and history of past medical condition with medication, patient allergic status, patient social habits/family history, and details of suspected drug cause for ADRs, causality assessment (using Naranjo's Scale). We defined adverse drug reactions according to the World Health Organization definition, as being all "noxious and unintended drug response, which occur at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function. By this definition, ADRs primarily include allergic reactions and adverse effects. Therefore, we excluded all the intentional overdoses, poisoning, abuse and misuse and wrong administration of drugs.

Patients who developed an ADR were interviewed from the day the ADR was reported with regard to consumption of any other medication and any co-morbidity identified to assess the causality relationship between the suspected drug and reaction and patient counseling were undertaken. The relationship between ADR and the suspected drug was assessed using Naranjo scale. The data were also analyzed as per severity using Hartwig criteria for severity for the suspected adverse drug reaction and categories as Mild, Moderate, Severe. All the reported ADRs were assessed for their appropriate management and proper steps were taken to prevent such ADR in future.

The data observed was analyzed in order to study the characteristics of the ADRs and to determine the nature and pattern of ADRs related to hospital admission and difference in the severity of ADRs and management and outcome of management of the reported ADRs.

Causality assessment is the method by which the extent of relationship between a drug and a suspected reaction is established. The assessment of causality relationship is often subjective, based upon an individual clinician's assessment. One clinician's judgment may appear unlikely to another clinician. If an ADR is suspected, the assessment starts with collection of all the relevant data pertaining to patient demographics, medications, including non-prescription (OTC) drugs, comprehensive ADR details including a description of the reaction, time of onset and duration of the reaction, complications and/or sequelae treatment of the reaction and outcome of the treatment and further relevant investigation reports. The collected data were used to correlate and categorize the relationship between the suspected drug and the adverse drug reaction.

### Statistical analysis

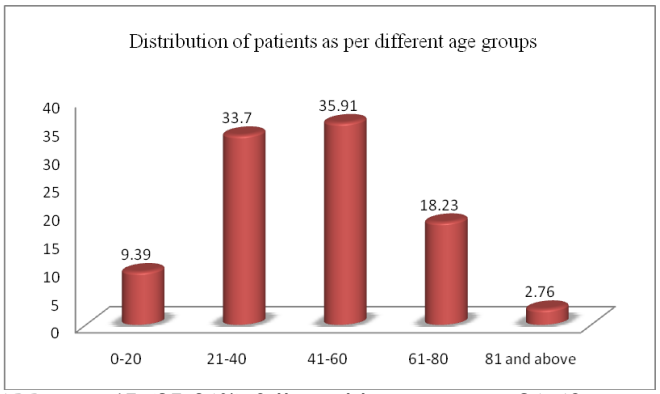
Statistical analysis was carried out using Chi-square test and regression analysis.

## RESULTS

The present study was initiated in order to study prevalence, causality, severity, classes of drugs involved in ADRs, organ system affected, underlying cause and management. In our study during 6months duration 181 patients were identified with ADRs. This includes 36, 20% ADRs after Hospital admissions (Group-1) and 145 (80%), ADR causing hospital admissions. The incidence of total ADRs was 5.6% (Group-1 (1.1%), Group-2 (4.53 %)). Out of 181 ADRs 116 (64.08%) were male and 65 (35.91%) were female.

### Distribution of patient pool as per age

All the ADRs were classified as per age group. Patients in age group of 41-60years showed the highest number of




ADRs i.e. 65 (35.91%) followed by age group 21-40 years (33.3%),61-80years (18.23),0-20years (9.39%),81 and above (2.7%) which accounted for the least .The present study revealed a predominance adults (36%) over geriatric (18.23%) (Figure 1).

**Figure 1.** Distribution of patients as per age groups.

### Number of ADRs associated with gender

A total of 181 patients with ADRs were identified during the study period, including 116 (64%) males and 65 (35.91%) females, but as per the hospital set up there were 160 beds for males and 80 beds for females for which ADRs in males were 116 and females were 65 (i.e. 80 beds, 65 ADRs **(80%)** in females and (160 beds, 116 ADRs (72.5%) in males. This implies ADRs in females were predominant (Table 1).

**Table 1.** Distribution of patient pool as per gender.

| S N | Sex | Bed size | Total Number of ADRs | % of ADRs as per the bed size |
|---|---|---|---|---|
| 1 | Male | 160 | 116 | 72.5 |
| 2 | Female | 80 | 65 | 80 |

### Number of ADRs associated with different Groups

From the total number of adverse drug reactions, drug reactions resulting in hospitalization (group-2) (80.11%) were maximum compared to ADRs occurring after hospital admission (group-1) (20%) (Figure 2).

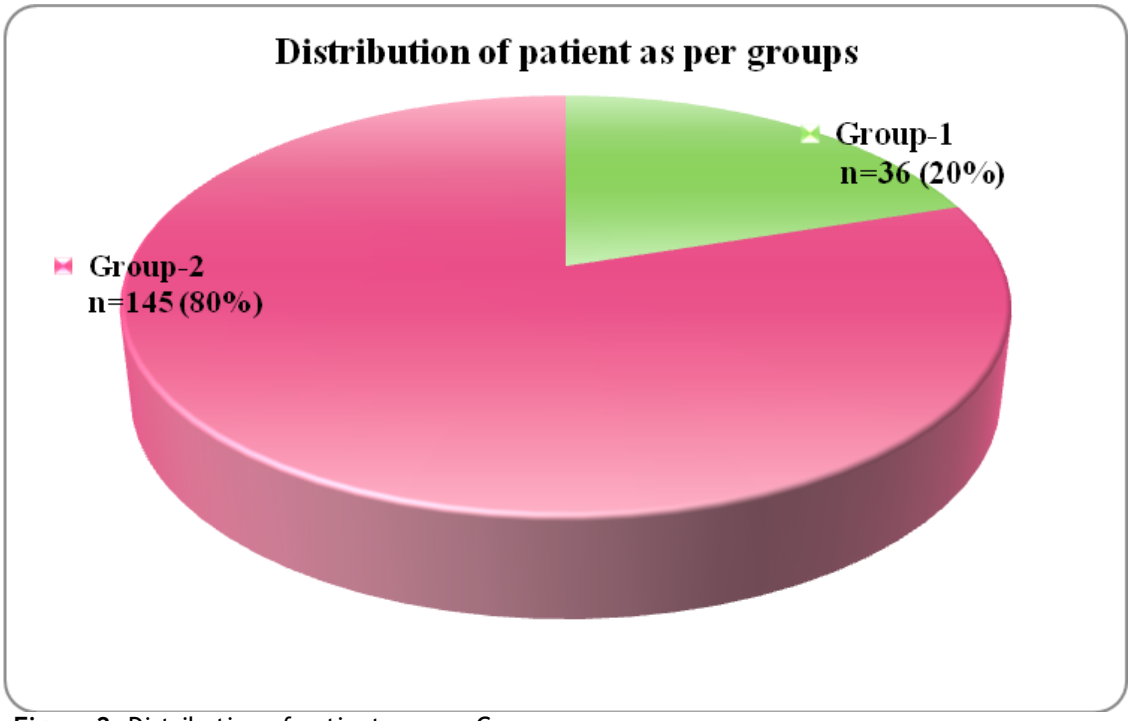



**Figure 2.** Distribution of patients as per Groups.
**Group 1.** ADRs occurring after hospital admission; **Group 2.** ADRs causing hospital admission.

**Classes of drugs involved in adverse drug reaction**

The most common drugs causing the ADRs and their occurrence in male, female, Group-1, Group-2 details are shown in (Table-2). Herbal medicines were associated with maximum of all the ADRs reported 38 (20.9%) following anti-tubercular and anti-connvulsants 19 (10.4%), ADRs with other drugs 17 (9.3%), antibiotics and anti-diabetic drugs 13 (7.1%), drugs acting on CVS 10 (5.5%), combinational drug therapy 9 (4.9%), steroids 7 (3.8%), anti retroviral therapy and diuretics 6 (3.3%), drugs acting on CNS 4 (2.2%) and least with immuno suppressant and anti-snake venom 3 (1.6%).

**Table 2.** Percentages showing ADRs in group-1, group-2, males, females involved with each drug category.

| Sl. No | Class of Drugs | M | % | F | % | G-1 | % | G-2 | % | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | NSAID | 8 | 4.41 | 6 | 3.31 | 0 | 0 | 14 | 7.73 | 14 | 7.73 |
| 2 | ANTIBIOTICS | 7 | 3.867 | 6 | 3.314 | 8 | 4.419 | 5 | 2.762 | 13 | 7.182 |
| 3 | ANTI-TUBERCULAR THERAPY | 15 | 8.287 | 4 | 2.209 | 2 | 1.104 | 17 | 9.392 | 19 | 10.497 |
| 4 | ANTI-RETROVIRAL THERAPY | 0 | 0 | 6 | 3.314 | 0 | 0 | 6 | 3.314 | 6 | 3.314 |
| 5 | ANTI-CONVULSANTS | 13 | 7.182 | 6 | 3.314 | 3 | 1.657 | 16 | 8.839 | 19 | 10.497 |
| 6 | DRUGS ACTING ON CVS | 5 | 2.762 | 5 | 2.762 | 2 | 1.104 | 8 | 4.419 | 10 | 5.524 |
| 7 | DRUGS ACTING ON CNS | 3 | 1.657 | 1 | 0.552 | 1 | 0.552 | 3 | 1.657 | 4 | 2.209 |
| 8 | ANTI-DIABETIC DRUGS | 6 | 3.314 | 7 | 3.867 | 0 | 0 | 13 | 7.182 | 13 | 7.182 |
| 9 | HERBAL MEDICINE | 27 | 14.917 | 11 | 6.077 | 0 | 0 | 38 | 20.994 | 38 | 20.994 |
| 10 | STEROIDS | 5 | 2.762 | 2 | 1.104 | 1 | 0.552 | 6 | 3.314 | 7 | 3.867 |
| 11 | IMMUNO-SUPRESSANT DRUGS | 3 | 1.657 | 0 | 0 | 1 | 0.552 | 2 | 1.104 | 3 | 1.657 |
| 12 | ANTI-SNAKE VENOUM | 3 | 1.657 | 0 | 0 | 3 | 1.657 | 0 | 0 | 3 | 1.657 |
| 13 | ADRS WITH DIURETICS | 6 | 3.314 | 0 | 0 | 5 | 2.762 | 1 | 0.552 | 6 | 3.314 |
| 14 | COMBINATIONAL DRUG THERAPY | 6 | 3.314 | 3 | 1.657 | 2 | 1.104 | 7 | 3.867 | 9 | 4.972 |
| 15 | ADRS WITH OTHER DRUGS | 9 | 4.972 | 8 | 4.419 | 8 | 4.419 | 9 | 4.972 | 17 | 9.392 |

G-1: Group 1, G-2: Group 2, M: Males, F: Females, T: Total.

Table 2 shows the percentages of ADRs with respect to different class of drug in males, females, Group-1 (all patients who develop ADRs after hospital admission) and Group-2 (all those patients who are admitted to hospital primarily due to ADRs).

**The organ systems affected due to ADRs.**

In this study, neurological ADRs was found to be maximum 42 (22.3%) followed by the gastrointestinal 22 (14.3%) ADRs, nephrotoxicity accounts for about 26 (13.8%), cutaneous ADRs 23 (12.2%), hepatotoxicity 19 (10.1%), haematological ADRs 18 (9.5%), cardio toxicity 17 (9%), ADRs with other systems 8 (4.2%), musculo-skeletal ADRs 5 (2.6%), respiratory tract ADRs 2 (1%), ototoxicity with the least number of ADRs 1 (0.5%).

**Table 3.** Percentages showing ADRs in group-1, group-2, males, females involved with each organ system.

| S.No. | Organ System Involved | M | % | F | % | G-1 | % | G-2 | % | T | % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | HEPATOTOXICITY | 14 | 7.734 | 5 | 2.762 | 0 | 0 | 19 | 10.497 | 19 | 10.11 |
| 2 | NEPHROTOXICITY | 20 | 11.05 | 7 | 3.87 | 6 | 3.31 | 20 | 11.05 | 26 | 13.83 |
| 3 | OTOTOXICITY | 1 | 0.55 | 0 | 0 | 1 | 0.55 | 0 | 0 | 1 | 0.53 |
| 4 | CARDIOTOXICITY | 8 | 4.42 | 7 | 3.87 | 10 | 5.52 | 5 | 2.76 | 17 | 9.04 |
| 5 | NEUROLOGICAL ADRS | 23 | 12.71 | 16 | 8.84 | 9 | 4.97 | 30 | 16.57 | 42 | 22.34 |
| 6 | GASTRO-INTESTINAL ADRS | 15 | 8.29 | 11 | 6.08 | 3 | 1.66 | 23 | 12.71 | 27 | 14.36 |
| 7 | CUTANEOUS ADRS | 14 | 7.73 | 9 | 4.97 | 3 | 1.66 | 20 | 11.05 | 23 | 12.23 |
| 8 | HAEMOTOLOGICAL ADRS | 13 | 7.18 | 3 | 1.66 | 0 | 0 | 17 | 9.39 | 18 | 9.57 |
| 9 | RESPIRATORY TRACT ADRS | 1 | 0.55 | 1 | 0.55 | 0 | 0 | 2 | 1.1 | 2 | 1.06 |
| 10 | MUSCULO-SKELETAL ADRS | 4 | 2.21 | 1 | 0.55 | 1 | 0.55 | 4 | 2.21 | 5 | 2.66 |
| 11 | ADRS WITH OTHER ORGAN SYSTEM | 5 | 2.76 | 3 | 1.66 | 2 | 1.1 | 6 | 3.31 | 8 | 4.26 |

(Group-1 all patients who develop ADRs after hospital admission) and group-2(all those patients who are admitted to hospital primarily due to ADRs).

**Classification of adverse drug reactions**

Details regarding classification and assessment of ADRs are given in Figure-3. Classification of ADRs showed that most of the reactions 84 (46.4%) were of type B followed by type A 71(39.2%), type C 20 (11%) and type E 6 (3.3%).

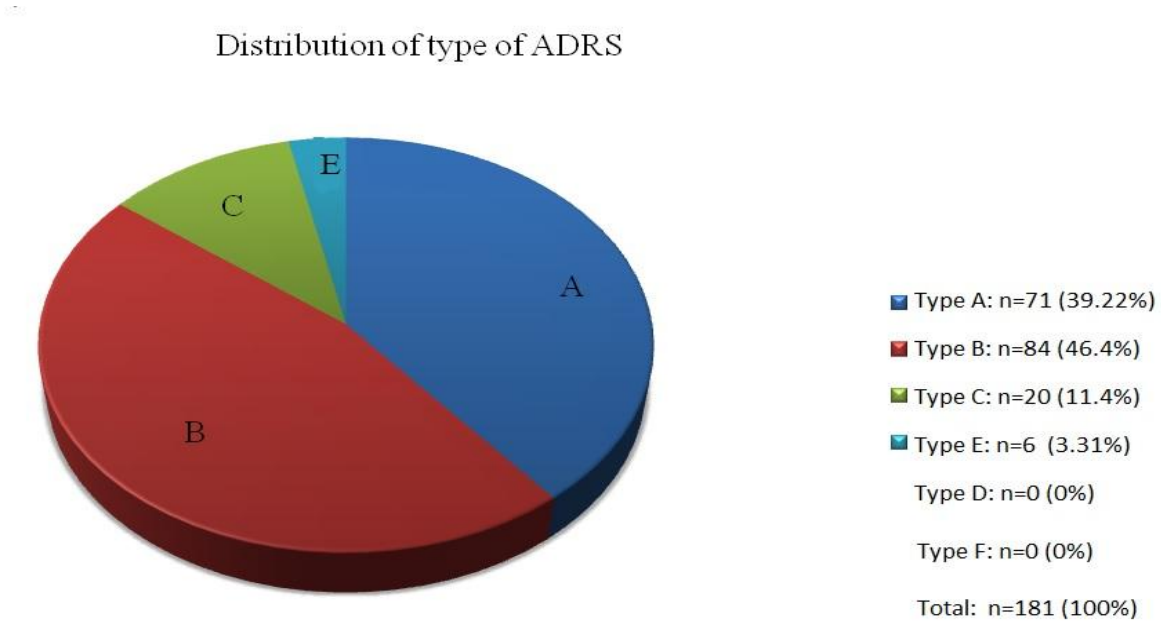



**Figure 3.** Classification of ADRs.

**Causality assessment by using Naranjo's algorithm**

To strengthen the validity of the findings of the study, causality assessment was done for individual cases by using Naranjo's algorithm. The suspected ADRs were assessed for their causality using the Naranjos Algorithm Probability Scale. It was observed that the majority of the reports were rated as probable 142 (78.45%), followed by possible 24 (13.25%) and definite 15 (8.28%) as shown in figure 4.

Causality assessment as per Naranjo's scale:

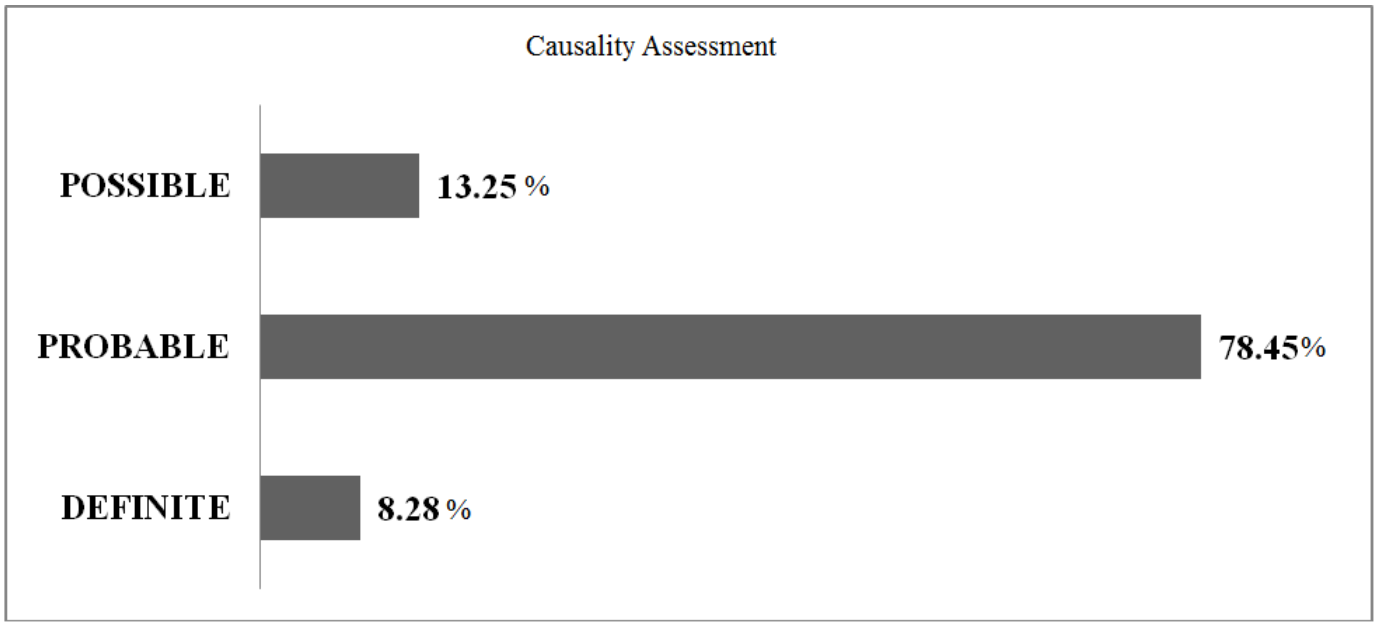



**Figure 4.** Shows the causality assessment based on Naranjo Algorithm probability scale.

**Severity assessment**

The ADRs were assessed for their severity using a Modified Hartwig scale, which is a standard scale for severity assessment. It was observed that out of 181 ADR reports, 36 cases (19.88%) were mild, 132 cases (72.92%) were moderate and 13 cases (7.18%) were severe. The severity assessment is shown in figure 5.

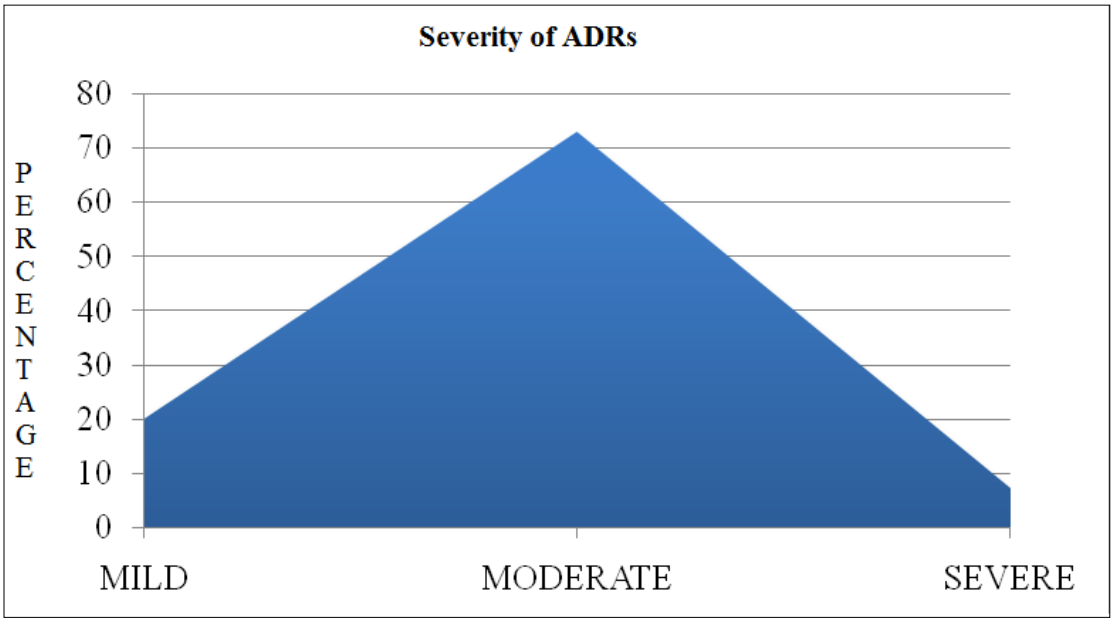



**Figure 5.** Severity of ADRs as per Modified Hartwig scale.

**CAUSE FOR ADVERSE DRUG REACTION**

Maximum ADRs were due to inter-individual variability 55 (30.3%) following the use of concomitant medical products including self medications and herbal remedies 43 (23.7%), inappropriate dosing 23 (12.7%), OTC medications 22 (12%), drug-drug interaction 18 (9.9%), inappropriate drug with respect to disease/symptoms 10 (5.5%), non-compliance 8 (4.4%) and lack of knowledge 12 (1.1%) accounting for the least (Table 4).

**Table 4.** Cause of adverse drug reaction.

| S. No. | Cause For Adverse Drug Reactions | Total | % |
|---|---|---|---|
| 1 | Drug-Drug Interaction | 18 | 9.94 |
| 2 | Self Medication/Otc Medication | 22 | 12.15 |
| 3 | Inappropriate Dosing/Wrong Dosing | 23 | 12.7 |
| 4 | Innappropriate Drug With Respect To Disease/Symptoms | 10 | 5.52 |
| 5 | Concomitent Medical Products Including Self Medications, And Herbal Remedies | 43 | 23.75 |
| 6 | Inter-Individual Variability | 55 | 30.38 |
| 7 | Non-Compliance | 8 | 4.41 |
| 8 | Lack Of Knowledge | 2 | 1.1 |
| **TOTAL** | | 181 | 100% |

**Management of adverse drug reaction**

In 87(48%) cases the suspected drug was withdrawn following symptomatic treatment was provided while in 30 (16.57%) cases the suspected drug was withdrawn, Symptomatic treatment was required in 16 (8.8%) cases, while 13 (7.18%) of the cases required specific treatment, the dose was altered in 12 (6.62%) case, dose alteration following symptomatic treatment was provided in12(6.6%), drug withdrawal following specific treatment for the reaction was provided for10 (5.5%) cases and no change was made with the suspected drug in 1 (0.5%) of the cases (Table 5).

**Table 5.** Management of reported adverse drug reactions.

| S.No. | Management | No of Cases | % |
|---|---|---|---|
| 1 | Drug withdrawal | 30 | 16.57 |
| 2 | Symptomatic treatment | 16 | 8.83 |
| 3 | No change | 1 | 0.55 |
| 4 | Dose altered | 12 | 6.62 |
| 5 | Specific treatment | 13 | 7.18 |
| 6 | Drug withdrawal+specific treatment | 10 | 5.52 |
| 7 | Drug withdrawal+symptomatic treatment | 87 | 48.06 |
| 8 | Dose alteration+symptomatic treatment | 12 | 6.62 |
| **TOTAL** | | **181** | **100%** |

**Rare Adverse Drug Reaction**

From the total number of ADRs rare adverse drug reactions accounts for about 11%, Details regarding rare adverse drug reactions are given in (Table 6).

**Details of death with ADRs**

Three deaths were reported with adverse drug reactions , one with efavirenz which was found responsible for causing exfoilative dermatitis and neuro-psychiatric manifestations, second with CAT-II regimen which was started to treat tuberculosis (relapse) which resulted in hepatitis following fulminant liver failure. Third with the use of herbal medicine responsible for liver failure, death (Table-8)

**Table 6.** Rare adverse drug reaction.

| S. No. | Adverse Drug Reaction | No of Cases |
|---|---|---|
| 1 | Vancomycin induced leucocytoclastic vasculitis | 1 |
| 2 | Metronidazole induced Aseptic meningitis | 1 |
| 3 | Metronidazole induced urticarial vasculitis | 1 |
| 4 | Ciprofloxacin induced TEN | 1 |
| 5 | Ciprofloxacin induced FDE | 2 |
| 6 | Monocef induced hematuria | 2 |
| 7 | Ethambutol induced anaphylaxis | 1 |
| 8 | CAT-I induced pedal edema | 2 |
| 9 | Efavirenz induced exfoilative dermatitis and neuro-psychiatric manifestations | 2 |
| 10 | Metformin induced skin rash | 1 |
| 11 | Metformin induced lactic acidosis | 1 |
| 12 | Herbal medicine induced liver failure | 2 |
| 13 | Decadran induced cushing syndrome | 1 |
| 14 | Furosemide induced hearing loss | 1 |
| 15 | Monteleukast induced thrombocytopenia | 1 |

**Life threatening Adverse Drug Reaction**

Details regarding life- threatening adverse drug reactions are given in( Table 7), which accounts for about 16 (8.8%).

**Table 7.** Life threatening adverse drug reaction.

| S. No. | Adverse Drug Reaction | No of Cases |
|---|---|---|
| 1 | Ciprofloxacin induced Toxic epidermal necrolysis | 1 |
| 2 | ethambutol induced anaphylaxis | 1 |
| 3 | Efavirenz induced exfoilative dermatitis and psychiatric symptoms | 2 |
| 4 | Phenytoin induced Toxic Epidermal necrolysis | 1 |
| 5 | Carbamazepine induced steven's johnson syndrome | 1 |
| 6 | Carbamazepine withdrawal status epilepticus | 1 |
| 7 | Warfarin induced subdural hematoma and bleeding gums | 1 |
| 8 | Insulin induced neuroglycopenic seizures | 1 |
| 9 | Metformin induced lactic acidosis | 1 |
| 10 | Herbal medicine induced liver failure | 1 |
| 11 | Cyclosporine induced marked thrombocytopenia | 1 |
| 12 | Mannitol induced sub-dural hygroma | 1 |
| 13 | Atropine induced tachycardia | 2 |
| 14 | Spironolactone+digoxin induced hyperkalemia | 1 |

**Table 8.** Deaths with adverse drug reaction.

| S. No. | Adverse Drug Reaction | Outcome |
|---|---|---|
| 1 | Efavirenz induced exfoilative dermatitis and neuro-psychiatric manifestation | Death |
| 2 | CAT-II induced hepatitis | Death |
| 3 | Herbal medicine induced liver failure | Death |

## DISCUSSION

Various studies have reported that the percentage of ADRs found was higher in adults than the geriatric population. The present study revealed a predominance adult (36%) over geriatric (18.23%). This might be due to the fact that most adult patient received multiple drug therapy and also presented with other co-morbidities such as Diabetes, Hypertension, Tuberculosis, Asthma and COPD this findings is consistent with the results of the previous study (Murphy et al., 1993) but differed

from the study which, reported that drug related hospitalization was significantly higher in the geriatric population (Lin et al., 1991). A total of 181 ADR cases were studied during the study period, including 116 (64%) males and 65 (35.91%) females, but as per the hospital set up there were 160 beds for males and 80 beds for females for which ADRs in males were 116 and females were 65 (i.e. 80 beds, 65 ADRs **(80%)** in females and (160 beds, 116 ADRs (72.5%) in males. This implies ADRs in females were predominant.

In this study, the drug class most commonly implicated with ADRs were the class of herbal medicine (20.9%) following anti-convulsants and anti- tubercular drugs with 10.49% of ADRs each, a similar study says NSAID, Anti-microbials, Herbal medicines and Anti-tubercular agents were the most commonly implicated drugs , which probably reflects their wide spread use (Hussain et al., 2010*)*. The most common organ system associated with ADRs were neurological (23.3%) this findings are similar to a previous study which reports ADRs related to CNS to be the second highest frequently manifested ADRs (Padmaja, 2009) and similar study reports. The most common systems associated with ADRs in their study were skin and the central nervous system (Arulmani et al., 2008). But this differs from the reports of a study which says dermatological ADRs were maximum. In the present study after neurological ADRs maximum ADRs were observed with GIT (14.36%) following nephrology (13.82%) and coetaneous ADRs accounts for about (12.2%).

In present study maximum ADRs were hypersensitivity (type-B i.e. 46.4%) followed by type-A (39.2%) which is consistent with a previous study which says hypersensitivity reactions to be the highest frequently manifested ADRs followed by augmented reactions (Arulmani et al., 2008).

To strengthen and further emphasize the validity of the findings of the study, causality assessment was done by using Naranjo's scale. Out of 181 ADRs reported, (78.45%) ADRs were probable, (13.25%) were possible and (8.28%) were definite. Severity of ADRs was evaluated by Modified Hartwig severity assessment scale, which showed that most of the ADRs reported in the study were of moderate severity (72.92%) which was consistent with the previous study (Arulmani et al., 2008).

We evaluated the underlying cause for ADRs and came to the conclusion that maximum (30.3%) number of ADRs were due to inter-individual variation towards different drug class followed by the use of concomitant medical products including self-medications and herbal remedies (23.7%), 50% of the total ADRs occurred due to multiple drug therapy, which is the second leading cause for ADRs in our study which are consistent with a study carried out previously (Patidar et al., 2013).

The most potent management was found to be drug withdrawal (Patidar et al., 2013) which is the second highest frequent management (16.5%) as per our study, Drug withdrawal followed by symptomatic treatment has proved out to be the most potent management in our study. Three deaths were reported in this study due to ADRs which is consistent with a previous study (Padmaja, 2009). Rare ADRs were identified in the present study which accounts for about (11%). Occurrence of life-threatening reactions in our study was (8.9%), while one of the previous studies reported these reactions to be (16%) (Hussain et al., 2010*)*. These variations may be due to difference in the sample size.

Reactions like Steven Johnson syndrome, toxic epidermal necrolysis, pose a significant risk to the patient's life. Worldwide studies have proved ADRs to be a major cause of morbidity and mortality. However Indian studies in this regard are very few but the pattern of reactions seems to be similar. Although there are certain characteristics of drug use in this present study, such as: large number of patients, poor doctor-patient ratio, self-medication, and drugs of alternative systems of medicine, malnutrition, widespread anemias, presence of counterfeit drugs and presence of the highest number of drug combinational products. The incidence of adverse drug reactions appears to be same as in the West or other countries. Unfortunately, in spite of the presence of well organized centers for drug monitoring in India, the number of ADR reported to these centers is far from satisfactory. There are number of reasons for incidence and prevalence of ADRs. These include the number of drugs prescribed are high, day by day increase in the number of new drug to market and the lack of a proper system for monitoring adverse drug reactions (Bates et al., 1997). While the exact epidemiology remains to be assessed in India, ADRs are becoming apparent cause of death. The management of drug-induced diseases are imposing additional burden to the treatment cost (Bremnan et al., 1991). Nevertheless, several studies have shown that most ADRs are avoidable, provided that the drugs are used rationally. Though, the most common system failure has been to spread the understanding of pharmacovigilance to the physicians (Cohen, 1999). Drug safety has been incorporated in curriculum guidelines for Indian medical undergraduates (MCI Curriculum Guidelines, 1997) but little has been attained in this regard (Leape, 1994).

## CONCLUSION

The results from this prospective, study shows that ADRs in patients are a significant Public health issue, impose a significant burden on patients through prolongation of patients hospital stay, increasing the admission rates, health care cost, morbidity, and mortality. ADRs monitoring has to be carried out by all the Doctors as the pattern of ADR may vary from place to place and time to time.

Most of the patients due to ignorance take on herbal medicines, OTC drugs and polypharmacy without proper medical supervision, which has led to severe life-threatening reactions such as SJS, TEN, AKF etc., cause for ADRs need to be recognized early, so that necessary actions may be taken to prevent mortality and morbidity from such reactions, appropriate management and careful consideration of ADRs involving planning and monitoring of drug therapy will lead to prevention of ADRs.

Since there are considerable social and economic consequences of ADRs and the majority of these adverse reactions are predictable and often preventable there is a necessity for a greater awareness among the healthcare professionals regarding not only the potential for adverse drug reactions resulting in hospital admissions, but also in the prevention (or) minimization of the occurrence of ADRs and the minimization of treatment costs. There is a need to engage health-care professionals, in a well-structured program to build synergies for monitoring ADRs to ensure maximum benefits for public health and safety. So there is a need to improve the pharmacovigilance system in order to protect the Indian population from probably suffering.

## FUTURE GUIDELINES

ADR monitoring has to be carried out by all the healthcare professionals as the pattern of ADR may vary from place to place and time to time. By early recognition of these reactions, necessary action can be taken to prevent mortality and morbidity from such reactions.

In this view support, co-operation from all higher health authorities, health care professionals, clinicians, pharmacists, and patients we hope we can bring about the change in the era of the prevalence of ADRs in patients and thereby decreasing the rate of morbidity and mortality.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. British Journal of Clinical Pharmacology. 2008;65(2):210–216.

Bates DW, Spell N, Cullen DJ. The costs of adverse drug reactions in hospitalized patients. Journal of the American Medical Association.1997;227:301-307.

Beijer HJM and Blaey CJ. Hospitalisations caused by Adverse Drug Reactions: A meta-analysis of observational studies. Pharmacy World Science. 2002; 24: 46–54.

Bremnan T, Leape L, Iared N. Incidence of adverse events and negligence in hospitalized patients. New England Journal of Medicine.1991;324:370-376.

Cohen JS. Ways to minimize ADRs-individualised doses and common sense are key. Journal of Postgraduate Medicine.1999;106:163-172.

Edwards IR, Aronson JK. Adverse drug reactions: Definitions, Diagnosis, and Management. Lancet. 2000; 356:1255–1259.

Gustafson JP, Bennett MD. The effect of telomeric heterochromatin from *Secale cereale* on Triticale (× *Triticosecale*). I. the influence of the loss of several blocks of telomeric heterochromatin on early endosperm development and kernel characteristics at maturity. Canadian Journal of Genetics and Cytology. 1982; 24(1): 83-92,10.1139/g82-008.

Hussain MM, Girhepunje K, Pal R, Siddiqua SS. Incidence of Adverse Drug Reactions in a Tertiary Care Hospital: ASystematic Review and Meta-Analysis of Prospective Studies. Der Pharmacia Lettre. 2010; 2(3): 358-368.

Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients:A meta-analysis of prospective studies. Journal of the American Medical Association. 1998;279(15):1200–1205.

Leape LL. Errors in medicine. Journal of the American Medical Association. 1994;272:1851-1857.

Lin SH and Lin MS. A survey on the drug related hospitalizations in a community teaching hospital. International Journal of Clinical Pharmacology, Therapy and Toxicology. 1991;31:66-99.

Mitchell SC, Smith RL, Waring RH. The menstrual cycle and drug metabolism. Current Drug Metabolism. 10 (5); 2009: 499–507.

Murphy BM, and Frigo LC. Development, Implementation and results of a successful multidisciplinary adverse drug reaction reporting program in university teaching hospital. Hospital Pharmacy Journal.1993;28:1199-1204.

Padmaja U. A Prospective Analysis of Adverse Drug Reactions in a South Indian Hospital. Online Journal of Health Allied Sciences. 2009;8(3):1.

Parthasarathi GA. Text Book of Clinical Pharmacy: Essential concepts and skills. Second Edition, Hyderabad, India, University press, 2011;102.

Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: Inappropriate prescription is a leading cause. Drugs Aging. 2005;22:767-777.

Patidar D, Rajput MS, Nirmal NP, Savitri W. Implementation and evaluation of adverse drug reaction

monitoring system in a tertiary care teaching hospital in Mumbai, India. Interdisciplinary Toxicology. 201323(1): 1–8.

Robert M. Adverse Drug Reactions and Clinical Toxicology. In: David B. Troy, Paul Beringer, editors. The Science and Practice of Pharmacy: Remington Pharmaceutical Sciences, Baltimore, Maryland, U.S.A, Lippincott William & Wilkins. 2006; 1221-1223.

Wester K, Jonnson AK, Sigset O, Druid H, Hagg S. Incidence of fatal adverse drug reactions: A population based study. British Journal of Clinical Pharmacology. 2008;65:573–579.

WHO, Safety of medicines in public health programs: Pharmacovigilance an essential tool, WHO; 2006. [http://www.who.int/hiv/pub/pharmacovigilance/safety/en/]

Wiffen P, Gill M, Edwards J, Moore A. Adverse drug reactions in hospital patients. A systematic review of the prospective and retrospective studies. Bandolier Extra. 2002:1–16.