A STUDY OF ADVERSE DRUG REACTIONS REPORTED TO THE ADVERSE DRUG REACTION MONITORING CENTRE AT A TERTIARY CARE TEACHING HOSPITAL, KUPPAM

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India.

INTRODUCTION

WHO defines ADR as “any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function”. Thus this definition excludes overdose (either accidental or intentional), drug abuse and treatment failure and drug administration errors.[1] Adverse Adverse reactions are recognized hazards of drug therapy. Adverse Drug Reactions (ADRs) are important causes of mortality and morbidity in both hospitalized and ambulatory patients. In many countries ADRs rank among the top 10 leading causes of mortality. So there is a need to study ADRs seriously to create awareness about ADRs among patients to motivate health care professionals in the hospital to report ADRs to minimize the risk. Early detection, evaluation and monitoring of ADR are essential to reduce harm to patients and thus improve public health.[2] ADRs are the 4th to 6th largest cause for mortality in the USA.[3] They result in the death of several thousands of patients each year, and many more suffer from ADRs. The percentage of hospital admissions due to adverse drug reactions in some countries is about or more than 10%.[4,5,6]

In addition suitable services to treat ADRs impose a high financial burden on health care due to the hospital care of patients with drug related problems. Some countries spend up to 15-20% of their hospital budget dealing with drug complications.[7]

The incidence and severity of ADRs can be influenced by patient- related factors like age, sex, concurrent diseases, genetic factors, and drug related factors like type of drug, route of administration, duration of therapy, and dosage. The other important risk factors associated
with adverse drug reactions are gender, increased number of drug exposures, advanced age, length of hospital stay and function of excreting organs.\[^8\] Health care professionals-doctors, dentists, pharmacists, nurses are the most preferred source of data collection related to ADRs. Indian Pharmacopoeia Commission (IPC), is functioning as National Coordination Centre (NCC) for Pharmacovigilance Programme of India (PvPI) since 15th April 2011 under the aegis of Ministry of Health & Family Welfare, Government of India.\[^9\] The major functions of NCC are to collect, collate and analyze Adverse Drug Reactions (ADRs) data to arrive at an inference to recommend regulatory interventions to Central Drugs Standard Control Organization (CDSCO), besides communicating risks to healthcare professionals and the public through PvPI Newsletters.\[^10\]-\[^13\] To collect the ADRs from patients ADR Monitoring Centers (AMCs) are set up under NCC. The rationale for setting up the AMCs is to make it possible to identify rare ADRs that could not be found through clinical trial programmes.\[^14\] NCC provides the logistic support and manpower to AMCs for their smooth functioning and reporting the ADRs. PESIMSR is an ADR monitoring centre (AMC) under Pharmacovigilance Programme of India (PvPI).

### Roles and Responsibilities of Personnel at AMCs

Each AMC under PvPI is assigned with a coordinator (department of pharmacology) and a Technical Associate responsible for its functioning. Their roles and responsibilities are:

- The designated Coordinator is responsible for the proper functioning of respective AMC. In absence of the coordinator, the designated deputy-coordinator is responsible for the smooth functioning of the centre.

- Other important responsibilities of coordinator is collection, checking completeness for a valid case, causality assessment and scrutinizing the ADRs reports as per SOPs

- The technical associate appointed is responsible for the collection and follow up of ADR reports, which have to be reported to the AMC coordinator, all the scrutinized and signed ADRs reports should be entered in VigiFlow. Every report has to be sent for the central assessment at NCC.

- The centre coordinator is responsible for sending the monthly reports of their AMC to NCC.

- Sensitization of the physicians/ healthcare professionals/ students/ patients of the catchment hospital for spontaneous ADR reporting by various mode (Lectures on ADR reporting, Email, telephone, pamphlet and newsletter) has to be undertaken by the centre coordinator.
Feedback to all healthcare professionals involved in reporting, to be sent by the AMC Coordinators.

METHODOLOGY
A prospective observational study was undertaken in various departments of a tertiary care teaching hospital (PES institute of Medical sciences and research, Kuppam, A.P) for 12 months from January 2015 to December 2015. PESIMSR is an ADR monitoring centre (AMC) under Pharmacovigilance Programme of India (PvPI). Patients of all age groups who developed Adverse Drug Reactions were included for the study. The data for the study were taken from case sheets, investigation reports of patients who had experienced an ADR, personal interviews with reporting persons or clinicians, personal interviews with patient or patient’s attendant, past history of medication use, which were generally obtained from, prescriptions from the past, reports of Medical and surgical interventions, referral letters, etc. Detailed drug and clinical history, and relevant information about suspected reaction, its onset, duration, temporal association with drug intake if any, were recorded in CDSCO suspected ADR reporting form. The causality assessment of the reported ADRs was carried out using the “WHO-UMC causality assessment scale”.[15]

RESULTS
Out of total 179 ADRs reported, 88 cases were reported in OPD while 91 were reported in IPD patients. Maximum number of ADRs were found in age group of 31-40 yrs. (n=77, 43.01%) followed by 21-30yrs. age group (n=51, 28.49%). Although ADRs were observed in both gender but slight male preponderance was seen (n=94, 52.51%) over female (n=85, 47.48%).

Maximum number of ADRs were caused by Antibiotics (n=62) 34.63% followed by NSAIDs (n=47) 26.25% and topical steroids (n=34) 18.99%.

According to the final causality assessment, 11 patients were classified under the category of certain, as rechallenge data was available, 89 as probably associated as only dechallenge data was available and 79 as having possible association with the drug, as dechallenge data was not available.
Table: 1 Distribution of parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Number</th>
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<tbody>
<tr>
<td>Age wise distribution</td>
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<tr>
<td>1-10 yrs</td>
<td>7</td>
<td>3.91%</td>
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<tr>
<td>11-20 yrs</td>
<td>13</td>
<td>7.26%</td>
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<tr>
<td>21-30 yrs</td>
<td>51</td>
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<td>31-40 yrs</td>
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<td>41-50 yrs</td>
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<td>51-60 yrs</td>
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<td>Above 60 yrs</td>
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<td>2.79%</td>
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<td>Gender wise distribution</td>
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<tr>
<td>Male</td>
<td>94</td>
<td>52.51%</td>
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<tr>
<td>Female</td>
<td>85</td>
<td>47.48%</td>
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<tr>
<td>Causality wise distribution</td>
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<td></td>
</tr>
<tr>
<td>Certain</td>
<td>11</td>
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</tr>
<tr>
<td>Probable</td>
<td>89</td>
<td>49.72%</td>
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<tr>
<td>Possible</td>
<td>79</td>
<td>44.13%</td>
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Fig.1 Age wise distribution

Fig.2 Gender wise distribution
DISCUSSION

ADRs are an important public health issue. Despite the efforts being made to reduce the incidence of medication-related adverse events, the morbidity and mortality due to drug-induced reactions continue to be unacceptably high. ADRs are one of the major causes of iatrogenic diseases. They are often not recognized and, even if they are recognized, they are underreported. Many health professionals are unaware of their importance and possible consequences.

Demographic details of our study showed male preponderance over females which is consistent with the earlier report by Gupta et al.\textsuperscript{[16]}
Pirmohamed et al have shown a greater percentage of geriatric population suffering from adverse reactions which is not consistent with the present results in which more number of ADRs were found in 31-40 years of age group followed by 21-30 years of age group.\textsuperscript{[17]}

In our study, maximum number of cases were reported from inpatient department (n=91, 50.83\%) which is consistent with the most of the studies which show maximum number of cases from inpatient department.\textsuperscript{[18-21]} Results in our study may be due to the active coordination of technical associate, Head and post graduate students of various departments, Nursing staff of various departments and their constant encouragement might have helped clinicians to notify ADRs, that resulted in better reporting than comparable studies in India. Studies have shown age, gender, co-morbidity, number of drugs, and length of stay in the hospital as significant risk factors for development of ADRs.\textsuperscript{[22-28]}

Our data analysis showed that most common type of ADR seen in all the wards was the skin rash that was commonly caused with the antibiotics. This finding is in favor of the previous study\textsuperscript{[30]} done in Chicago by Murphy and Frigo developed and implemented an ADR reporting program in Loyola University Medical Center, a 563-bed tertiary care teaching hospital located in the western suburbs of Chicago. Another study revealed that the most common adverse reactions were rash; and antibiotics were the most commonly implicated drug class.\textsuperscript{[31]} We also found out that NSAIDs also had caused fatal and severe ADR than by the other drugs.

Drug class most commonly involved in the reactions was Antibacterials (n=62) 34.63\% followed by NSAIDs (n=47) 26.25\%; a finding consistent with other studies in which antibacterials or analgesics were most commonly associated.\textsuperscript{[28,29]} Reason for this may be due to self-medication which we observed in our study.

Causality assessment was done by using WHO-UMC scale. The assessment done by using WHO scale reveals that 49.72\% of ADRs were probably drug related, 44.13\% of ADRs were possibly drug related, whereas 6.14\% were classified as certainly related to drug similar to the results in another study by Suh et al.\textsuperscript{[29]}

Assessment of severity of the suspected ADRs revealed that 27.37\% of suspected ADRs were severe, 47.48\% of ADRs were moderate in severity and 25.13\% of ADRs were mild in severity.
CONCLUSION
The study concluded that the spontaneous reporting of Adverse Drug Reactions is fairly good in our hospital setting. The effort of this study revealed the occurrence of comparatively less number of adverse reactions and their impact on patients of a developing country like India. The results provided an insight to the healthcare providers on the importance of monitoring and reporting of Adverse Drug Reactions. Adverse Drug Reactions are one of the drug related problems in the hospital setting and is a challenge for ensuring drug safety. Antibiotics comprise the major volume of the drug family and inpatient prescriptions and thus are the most irrationally prescribed drug class. So implementation of antibiotic guidelines for the hospital scenario and strict adherence should be ensured to promote the rational use. The development and use of clinical decision support systems can promote rational antibiotic use. The health system should promote the spontaneous reporting of Adverse Drug Reactions to antibiotics and other drugs, proper documentation and periodic reporting to ADR Monitoring centers (AMC) to ensure drug safety. The active involvement of a well trained clinical pharmacist for detecting the Adverse Drug Reactions and delivering the awareness classes for the healthcare professionals regarding the need of reporting the incident could improve the scenario in under-reported hospitals. The healthcare system should promote the spontaneous reporting of dermatological adverse drug reaction to Pharmacovigilance centres for ensuring drug safety.

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REFERENCES


