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Research Article

**DETECTION, PREVENTION AND MANAGEMENT OF  
ADVERSE DRUG REACTIONS IN AN URBAN QUATERNARY  
CARE HOSPITAL**

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**Abstract:**

*Pharmacovigilance also known as drug safety is defined as the science and activities relating to the collection, detection, assessment, monitoring and prevention of adverse effects or any other drug-related problems. The occurrence of adverse drug reaction is a price the patient pays for the benefits produced by modern medicine. Adverse drug reactions can result in diminished quality of life, increased health care costs, more frequent physician visits, hospitalizations, and even death.*

*This is a retrospective and prospective observational study, conducted at a quaternary care hospital for a period of six months. The main aims of this study is to assess the incidence, pattern of ADRs, causality, offending drugs, monitoring and documenting suspected ADR(s) and to prevent the occurrence. Each reported ADR was assessed for its causality by using Naranjo's scale. The severity of each reported ADR was assessed using modified Hartwig & Siegel scale and preventability of ADRs by modified Schumock & Thornton scale.*

*Study strongly suggests there is a greater need for streamlining of hospital based ADR reporting as well as monitoring system to create awareness, and promote more accurate reporting of ADR(s) among healthcare professionals.*

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**INTRODUCTION:**

Pharmacovigilance also known as drug safety is defined as the science and activities relating to the collection, detection, assessment, monitoring and prevention of adverse effects or any drug-related problems [1]. In other words it ensures medications are used to maximal benefit while minimizing risks of treatment. It has the potential to minimize harm through promoting broader safety concerns for newly introduced as well as already established products.

The World Health Organization (WHO) defines an ADR as 'a response to a drug that is noxious, unintended and occurs at doses normally used in man for prophylaxis, diagnosis, therapy of disease, or for modification of physiological function [2]. Adverse drug events can occur from single dose or prolonged administration of a drug or results from combination of two or more drugs. ADR monitoring can predict hazards that may occur from future administration and warrants prevention, specific treatment, alteration of dosage regimen, or even withdrawal of drug. ADRs occur in daily clinical practice, not only clinical trials thus post-marketing medication safety monitoring including spontaneous reporting and observational studies helps provide means of ADR detection, quantification and prevention [3].

The importance of ADR(s) is often underrated; they are of major clinical concern and account for 3% to 6% of all hospital admissions; and account for 6% to 15% of hospitalized patients experiencing serious adverse drug reactions [4,5]. A published meta-analysis of incidence of ADR(s) in hospitalized patients concluded as fourth to sixth leading cause of death in the United States and the overall incidence of serious ADRs accounted for 6.7% of hospitalized patients [6]. They can be life threatening and unnecessarily expensive since there are wide range of drugs available, the manifestation of toxicity varies and can affect any organ system. According to a study carried out at a private tertiary care hospital in South India, the incidence of ADRs was found to be 1.8%, out of which 12% of suspected ADRs were severe and 49% ADRs were moderate in severity [7]. A study by Arulmani *et al.* in India carried out in a secondary care hospital reported an overall 9.8% incidence of ADRs, of which 3.4% of ADRs were associated with hospital admissions [8]. Another study carried out in a tertiary care referral center in South India showed that admissions due to ADRs accounted for 0.7% of total admissions and deaths due to ADRs accounted for 1.8% of total ADRs [9]. The pattern of toxicity is likely to change with introduction of new products. It is therefore important for prescribing clinicians to become more aware of the toxicity profile for the drugs prescribed

and to be vigilant for the occurrence of unexpected adverse reactions [10].

Tracking of adverse drug reactions is now required by regulatory agencies in order to identify and prevent adverse drug reactions. Methods that can accurately predict those most at risk for adverse drug reactions have been developed. The most commonly used method is the spontaneous adverse drug reaction reporting scheme also known as the yellow card system in place in the United Kingdom [11]. The yellow card scheme is important in identifying previously undetected adverse reactions and has provided many early warnings of drug safety hazards to allow appropriate drug regulatory action to be taken [12].

**Methods of detecting an ADR**

The first step in detection of ADRs is collection of data. The data to be collected includes patient's demographic data; presenting complaints; past medication history; drug therapy details including over-the-counter drugs, current medications and medication on admission; and lab data such as hematological, liver and renal function tests. Details of the suspected adverse drug reaction such as time of onset and duration of reaction, nature and severity of reaction; details of the suspected drug including dose, frequency, time of administration, duration of treatment, plasma concentration of drug; previous reports on reported reactions; data on any other causes including risk factors and predisposing factors are useful. Every healthcare practitioner should see it as a part of his/her professional duty to report any suspicion of a drug unexpectedly causing a risk situation for a patient under his/her cares [13].

**Reporting ADRs:**

Case Report Forms used have four main sections:

- Patient information / demographics
- Adverse event
- Suspected medication(s)
- Reporter

**Prevention:**

Multiple factors may contribute to adverse drug events (ADEs) which occur in inpatient, outpatient, and other health care settings (e.g., long-term care facilities, group homes), or during care transitions. The delivery of safe health care depends on creation of reliable health care system that considers systems, organizational, technical, provider, and patient factors that contribute to harm. The Joint Commission patient safety event taxonomy model helps to potentially identify key determinants of ADEs [14]. This model categorizes root causes of patient safety events into proximate (e.g., human) and

latent (e.g., organizational and system) factors. Proximate factors that contribute to ADEs include those that involve the patient and/or provider. Provider factors which may contribute to ADE(s) involve physicians, pharmacists, nurses, and caregivers who are certified to administer medication [15]. As indicated these may include errors in medication prescribing, dispensing, or administration [16].

Organizations may use this model of key determinants of ADE(s) to ensure that patient, provider, technical, organizational, and systemic factors are considered in efforts to prevent ADE(s). Organizations may conduct a careful root cause analysis of ADE(s) that identifies underlying causes and potential targets for intervention, with the goal of preventing their recurrence. By determining and

verifying probable causal pathways that led to adverse drug event, root cause analysis allows organizations to identify appropriate corrective and/or preventive actions, as well as to encourage the development of a culture of safety.

#### Management of ADR:

First and foremost step is withdrawal of suspected drug(s), if the reaction is likely to be dose related, dose reduction should be considered, and treatment for suspected reaction. While managing an ADR, always have a clear therapeutic objective in mind, do not treat for longer than necessary, review the patient regularly and simplify management. Commonly used plan of action while dealing with suspected adverse drug reaction is as follows:

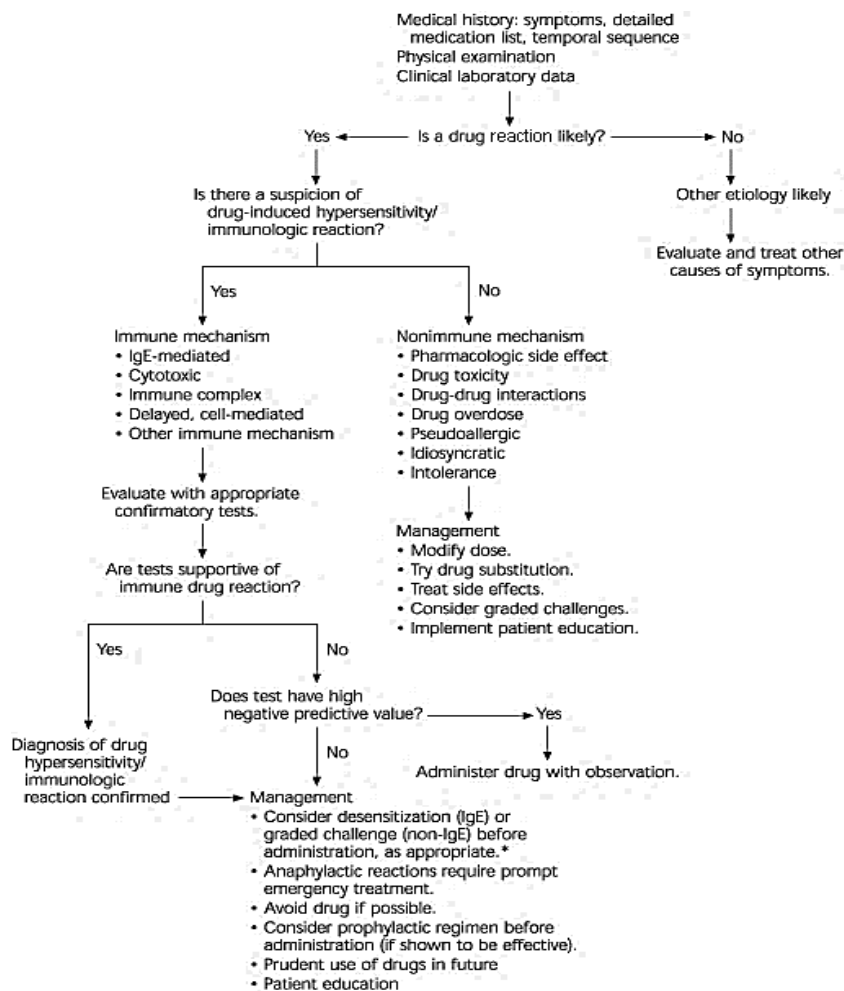


Fig 1: Management of ADRs

**Role of Pharmacist in Management of ADR:**

The fundamental role of health care providers (HCPs) is to identify potential and actual drug related problems, resolve problems, and prevent potential drug-related problems. HCPs are encouraged to take responsibility in development of Adverse Drug Reaction Monitoring and Reporting Programs to increase awareness of ADR(s), increase reporting of ADR(s), and increase opportunities to review drug selection and prescribing practices directly affecting patient outcome.

The pharmacist's role is to promote development, maintenance, and ongoing evaluation of programs to reduce the risk of ADR(s) through detecting, reporting and assessing any suspected ADR [17]. Investigate every suspected ADR for its nature, probability, and severity, Develop risk reduction strategies as part of an ongoing program. Enlist the continued support of other health professionals in this program, Provide information to other health care professionals to better identify ADR(s). Report serious or unusual ADR(s) through the FDA's Med Watch program; disseminate information about previously unreported ADR(s).

National Pharmacovigilance Program in India was started with the objectives of monitoring the safety of drugs and creation of an adverse drug reaction database for the Indian population [18]. Encouraging health care providers to take responsibility in the development of Adverse Drug Reaction Monitoring and Reporting Programs leads to heightened awareness of ADRs, increased reporting of ADRs, and increased opportunities to review drug selection and prescribing practices affecting patient outcome [19].

**METHODOLOGY:****Study design**

- Prospective and retrospective observational study.

**Study period**

- Study was carried out for a period of six months.

**Source of data**

- Data was collected from
  - Case files of patient who was admitted for more than 24 hours in the hospital.

**Inclusion criteria:**

1. All patients admitted to the hospital
2. Both gender

**Exclusion criteria:**

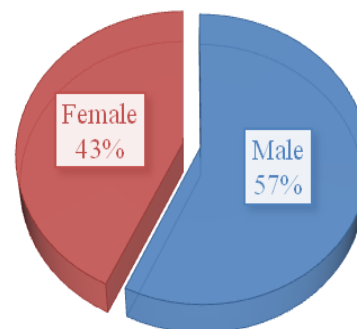
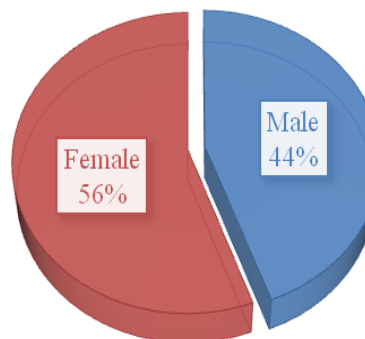
1. Clinical trial patients
2. Pregnant patients
3. Neonates

**Method of data collection:**

- Case series study
- Spontaneous reporting

**Analysis:**

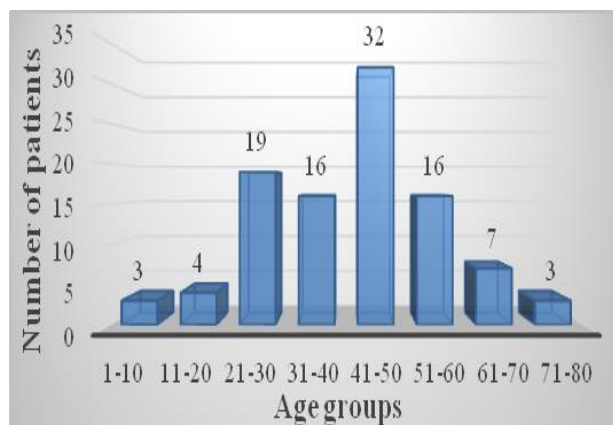
- Microsoft Excel

**RESULTS AND DISCUSSION:****Fig 2: Gender Distribution (Retrospective Study)****Fig 3: Gender Distribution (Prospective Study)**

Our retrospective study showed (fig 2) the incidence of ADRs during treatment was more common in men (57%) compared to women (43%). Whereas our prospective study shows (fig 3) women (56%) experienced more ADRs than men (44%).

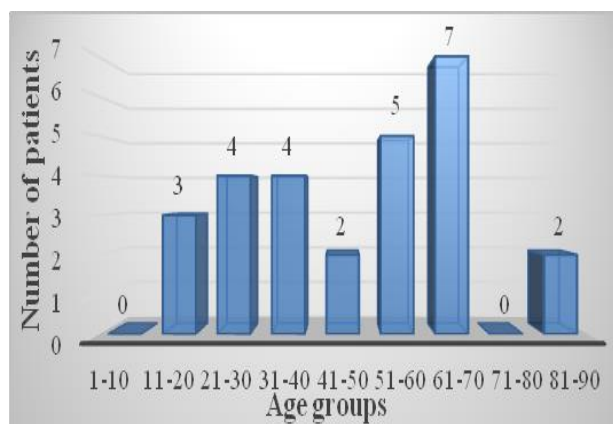
A study conducted by Sriram S et al in private tertiary care hospital in south India there were 57 documented ADRs from the 3,117 admitted to the General Medicine ward. The incidence was more common in males than female [20].

The above shows the incidence of ADRs depends on the population involved in the study and that incidence of ADR(s) does not significantly differ with men or women.



**Fig 4: Age Group Distribution (Retrospective Study)**

Highest numbers of patients with ADRs were found in the age group of 41-50 and lowest numbers of patients with ADRs were found in the age group between 1-10 & 71-80 (fig 4).



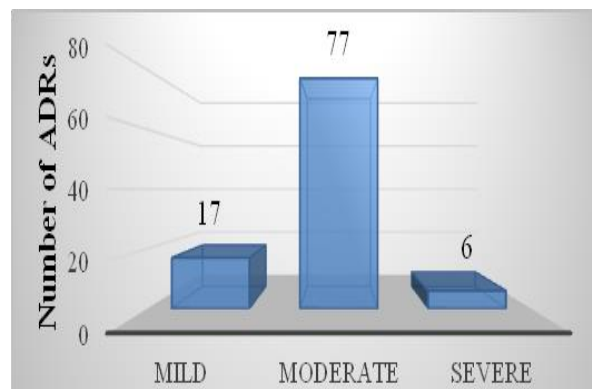
**Fig 5: Age Group Distribution (Prospective Study)**

The highest number of patient with ADR were found (fig 5) in age group 61-70 and lowest number of patient with ADR were found in age group between 41-50 and 81-90.

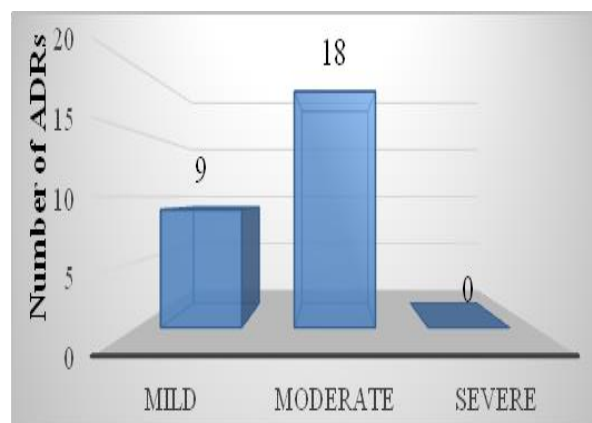
A study conducted by Sriram *et al*, in a private tertiary care hospital, results of age categorization revealed that patients of 60 years and above age group experienced maximum ADRs, followed by age group between 30-59 years and 18-29 years age group [20].

The above shows the incidence of ADRs among age groups depends on the population involved in the study although the incidence of ADRs increases greatly after the age group of 35 this also can differ

significantly according to the population being studied.



**Fig 6: Severity Assessment (Retrospective Study)**



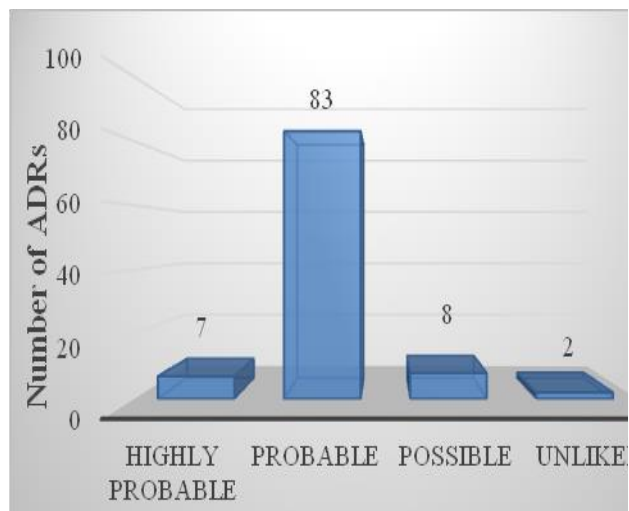
**Fig 7: Severity Assessment (Prospective Study)**

According to Severity Assessment by Modified Hartwig and Siegel Scale our retrospective study shows that ADRs were of moderate severity (77%) followed by mild (17%) and severe (6%), prospective study shows that moderate (66.6%) followed by mild (33.3%) and severe(0).

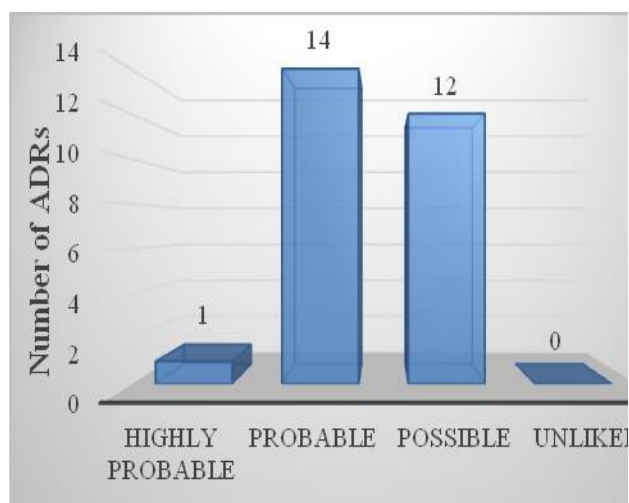
Sivanandy Palanisamy *et al* conducted a study on assessment, monitoring and reporting of adverse drug reactions in Indian Hospital. According to Severity Assessment by Modified Hartwig and Siegel Scale showed that 35 (18%) ADRs were moderate, 21 (9%) ADRs were mild and 4 (1%) ADRs were severe. No lethal effects were observed or produced [21].

Our retrospective as well as prospective analysis resulted in very few occurrences of severe ADRs possibly due to intervention and majority of ADRs were of moderate severity.





**Fig 8: Causality Assessment Scale (Retrospective Study)**



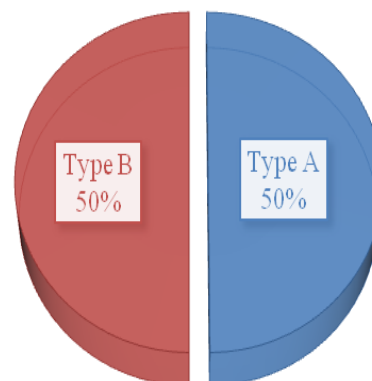
**Fig 9: Causality Assessment Scale (Prospective Study)**

Naranjo causality scale assessment for retrospective data showed that out of 100 ADR's 83 (83%) ADR's were probable, 8 (8%) were classified as possible and 7 (7%) were highly probable and unlikely 2 (2%). Our prospective analysis out of 27 ADRs 14 (51.8%) were probable, 12 (44.4%) were possible and 1 (3.7%) highly probable and unlikely none results were shown in fig 8 & 9.

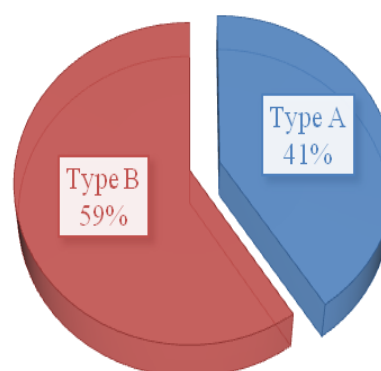
A study in Indian hospital on ADRs, assessed by Naranjo's scale showed out of 60 ADRs 44 (73.33%) were possible, 16 (26.67%) were classified as probable and 0 (0.0%) were definitely related to the drug [21].

Our study found majority of ADRs reported were probable according to Naranjo's causality assessment

scale. This may be due to fact that most of the ADRs were not confirmed by re-challenge of drug.



**Fig 10: Rawlings and Thompson's Classification (Retrospective Study)**



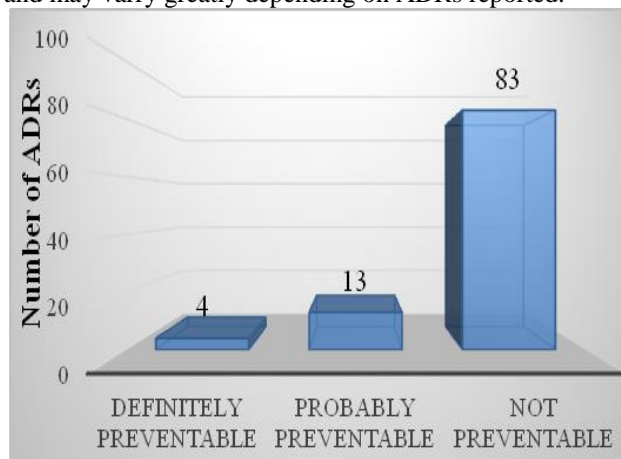
**Fig 11: Rawlings and Thompson's Classification (Prospective Study)**

According to Rawlings and Thompson's classification ADRs are classified into type A and Type B, analysis of reported ADRs by this method shows incidence of both the type of ADRs were in ratio 1:1 in retrospective study, whereas predominance of Type B reactions (59%) over Type A (41%) in our prospective study (fig 10 & 11).

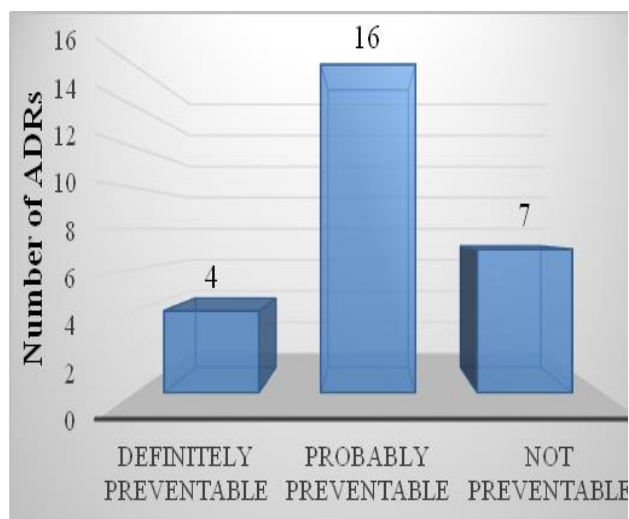
Prospective results are in line with study conducted by Oshikoya *et al.* and Starveva *et al.* but in another study by Suthar and Desai, all the reported reactions were Type B reactions [22]. Type A reactions are dose related and thus were preventable from their known pharmacology and therefore all of them were potentially avoidable. Type B reactions comprise

approximately 10–15% of all ADRs and include hypersensitivity drug reactions [23].

The above study shows the incidence of Type A or Type B ADRs depends on the occurrence of ADRs and may vary greatly depending on ADRs reported.



**Fig 12: Preventability Assessment (Retrospective Study)**

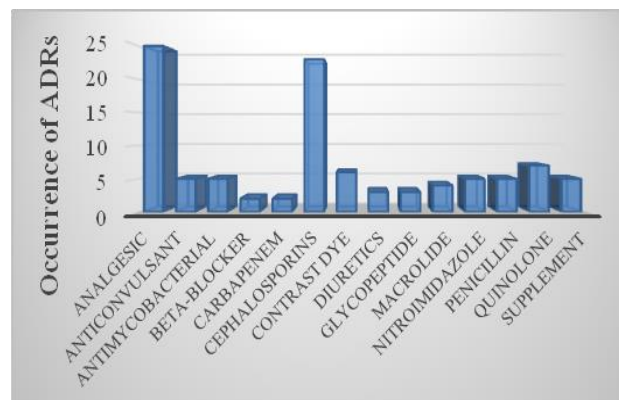


**Fig 13: Preventability Assessment (Prospective Study)**

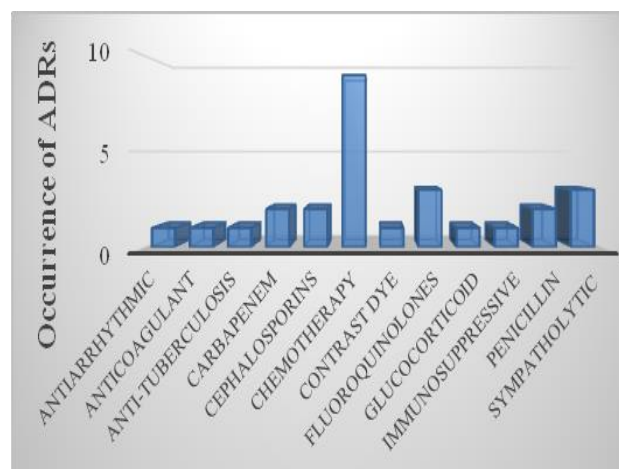
Preventability analysis through modified Schumock and Thornton scale for retrospective study revealed the majority of reactions were not preventable (82%) followed by probably preventable (13%) with only few reactions being not preventable (4%). In case of prospective study majority of reactions were probably preventable (59.2%) followed by not preventable (25.9%) with only few reactions being definitely preventable (14.8%).

According to a study conducted by Bates, antibiotics were responsible for 9% of preventable ADRs and 30% of non-preventable ADRs [24]. Our study

resulted in most of reactions being not preventable and probably preventable. Whereas actual preventable ADRs were fewer in number, reflecting occurrence of ADRs due to medication errors such as incorrect dose, route of administration, duration or even inappropriate drug were not common in this hospital.



**Fig 14: Class of Drugs Associated with ADRs (Retrospective Study)**



**Fig 15: Class of Drugs associated with ADRs (Prospective Study)**

In our retrospective study ADRs were commonly associated with Analgesic (25%) followed by Cephalosporins (23%), Quinolones (7%) and Contrast Dye (6%). Our prospective study shows that ADRs were most common in Chemotherapy (33.3%) followed by Fluroquinolones and Sympatholytics (11.1%)

A study by S Sriram *et al* on Prevalence of adverse drug reactions in a private tertiary care hospital in South India associated Antibiotics as 23% followed by NSAIDs as 19% of drug classes causing ADR [20].

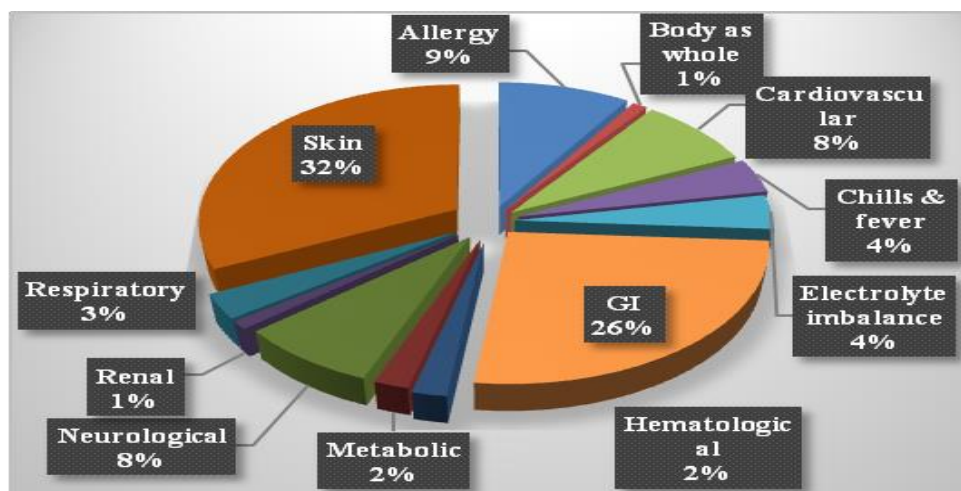


Fig 16: Organ Systems Affected by ADRs & commonly Occurring Reactions (Retrospective Study)

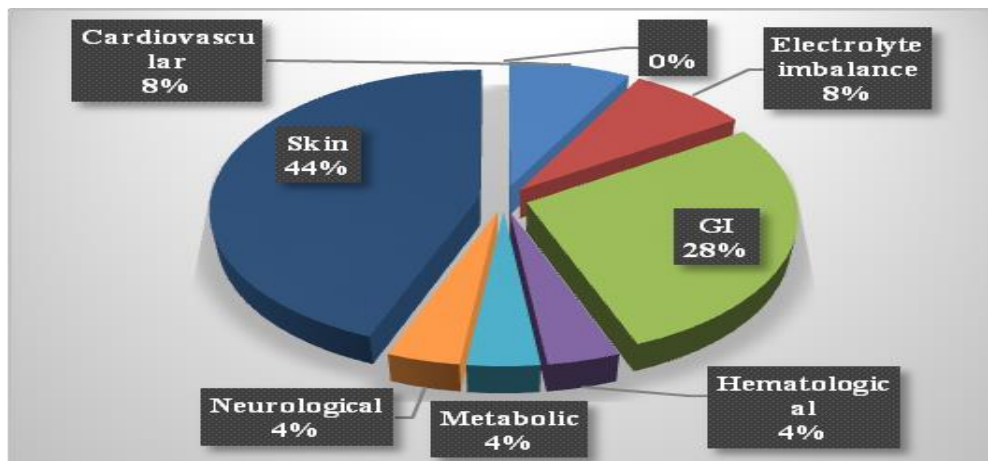


Fig 17: Organ Systems Affected by ADRs & Commonly Occurring Reactions (Prospective Study)

Our retrospective data shows the organ systems most commonly affected by ADRs were Skin (32%) followed by Gastrointestinal System (26%), Allergies (9%) and Neurological (8%). Our prospective analysis shows that Skin (11%) and Gastrointestinal system (7%) predominance.

Study by S Sriram *et al* showed organ systems most commonly affected by ADRs were Gastrointestinal in 37% of patients, Dermatological in 25% of patients, Central Nervous System in 14% of patients, followed by Cardiovascular in 12% of patients [20].

Our results were comparable with an international study conducted by Suh *et al*, which revealed that the system most badly affected was the dermatological and gastrointestinal system [25].

### CONCLUSION:

This study strongly suggests there is a need for streamlining hospital based ADR reporting and monitoring system in order to create awareness and to promote the reporting of ADR among HCPs. The present study concludes pharmacist's involvement greatly increases the reporting rate as well as quality of reporting. Hospital/clinical pharmacists also have a great role to play in the area of pharmacovigilance to strengthen the national pharmacovigilance program. Conducting educational classes for HCPs, developing and maintaining electronic documentation of patient's medical records may serve as a valuable tool to detect early signals of potential ADRs. In addition, proper record systems for patient medical records may help ease access for healthcare



professionals in detection and prevention of ADRs. Implementation of a computerized reporting system is highly recommended in this hospital setup since it will improve detection as well as reporting of ADRs.

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