

## To study the pattern of adverse drug reactions among patients hospitalized in the medical wards of a tertiary care hospital

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### ABSTRACT

**Background:** ADRs have a major impact on public health, quality of life. ADRs are a recognized hazard of drug therapy. Although some ADRs are minor and resolve without sequel, others can cause permanent disability or death. Despite the methodological rigor of clinical trials, it is generally not possible to identify all safety issues associated with drugs during the pre-marketing research phase. The only way to find out such occurrences is to be on active-look out for adverse events over a long time horizon in large population and in different host conditions. The information may be useful in identifying and minimizing preventable ADRs, while generally enhancing the knowledge of the prescribers to deal with them more efficiently.

**Methods:** This retro-prospective study was conducted in a tertiary care hospital for one year. Data of those patients who experienced ADRs was recorded in detail from internal Medicine ward. An assessment of causality was done. Data was evaluated to determine the class of drugs and the organ systems frequently associated with ADR within the settings of the institute.

**Results:** The total incidence of ADRs was 7.59% in hospitalized patients with male predominance. Most common system involved was GIT followed by CNS and CVS. Antibiotics were most common culprits for ADRs followed by NSAIDs and hypoglycemic agents. In causality assessment probable ADRs were much more than possible ADRs. Severity of reaction in most of the patients was moderate. Majority of ADRs were Type A and maximum were probably preventable.

**Conclusions:** There is need to explore the reasons for this relatively low incidence rate of ADR's in the Indian population. Under-reporting is one of the major factors with a lack of proper pharmacovigilance system which is still in budding state in India.

**Keywords:** Adverse drug reactions, Hospitalized patients, Retrospective, Prospective, Medical wards

### INTRODUCTION

ADRs in hospital patients can be divided into two broad categories: those that cause admission to hospital, and those that occur in patients after hospital admission. Approximately 5% (range 2–20%) of reported hospitalizations are because of an ADR and at least one ADR has been reported to occur in 10–20% of hospitalized patients. An ADR is associated with a significantly prolonged length of stay, increased economic burden, and almost two-fold increased risk of death. ADRs have a major impact on public health; reducing patients' quality of life and imposing a considerable financial burden on the health care systems and on patient at a time when many health care systems are under considerable financial strain. These are a

recognized hazard of drug therapy. Although some ADRs are minor and resolve without sequel, others can cause permanent disability or death, and contribute to the incidence of adverse drug reactions, resulting in increasing health care costs.<sup>1-3</sup>

Drugs that are approved by the national regulatory authorities for marketing are required and expected to be safe. Despite the methodological rigor of clinical trials, it is generally not possible to identify all safety issues associated with drugs during the pre-marketing research phase due to the fact that the size and characteristics of the subject population, drug doses, and duration of use and concomitant therapies that exist in actual post-marketing reality cannot be exactly mirrored in a clinical trial. The only way to find out such occurrences is to be

on active-look out for adverse events over a long time horizon in large population and in different host conditions with regard to ethnicity, age, gender and physiological state.<sup>4</sup>

Pharmacovigilance, which is an evolving science dedicated for reducing medicine related harm to patients, is a good tool for ensuring safe and effective use of medicine. The information may be useful in identifying and minimizing preventable ADRs, while generally enhancing the knowledge of the prescribers to deal with them more efficiently. Hospitalized patients are an important study population as they differ markedly from the populations included in clinical trials. The huge inflow of patients makes Dr. Rajendra Prasad Government Medical College an ideal venue for initiation of pharmacovigilance activities in order to ensure safe, rational and effective drug therapy to the patients.

The present study was aimed to study the pattern of adverse drug reactions in indoor patients in the department of internal medicine, Dr. Rajendra Prasad Government Medical College, Kangra at Tanda and to assess the class of drugs and organ systems frequently associated with ADRs.

## METHODS

### Study design

A retro-prospective, observational study that was conducted in the department of pharmacology and department of internal medicine, Dr. Rajendra Prasad Government Medical College Kangra at Tanda. All the patients admitted in the department of internal medicine over a period of 12 months were enrolled in the study.

### Ethical clearance

The study protocol was approved from Scientific Review Committee and Human Ethics Committee of the institution before starting the study. All consecutive patients of either sex or age admitted in the Internal Medicine wards for one year were included in the study. Data of those patients who experienced ADRs was recorded in detail and analysed.

### Monitoring of adverse drug reactions

WHO definition of adverse drug reaction was used and all reactions to drugs administered at appropriate dosages were recorded.

### Prospective

A record of all the patients admitted in medicine wards was collected from the internal medicine department. To monitor ADRs rounds of the wards were made twice a week. Data of the patients experiencing any drug reaction was collected in detail by interviewing the patient.

### Retrospective

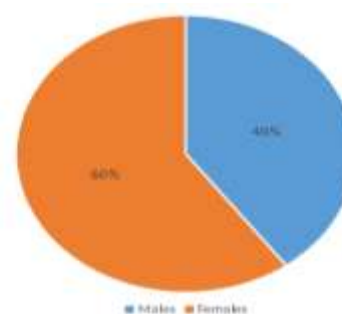
Regular visits had been made to the case record section of the hospital to collect data retrospectively of those patients who were left out from prospective part of study because of any reason.

### Causality assessment

An assessment of causality was done by using UMC–WHO scale.<sup>5</sup> Classification of ADRs were done by using Rawlins and Thompson classification.<sup>6</sup> Severity of ADRs was assessed using the modified Hartwig and Siegel scale.<sup>7</sup> Modified Shumock and Thornton criterion was used to assess the preventability of ADRs.<sup>8</sup> Adverse Reactions were coded using WHO adverse drug terminologies.<sup>9</sup> Data was evaluated to determine the class of drugs and the organ systems frequently associated with ADR within the settings of the institute.

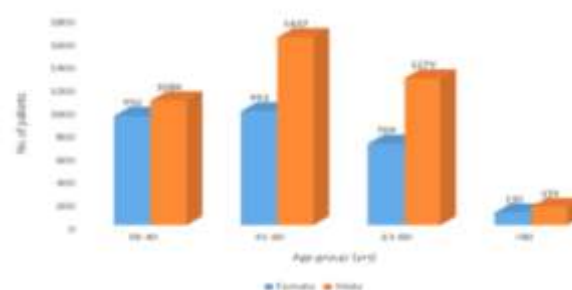
## RESULTS

A total of 6922 patients were admitted in the department of internal medicine during study period of 12 months. Out of total 6922 patients, 2763 were females and 4159 were males as shown in Figure 1.



**Figure 1: Sex distribution of study subjects.**

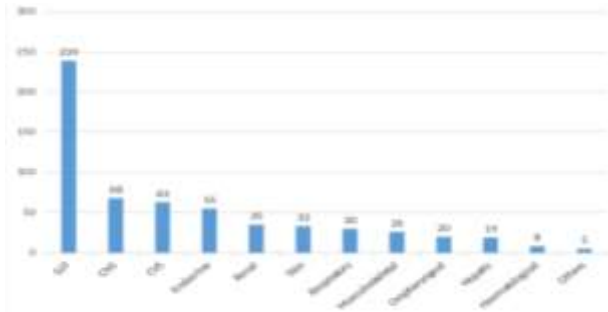
There were total 2036 patients in age group 18-40 years, 2629 in age group 41-60 years, 1988 in age group 61-80 years and 269 above 80 years as in Figure 2.



**Figure 2: Age and sex distribution of study subjects.**

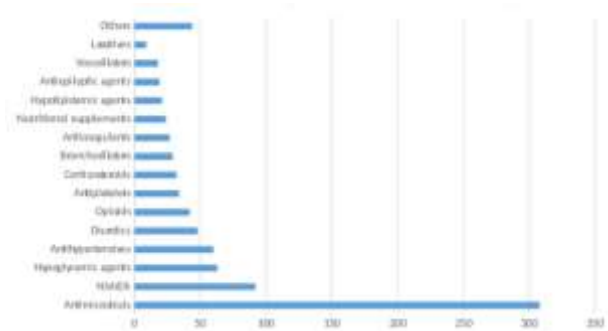
Out of these 526 patients were found having documentation of adverse drug reactions that constitutes 7.59% of total case records screened retro-prospectively.

Out of total 526 patients with ADRs, 242 were females and 284 were males. There were total 126 patients in age group of 18-40 years, 202 in age group 41-60 years, 178 in age group 61-80 years and 20 in age group more than 80 years. The incidence of ADRs was 7.59% in hospitalized patients. GIT was the most common organ system involved (39.7%) followed by CNS (11.3%) and CVS (10.4%) as given in Figure 3.



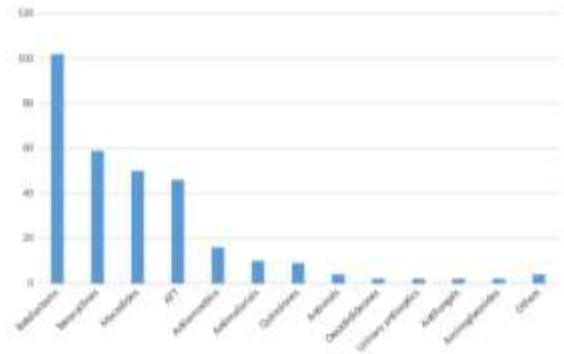
**Figure 3: Organ systems affected by ADRs in study subjects (n=526).**

Most common class of drug associated with ADRs were antimicrobials (35.4%) followed by NSAIDs (10.57%) and hypoglycemic agents (7.24%) as shown in Figure 4.

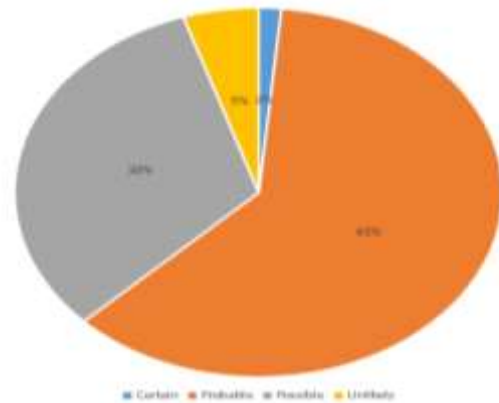


**Figure 4: Frequency distribution of drugs attributable to various drug classes.**

Most common antimicrobial agents attributable to ADRs are betalactams (33.11%) followed by tetracyclines (19.15%) and macrolides (16.23%) as given in Figure 5. Number of drugs received by an individual patient ranged from 1 to 15 with an average of 5.82. 25% patients received up to 4 drugs while 50% received 4-8 drugs and 50% received more than 8 drugs. Total duration of hospital stay in the patients with ADRs ranged from 1 day to 33 days with mean duration of 6.76 days. 25% of patients stayed up to 4 days, 50% stayed for 5-8 days and 25% for more than 8 days. Among male patients 62.5% ADRs were probable and in female patients 59.8% were probable. Overall 1.5% ADRs was certain, 61.2% probable, 32.3% possible and 5% unlikely in causality assessment as in Figure 6.

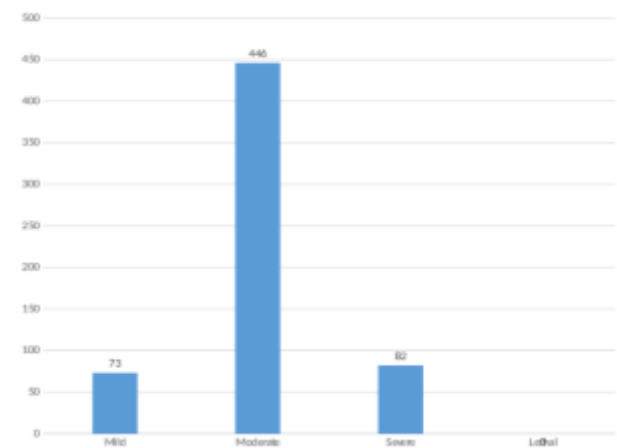


**Figure 5: Antimicrobial agents attributable to ADRs in study subjects.**



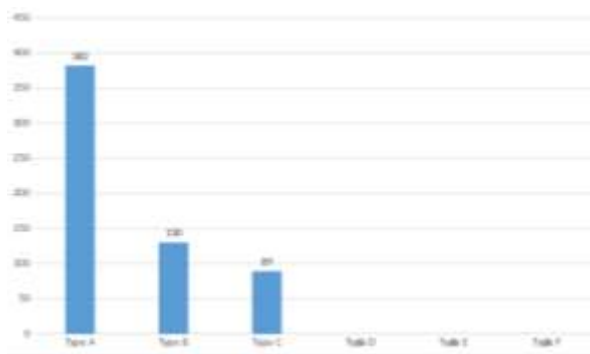
**Figure 6: Causality assessments of ADRs.**

Overall 12.1% were mild, 74.2% were moderate and 13.6% were severe. No case of lethal ADR was reported as displayed in Figure 7.

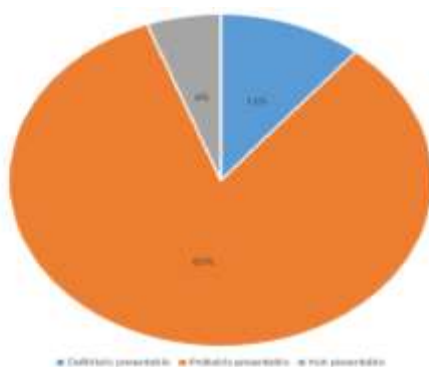


**Figure 7: Classification of ADRs on the basis of severity.**

63.57% of the ADRs were type A, 21.63% were type B and 14.8% were type C according to reaction type. No ADRs of type D, E and F were found as in Figure 8. Maximum number of ADRs was probably preventable as shown in Figure 9.



**Figure 8: Classification of ADRs on the basis of reaction type.**



**Figure 9: Classification of ADRs on the basis of preventability (n=601).**

## DISCUSSION

This retro-prospective study was conducted in medical ward of a tertiary care hospital in order to determine the pattern of adverse drug reactions. It analysed ADRs in varied spectrum i.e. in terms of their assessment of causality, severity, preventability, reaction type, organ system involved and the drug class frequently associated with them. Total patients enrolled in the study were 6922. In this study we found that 526 (7.59%) patients developed ADRs. Comparable observations have been made by Hurwitz (10.2%) De Vries *et al* (9.2%) and Moore *et al* (6.6%) about Hospitalized patients.<sup>10-12</sup>

The demographic detail of our study showed higher incidence of ADRs in females (8.75%) in comparison to (6.82%) in males whereas within ADRs patients (n=526), there is higher incidence in males (54%) as compare to females (46%). Similar results were reported by Goyal *et al* (59.3%), Chen *et al* (68.5%) and Palanisamy *et al* (59%) in male and (41%) were female whereas Lobo *et al* and Koh *et al* concluded in their studies that gender was not a risk factor to develop ADRs.<sup>13-17</sup>

In our study age group 41-60 years showed high incidence of ADRs (38.4%) in both the genders. Similar findings were shown by Palanisamy *et al* who observed the same age group (41-60 years) with 42.71% of ADRs.<sup>15</sup>

In present research we observed that polypharmacy lead to significant increase in the number of ADRs. The no. of medication consumed ranged from 1-15 with mean 5.82 (SD+2.71) and median 6.

We concluded in the study the mean duration of stay in the hospital I was 6.75 days with SD+4.76. In a study by Pirmohamed *et al* concluded the median bed stay 8 days. In another study by Patel *et al* evaluated median duration 5 days.<sup>18,19</sup>

Regarding the reaction type of ADRs, we observed majority belong to type A (63.57%) as compared to type B (21.63%) and type C (14.80%). The study by Lobo *et al* observed the same that type A reactions were most common (82.1%). The study by Goyal *et al* confirmed the same as above type A (73%) and type B (27%).<sup>13</sup> Moore *et al* concluded that 77% of ADRs were related to pharmacological properties of the involved drugs.<sup>12,13,16</sup>

The most common system associated with the ADRs was gastrointestinal system (39.7%) that was followed by CNS (11.3%) and CVS (10.4%). The findings are supported by the study of Sriram *et al*, Goyal *et al* and Uchit *et al* where GIT was found to be most commonly affected organ system.<sup>13,20,21</sup>

In our study drug class most commonly involved was Antimicrobials (35.4%) followed by NSAIDs (9.93%) and antihypertensive (10.57%). Gor and Desai *et al* support this study with Antimicrobials topping the list 72.2%. These findings are further consistent with the studies reported by Karthikeyan *et al* and Sriram *et al* who evaluated the maximum prevalence of antimicrobial drugs as 26.8% and 23% respectively.<sup>20,22,23</sup>

Causality assessment concluded that most common were probable ADRs (61.2%) followed by possible (32.3%), unlikely (5.0%) and certain (1.5%) respectively. Which was similar to the study by Goyal *et al* and Palanisamy *et al*.<sup>13,15</sup> Considering the severity of reaction 74.2% ADRs were observed moderate in nature, 13.6% severe and 12.1% mild. But different results were recorded by Arulmani *et al* that showed 53.7% mild reactions. Hurwitz observed 80% of moderate severity. Palanisamy *et al* 61% of ADRs were moderate in severity.<sup>10,15,24</sup>

83.36% ADRs were probably preventable, 10.98% were definitely preventable and non-preventable were 5.25% in the present study. Similar records were observed by Samoy *et al*, Chen *et al* and Wilson *et al* i.e 72.1%, 73% and 83% preventable ADRs respectively. Whereas De Vries *et al*, Palanisamy *et al*, and Sriram *et al* concluded definitely preventable ADRs, 43.5%, 40% and 28% respectively.<sup>11,14,15,20,25,26</sup>

In our study it was found that 42.9% ADRs remitted by dechallenging the suspected drugs. Similar study by Rao *et al* suggested that the suspected drug was withdrawn for management of the ADRs in majority (56.6%) of the



reports. According to study by Palanisamy et al most of ADRs were treated by withdrawing offending drugs (81.25%). Rao et al and Lobo et al concluded that at least one predisposing factor was present in 79.9% of the reports and most common were polypharmacy and multiple diseases.<sup>15,16,27</sup>

There is need to explore the reasons for this relatively low incidence rate of ADR's in the Indian population. Under-reporting is one of the major factors with a lack of proper pharmacovigilance system. There are various factors affecting the ADR incidence e.g. age of patients, gender, number of drug exposure, length of hospital stay, genetic factors, ethnicity, dietary and environmental factors etc. The main factor affecting the ADR incidence could be attributed to inconsistent or contradictory methods among the individual studies. Another example of inconsistent methodology is the problem that some investigators include error in administration of drugs, overdose of drug for reporting ADR.

#### **Limitations of the study**

Although this was a retro prospective study conducted in a substantially good sample size of hospitalized patients it was confined to the medicine ward only. Better insight would have been provided by the involvement of other departments. Patients who were transferred from other departments into the medicine wards; any ADRs during their stay in the other ward was not ascertained. Though the employed methodology was based on data obtained during daily ward rounds, from the prescribing physician and from the patients' medical records, the drawback was the identification of the ADRs by the investigator only at any given time. In addition to the lack of information on drugs and clinical data in the medical records, it is quite possible that certain clinical interurrences that could lead to the suspicion of a ADRs was not recorded leading to an underestimation. Lastly due to constraints of time and manpower the economic burden associated with ADRs could not be taken up in this study

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