

Research Article

Preventability, Predictability and Seriousness of Adverse Drug Reactions amongst Medicine Inpatients in a Teaching Hospital: A Prospective Observational Study

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ABSTRACT

People in every country of the world are affected by adverse drug reactions (ADR) and it is estimated that at least 60% of ADRs are preventable (WHO fact sheet). Data from various studies have shown that about 20 - 80% of ADRs are preventable. Majority of hospitals in India do not have an ADR reporting and monitoring programme. Moreover, assessment of the impact and potential for prevention was limited because many studies did not assess seriousness and preventability. Therefore we tried to analyze the preventability of reported ADRs in this study. Primary objectives were to assess the preventability and seriousness of reported ADRs. We have also tried to analyze the predictability, effect of length of hospitalization and predisposing factors responsible for ADRs. A prospective observational study was carried out for the duration of 8 months amongst medicine inpatients of a teaching hospital. Preventability, Predictability and Seriousness were assessed for each suspected ADR. In addition to this, effect of length of stay on happening of an ADR was also assessed. Our finding showed about 34% ADRs were "Definitely preventable", 21% were "Probably preventable" while remaining 45% were "Not preventable". 72.71% of the reactions prolonged the hospitalization of patients whereas 25.18% of the reactions required intervention to prevent permanent damage and only 2.10% of the reactions were life threatening. Almost 69% ADRs deemed predictable. Although ADRs encountered in the study are non serious and not preventable, management of such ADRs through therapeutic interventions would be beneficial in better patient outcome.

Keywords: Adverse Drug Reaction, Prospective Observational, Preventability, Intervention.

INTRODUCTION

Patient safety has become a leading topic at the national level. The overall rate of adverse drug reactions (ADRs) is estimated to be 6.5% and 28% of these ADRs are preventable.¹ One meta-analysis found an adverse-drug-reaction (ADR) rate of 6.7% among hospitalized patients.² An ADR can lead to significant morbidity, mortality and financial costs. ADRs that may be preventable might be considered a form of medication error.³

People in every country of the world are affected by ADRs. According to WHO factsheet, it is estimated that at least 60% of ADRs are preventable. In some countries ADR-related costs, such as hospitalization, surgery and lost productivity, exceed the cost of the medications.⁴ Historically, studies have

shown that between 20% and 80% of ADEs and ADRs are preventable with the majority of latter studies⁵ showing around 60- 70% preventability.⁵

A systemic meta-analysis using Medline and Embase as databases for literature published between 1980 and June 2002 on the incidences of ADEs and their preventability in hospital settings showed that upto 56.6% these events were judged to be preventable.⁶ An ADR was classified as preventable if the drugs involved were not appropriate for the patient's clinical condition; the dose, route or frequency of administration was not appropriate for the patient's age, weight or disease; the patient required therapeutic drug monitoring or other necessary laboratory tests that were not performed or not performed

frequently enough; the patient had a history of allergy or previous reaction to the drug; a known drug interaction was the suspected cause of the reaction; a serum drug concentration above the therapeutic range was documented; non-compliance was associated with the reaction; or a medication error was associated with the reaction.⁷

Although India is a developing country, most hospitals in India do not have an ADR reporting and monitoring programme.⁸ Assessment of the impact and potential for prevention was limited because many studies did not assess seriousness and preventability. Moreover findings of our previous study showed overall incidence of ADRs in hospital patients was 4.75% and the financial burden of Rs 412.79 per patient.⁹ Therefore we tried to analyze the preventability of reported ADRs in this study. The main primary objective of this study was to assess the preventability and seriousness of reported ADRs. Other secondary objectives were the assessment of predictability, effect of length of hospitalization on ADR and predisposing factors responsible for ADRs.

MATERIALS AND METHODS

We prospectively studied patients who were admitted to internal medicine departments and medicine ICU at Bharati Hospital and Research Centre, a 850 bedded tertiary care teaching hospital in Pune, Maharashtra. All the patients who were admitted in medicine units for >24 hours and developed an ADR were included for analysis. Patients admitted due to the reason of an ADR were also included. Study was carried out for the duration of 8 months from November 2010 to June 2011. ADR monitoring was performed by pharmacist who reviewed the patient's drug therapy, monitored the laboratory data, assessed for fresh complaints and interviewed the patients. Additionally duration of drug use, duration of hospitalization, effect of duration of hospitalization of ADRs, treatment of ADRs, co-existing disease and drug suspected to cause ADR and description of ADRs were recorded. The collected information was used to assess the probability that reaction was drug related, predisposing factors for an ADR and also to assess the preventability, seriousness and predictability of the ADRs. The preventability was determined using modified criteria adopted from Schumock and Thornton.¹⁰ Seriousness of reaction were categorised according to FDA criteria¹¹ while predictability was determined by classifying the ADRs.¹² Criteria for preventability correspond directly to the questions published

by Schumock and Thornton (Table 1). Any answer of "yes" to any question suggests that the ADR might have been preventable. Patient and drug therapy were evaluated to identify various predisposing factors responsible for an ADR. In addition to this, effect of length of stay on happening of an ADR and impact of hospitalized ADR and ADR related hospitalization with preventability was assessed. Both preventable and non-preventable ADRs were compared in the view of types of ADR and age group. Finally collected information were compared and reviewed by clinical pharmacists to assess their significance.

RESULTS

A total of 143 ADRs were found during the study periods which were analyzed for the preventability criteria. About 48 (34%) ADRs were "Definitely preventable", 30 (21%) were "Probably preventable" while remaining 65(45%) were "Not preventable" as shown in Fig. 1. Amongst 143 ADRs, 90 reactions occurred in hospitalized patients of which 42 were deemed preventable while remaining 53 lead to hospitalization, of which 36 were preventable (Table 2).

Seriousness criteria assessment showed 72.71% of the reactions prolonged the hospitalization of patients whereas 25.18% of the reactions required intervention to prevent permanent damage and only 2.10% of the reactions were life threatening (Table 3). Effect of length of stay on the ADR showed that as the length of hospitalization increases the probability of developing ADR per patient increases. On the stay of 1 week average number of ADRs/patient was 1.75 which was increased to 2.6 in case of stay of more than 2 weeks (Table 4). Average length of stay per patient was found to be 7.78 days/patient in our study.

Predictability assessment was carried out by categorizing the ADRs and found that almost 98(69%) ADRs deemed predictable while remaining 45(31%) were found non-predictable (Fig. 2). Amongst the several predisposing factors, polypharmacy constituted the highest percentage in causing ADR (48.95%) followed by co-morbidity and age (40.56% and 20.28% respectively). Other predisposing factors are shown in Table 5.

DISCUSSION

An epidemiological research performed in the United States shows the occurrence of ADRs in 10–20% of all hospitalized patients.¹³ It is estimated that ADRs are responsible for 3.2–6.5% of admissions to hospital¹⁴ and about

28% of ADRs were preventable in USA.¹⁵ Our findings on preventability showed about 55% of ADRs were deemed preventable while 45% were non-preventable. Amongst the preventable ADRs 34% were definitely preventable because of an inappropriate selection of drug for patient's condition and there is known treatment of found ADRs. Remaining 21% were found probably preventable as necessary laboratory tests not performed or preventative measures not prescribed when administering drug to patient. Our study results were comparable with the studies carried out by James BC and McDonnell et al^{16, 17} showing 60.5% and 62.3% of the ADRs as preventable respectively. However, our findings varied with the data from western studies carried out in USA¹⁵, Germany¹⁸ and France¹⁹ which found 28%, 28.5% and 80% of ADRs as preventable respectively. Another study in Australia showed 5.5% ADRs were definitely preventable and 60% as possibly preventable.²⁰

According to US-FDA criteria any adverse reaction denoted as serious if the patient outcome fall within categories such a death, life-threatening, hospitalization (initial or prolonged), disability or permanent damage, congenital or birth defect or required intervention to prevent permanent damage to patient.¹¹ Comparative data on seriousness of ADRs was not found from any of the western studies however some of the Indian studies mentioned the data on seriousness. Life threatening reactions were just 2.20% in our study. No fatality was observed. About 73% of ADRs were responsible for prolongation of hospitalization of patient. Life threatening reactions found in our study were AKT induced hepatitis (2 cases) and suspected Steven Johnson Syndrome with use of Antibiotics. Our findings on seriousness differ from an Indian study carried out by Vora MB et al which showed 4.25% death, 29.79% life threatening cases and prolonged hospitalization in 62.84% of the cases.²¹

ADRs may prolong hospital stay, it is important to appreciate that those patients who stay longer in hospital are at an increased risk of ADRs, and therefore an association of an ADR with longer stays does not necessarily reflect cause and effect^{22, 23} There is a definite association between ADRs and increased length of stay across several studies.⁵ As mentioned above in Vora et al study,²¹ In 62.84% cases ADR prolonged the hospitalization. Another study by Moore et al found that patients admitted with ADRs did not stay in hospital significantly longer than

patients without ADRs, whereas patients with ADRs in hospital did²⁴ which correlates that length of stay in hospital is directly proportional to the number of ADRs to the patient. Our findings showed that on the stay of 1 week, average number of ADRs was 1.75 but in case of stay of more than 2 weeks average number of ADRs increased from 1.75 to 2.6/patient. Average length of stay was found to be 7.78 days/patient in this study.

Type A (augmented) reactions are predictable through knowledge of the drug's pharmacology and are dose-dependent while by contrast Type B (bizarre) reactions are unpredictable from the known pharmacology of the drug, and do not show a clear dose-response relationship.^{25, 26} In this study 69% of the ADRs were categorized as predictable in contrast with the international report showing 96.1% of the ADRs as predictable.²⁷

Occurrence of ADR depends on various predisposing factors such as polypharmacy, age, gender, race, genetics, multiple/ inter-current diseases, inadequate knowledge of patients and allergy which leads to morbidity and mortality in individual patient.²¹ Factors associated with increased incidence of ADR were increasing age (especially > 70 years) increasing number of medicines and particular classes of medicine.²⁸ Polypharmacy is a recognized risk factor for ADRs particularly in the elderly and is likely to increase since therapeutic guidelines indicate use of multiple therapies to manage and control the diseases.⁵ Similarly, Patients with multiple diseases are at an increased risk of developing ADR due to multiple drug use of their multiple diseases. Similarly, patients with impaired hepatic or renal status are also at a high risk of developing an ADR to drugs which are eliminated by these organs.²⁹

Polypharmacy (48.95%) and comorbidities (40.56%) are the most common predisposing factors responsible for ADRs in this study. An Indian study by Jose J et al revealed polypharmacy (93.1%) and multiple disease state (52.9%) as the most prevalent predisposing factors in the patients who developed ADRs along with age (32.4%).³⁰ Another Indian study by Sriram S et al showed that multiple drug therapy (68%), age (56%) and comorbid diseases (42%) were identified as the major predisposing factors.³¹

CONCLUSION

Though use of non-prescription drugs, self medication and drug abuse remains significant problem for occurrence of ADRs, the ADRs encountered in the study are non serious and not preventable. It implies that patients are

harmful with ADRs with normal use of drugs in comorbid patients. Management of such ADRs through therapeutic interventions would be beneficial in better patient outcome. A more

focus on medication errors would not suffice the prevention of ADRs.

Table 1: Preventability criteria according to Schumock and Thornton scale

Definitely Preventable	
1.	Was there a history of allergy or previous reactions to the drug?
2.	Was the drug involved inappropriate for the patient's clinical condition?
3.	Was the dose, route or frequency of administration inappropriate for the patient's age, weight or disease state?
4.	Was a toxic serum drug concentration (or laboratory monitoring test) documented?
5.	Was there a known treatment for the Adverse Drug Reaction?
Probably Preventable	
6.	Was required Therapeutic drug monitoring or other necessary laboratory tests not performed?
7.	Was a drug interaction involved in the ADR?
8.	Was poor compliance involved in the ADR?
9.	Were preventative measures not prescribed or administered to the patient?
Not preventable	
If all above criteria not fulfilled	

Table 2: Preventability analysis with ref. to types of ADR and gender

	DEFINITELY PREVENTABLE	PROBABLY PREVENTABLE	NOT PREVENTABLE	TOTAL
ADR related hospitalization	27	9	17	53
Hospitalized ADR	21	21	48	90
Adults	35	21	59	115
Geriatrics	13	9	6	28

Table 3: Seriousness of Reaction (According to US-FDA)

	NUMBER OF ADRs (n=143)	% OF ADRs
Life threatening	3	2.10%
Hospitalization initial/prolonged	104	72.71%
Req. intervention to prevent permanent damage	36	25.18%

Table 4: Effect of length of stay on ADR

LENGTH OF HOSP. STAY (WEEK)	NUMBER OF PATIENTS	NUMBER OF ADR's	AVG. NUMBER OF ADR/PATIENT
1- 7 days (1 week)	28	49	1.75
8- 14 days (2 week)	11	18	2.54
15- 24 days (> 2 weeks)	5	13	2.6

Table 5: Predisposing factors for ADRs

	NUMBER OF ADRs (n=143)	% OF ADRs
Polypharmacy	70	48.95%
Co-morbidity	58	40.56%
Age	29	20.28%
Inadequate knowledge of patients	10	6.99%
Genetics	7	4.89%

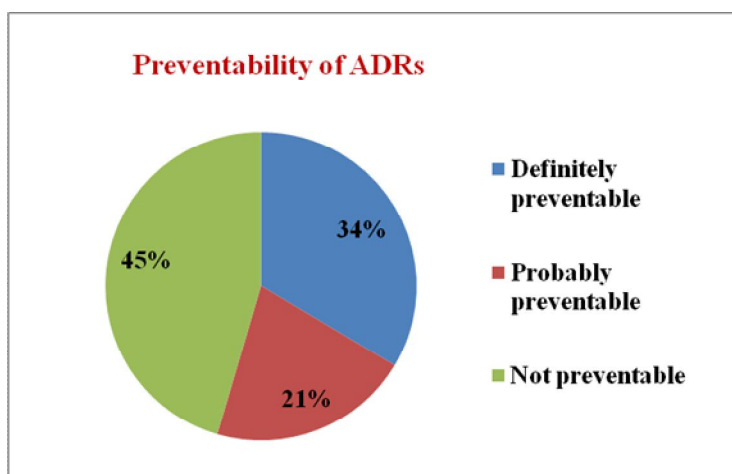


Fig. 1: Preventability of ADR by using Modified Schumock and Thornton Scale

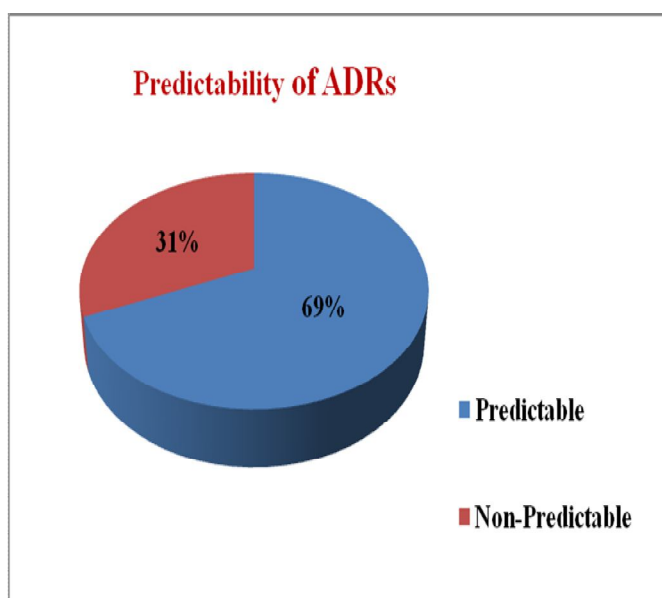


Fig. 2: Predictability analysis of suspected ADRs

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