

ADVERSE DRUG REACTIONS IN ADULTS LEADING TO EMERGENCY DEPARTMENT VISITS

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ABSTRACT

Medication-related visits to the emergency department are an important but poorly understood phenomenon. A large number of adverse drug event-related visits and admissions are preventable which highlights the importance of public education on the proper use of drugs. The aim of this study was to determine about the frequency, preventability and severity of adverse drug events resulting in emergency department visits.

A prospective observational study was conducted including selected adults presenting to the emergency department with adverse drug reactions over a period of 1 year during 2011-2012. The present study tried to determine the same in patients attending a tertiary care teaching hospital in and around kolar. WHO guidelines were strictly applied for classifying adverse drug reactions. Drug-related visits were assessed by two physicians. Discrepancies were adjudicated by two independent reviewers. Also, all patients (relatives, if patients were unconscious) were interviewed to elicit more information and reassess the causes for the emergency room visit and hospital admission.

Among the 133 patients included in the study, the emergency department visit was identified as drug-related adverse reactions for 50 patients (37.59%); of these 9 visits (18%) were deemed preventable. Severity was classified as mild in 14%, moderate in 68% and severe in 18% among adverse drug events. The most common Adverse drug reactions (ADR) were neuropsychiatric events ($n=10$ [28.57%]), gastrointestinal reactions (37.14%) and angioedema (11.42%). The most common drug classes involved were NSAID (32%), Glucocorticoids (20%), Fluoroquinolones (8%) and Insulin (6%). A patient having one or more co morbidities (p -value 0.0002) has a more chance of developing an ADR. A patient going to more than one physician (p value 0.0124) and pharmacy (p value 0.0002) along with a daily intake of more than two medications (p value <0.0001) has a greater chance of developing an ADR.

In the present study, we estimated the proportion of drug-related visits to be 1.3 % and the frequency of adverse drug reactions was 1%. More than 1 in 100 emergency department visits are due to drug-related adverse events, a potentially preventable problem in our health care system. Physicians should prescribe NSAIDs and glucocorticoids with caution to patients along with adequate counseling regarding adverse drug reactions.

Keywords: Adverse drug reaction, Emergency room, Drug related problems, Adverse Drug Events

INTRODUCTION

Adverse drug-related events have recently been evaluated in ambulatory care settings and among patients admitted to hospital¹⁻⁵, and it has been estimated that 5%-25% of hospital admissions are drug-related^{3,4}. Unfortunately, emergency department visits are not reflected in most hospital studies, because patients seen in the emergency department for an adverse drug-related event are typically not admitted⁶.

Adverse drug events (ADEs) account for a sizable proportion of all visits to a medical emergency unit and some are serious enough to require hospitalization. A large number of adverse drug event-related visits and admissions are preventable which highlights the importance of public education on the proper use of drugs, and also the need for regulation of the practice of unregistered medical practitioners in developing countries.

In addition, most research evaluating drug-related visits to the emergency department has involved retrospective studies or analysis of administrative data⁷⁻⁹. Retrospective studies may underestimate the incidence of drug-related visits because information may be missing or inaccurately documented¹⁰. Finally, studies performed to date have used variable definitions of "drug-related events," which limits comparative evaluation and generalisation. The studies on drug-related visits to the medical emergency department and hospital can contribute to a more comprehensive evaluation of drug related problems, that arise from prescriptions of general practitioners.

The information generated from such prospective studies can be utilized in such a manner, to try and establish as to what proportion these events are avoidable, so that an intervention can be carried out in future.

Adverse drug events (ADEs) are a substantial cause of hospital admissions. However, little is known about the frequency, preventability and severity of Adverse drug events resulting in emergency department visits. To address this issue, we need to conduct a study confining to the region of kolar

METHODOLOGY

The present study was a prospective observational study. All visits to the emergency room of R.L Jalappa hospital, Kolar over duration of one year were recorded. R.L Jalappa hospital is an 850-bedded tertiary care hospital. The residents on round-the-clock duty in the emergency room informed about the study objectives. They were asked to elicit information from all patients regarding whether the patient's visit was due to an ADR, drug interaction, or patient non-compliance. Drug-related visits were assessed by two physicians (Figure 1).

Discrepancies were adjudicated by two independent reviewers. Also, all patients (relatives, if patients were unconscious) were interviewed to elicit more information and reassess the causes for the emergency room visit and hospital admission.

For each patient, the following information was recorded: demographic characteristics, diagnosis, drug history, type of ADE and clinical condition. The cases of suspected ADEs were followed-up to find out whether they were discharged from the emergency room itself, or whether they subsequently required hospitalisation.

An emergency department visit was deemed to be related to medication use if the presentation was directly related to the presenting chief complaint and could be classified into 1 of 8 predefined drug-related categories: adverse drug reaction, drug interaction, improper drug selection, untreated indication, sub therapeutic dosage, supratherapeutic dosage, nonadherence and drug use without indication.

DEFINITIONS

The World Health Organisation (1970) defines an adverse drug reaction as: "Any response to a drug which is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy".

Causality was determined by both the modified World Health Organization algorithm and the modified algorithm of Naranjo and

associates. An adverse drug-related event was considered to be present if assessment by the World Health Organization algorithm indicated a "certain" or "probable" drug-related event, or if assessment by the Naranjo algorithm indicated a "definite" or "probable" drug related event.^{22,23}

Severity was classified as mild (laboratory abnormality or symptom not requiring treatment), moderate (laboratory abnormality or symptom requiring treatment or admission to hospital or resulting in no permanent disability), severe

(abnormality or symptom that was life-threatening or resulted in permanent disability) or fatal.¹⁸

Drug-related visits were defined as preventable if drug treatment or lack thereof, was inconsistent with current best practice. Such inconsistencies included inappropriate drug, dosage, route or frequency for the patient's clinical condition, age, weight or renal function; known drug allergy or previous reaction to drug; known drug interaction; nonadherence; lack of laboratory monitoring; and prescribing, dispensing or administration errors

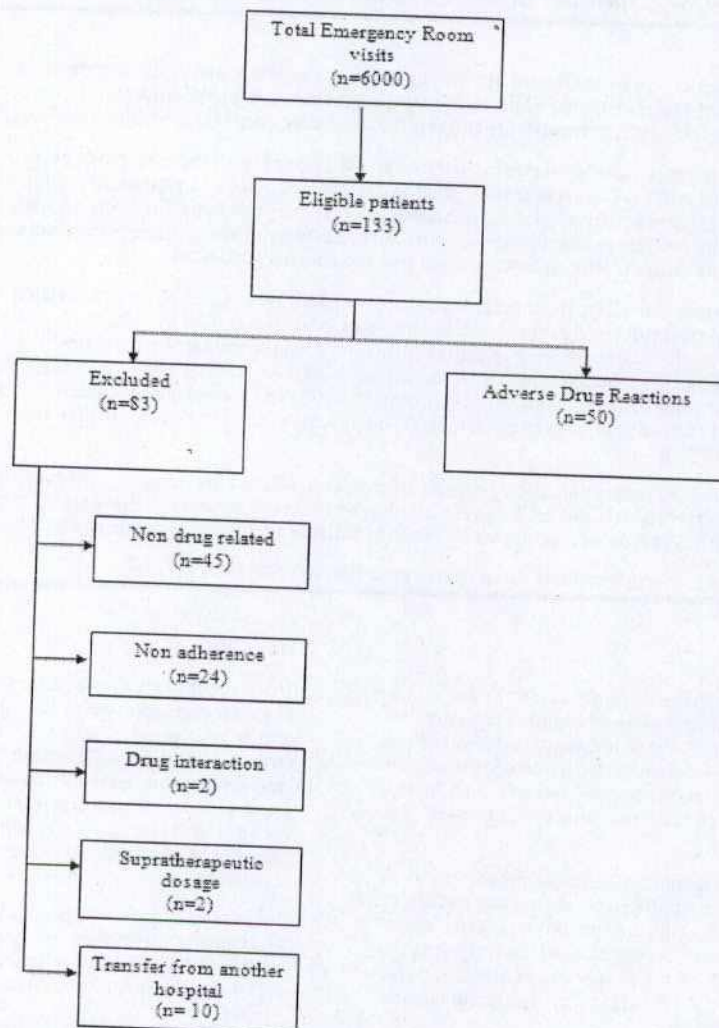


Fig. 1: Patient flow in a study of medication-related visits to the emergency department.

STATISTICAL ANALYSIS

Students 't' test was used to compare the mean number of drugs prescribed between patients whose visit was due to an ADE, and patients whose visit was not due to an ADE. The chi-square test was used to compare the percentage of ADE that occurred between different age groups of patients. A 'p' value of less than 0.05 was considered to be statistically significant. The Statistical Package for the Social Sciences (SPSS) programme was used for analysis.

RESULTS

Among the 133 patients included in the study, the emergency department visit was identified as drug-related adverse reactions for 50 patients (37.59%); of these 9 visits (18%) were deemed preventable. Age distribution of the patients studied showed 60% (n=30) were above the age of 50 years (Table 1).

Table 1: Age distribution of patients studied with adverse drug reaction (n=50)

Age category (yr)	No. of Patients (%)
20-29	5 (10)
30-39	6 (12)
40-49	9 (18)
50-59	9 (18)
60-69	19 (38)
70-79	2 (4)

The most common Adverse events were neuropsychiatric events (n=10 [28.57%]), gastrointestinal reactions (n=13 [37.14%]) and angioedema (n=4 [11.42%]). The most common drug classes involved were NSAID (n=16 [32%]), Glucocorticoids (n=10 [20%]), fluoroquinolones (n=4 [8%]) and Insulin (n=8 [16%]) (Figure 2).

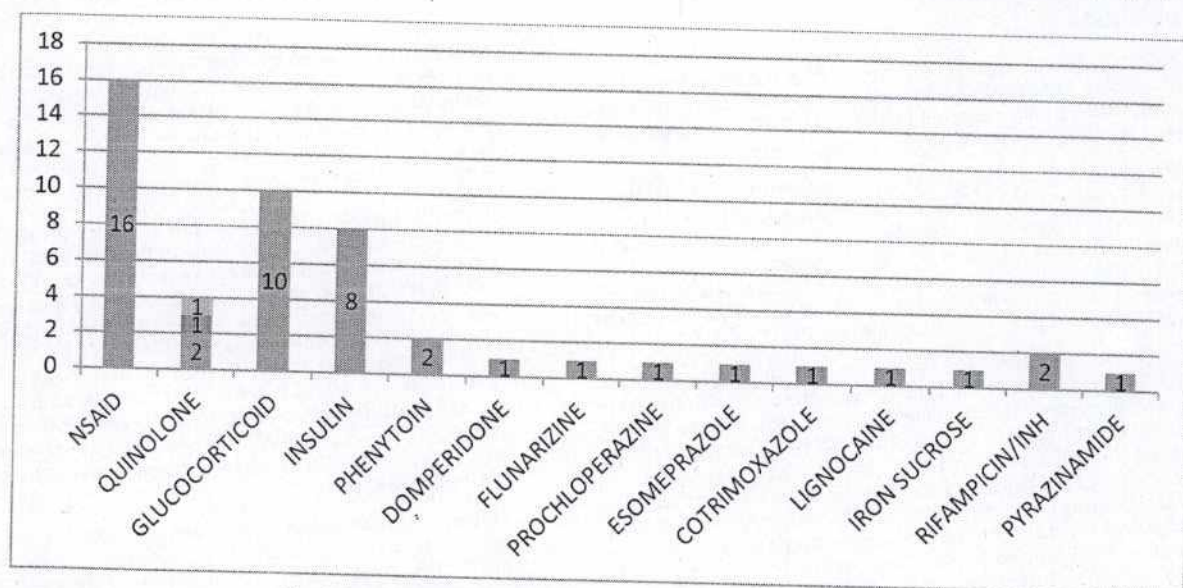


Fig. 2: Common drugs involved that caused adverse drug reactions.

Quinolone - Blue: Ciprofloxacin, Red: Ofloxacin, Green: Gatifloxacin

Gender distribution showed 58% (n=29) were females and 42 % (n=21) were males (Table 2). A patient having one or more co morbidities (p-value 0.0002) has a more chance of developing an ADR (Table 2). A patient going to more than one physician (p

value 0.0124) (Table 2) and pharmacy (p value 0.0002) (Table 2) along with a daily intake of more than two medications (p value <0.0001) (Table 2) has a greater chance of developing an ADR.

Table 2: Demographic characteristics of patients with visits to the emergency department for Adverse drug reactions (n=50)

Sex	No. of Patients (%)
Male	21 (42)
Female	29 (58)
Number of Physician prescribers	
< 1	17 (34)
Greater than 1	33 (66)
Number of Co morbidities by category	
0	26 (52)
1	21 (42)
2	3 (6)
Number of pharmacies	
< 1	8 (16)
Greater than 1	42 (84)
Number of medications by category	
1-3	41 (82)
4-6	9 (18)

Severity was classified as mild in 14%, moderate in 68% and severe in 18% (Table 3) of visits among adverse drug events.

Table 3: Severity - number (N) and percentage of visits among adverse drug events

Mild	Moderate	Severe
N=7	N=34	N=9
14%	68%	18%

The factors associated with adverse drug reaction related visits to the emergency department (Table 4) found in this study were the number of co morbidities a patient has, total number of pharmacy visits, total number of physicians prescribers and total number of medications a patient takes at a given period. Another observation made during this study is that patients usually make multiple visits to the local pharmacy with the same prescription and get the drugs over the counter.

Table 4: Univariable analysis of factors associated with adverse drug reaction related visits to the emergency department

Factor	ADR N=50	Non Drug Related N=45	95% CI	P value
No. of co morbidities, mean (SD)	0.54 (0.61)	0.13 (0.34)	0.2- 0.61	0.0002
Total No. of medications, mean (SD)	2.52 (1.16)	1.13 (0.59)	1.00-1.77	<0.0001
Greater than one Pharmacy	42/50 (0.84)	15/45 (0.33)	0.31-0.93	0.0002
> 1 Physician Prescriber	33/50 (0.66)	19/45 (0.42)	0.14-1.11	0.0124
Age, mean (SD)	50.11 (16.30)	45.56 (17.21)	-2.99 - 12.10	0.2327

DISCUSSION

Amidst increasing reports of adverse drug reactions, the present prospective study tried to determine the same in patients attending a tertiary care teaching hospital in and around kolar. WHO guidelines were strictly applied for classifying adverse drug reactions.

In the present study the emergency department visit was identified as a drug-related adverse reaction for 50 patients (37.59%); of these 9 visits (18%) were deemed preventable. As compared to a previous study by Sanchez Munoz et al, 45% of adverse drug events were detected at the Emergency Department ($n = 72$) and 55% ($n = 88$) were detected during hospitalization. 62.3% of adverse drug events were considered potentially avoidable ($n = 109$)¹⁵.

Sanchez Munoz et al found 38.1% of adverse drug events were serious, 40.0% moderate and 21.9% mild. Drugs most commonly involved in adverse drug events sample studied included: antimicrobials (24.0%), systemic corticoids (15.4%), NSAIDs (11.4%), diuretics (10.3%), digoxin (9.1%), insulin and oral hypoglycaemic agents (5.7%), anticoagulants and heparin (5.7%)¹⁵. In our study we found that 18% of adverse drug events were serious, 68% moderate and 14% mild. Drugs most commonly involved in adverse drug events sample were NSAID's (32%), Glucocorticoids (20%), Quinolones (8%) and Insulin (16%), which probably reflects their widespread use. In another study by Malhotra S et al, Non-steroidal anti-inflammatory agents, oral hypoglycaemic and antitubercular drugs were responsible for 37% of all adverse drug reactions¹⁶.

Age distribution of the patients in our study showed 60% were above the age of 50 years. As compared to a previous study, more than 14% - 28.2% of elderly admissions were due to drugs¹¹⁻¹². Elderly age group patients are at high risk of developing drug related adverse effects because of increased sensitivity to the unintended side effects or adverse drug reactions of medications that could result from incorrect dosing, and their use of more medications. Because of the increasing number of drugs, regimen complexity, continuously changing drug interactions and adverse effects, physician memory can no longer serve as a reliable bridge between research advances and clinical practice. We must remember that "there are no biologically safe drugs; there are only safe physicians"¹³. A study by Fita Rahmawati et al showed that elderly people receive a higher number of prescriptions in hospital and in the community than do younger patients. This research showed of the sampled geriatric hospitalized patients, 36 patients taking more than five drug/day during hospitalization, with range 0.3 - 8.5 drugs per day. Of the 100 selected hospitalized geriatric patients, 66 % were women and their ages range from 60 to 90 years. The majority of patient's ages were between 60-79 years old, with the average age was 71.24 ± 5.87 (\pm SD) with increasing age comes an increasing vulnerability to develop diseases and, in the elderly, the tendency to acquire multiple and chronic diseases. This population therefore is prescribed and uses more drugs than younger populations¹⁹.

In addition there is convincing evidence from the study of Malhotra S et al, showing that the highest percentage of adverse drug events was observed in the age group less than 20 and more than 80 years. Adverse drug reactions accounted for 45% of all drug related visits, followed by patient non-compliance (28%). Patient and physician non-compliance were the main causes of drug-related hospital admissions. 52% of all adverse drug events-related visits and 55% of adverse drug events-related admissions were considered to be preventable. Non-compliance was mainly seen in hypertensives, asthmatics and epileptics¹⁶.

The most common adverse events in the present study were neuropsychiatric events (28.57%), gastrointestinal reactions (37.14%) and angioedema (11.42%). In another study done by Peter J. Zed et al showed that of the types of adverse events leading to the 122 drug related visits, the most common were neuropsychiatric events (15.6%), pain (14.8%) and gastrointestinal reactions (11.5%)¹⁷.

In the present study, we estimated the proportion of drug-related visits to be 1.3 % and the frequency of adverse drug reactions was 1%. In a study by Saha L et al, they estimated the proportion of drug-related visits to be 4.2%¹⁸.

Most studies reviewed by Bhatt AD et al, suggest that a significant percentage of adverse drug reactions are preventable¹³. In our study, 18% of ADRs were preventable. 0.4% of patients who presented to emergency room were due to non adherence. The causes of patient non-adherence were due to a majority of them switching over to alternative systems of medicine.

In a multivariate analysis by Lazarou J et al, only age and the number of medications taken were significantly associated with adverse events. In total, 410 drugs were incriminated in the occurrence of 328 adverse drug events. The most frequently incriminated drug classes were: (i) psychotropic agents ($n=84$; 20.5%); (ii) diuretics ($n=48$; 11.7%), anticoagulants ($n=38$; 9.3%) and other cardiovascular drugs ($n=63$; 15.4%); and (iii) analgesics, including NSAIDs ($n=57$; 13.9%). Preventability could be assessed in 280 of the 328 cases. In 106 cases (37.9%), the adverse drug events was judged to be preventable.¹ Many health care delivery systems, especially in hospitals, could be redesigned to significantly reduce the likelihood of error¹⁴.

In our study we found that several factors can influence the occurrence of an adverse drug reaction including the number of comorbidities, total number of medications at a given period, number of pharmacy's and physicians a patient goes for his or her treatment.

However larger studies with more generalised population are necessary to determine about the frequency, preventability and severity of adverse drug events resulting in emergency department visits.

Many health care delivery systems, especially in hospitals, could be redesigned to significantly reduce the likelihood of error¹⁴. In a study conducted by Bhaskar H et al, 95% of Doctors are not undergone any Drug interaction / Adverse Drug Reaction Training Program. Seventy five percent of Doctors expressed their interest for attending Drug interaction / Adverse Drug Reaction Training. Most of the doctors evaluate the Drug interaction at the time of prescription writing, from memory (42%), book reference (22%) and both (28%). 40% of doctors felt that the ideal method for evaluating Drug interaction is from book reference. 95% of writing their prescription by hand written. 92% of Doctors need a better solution to identify the Drug interaction²⁰.

CONCLUSION

More than 1 in 100 emergency department visits are due to drug-related adverse events, a potentially preventable problem in our health care system. Patients prescribed with more than two drugs and going to more than one pharmacy and physician for treatment have higher risk for developing adverse drug reactions. Physicians should prescribe NSAIDs and glucocorticoids with caution to patients along with adequate counseling regarding adverse drug reactions.

LIMITATION

Our study has a few limitations. Although the team used a standardized approach, bias may have occurred in the determination of whether a visit was drug-related. We attempted to minimize this potential bias through an independent adjudication process. Increased attention to the subject of drug-related visits resulting from this study may have heightened emergency physician's awareness of drug-related issues and introduced a Hawthorne effect. Given the study location, our results are not necessarily projected to the community or paediatric hospitals.

ABBREVIATIONS

ADR - Adverse Drug Reactions

ADE - Adverse Drug Event

DRP- Drug Related Problem

NSAID- Non steroidal anti inflammatory drug

SPSS - Statistical Package for the Social Sciences

Author's contribution

Dr. Jayarama N, Dr. Shiju K Sreeba and Dr. Prabhakar conceived the strategies for the study. Dr. Jayarama supervised the project. Dr. Shiju K Sreeba designed the study, analysed data and wrote the paper. Data was validated by Dr. Prabhakar, and Dr. Jayarama. All authors discussed the results and implications and commented on the manuscript at all stages.

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