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Incidence and Severity Associated With Adverse Drug Reactions in Surgery Inpatients

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Abstract

Aim:
Present study was carried out to assess the incidence of adverse drug reactions (ADR) and assessment of causality and severity associated with reported suspected ADRs.

Materials and Methods:
A prospective cross sectional spontaneous reporting study was conducted over a period of six months in inpatients of Surgery wards of Prince bijaysingh memorial (PBM)Hospital ,Bikaner Rajasthan. Naranjo Probability scale was used for causality assessment. Reported ADRs were classified according to Rawlin and Thomson classification and assessed for severity using scale developed by Hartwig et al.

Results:
A total of 45 suspected Adverse Drug Reactions report forms were reported during the period of 6 months of study in 3565 admitted patients in general surgery wards showing an overall incidence of 1.26%. Gastrointestinal system (51.7%) was most commonly involved. Drug class most commonly associated was Antimicrobials(80.2%). 95.6% of ADRs were classified as "Possible" in view of causality, while 91.2% were found to be "mild" in case of severity. Most patients recovered (66.7%) from the ADR's. 73.3% ADR's were augmented or type A.

Conclusion:
Awareness about ADR reporting is still poor amongst healthcare professionals in India. The incidence and severity of ADRs documented in our study are lower than those reported in other studies. Antibiotics comprise the major drug family associated with ADRs so should be rationally prescribed . Improved communication between the physicians and nurses with the pharmacovigilance centre in the hospital is suggested.

Keywords: Adverse drug reaction, Prospective Spontaneous reporting, Causality, Severity

INTRODUCTION

Drugs are double edged weapons ; they can save life , also can cause adverse drug reactions [ADRs] and are major cause of morbidity and mortality worldwide[1]. ADRs are of great concern to the general public, medical practitioners, pharmaceutical industries and the regulatory authorities[2]. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse drug effects or any other possible drug related problems[3]. India rates below 1% in Pharmacovigilance as against the world rate of 5%[4].

Most of the advanced countries have set up an ADR reporting system at the national level. An ADR reporting programs on an institutional basis can provide valuable information about potential problems in drug usage in that institution. Furthermore, reviewing pooled data from diverse geographic, social and medical population enhances the ability to identify rare events and to generate new signals and thus in setting up a sound Pharmacovigilance system in the country[5] .

The majority of ADR studies have been undertaken in general medical units. A 1982 multi-centre study of surgical patients demonstrated that ADRs were associated with 2.2% of prescriptions, majority of reactions were relatively minor[6]. In a study for search of ADE's in surgical hospitalized patients in Embase and Medline found occurrence of 2- 27.7% per 100 admissions with preventable ADEs of 18-54% [7] . Accurate registration of adverse surgical outcomes is essential to detect areas for improvement of surgical care quality[8].

It is estimated that only 6-10% of all ADRs are reported . ADRs have an economic burden on the patients as well as on the health care establishment,.In India there is absence of vibrant ADR monitoring system and lack of reporting system among health care workers[9]

Pharmacovigilance is carried out in India by the sponsors as part of regulatory requirement and in collaboration with WHO (Uppasala Monitoring Centre,Sweden) as Pharmacovigilance Programme of India (PvPI). The Uppsala Monitoring centre (UMC, WHO), Sweden is maintaining the international database of adverse drug reaction reports[9,10] .Spontaneous reporting of ADRs is a common method of detecting undesirable responses to the drugs Under reporting, is a major drawback[11]

The present study was carried out in department of surgery of Prince bijaysingh memorial (PBM)Hospital ,Bikaner Rajasthan ,a multispecialty tertiary care teaching hospital. The objective of this study was to assess incidence and characteristics of ADRs occurring in the surgery inpatients, causality of drug to these reactions and their severity.

MATERIALS AND METHODS

This is a prospective cross-sectional study to analyse the occurrence of ADRs in hospitalized patients of General surgery at the PBM hospital and an approved pharmacovigilance centre.

All patients admitted in General surgery wards are included in study. 3565 patients were admitted during study period of 6months from March 2014 to August 2014.

Suspected ADRs Reporting forms (downloaded from CDSCO website) were distributed to surgery department personally .It is a structured and pretested format.ADR data was collected by spontaneous reporting. Spontaneous reporting is the core data generating system of international pharmacovigilance, relying on health care professionals to identify and report voluntarily

Approval of the Institutional Human Ethics Committee and permission from the superintendent of the hospital were obtained. Informed consent was obtained from all the patients suspected of ADRs before documentation.Patients with intentional and accidental poisoning and patients with drug abuse were excluded from the study.Prior to the study, there was no organized pharmacovigilance programme in the hospital.Awareness on ADR monitoring was created through clinical meetings with health and allied healthcare professionals of the hospital.The ADRs were defined according to the WHO definition of an ADR.In the suspected cases,past medical/medication history of patients were collected.

Patients were interviewed, monitored daily throughout their hospital stay and their medical records were reviewed. The suspected ADRs were carefully analyzed and documented. All relevant data including all drugs the patients received prior to the onset of the reaction, their respective dosage, route of administration with frequency, date of onset of reaction and the patients' allergy status (to drugs and foods) were noted. In addition the patient medication history and other comorbidities were also identified.

The causality relationship between the ADR and the suspected drug therapy was assessed using the Naranjo probability scale. No rechallenge was attempted in any patient.

The ADRs were classified . The severity of the reaction was determined according to Hartwig *et al.*as given below:

Mild reactions which were self-limiting and able to resolve over time without treatment and did not contribute to prolongation of length of stay.

Moderate ADRs were defined as those that required therapeutic intervention and hospitalization prolonged by 1 day but resolved in <24 h or change in drug therapy or specific treatment to prevent a further outcome.

Severe ADRs were those that were life threatening, producing disability and those that prolonged hospital stay or led to hospitalization, required intensive medical care, or led to the death of the patient.

The most common class of drugs causing ADRs were identified and documented

Patient outcomes were reported as: Fatal,Fully recovered (Patient fully recovered during hospitalization),Recovering (Patient recovering, but not fully recovered during hospitalization),Unknown

RESULTS

A total of 51 cases of suspected adverse adverse drug reactions report form were recorded during the period 6 months of study in 3565admitted patients in general surgery ward. Out of this 6 cases were excluded either because the offending drug was not identified or the data was insufficient to make any analysis. The remaining 45 cases were analyzed as under:

DATA ANALYSIS

Out of 45 patients 20 (44.4%) were male and 25 (55.6%) were female . Maximum patients (42.2%) belonged to the age group of ≥60 followed by 40-59(37.8%) and 20-39 (20%) (table 1,figure1)

Gastrointestinal tract system (GIT) is the most commonly involved system in 51.7% ADR's ,followed by skin(29.3%) then urinary system(5.2%) and in respiratory system 5.2% ADR's found Others (CNS) included 8.6% ADR's(table 2,figure 2)

Ceftriaxone caused highest 16% of the adverse drug reactions, Amoxicillin+clavulinic acid combination caused 13.3% Ceftazidine, Ampicillin and metronidazole caused 11.1% each. Amikacin and ofloxacin caused 6.6% each.Cefotaxime,Diclofenac,Tramadol,Ibuprofen and Lidocaine caused 4.4% ADR's while and Paracetamol caused 2.2% ADR's (table 3,figure 3).

According to Rawlin and Thomson classification out of 45 ADR's ,73.3% were typeA and 26.7% were type B. (table 4 figure 4).Out of 45 ADR's reported 91.2% were mild and 6.6% were moderate and 2.2% severe in severity (table 5 figure 5). Using Naranjo scale 4.4% (n=2) cases rated as probable and 95.6%(n=43) cases reported as possible (table 6,figure 6). Outcome was 33.3% (n=15)of cases were reported recovering,while 66.7 %(n=30) fully recovered(figure7)

TABLE- 1:Sex and age wise distribution of ADRs

Age(years)	Male	Female	Total No. Of ADRs	Percentage (%)
20-39	5	4	9	20
40-59	6	11	17	37.8
≥60	9	10	19	42.2
Total	**20**	**25**	**45**	**100**

TABLE-2 Organ System affected due to ADR's

System affected	Male	Female	Total	Percentage (%)
GIT	14	16	30	51.7
Skin	8	9	17	29.3
Urinary System	1	2	3	5.2
Respiratory system	1	2	3	5.2
CNS	2	3	5	8.6
Total	**26**	**32**	**58**	**100**

TABLE-3 Drugs causing ADR's

Drug	No. Of ADR's	Percentage
Ceftriaxone	7	16
Amoxicillin+Clavulinic acid	6	13.3
Ceftazidine	5	11.1
Ampicillin	5	11.1
Metronidazole	5	11.1
Ofloxacin	3	6.6
Amikacin	3	6.6
cefotaxime	2	4.4
Diclofenac	2	4.4
Tramadol	2	4.4
Ibuprofen	2	4.4
Lidocaine	2	4.4
Paracetamol	1	2.2
Total	**45**	**100**

TABLE-4 Type of reaction (classification according to Rawlin and Thomson)

Category	No. Of ADR's	Percentage (%)
Type A	33	73.3
Type B	12	26.7
Total	45	100

TABLE 5: Level of severity (Hartwig Scale)

Level of severity	No. Of ADR's	Percentage (%)
Mild	41	91.2
Moderate	3	6.6
Severe	1	2.2
Total	**45**	**100**

TABLE-6 Causality analysis (according to Naranjo scale)

Causality Parameters	No. Of ADR's	Percentage (%)
Definite	0	0
Probable	2	4.4
Possible	43	95.6
Unlikely	0	0
Total	**45**	**100**

TABLE-7 OUTCOME

Parameters	No. Of ADR's	Percentage (%)
Fatal	0	0
Recovering	15	33.3
Recovered	30	66.7
Unknown	0	0
Others	0	0
Total	**45**	**100**

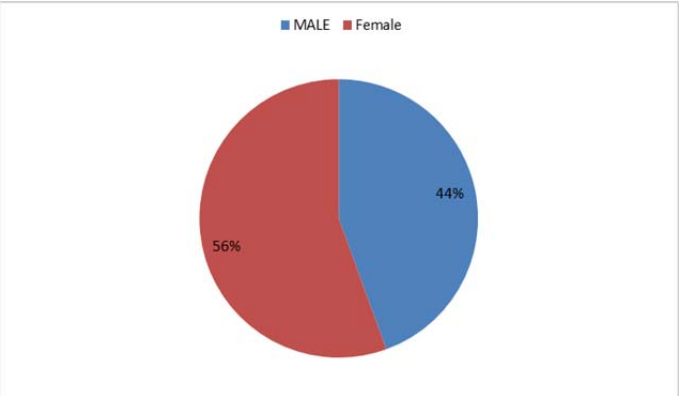


Figure 1--Sex wise distribution of ADRs

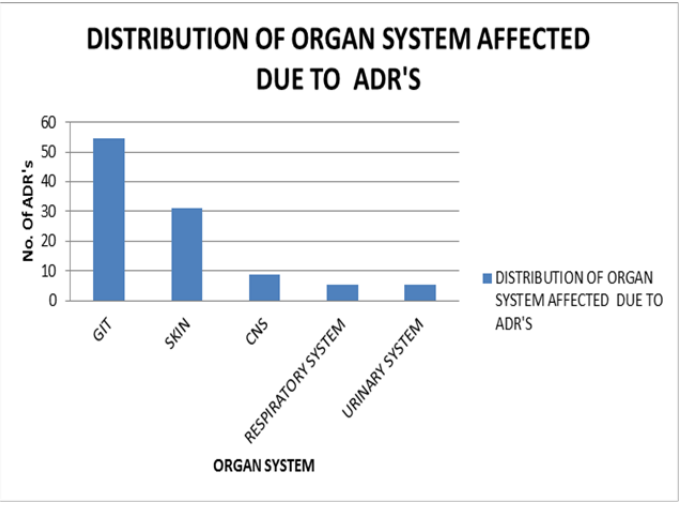
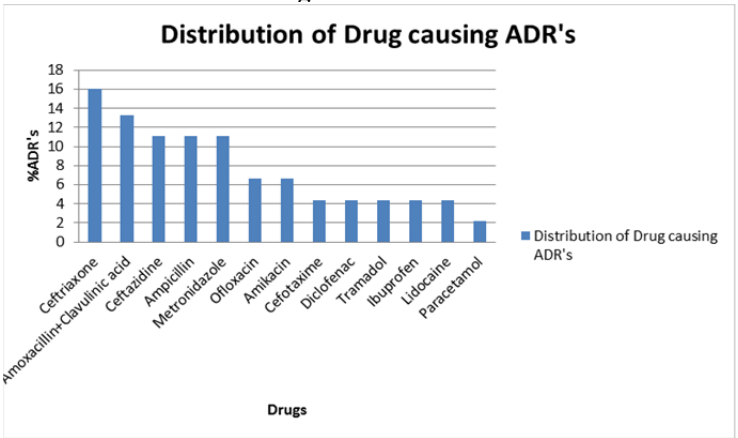


Figure-2



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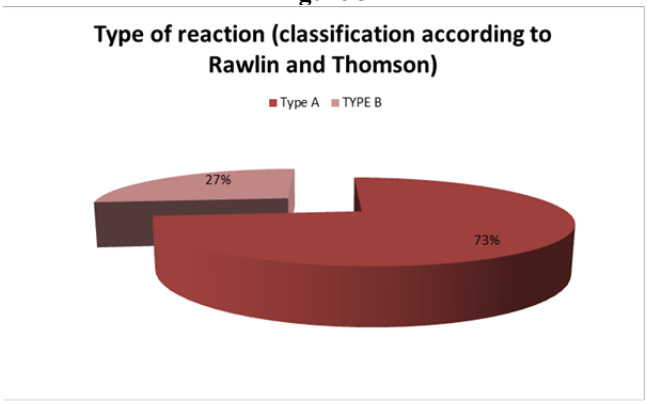

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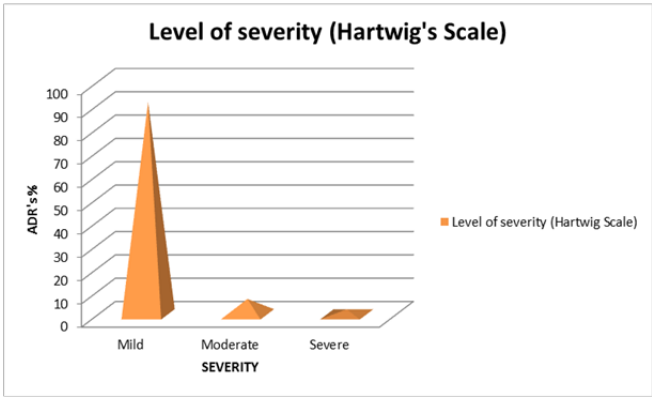

Figure-5

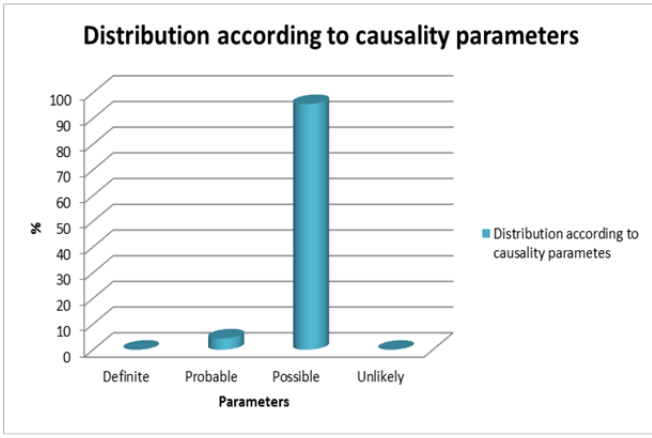

Figure 6

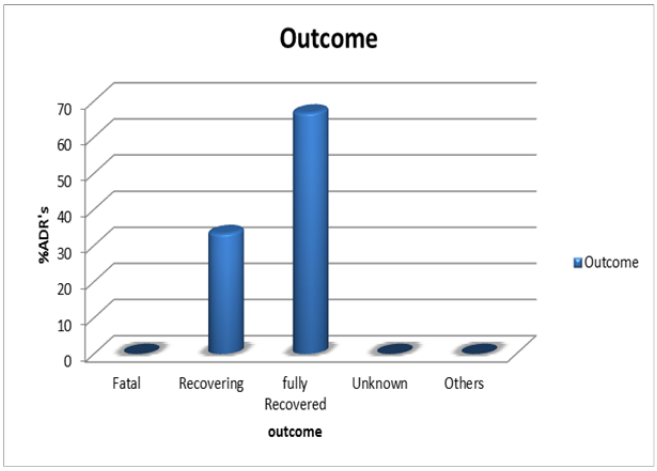

Figure-7

DISCUSSION

Registration of surgical adverse outcomes appears valuable but is largely depending on the reliability of the underlying sources[8].

The number of reports we received were 45 out of 3565 patients admitted , which amounted to an incidence of 1.26 % in our set up In comparison with the study for search of ADE's in surgical hospitalized patients in Embase and Medline found occurrence of 2- 27.7% this can be considered as underreporting[7]. It is a universal problem and many reasons are identified such as busy schedule of clinicians, lack of knowledge about the exact authority to report ADRs to, unavailability ofADR reporting forms, lack of incentives, reporting process being tedious and inadequate expertise . Our verbal discussions with clinicians revealed similar reasons for underreporting in our institution.

The demographic details of our study population showed female gender predominance over males, which was similar to that reported in other studies found in the literature[12,13,]. This might be due to higher emotion quotient in females, which makes them more sensitive to the pharmacological actions of medicines, Rational dose titration may lead to minimization of ADRs in females[14]

Incidence of ADRs was found to be higher in older patients Compromised organ functions, decreased BMR (basal metabolic rate), concomitant disease conditions and multiple drug regimens might be likely reasons for higher incidence[14]

In the study,the drug class most commonly implicated with ADRs was antibiotics . This result is consistent with the study carried out by Murphy *et al*[15]. (1993), Carnasos *et al*[16]. (1974) and Rajesh *et al*[17]. (2008) The documented antibiotic Adverse Drug Reactions are mainly affecting the GIT and skin . The study of Benjamin Horen et al. and Annie also found the predominance of the gastrointestinal system followed by the skin in ADR occurrence (Horen, 2002; Pierre Jonville-Bera, 2002)[18,19]. Four other studies showed the predominane of cutaneous manifestations (Mohammed Misbahet al., 2010; Oshikoya et al., 2007; Jose, 2008)[20,21,22]

The cephalosporins and fluoroquinolones were the most used antibiotic class in the inpatient settings, so that the reported ADRs were also more in these drug classes. A study conducted by Stavreva et al[23]. also revealed the predominance of cephalosporins whereas fluoroquinolones were most accounted in a study conducted by others[20]. Thus implementation of antibiotic guidelines for the hospital scenario and strict adherence should be ensured to promote the rational use.

Analysis of the type of reported ADRs according to Rawlin and Thompson revealed Type A predominance. This result is in line with the study conducted by Oshikoya et al.[21] and Starveva et al[23] . Type A reactions are dose related and thus were preventable from their known pharmacology and therefore all of them were potentially avoidable. Eva states that Type B reactions comprise approximately 10–15% of all ADRs and include hypersensitivity drug reactions (Gomes and Demoly, 2005)[24]. Even though, most of them were moderate reactions, they resulted in an increased health care cost due to an increased length of stay and need of some medical interventions as a result of incidence of Adverse Drug Reactions

Most of the adverse drug reactions are preventable. This calls for the urgent need to reinforce the monitoring of adverse reactions to drugs, public education against self-medication, inclusion of reaction monitoring, and an introduction to drug-safety in the curriculum of medical undergraduates, as well as systemic and periodic medical education of health professionals. This multi-pronged strategy could lead to a reduction in the incidence of adverse drug reaction be assessed in india[25]

CONCLUSION

The reporting rate appeared to be low so there is need for increasing knowledge and awareness. Geriatrics and females were most affected with ADRs. Antimicrobial drugs being mostly affecting class of drugs. There is need for establishing ADR monitoring centre at every multidisciplinary hospital. Also, more original studies need to be conducted in Indian population to know the exact prevalence of ADRs in Indian hospitals.

The pattern of ADRs reported in our hospital is comparable with the results of other studies. It provides a database of ADRs due to common drugs used in our hospital, which will help clinicians for optimum and safe use of these drugs. Hence strict vigilance is required for the use of these likely drugs and their
safety assessment.

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