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Original Research Article

A study of reporting pattern of adverse drug reactions in a tertiary care teaching hospital

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ABSTRACT

Background: Adverse drug reactions (ADRs) are one of the prime causes of morbidity and mortality, increase in hospital stay and socioeconomic burden on the patients. Periodic monitoring aids in formulating methods for safe usage of medicines in hospitals. Identification of ADRs and their reporting pattern can provide useful information for their prevention. Hence this study was done to see the pattern of reported ADRs in Patna Medical College and Hospital, Patna in a 3 months of study.
Methods: It was an observational and retrospective study carried out between July 2022 to September 2022. Both outpatients and inpatients were included in the study. The ADRs in the form of Individual Case Safety Reports (ICSRs) were sent to the nearby adverse drug reaction monitoring centre (AMC).
Results: The occurrence of ADRs was more common in females (56.25%) as compared to males (43.75%). Patients of age-group 21-40 years (40.625%) were most commonly involved. Medicine department (34.375%) reported the maximum percentage of ADRs. Antimicrobials (37.50%) was the most common drug-group causing ADRs. Maximum reported ADRs (81.25%) were probable, 9.375% were possible, 6.25% were certain, while 3.125% were unlikely with the suspected drug as per Naranjo scale.
Conclusions: The pattern of ADRs reported in our hospital is comparable with the results of studies conducted in hospital setup elsewhere, along with a few differences. The study results revealed opportunities for interventions in ADR management especially for the preventable ADRs to ensure safer drug use.

Keywords: Adverse drug reactions, Pharmacovigilance, Individual case safety reports, Health care professionals

INTRODUCTION

An adverse drug reaction has been defined as 'any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug'. This definition excludes trivial or expected side-effects and poisoning or over dose. The drugs which are available for use by millions of populations have undergone trials on only few thousands of volunteers in routine preclinical and clinical trials. When a new drug is released into the market, its real test begins as various co-morbidities throw up important challenges to this molecule. Adverse drug reactions (ADRs) have a major impact on public health. Pharmacovigilance has become a very important tool to analyse these ADRs. Modern medicines have a major impact on quality of life nowadays by reducing morbidity and enhancing the life expectancy associated with a number of diseases. But, inspite of these benefits, adverse drug reactions (ADRs) play a major role in hampering the quality of life of patients and also put an economic burden on patients and society. So, benefits and ADRs are the two sides of the same coin. Across the world,

several studies have reported ADRs during hospital stay ranging from 1.7% to 32.7%, whereas patients admitted with ADRs were between 2.5% and 21.4%. The reported incidence of adverse drug reactions in India ranges from 3.7% to 32.7%.[1] There is a vast difference in disease prevalence, ADR reporting system, drug use pattern and drug management system between developed and developing countries which impacts the frequency of ADRs development and economic burden.[2]

Pharmacovigilance (PV) was officially introduced in December 1961 with the publication of a letter (case report) in the Lancet by Mc Bride et al the Australian doctor who first suspected a causal link between serious fetal deformities (phocomelia) and thalidomide, a drug used during pregnancy. Thalidomide was used as an antiemetic and sedative agent in pregnant women.[3] In 1968 the World Health Organization (WHO) promoted the "programme for international drug monitoring", a pilot project aimed to centralize world data on adverse drug reactions (ADRs). In particular, the main aim of the "WHO Programme" was to identify the earliest possible PV signals. The term PV was proposed in the mid-70s by a French group of pharmacologists and toxicologists to define the activities promoting "The assessment of the risks of side effects potentially associated with drug treatment".[4] PV is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, blood products, herbals, vaccines, medical device, traditional and complementary medicines with a view to identifying new information about hazards associated with products and preventing harm to patients. The challenge of maximizing drug safety and maintaining public confidence has become increasingly complex. Pharmaceutical and biotechnology companies must not only monitor, but also proactively estimate and manage drug risk throughout a product's lifecycle, from development to post-market.[5] Since very few new drugs were discovered in India and hardly any new drug was launched for the first time in India in the past, there was no major compulsion to have a strong PV system to detect ADRs of marketed products. The experience from the markets where the drug was in use for several years before its introduction in India, was used by the companies and the regulatory agencies to assess the safety parameters and take corrective actions, such as the withdrawal or banning of the drug in question. The evolution of a new patent regime in the Indian pharmaceutical and biotechnology industries as a Trade Related Intellectual Property Rights and Services (TRIPS) makes it incumbent upon India to no longer copy patented products and market them without licence from the innovator company. The leading Indian companies, realizing the compulsions of the new regime, have already initiated investments of substantial resources for the discovery and development of new drugs needed for both Indian and International markets. This in turn means that during the coming year, research and development by the Indian pharmaceutical and biotech companies will hopefully lead to new drugs based on pre-clinical and clinical data generated mostly in India. In such cases, the Indian regulatory agencies cannot count on the experience of other markets to assess the incidence and prevalence of importance of a properly designed PV system in India. With the Indian companies' capacity to develop and market new drugs out of their own research efforts, it is important that adequate PV standards are introduced to monitor ADRs of products first launched in India. Looking the importance of pharmacovigilance, a study was conducted on ADRs reported from different clinical departments of Patna Medical College and Hospital, Patna from July 2022 to September 2022.

Aim and objectives

The present study was conducted with the following objectives: to study the demographic distribution of reported ADRs; to assess the frequency of ADRs reported from various clinical departments of Patna medical college and hospital, Patna; to find out drugs most commonly causing ADRs; and to study the causality assessment of reported ADRs.

METHODS

This was an observational, retrospective, non-interventional study of voluntarily reported ADRs forms at Pharmacovigilance unit, department of pharmacology, Patna medical college, Patna from July 2022 to September 2022 over a period of 3 months.

Inclusion and exclusion criteria

All patients of either sex, any age, inpatients, outpatients from all clinical departments with suspected ADRs were included in the study. Patients taking alternative systems of medicines like Ayurveda, Homeopathy, Unani, Siddha, suspected toxicities, over dosage, unconscious and patients unable to respond to verbal questions were excluded from the study.

Procedure

Demography of patient, causative drug, reaction, outcome, and severity were recorded in the central drug standard control organization approved ADR reporting form. Confidentiality of data was maintained. Analysis and evaluation of the reported data done on several parameters viz: Demography of patient: age-group and gender were analysed. Clinical departments reporting ADRs: reported ADRs were analysed for their reporting clinical departments. Suspected medications causing ADRs: the drugs most likely to cause the ADRs were analysed. Causality assessment: done by Naranjo's adverse drug reactions probability scale and classified into definite, probable, possible and doubtful.

RESULTS

Total of 32 cases of suspected ADRs were reported by different clinical departments of PMCH, Patna from July 2022 to September 2022. Out of 32 reported ADRs, 18 ADRs were reported in females and rest 14 were reported in males as shown below (Table 1, Figure 1).

Table 1: Total number of cases according to sex distribution.

Sex	Total number of ADRs reported out of 32	Percentage of total ADRs
Male	14	43.75
Female	18	56.25

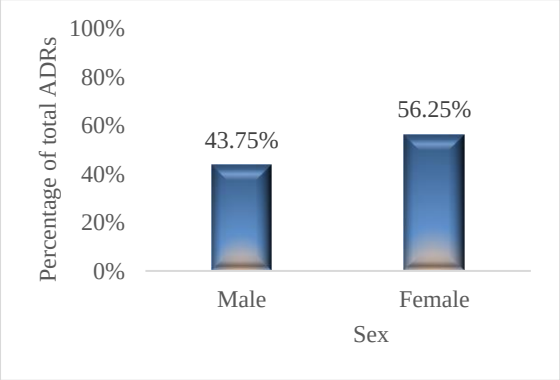

Figure 1: Total number of cases according to sex distribution.

Table 2: Distribution of demographic details and ADRs.

Age group (years)	No. of ADRs (%)	Female (%)	Male (%)
0-20	2 (6.25)	0 (0)	2 (6.25)
21-40	13 (40.625)	6 (18.75)	7 (21.875)
41-60	5 (15.625)	3 (9.375)	2 (6.25)
61-80	12 (37.50)	9 (28.125)	3 (9.375)
>80	0 (0)	0 (0)	0 (0)

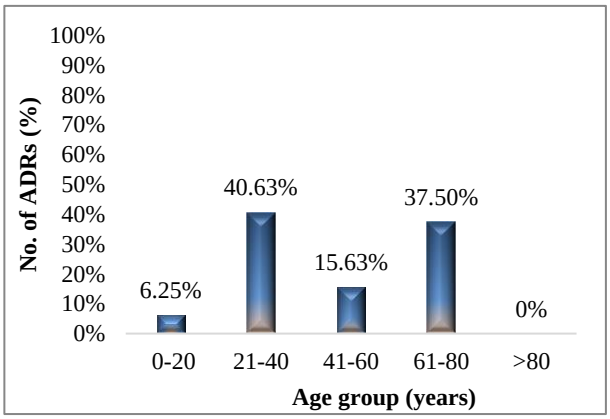

Figure 2: Distribution of demographic details and ADRs.

The patients within the age group 21-40 years were most commonly involved followed by age group 61-80 years. ADRs were very less reported in age-group 0-20 years and >80 years age-group. The distribution of demographic details (age group and gender) and the number of ADRs summarised below (Table 2, Figure 2 and 3).

Medicine department reported the maximum number of ADRs followed by Skin and VD department. Neurology, psychiatry, TB and chest, ophthalmology, urology, orthopaedics and obstetrics & gynaecology department also reported ADRs as shown below (Table 3, Figure 4).

Table 3: Frequency of ADRs reported from different clinical departments.

Department	Number of ADRs reported out of 32	Percentage of total ADRs
Medicine	11	34.375
Skin and VD	10	31.25
Neurology	4	12.50
Psychiatry	2	6.25
TB and Chest	1	3.125
Ophthalmology	1	3.125
Urology	1	3.125
Orthopaedics	1	3.125
Obstetrics & gynaecology	1	3.125

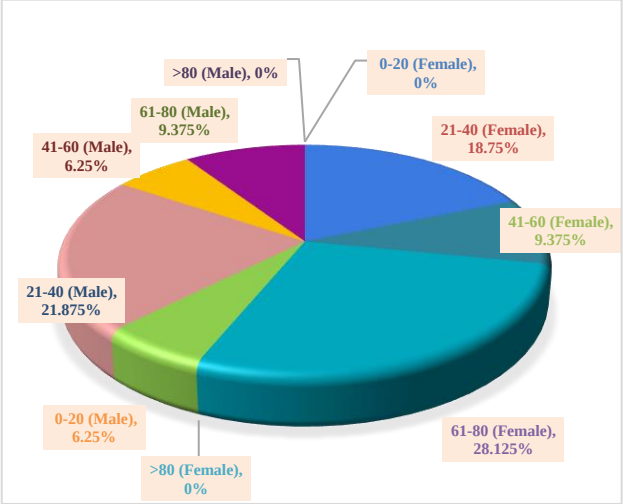

Figure 3: Distribution of reported ADRs as per demographic details.

Maximum ADRs were reported due to antimicrobials followed by drugs acting on CNS as shown in Table 4 and Figure 5. Among antimicrobials, HRZE and cephalosporin group drugs contributed maximum in reported ADRs. Other antimicrobials were metronidazole, amoxicillin & clavulanate, ofloxacin & ornidazole, vancomycin, albendazole and dapsone causing ADRs. The most common drug causing ADR in

the study was paracetamol and HRZE. 3 cases out of 32 cases (9.375%) were due to paracetamol and also 3 cases out of 32 cases (9.375%) were due to HRZE as shown in Table 4 and Figure 6. Majority of the reported ADRs causality assessment by Naranjo scale was probable followed by possible. Very few ADRs having causality assessment certain and doubtful were reported as shown below (Table 5, Figure 7).

Table 4: Different classes of drugs causing ADRs.

Group of drug	Number of ADRs reported out of 32	Percentage of total ADRs
Antimicrobials	12	
HRZE	3	
Ceftriaxone	2	
Cefoperazone	1	
Metronidazole	1	
Amoxicillin & Clavulanate	1	37.50
Ofloxacin & Ornidazole	1	
Vancomycin	1	
Albendazole	1	
Dapsone	1	
CNS drugs	10	
Oxcarbazepine	2	
Levodopa	2	
Gabapentin-NT	2	
Pregabalin-NT	1	31.25
Olanzapine	1	
Chlorpromazine	1	
Phenobarbitone	1	
CVS drugs	4	
Lisinopril	1	
Propranolol	1	
Torsemide & Spironolactone	1	12.50
Tamsulosin Solifenacin	1	
NSAIDs	4	
Paracetamol	3	12.50
Diclofenac	1	
Antidiabetic drugs	1	3.125
Gliclazide	1	
Eye drops	1	3.125
Atropine eye drop	1	

Table 5: Causality assessment of reported ADRs as per Naranjo scale.

Causality assessment	Total number of ADRs reported out of 32	Percentage of total ADRs
Probable	26	81.25
Possible	3	9.375
Certain	2	6.25
Doubtful	1	3.125

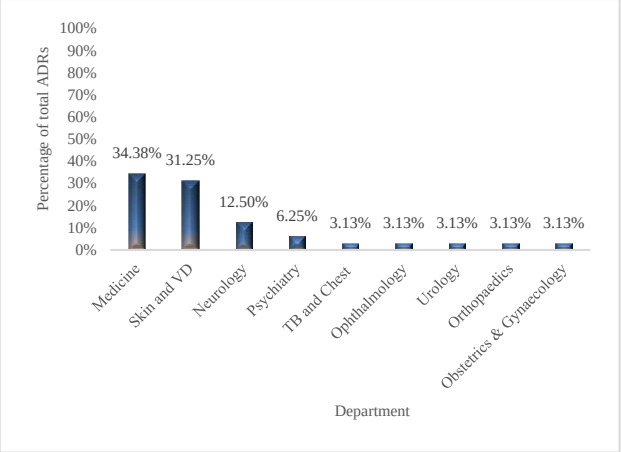

Figure 4: Frequency of ADRs reported from different clinical departments.

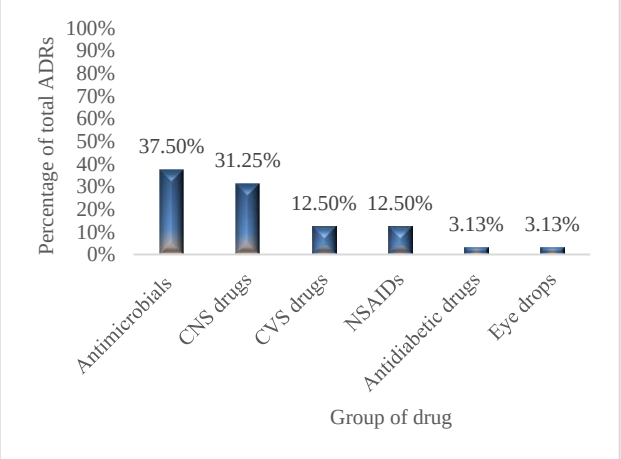

Figure 5: Different classes of drugs causing ADRs.

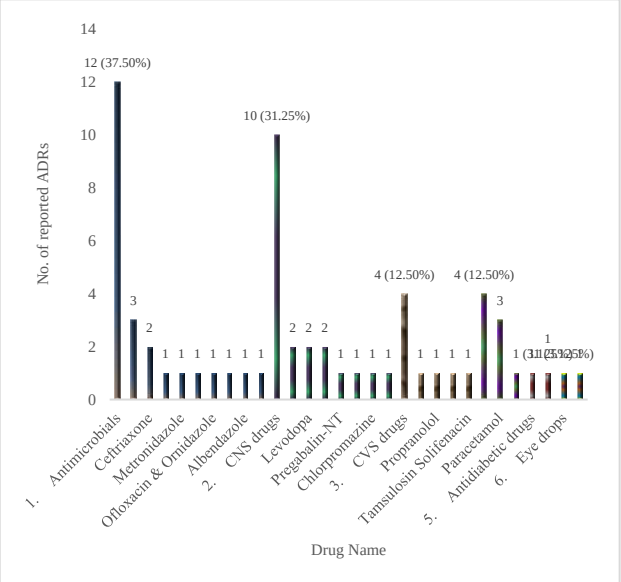

Figure 6: Different drugs causing ADRs.

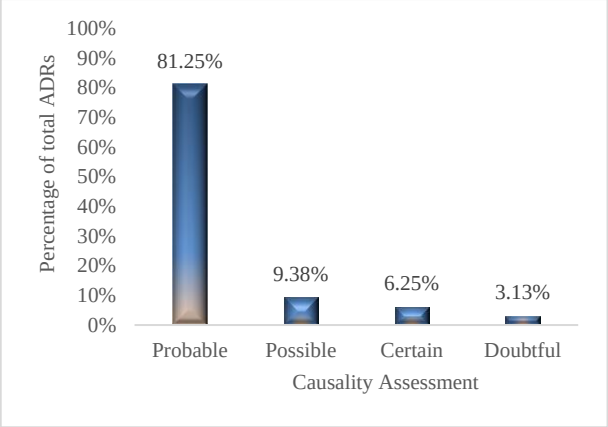

Figure 7: Causality assessment of reported ADRs as per Naranjo scale.

DISCUSSION

In the present study total 32 ADRs were reported over a period of 3 months. All of them were sent to nearby AMC after properly recording in ADR reporting form. In the present study, ADRs occurred slightly more in 18 (56.25%) females than 14 (43.75%) males. This result was in concordance with the results of several previous studies, while few studies also showed male preponderance.[6-11] Women experience adverse reactions more frequently than men do. This finding may be because women and men show different pharmacokinetic and pharmacodynamic responses to drugs. Pharmacokinetic differences arise because of differences in body weight, body mass index, fat composition and liver metabolism. Hormonal changes during puberty, menstruation, menopause and the genomic constitutional differences may also influence the levels of various drug metabolizing enzymes in females. These differences can ultimately influence dosing of drugs with narrow therapeutic index. In addition to these, women take more medications than men and are more likely to experience an adverse event due to drug-drug interactions. Other factor which may predispose to ADRs in general, is the genetic constitution e.g., the HLA type may predispose to reactions to drugs like aspirin and slow N-acetylation phenotype may predispose to sulphonamide reactions. Familial predisposition to antimicrobial drugs has also been reported while the role of atopy in predisposing to drug reactions is controversial.

The patients within the age group 21-40 years (40.625%) were most commonly involved followed by age group 61-80 years (37.50%). This result was somewhat in concordance with some previous studies.[12] Adverse drug reactions have been reported to occur mainly in young and middle-aged adults. Reason could be that the patients of this age group are more prone to diseases, are often on multiple drug therapy and frequently visits the outpatient department for their regular check-ups. Most of the ADRs were reported from medicine department (34.375%) followed by Skin and VD department (31.25%). This result was exactly in concordance with some previous studies.[13-15] While some studies also showed that most commonly ADRs were being reported from Skin and VD department.[12] Antimicrobials (37.50%) was the most common causative drug group in the reported ADRs. This finding was similar to findings of numerous previous studies.[12,16-19] The reason could be that antimicrobials are the most common class of drugs to be used in hospital settings. So, the chances of ADRs being reported due to them are also high. Among antimicrobials, most commonly HRZE and cephalosporin group drugs (Ceftriaxone and Cefoperazone) were reported to cause ADRs. The Naranjo scale was used for assessing causality of reported ADRs. According to this criteria, maximum ADRs (81.25%) were probable, 9.375% were possible, 6.25% were certain, while 3.125% were doubtful with the suspected drug. This result was in concordance with some previous studies.[18,19] The reason for being most of the ADRs under probable or possible causality assessment was due to lack of information provided by patients on causality assessment by Naranjo scale. And also due to many ethical issues rechallenging was hardly done. So, certain association of ADRs with suspected drug was very- very less in the study. In phase-IV clinical trial of drugs, it is responsibility of health care professionals to report the suspected ADRs for better safety of drugs. Sadly, in India very few ADRs are reported and so more sensitization is required in this aspect of pharmacology. A continuing adverse reaction preventive program in a hospital can guide us on the safety of drug therapies, measure the incidence rates, educate and increase awareness amongst healthcare professionals on detection and reporting of adverse reactions.

Limitations

The scope of the present study was grossly limited due to lesser number of total ADRs reported. Also due to various ethical issues, rechallenging was hardly, if ever performed. So, the majority of the ADRs were under probable and possible causality assessment.

CONCLUSION

From our study we concluded that females had more ADRs. Antimicrobials was the most common class of drugs causing ADRs. Medicine department reported the maximum number of ADRs. ADR reporting is a continuous and evolving process. The current study as well as many studies concurrently going on as well as being planned will definitely help to reinforce and suggest ways to better ADR reporting.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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