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Research Article

A CROSS-SECTIONAL PHARMACOVIGILANCE STUDY ON ADVERSE DRUG REACTION IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objectives: This study was conducted to identify and report the adverse drug reactions (ADRs) which are occurring in pediatric and medicine departments in a tertiary care hospital at Vadodara.

Methods: A cross-sectional study was conducted for 6 months in-patient at a tertiary care teaching hospital. We enrolled the patients based on inclusion criteria and data was analyzed with the help of MS excel 7 and Graph pad Prism. Further, the assessments of type, severity, and preventability of reported ADRs were done using Wills and Brown classification, modified Schumock and Thornton severity scale, modified Hartwig and Siegel preventability scale.

Results: Data were collected from a total of two hundred patients of which twenty-six (13%) patients were affected with ADRs. Among twenty-six patients, females (64%) were more affected with ADRs when compared to males (36%). According to the department, most ADRs were observed in the medicine ward than in the pediatric. The highest number of ADRs was associated with antibiotics (46.1%). Based on the type of ADRs, Type B ADRs (77%) were more observed followed by Type A (7%) and Type C (8%).

Conclusions: The information obtained from our study will help clinical pharmacists and healthcare professionals to take precautions in the future and adopt certain measures for preventing the ADRs and hence help in promoting safer and rational drug use in institutions and improving the quality of patient care.

Keywords: Adverse drug reaction, Adverse drug reaction reporting form, Adverse drug reaction incidence, CDSCO reporting form, WHO causality assessment scales.

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INTRODUCTION

The World Health Organization (WHO) defines adverse drug reactions (ADRs) as any response to a drug that is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or the modification of physiologic function. ADRs have been considered as a leading cause of considerable morbidity and mortality. Thus this definition eliminates excessive consumption of drugs (either accidental or intentional), drug abuse, and treatment failure, and drug administration errors [1]. ADRs are considered as the main cause of morbidity and mortality in both hospitalized and ambulatory patients. Hence, there should be awareness in the patients and healthcare professionals about the importance of early detection, evaluation, monitoring, and reporting of ADRs which will help in minimizing the risk to patients and thus improve the health of the public [2].

ADRs are more prone in genetically predisposed individuals acting as risk factors for developing ADRs [3]. Safety and efficacy are the major concerns of healthcare professionals when it comes to rational drug therapy and this is because it is common to find unwanted effects such as adverse reactions and side effects in every drug. Apart from these, drug interactions between different kinds of medications contribute to the added concern of safety and efficacy of drug therapy. To avoid such unwanted effects of drug therapy health care professionals should practice the use of the best and safest medicines according to individual patient requirements [1].

ADR reporting programs encourage surveillance for ADRs, promote the reporting of ADRs, and stimulate the education of health professionals regarding potential ADRs. The data generated from this type of work will further contribute to national and international databases which will further contribute to drug safety by product labeling revision and plan patient education. Therefore, the present work is designed to identify and report the ADRs which are occurring in pediatric and medicine departments in a tertiary care hospital.

METHODS

A cross-sectional study was carried out in a tertiary care teaching Hospital, Vadodara, Gujarat for a period of 6 months (Oct 2019-Mar 2020) to report the ADRs occurring in pediatric and medicine wards. The study protocol was approved by Parul University Institutional Ethics Committee for Human Research in October 2019 (PUIECHR/PIMSR/00/081734/2308). Patients with ADR of any age of either sex, inpatient setup of Paediatric and Medicine department of Parul Sevashram Hospital were included. Patients who are unwilling to take part in the study were excluded. CDSCO form was used for reporting suspected ADRs.

Case records of all the patients were observed and; (1) the demographic details like age, sex, complaints of admission and present illness, medical and medication history, any allergies previously present, (2) habits like a type of diet, smoking, alcohol consumption, (3) laboratory findings such as haemogram, serum biochemistry, blood pressure were obtained from the patients. The informed consent form was designed and explained to the enrolled patients emphasizing the benefits, risk factors of the study as well as outcomes. Data were analyzed with the help of MS excel 7 and Graph pad Prism. Further, the assessments of type, severity and preventability of reported ADRs were done using Wills and Brown classification, modified Schumock and Thornton severity scale, and modified Hartwig and Siegel preventability scale.

RESULTS

ADR was found in a total of 26 patients among 200 inpatient admissions during the study period. The incidence rate was found to be 0.13% and also more common in female patients when compared to male patients.

We observed 9 ADRs in the 46–60 age group followed by 7 ADR in the 0–15 age group then 31–45 as 6 and 16–30 as 4 respectively (Fig. 1). Hence, ADRs were seen more commonly in the age group of older adults. This may be because the number of hospital admissions of geriatrics was more compared to the other two age groups.

ADRs are differentiated according to the department i.e. Pediatric ward and medicine ward. ADRs were found more in the medicine department compared to the pediatric ward, i.e., Out of 26 patients, seven patients were of the pediatric department and 19 patients of medicine ward and the findings were significant *p=0.0352.

According to the treatments given to the ADRs occurred. Out of twenty-six (26) patients; 17 (64%) patient's medication was stopped due to ADR, the addition of a new drug for treating ADR was found to be 1 (4%), in 6 (24%) patients another drug was substituted instead of the drug that is responsible for causing ADR and no change in therapy was seen in 2 (8%) patients, and the findings were significant **p<0.0001 (Fig. 2).

According to the outcomes of ADR treatment; out of 26 patients that had ADR, we found 14 cases of ADR where patients recovered before getting discharged, five cases of recovering, one continuing, and unknowns and the findings were significant *p=0.0128

ADR occurrence is differentiated into two types i.e., ADR which occurred led to hospitalization, ADR occurred after hospitalization. Out of 26 patients, 50% (13) of the population had been presented with ADR after hospitalization while ADR which led to hospitalization were found in 50% (13) of the population.

For assessing causality WHO-ADR Monitoring Centers (AMC) scales were also used. According to the WHO causality assessment, probable and possible ADRs were mostly seen. We found that 13 (52%) and 12 (48%) cases are probable and possible respectively. Most of the ADR found during the study were of the type Probable when compared to Possible, and the findings were significant **p<0.0001.

According to the differentiation of the class of drugs, it was found that the major class of drugs causing ADR was Antibiotics. ADR occurrence in sequence of descending order, Antibiotic (12) followed by Non-Steroidal and Anti-Inflammatory Drugs (5), then multivitamins, steroids and anticonvulsant which was found to be 3 followed by other classes of drugs, and the findings were significant **p<0.0001 (Fig. 3).

In our study, we observed that the dermatology system is majorly affected due to adverse effects. Among 200 patients screened, 17 patients' dermatology systems were affected, i.e., major cases of itching and rash all over the body. Followed by four cases of edema, two cases that affected the ear and mouth, one each case that affected the gastrointestinal system, cardiovascular system, and liver, and the findings were significant** p=0.0015 (Fig. 4).

Assessment of ADRs

Our study observed different types of ADR, which was then stratified based on their types. Out of 26 ADR cases, 17% cases of ADR were of Type A, i.e., Augmented (4 out of 26), 77% cases were of Type B, i.e., Bizarre (20 out of 26) and 8% of cases were of Type C, i.e., Continuous (2 out of 26), and the findings were significant **p=0.0036.

We also assessed the severity of ADR according to Hart-wig and Siegel Severity Scale. In which 16 mild cases, ten moderate cases, and none severe cases of ADR were observed. Hence, most of the ADR caused were mild to moderate, and the findings were significant **p=0.0013.

According to the Schumock and Thornton Preventability scale, we remarked that 18 ADR cases were definitely preventable, five cases were probably preventable and three cases were not preventable. Hence, the outcome of most of the ADR caused was definitely preventable, and the findings were significant *p=0.0138 (Fig. 5).

Table 1: Details of Adverse Drug Reaction caused in hospitalized patients

S. No	Patient details	Adverse reactions	
		Drugs	Reaction
1	KR–2/F	Ceftriaxone, PCM	Rash
2	SP–57/F	Phenytoin, PCM	Itching and rash all over body
3	TB–10/M	Metronidazole, cefixime	Severe diarrhea
4	PP–48/F	Gentamicin, cefuroxime	Steven Johnson syndrome
5	LY–36/M	Spironolactone	Anasarca
6	DD–11 months/F	Asthalin	Itchiness over cheeks
7	CD–60/F	Bisoprolol	Bradicardia
8	NK–53/F	Prednisolone, cefixime	Pemphigus vulgaris
9	SD–19/F	Levofloxacin, hydrocortisone	Itching and rash all over the body
10	DK–5/F	Amoxicillin+clavulanic acid	Itching and rash all over the body
11	KP–35/F	Amoxicillin, dextromethorphan	Rash all over the body and oral cavity
12	RB–40/F	Phenytoin	Viral hepatitis
13	SV–18 months/M	Solvin cold	Itching in whole body
14	SK–18 months/F	OPV and RVV (vaccine)	Fever, rash all over the body
15	IT–2 months/F	Vancomycin, meropenem	Redness all over the body
16	DM–41/F	Streptomycin	Hearing loss
17	RG–40/F	Flurazolidone	Itching all over the body
18	MR–23/M	Diclofenac, PCM	Gingivitis
19	RB–49/M	Phenytoin	Skin lesion and itching over groin region
20	TS–53/M	Amlodipine	Pedal edema
21	RG–21/M	Torsemide B-plex forte, cyanocobalamin	Skin lesions on B/L leg, itching, and eruption on-ear
22	AB–32/F	Ceftriaxone	Angioedema
23	JB–53/F	Atenolol	Itching over body
24	BB–26/F	Ornidazole	Fixed drug reaction over lips
25	LB–58/M	Paracetamol	Fixed drug reaction
26	RK–56/F	Methylprednisolone	Facial puffiness

According to the onset of ADRs, most of the cases were observed after 2 days, i.e., 18 cases of ADR followed by seven cases and one case of ADR observed within 1–24 h and 1 h, respectively.

According to ADR predictability, 77% of ADR was not predictable and 23% of ADR was predictable according to medications prescribed. According to different types of ADR, Type B was not predictable.

DISCUSSION

ADR not only affects the patient's health but also their financial condition. Hence, proper monitoring of ADRs is mandatory. Our study involves the identification, reporting, and monitoring of ADR. According to our study, the incidence rate was found to be 0.13. It may differ across the hospitals, state, and country [4,5].

Our study shows that the incidence rate of ADRs was found to be more for females when compared to males [5]. Our studies also show that older adults between the ages of 46–60 years were found to have a higher frequency of occurring ADRs followed by children, adults, and young adults, respectively. This result depends upon the admission of the age group to the hospital [6]. According to department-wise differentiation, we found that patients admitted in the medicine department were more prone to ADR compared to that of the Paediatric department which is parallel to the study conducted by Shamna *et al*. [2].

Arulmani *et al.* concluded that in 37 patients ADR causing drugs were stopped, in 27 patients ADR causing drugs were substituted with another drug, in 16 patients other drugs were added to treat symptoms, in nine patients dose was decreased and in 32 patients no change in therapy was observed [7]. In our study, we observed 17 patients in which ADR-causing drugs were stopped, six patients in which the offending drug was substituted with another drug, one patient in which other drugs were added to treat symptoms, and in two patients no change was observed.

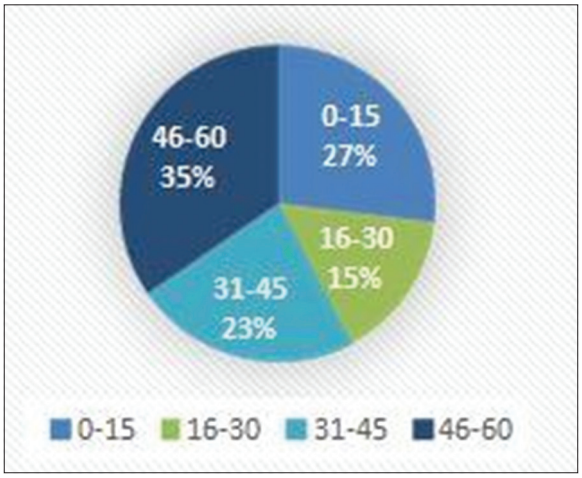

Fig. 1: Adverse drug reaction distribution according to age

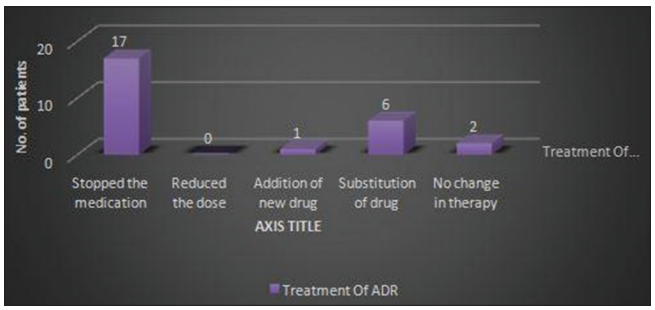

Fig. 2: Differentiation According to the treatment given to adverse drug reactions

Among 26 ADRs the outcomes observed were, 15 cases of recovered ADRs, five cases of recovering, five cases had unknown outcomes, one case is continuing which was consistent with the study done by Arulmani *et al*. None fatal cases were found in both the studies. Both studies concluded that the numbers of recovered cases were found more [7]. According to S. SreAkshayaKalyani *et.al.,* ADR that occurred after hospitalization was more compared to the ADRs that lead to hospitalization [5]. But according to our study the ADR that occurred after hospitalization and ADR that lead to hospitalization are the same.

For assessing causality WHO-AMC scale is used. According to the WHO scale, the results were probable 14 and possibly 12. Here probable cases were more found as compared to the possible. These findings were the same as the study conducted by S. SreAkshayaKalyani *et.al* [5,8-12].

Our study found that antibiotics were the class of drugs more prone to ADRs. This may be due to the wide usage of antibiotics in our study site [3,10]. According to the organ affected analysis, our studies concluded that the dermatology system was more affected by the

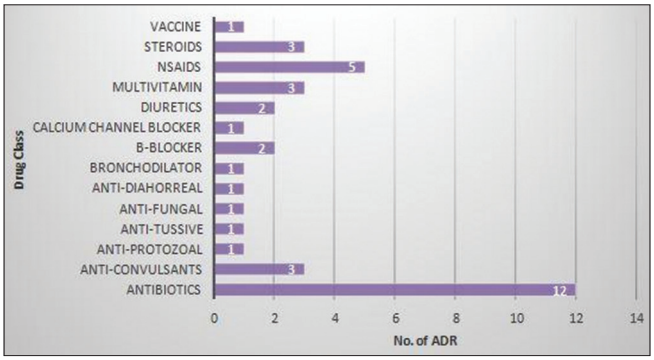

Fig. 3: Differentiation according to the class of drug that caused Adverse drug reaction

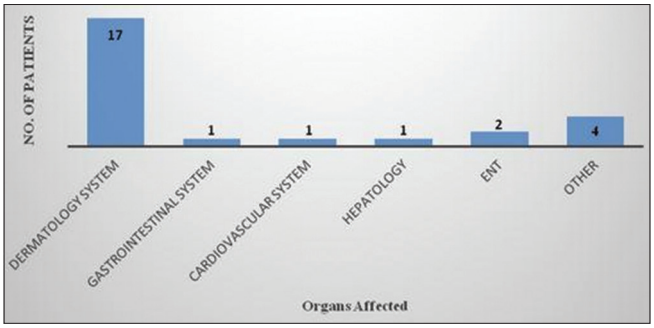

Fig. 4: Differentiation of ADR according to organs affected

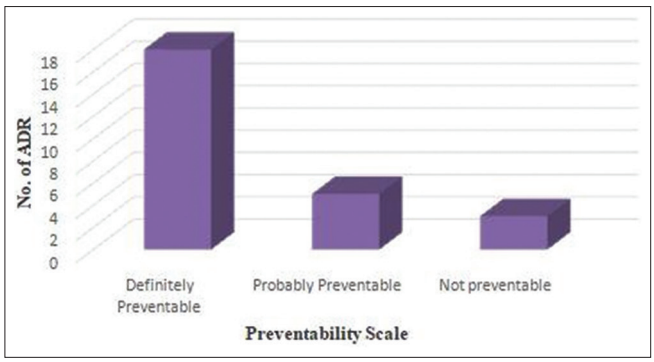

Fig. 5: Differentiation according to Schumock and Thornton preventability scale

ADRs compared to other systems, Skin rash was commonly seen in the dermatology system. Our findings were similar to the study conducted by Kalyani *et al*. [5].

In our studies, we observed four cases of type A reaction (Augmented), 20 cases of type B reaction (bizarre), and two cases of type C reaction (continuous). Type B reactions were more found as compared to type A followed by type c, respectively. Our findings were similar to the study conducted by Venkaraddi *et al*. [4].

Severity was evaluated using Modified Hartwig and Siegel scale. According to our study, we found 16 (61.53%) cases of mild and 10 (38.46%) cases of moderate. No case of severe was observed in our study [8].

To assess the preventability of ADRs we have used the Schumock and Thornton scale. According to our study, 18 (69.23%) cases of ADR were definitely preventable, 5 (19.23%) cases of ADR were probably preventable and 3 (11.53%) cases of ADR not preventable were observed [11,13].

According to our study 6 (23.07%) were predictable and 20 (76.92%) were not predictable. Not predictable was found more in our study as compared to predictable that may be due to hypersensitivity reactions were more observed which belong to type B reaction, i.e., not predictable [9].

CONCLUSIONS

ADRs can occur from any medication and to any person which may also be life-threatening or fatal. ADR is a major concern and there should be continuous monitoring and reporting of ADR, which will help in minimizing the risk of occurrence. The individual effect of drug-related information like age, gender, and hypersensitivity is not observed during clinical trials but can be obtained during post-marketing surveillance.

The information obtained from our study will help clinical pharmacists and healthcare professionals to take precautions in the future and adopt certain measures for avoiding the avoidable ADR and hence help in promoting safer drug use in institutions and improving the quality of patient care.

AUTHORS' CONTRIBUTIONS

The author and the co-authors equally contributed to the study conception and design. Material preparation, result interpretation and analysis were performed by Princy Easow, Olisha Delvita Mendonca, Dhaval Sidhdhapuria and Jitendra Vaghasiya. The author and co-authors have read and approved the final manuscript.

CONFLICTS OF INTEREST

We state that we do not have any conflict of interest.

AUTHORS' FUNDING

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