

ADVERSE DRUG REACTIONS IN PEDIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL IN KOLLAM

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ABSTRACT

Objective: Adverse drug reactions have not been as thoroughly studied in children as they have in adults. Extrapolation of efficacy, dosing regimens, and ADRs from adult data are inappropriate owing to developmental changes in physiology and drug handling. There is a lack of local data regarding the potential risk of ADRs in pediatric patients. Objective of this study is to identify the adverse drug reaction (ADR) profile in pediatric patients.

Methods: In this cross-sectional study, 450 children attending the pediatric inpatient and outpatient department were selected, and the CDSCO reporting form for suspected ADR reporting forms was collected from those who had any adverse events by the consulting pediatrician. Later, this form was analyzed for the details for ADRs and assessed for causality, severity, and preventability using Naranjo's algorithm, Hartwig and Siegel scale, and modified Schumock and Thornton scale of adverse drug reactions.

Results: The cross-sectional study revealed a prevalence of 12.89%. Antibiotics caused more ADRs than any other group of drugs. Dermatological ADRs were the most common. Most ADRs were not preventable and were of moderate severity. The causality assessment showed that most ADRs were possible category.

Conclusion: The ADRs are often unrecognized. We need more strict monitoring for early detection, treatment, and more importantly prevention of these events in the future. For that, more awareness programs, CMEs and teamwork are extremely important among the caregivers.

Keywords: Pediatric ADR, Pharmacovigilance, Adverse drug reaction, ADR monitoring.

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INTRODUCTION

Pharmacovigilance in children requires special attention. Drugs are the mainstay of treatment in pediatric practice, yet a high proportion of drugs has not been tested in children. This leads to irrational prescribing, the use of inappropriate doses, the use of age-inappropriate formulations, which may result in underdosing or overdosing, and drug development without due regard for regular development process of a child. Children are more vulnerable to ADRs as the pharmacokinetics and pharmacodynamics of many commonly used drugs vary significantly in pediatric patients [1]. The joint WHO-UNICEF report of 2006 states: "Children are not small adults when taking a drug." The capacity of absorption, distribution, metabolism, and elimination of a drug is very different between adults and children, and they continue to change during the stage of development [1,2]. The purpose is to identify new information about hazards associated with medicines and preventing harm. In consideration of all these, our objective was to find the proportion of adverse drug reaction (ADR) in pediatric patients in a tertiary care hospital and to assess causality, severity, and preventability of adverse drug reactions using various standard scales.

METHODS

A cross-sectional study was done in the outpatient and inpatient department of Paediatrics, Govt. Medical College, Kollam. All patients of either sex between the ages 0 and 12 years coming as outpatient or who are hospitalized are included in the study. Sample size was determined by the formula $Z\alpha^2 pq / d^2$, and the sample size has been calculated as 384. All consecutive cases attending pediatric OPD and as inpatients till the sample size is satisfied.

After obtaining IRC and IEC approval for the study, CDSCO-ADR reporting form reported by the pediatricians was collected and

analyzed from OPD and IPD. The ADR data were analyzed to find the demographic profile, type of ADR, its severity, frequency of occurrence, drugs implicated, outcome, drug interactions, if any. The causality of ADR was assessed with Naranjo's algorithm scale [3]. The severity of ADRs was assessed by Modified Hartwig and Siegel scale [4]. Examples of ADRs assessed as severe are those that cause death, directly life-threatening, lengthened hospitalization, or entailed shift to a higher level of clinical care. The preventability of ADR was assessed using Modified Schumock and Thornton scale [5].

RESULTS

Prevalence of ADRs

Of the 450 patients studied in pediatric OPD and IPD, we got ADRs in 58 patients. The prevalence of ADR among pediatric patients is 12.89%.

Sociodemographic profile

32.8% of ADRs were reported in children more than 10 years of age as shown in Fig. 1. Mean age was 7.23 years with a SD of 5.28. Among them, 56.9% were males and 43.1% were females.

System affected and ADRs reported

Dermatological system was most commonly affected (44.9%) followed by gastrointestinal system (43.1%). Neurological and circulatory ADRs were also reported in 10.3% and 1.7%, respectively (Fig. 2). Urticaria was the most commonly observed ADR followed by rashes.

Drugs causing ADR

Among the drugs, antibiotics (56.8%) were responsible for majority of ADRs since it was the most commonly prescribed drugs (Table 1). Of this, amoxicillin + clavulanic acid caused most ADRs. NSAIDs came next with a percentage of 19 followed by bronchodilators (5.2%) and antipsychotics (3.4%). About 3.4% ADR were noted for an ayurvedic

preparation (Uramarunnu). Concomitant drug therapy was present for majority of ADRs (56.9%).

Assessment of ADRs

The ADRs reported were assessed using Naranjo's algorithm scale [15] (for causality), Modified Hartwig and Siegel scale (for severity), and Modified Schumock and Thornton scale (preventability). The highest causality of ADRs belonged to category possible (51.7%), followed by probable (46.6%). Definite was only 1.7%. Most of ADRs belonged to a Naranjo score of 2 and 3 (both 31.03%) (Tables 2 and 3).

Considering the preventability, most of the ADRs were not preventable (56.9%), followed by probably preventable (29.3%). Nearly 13.8% of ADRs were definitely preventable (Fig. 3).

About 75.9% of the ADRs was of moderate severity (severity level 3 followed by 4a) followed by 24.1% mild ADRs. No severe ADRs were reported (Table 4 and Fig. 4).

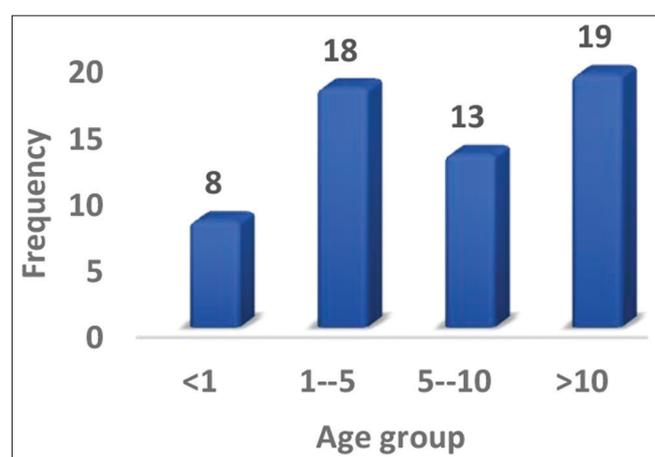


Fig. 1: Age distribution

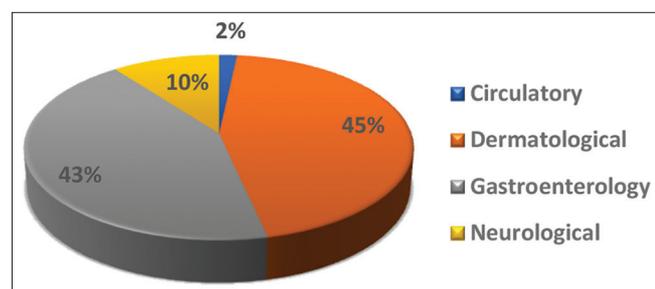


Fig. 2: System-wise distribution of ADRs reported

Table 1: Drugs with most reported ADRs

Drug class	Frequency (n=58)	Percentage
Antacid	1	1.7
Antibiotic	30	51.7
Antibiotic tubercular	2	3.4
Antifungal	1	1.7
Antihistamine	1	1.7
Antipsychotic	2	3.4
Antiulcer	1	1.7
Antiviral	2	3.4
Ayurvedic	2	3.4
Bronchodilator	3	5.2
Decongestant	1	1.7
NSAID	11	19.0
Vaccine	1	1.7

DISCUSSION

Of the 450 patients studied in pediatric OPD and IPD, we got ADRs in 58 patients. Hence, the prevalence of ADR among pediatric patients is 12.89%. The prevalence was low compared to the study by Mandha *et al* [6] and Clavenna *et al* [7]. The tertiary care center where the study was done started only in the year 2016 and is still in the infant stage. Inadequate manpower in all the sectors including doctors, nurses, and pharmacists may have contributed to the low prevalence. Lack of awareness about pharmacovigilance program was also an important reason. Maximum number of ADRs were reported by treating pediatricians followed by nurses.

In the present study, 32.8% of ADRs were reported in children more than 10 years of age. This was in contrast to study by Priyadarsini *et al*. [8] and Khan *et al*. [9]. Among them, 56.9% were males and 43.1% were females.

Dermatological system was most commonly affected (44.9%) followed by gastrointestinal system (43.1%). Neurological and circulatory ADRs were also reported in 10.3% and 1.7%, respectively. This was in accordance with study by Priyadarsini *et al*, Khan *et al*, and Mandha *et al*. Most common ADR reported was urticaria followed by rashes and diarrhea. More ADRs were reported for oral medications compared to parenteral route. This may be due to low admission rate in our hospital due to lack of infrastructure and manpower at that time.

In the present study, antibiotics (56.8%) were responsible for majority of ADRs since it was the most commonly prescribed drugs. Of this, amoxicillin + clavulanic acid caused most ADRs as it was the readily available antibiotic in government supply. Similar results were obtained in studies by Mandha *et al* [6], Shamim M *et al* [10] where beta lactams were the commonest antibiotic causing ADRs. NSAIDs came next with a percentage of 19 followed by bronchodilators (5.2%) and antipsychotics (3.4%). 3.4% ADR were noted for an ayurvedic preparation (Uramarunnu) as a good percentage of population belong to rural area with traditional beliefs. Concomitant drug therapy was present for majority of ADRs (56.9%).

The ADRs reported were assessed using Naranjo's algorithm scale (for causality), Modified Hartwig and Siegel scale (for severity), and

Table 2: Causality assessment

Causality	Frequency	Percentage
Definite	1	1.7
Possible	30	51.7
Probable	27	46.6
Total	58	100.0

Table 3: Naranjo scores of the ADR reported

Naranjo score	Frequency	Percentage
2	18	31.03
3	18	31.03
4	10	17.24
5	7	12.07
6	2	3.45
7	2	3.45
9	1	1.72
Total	58	100.0

Table 4: Analysis of ADRs based on severity

Severity	Frequency	Percentage
Mild	14	24.1
Moderate	44	75.9
Total	58	100.0

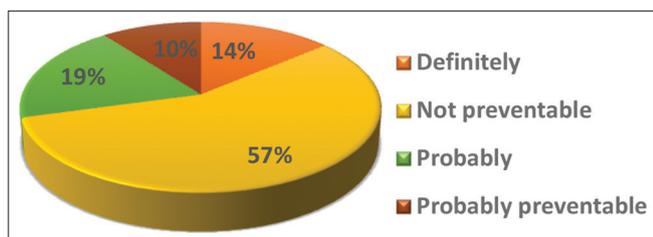


Fig. 3: Preventability criteria

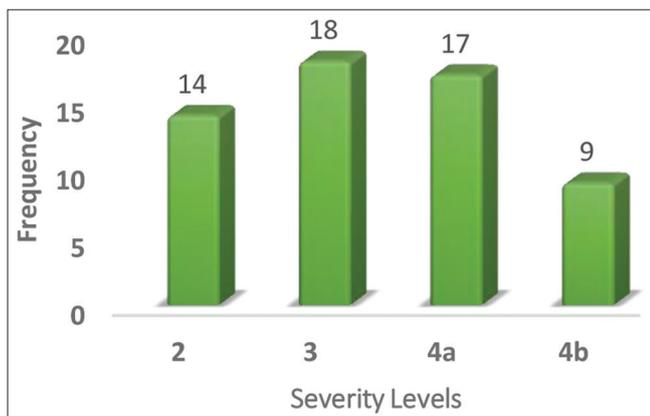


Fig. 4: Severity levels of ADRs reported

Modified Schumock and Thornton scale (preventability). The highest causality scores of ADRs were possible (51.7%), followed by probable (46.6%). Definite was only 1.7%. Most of ADRs belonged to a Naranjo score of 2 and 3 (both 31.03%) Considering the preventability, most of the ADRs were not preventable (56.9%), followed by probably preventable (29.3%). About 13.8% of ADRs were definitely preventable. Almost 75.9% of the ADRs were of moderate severity (severity level 3 followed by 4a) followed by 24.1% mild ADRs. No severe ADRs were reported. Severe ADRs are generally not observed and are rare in recent studies also [5,6,10]. This was in accordance with study by Mandha *et al.* and Digra *et al.* [13].

CONCLUSION

The joint WHO-UNICEF report of 2006 states: "Children are not small adults when taking a drug." ADRs are one of the major causes of iatrogenic diseases which are often unrecognized and underreported. In the study, majority of ADRs were reported among children more than 10 years. Antibiotics contributed more to the ADRs followed by NSAIDs. Most of the reactions were of moderate severity. This stipulates the need for regular and strict ADR monitoring among children to ensure the safety of drug therapy. Family pediatricians can play very important role in reporting suspected ADRs in harmony with pharmacovigilance projects. Risk management programs along with active observation will help to plan effective steps in the future reducing risks for the community [3]. Pharmacovigilance awareness programs should be conducted among various levels of health-care professionals to enhance the impact of understanding and spontaneous reporting of ADRs [14].

AUTHORS CONTRIBUTION

The study design and concept were done by Dr. Reeja R and Dr. Beena JS. And Dr. Reeja R wrote the paper, performed data collection, performed data analysis, drafted the manuscript, and contributed to the final manuscript. Dr. Beena JS cowrote the paper, drafted the manuscript, and contributed to the final manuscript. Dr. Ajithkrishnan AS helped in data collection and made it feasible. Dr. Bindulatha Nair R supervised the research and contributed to the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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