

Research Article



Drug-Related Problems and Their Preventability among Admitted Patients in Paediatrics Department of a Tertiary Care Institute from Eastern India - A Prospective Study

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ABSTRACT

Patients with different manifestations and different diagnoses are admitted in Paediatric department. In admitted cases, drug therapy usually consists of multiple drugs including antibiotics, anticoagulants, glucocorticoids, antihypertensive, anti-diabetics, etc. Due to the prescription of multiple drugs, the chance of drug interactions is high. Early detection of DRP can help prevent any harm to patients. It is therefore possible to thoroughly evaluate various drug-related problems and prevent some of them in the paediatric inpatient department. The aim was to find out the drug-related problems during management of patients under paediatric department, to find out the magnitude and preventability. In addition, we hoped to provide insights into the DRPs encountered among hospitalized paediatric patients that can help in finding the appropriate solutions. All children's medical records were identified, collected and analyzed by trained clinical pharmacologists to identify DRP according to the well recognized and appropriate criteria system established by the Pharmaceutical Care Network Europe (PCNE). For standardization, patient demographics (age, gender, location and diagnosis) were recorded using WHO ICD version. Drugs were grouped into different categories using the Anatomic Therapeutic Chemical (ATC) classification (WHO-ATC). Descriptive analysis was done to summarize the findings of this study. Of 534 patients, 193 patients (36.1%, 193/534) had at least one DRP. A total of 262 DRPs were identified in 193 patients, of which 230 DRPs (87.8%, 230/262) were considered preventable. The vast majority of DRPs were related to dose selection (74.78%, 172/230). The second most common cause was related to drug choice (23.04%, 53/230) and drug use (2.5%, 5/280). We found that an increase in the number of drugs also increases the chances of having DRP by 1.31 times (95% CI, 0.89 to 1.81, P=0.00005). There is high incidence of preventable drug related problems which is generally ignored if not thoroughly investigated. Most of the DRPs are associated with dosing and drug choice problems.

Keywords: Paediatric, Prescription, Drug Related Problem, Medication Error, Adverse Drug Reaction.

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INTRODUCTION

Drug-related problems (DRPs) are generally defined as “an event or circumstance that involves drug therapy that interferes or has potential to interfere with desired health outcomes”.¹ The term DRP comprises medication errors (MEs), adverse drug events (ADEs) and adverse drug reactions (ADRs). An ME is any event that is preventable and may cause or lead to inappropriate use of medicine or patient harm while the medication is in the control of the healthcare professional, patient or consumer.² An ADE can be defined as an injury that may be or not causally related to the use of a drug.³ ADRs can

be defined as “any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of diseases, or for the modification of physiological functions”.⁴

Based on the definition of MEs and DRPs, DRPs are most likely to be related to MEs. Studies on DRP in the paediatric population are limited. Results from the Harvard Medical Practice Study showed that nearly 4% of long-term hospitalization patients were caused by medical injuries, and nearly 70% of identified medical injuries were the result of preventable errors.^{5,6} Drug use complications were found to be the most frequently identified medical injuries, which accounted for 19.4%.⁷ Nearly 80% of identified ADEs occurred at the drug ordering stage, with 34% related to incorrect dosing.⁸ Several studies have found that paediatric hospital admissions and emergency room visits secondary to DRP are more common in children than in adults.^{9,10}

Prescribing a drug for children is considered a challenging process for all health care professionals and represents an



economic burden for the health care system.¹¹ A recent systematic review that investigated the incidence and preventability of DRPs associated with re-hospitalization showed mixed results. They have found that, in 5–87% of cases (median 69%, IQR 19–84%), readmission was preventable with a median drug readmission rate of 21% (IQR 14–23%). Due to the limited number of included studies that investigated on preventability, the authors stated that "a precise estimate of the proportion of preventable drug-related readmissions is impossible".¹²

Patients with different manifestations and different diagnoses are admitted in Paediatric department. In admitted cases, drug therapy usually consists of multiple drugs including antibiotics, anticoagulants, glucocorticoids, antihypertensive, anti-diabetics, etc. Many of them have a low therapeutic index. Due to the prescription of multiple drugs, the chance of drug interactions is high. Early detection of DRP can help prevent any harm to patients. It is therefore possible to thoroughly evaluate various drug-related problems and prevent some of them in the paediatric inpatient department.

Case reports and a few studies of such evaluation are published. However, reports of any thorough prospective evaluation of DRPs in admitted patients under Paediatrics are scarce from this part of the world.

There might be various categories of drug-related problems related to management of admitted patients in IPD of Paediatrics in a tertiary care hospital. There are preventable drug-related problems which can be found early after regular analysis of the chart order (prescription for admitted patients) and appropriate preventive measures can be taken.

Therefore, we plan to undertake the current study for analysis of the drug related problems in admitted patients under Department of Paediatrics at our centre which is a reputed tertiary care medical college and hospital in Eastern India.

The aim was to find out the drug-related problems during management of patients under paediatric department, to find out the magnitude and preventability. In addition, we hoped to provide insights into the DRPs encountered among hospitalized paediatric patients that can help in finding the appropriate solutions.

MATERIALS AND METHODS

Ethical Approval

Informed consent was obtained from the parent or legal guardian of all patients after providing them written informed consent and patient information sheet to participate in this research, in accordance with the Good Clinical Practice and Declaration of Helsinki. This study was approved in October 2021 by the Institutional Ethics Committee.

Study Design

A prospective observational study was conducted at a tertiary care institute of eastern India. We used the same chart review method for data collection that was proposed by Ghaleb et al¹³ and Dean et al.¹⁴ to study ME to address preventable adverse drug reactions in children. Patients recruited in our study were children aged ≤ 15 years who were admitted in emergency ward, paediatric surgery department, paediatric medical department, paediatric intensive care unit (PICU) and neonatal intensive care unit (NICU). Patients admitted to the paediatric oncology department were excluded. Data collection was done over a period of 6 months (January 01 to June 30, 2022). Study participants were classified into five age groups adjusted according to the guidelines of the International Conference on Harmonization E11 as follows: ≤ 1 month; >1 month to ≤ 2 years; >2 to ≤ 6 years; >6 to ≤ 12 years; and >12 to ≤ 15 years.¹⁵

Data Collection

All children's medical records were identified, collected and analyzed by trained clinical pharmacologists to identify DRP according to the well-recognized and appropriate criteria system established by the Pharmaceutical Care Network Europe (PCNE).¹⁶ For standardization, patient demographics (age, gender, location and diagnosis) were recorded using WHO ICD version.^{10,17} Drug table was prepared with the number and type of drugs. Drugs were grouped into different categories using the Anatomic Therapeutic Chemical (ATC) classification (WHO-ATC).¹⁸

As per the protocol of this study and standard guidelines, if the identified DRPs were due to errors in the medication use process such as during prescribing, dispensing, administering or monitoring, it was then classified as a medication error (Preventable DRP). Consensus discussion and mutual agreement within the group of clinical pharmacologists was sought in order to reach a final decision about validation of DRPs. Subsequently, each DRP case was reviewed and analysed independently by two members of the group to check preventability using the criteria provided by Schumock and Thornton (1992).¹⁹

Classification of DRPs

The PCNE system is well structured and most recognised with various domains and has distinct protocols for drug related problems, their causes, and potential interventions. On this background, the PCNE classification system (Version 9.1) was utilized for the definition and classification of DRPs.¹⁶

Statistical Analysis

A descriptive analysis was done to summarize the findings of this study and for describing the characteristics of the study population based on age, gender, diagnosis, and medication class using WHO-ATC. Data were collected and summarised using Microsoft Excel 365 and presented in the form of number, percentage, median, and inter-quartile range (IQR). The rates of DRPs were calculated by



dividing the number of patients who experienced at least one preventable DRP by the total number of study participants. Bivariate analysis was done using chi-square and *t*-statistic test for determining the association of DRPs' occurrence with number of medications. The result obtained from above analysis was reported as odds ratio (OR). Any P value of less than 0.05 was taken to be statistically significant. Statistical analysis was done using the SPSS software.

RESULTS

A total of 534 paediatric patients were monitored during the study period (January 1 to June 30, 2022). Of these 534 patients, 193 patients (36.1%, 193/534) had at least one DRP and were thus included in the study. The male (n=112) to female (n=81) ratio was 1.38 to 1 with a median age of 1.5 years, IQR (6 months to 6 years). A total of 1018 medications were recorded during the observation periods as follows: a total of 153 medications were administered

to 53 patients identified as having less than 5 prescription medications, 736 medications were administered to 129 patients who received 5 to 10 medications on their prescription, and 129 medications were noted in 11 patients who received more than 10 prescription drugs. The largest age group included was more than a month to less than 2 years. Table 1 provides details of patient characteristics.

Total Diseases Associated with Identified DRPs

The number of patients with at least one DRP was 193. Using the WHO-ICD 10 classifications for disease diagnoses, a total of 23 different diagnoses were identified in 193 patients, with respiratory system diseases (pneumonia and bronchiolitis) being the most frequently reported diseases, followed by infectious diseases (sepsis, upper respiratory tract infection, urinary tract infection, wound infection). Figure 1 shows the recorded frequency of disease in 193 patients with DRP.

Table 1: Patients characteristics

Parameters	Emergency Ward n=40	Paediatric Surgery Ward n=51	Paediatric Medicine Ward n=62	PICU n=18	NICU n=22	Total N=193
Age						
0-1 month	1	3	3	4	10	21
>1 month to ≤ 2 years	24	14	29	13	12	92
>2 years to ≤ 6 years	8	19	14	0	0	41
>6 years to ≤ 12 years	6	13	15	1	0	35
>12 years to 15 years	1	2	1	0	0	4
Gender						
Male	25	29	34	11	13	112
Female	15	22	28	7	9	81
Number of Prescribed Drugs per Patient						
<5	20	13	12	0	8	53
5-10	19	35	46	15	14	129
>10	1	3	4	3	0	11

n - number of included patients with DRPs per study area; N - total number of patients with DRPs.

Table 2: Frequency of Detected Preventable DRPs

	Emergency Ward n=39	Paediatric Surgery Ward n=63	Paediatric Medicine Ward n=76	PICU n=25	NICU n=27	Total N=230
Age						
0-1 month	1	3	3	1	11	19
>1 month to ≤ 2 years	25	16	36	18	16	111
>2 years to ≤ 6 years	6	25	16	0	0	47
>6 years to ≤ 12 years	5	18	16	6	0	45
>12 years to 15 years	2	1	5	0	0	8
Gender						
Male	21	38	41	15	21	136
Female	18	25	35	10	6	94



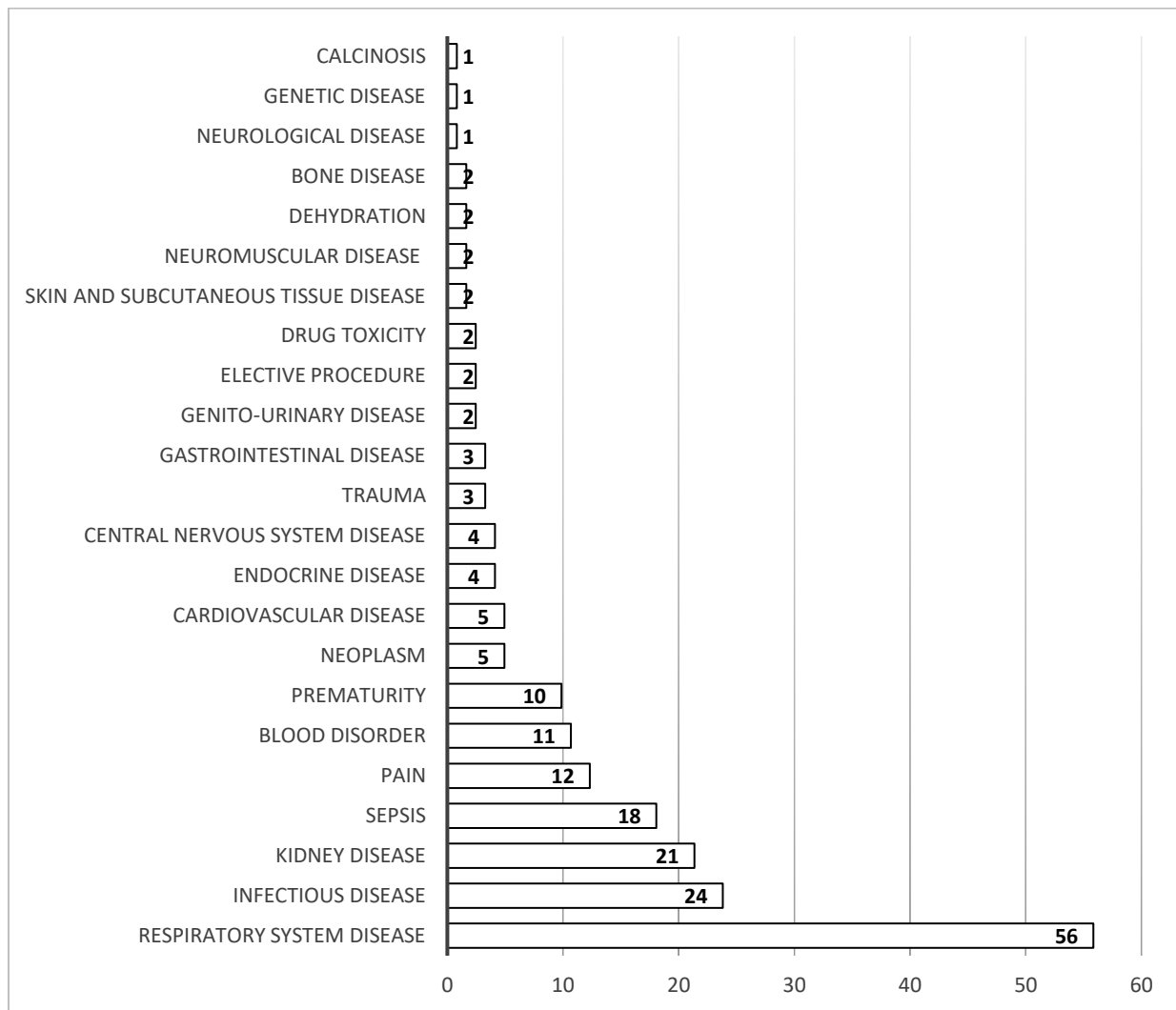


Figure 1: Frequency of 223 disease systems recorded in 193 patients with DRPs.

Incidence of Preventable DRPs

A total of 262 DRPs were identified in 193 patients, of which 230 DRPs (87.8%, 230/262) were considered preventable. The incidence of preventable DRPs of the identified total DRPs per study area was 76 preventable DRPs in the medical department (33.0%, 92/319), followed by 63 in the surgical department (27.4%, 77/230), 39 in the ED (17, 0%, 48/230), 27 in the NICU (11.7%, 33/230) and 25 in the PICU (10.9%, 30/230) in which one child may contribute to more than one DRP that can be prevent. Table 2 details the frequency of preventable DRPs in each study area.

Drug Classes Involved with the Occurrence of Preventable DRPs

Using the WHO-ATC classification system for medication, nine drug groups matching with ATC anatomical group (1st level) were reported. The most often drug groups involved in the preventable DRPs were “anti-infective agent for systemic use” (J), followed by “drug related to blood and blood forming organs” (B), and “drug related to alimentary tract and metabolism” (A). Table 3 provides details of the most frequently found ATC anatomical group with preventable DRPs.

Table 3: Drug classes involved with the occurrence of preventable DRPs

ATC Code	Drug Groups	Frequency (N=230)	Percentage
A	Alimentary tract and metabolism	57	24.78
B	Blood and blood forming organs	57	24.78
C	Cardiovascular system	2	0.87
H	Systemic hormonal preparations	4	1.74
J	Anti-infective for systemic use	75	32.61
L	Antineoplastic and immune-modulating agents	2	0.87
M	Musculoskeletal system	9	3.91
N	Nervous system	16	6.96
R	Respiratory system	7	3.04



Epidemiology of DRPs

Overall, three main causes were reported for the 280 preventable DRPs identified. The vast majority of DRPs were related to dose selection (74.78%, 172/230). The second most common cause was related to drug choice (23.04%, 53/230) and drug use (2.5%, 5/280). Table 4 summarizes the categories and most commonly reported preventable causes of DRPs by PCNE classification.

Table 4: Frequency of identified preventable DRPs according to PCNE classification

DRPs Category (% , n/N)	Classification	Incidence	Percentage
Dosing problems (74.78%, 172/230)	Dose too low	135	58.70
	Dose too high	37	16.09
Drug choice problems (23.04 %, 53/230)	Duplication of Drug	1	0.43
	No clear indication	20	8.70
	Contraindication	5	2.17
	Inappropriate Drug	25	10.87
	Drug interaction	2	0.87
Drug use problems (2.17%, 5/230)	Therapy duration too long	2	0.87
	Inadequate drug monitoring	1	0.43
	Drug omission	2	0.87

We found that an increase in the number of drugs also increases the chances of having DRPs by 1.31 times (95% CI, 0.89 to 1.81, P=0.00005).

DRPs' Severity

None of the identified preventable DRPs was life-threatening or fatal. The majority of preventable DRPs were assessed as moderate in severity (90.86 %, 209/230), minor (8.70 %, 20/230), and severe (0.43%, 1/230).

DISCUSSION

The result of our study showed that a significant number of preventable DRPs were reported from the hospitalized children. The number of patients who experienced at least one DRP was 193. 262 DRPs were recorded among them. The overall incidence of drug related problem was 49.06% (262/534). The preventability rate of all identified DRPs was 87.8% (230/262), which alerts a safety concern. The high incidence of preventable DRPs in our study was similar to that reported in the Hong Kong study (51.2%).²⁰

The medical ward was identified to have the highest recorded number of preventable DRPs (76/230, 33.04%) as compared to other paediatric wards. Overall, the most frequent reported cause and type of preventable DRPs in

paediatric wards was dosing problems 74.78% (172/230), which is comparable with findings from previously published studies that looked at DRPs in paediatric patients at ward level and in emergency departments.^{21,22} Several study results have shown that most DRPs were associated with inappropriate drug selection, drug dosage, and dosing interval.^{23,24} Similarly, dosing problems were the most frequently found cause of preventable DRPs in each paediatric ward. A standardized medication dosing guide has been used as a strategy to eliminate medication dosing errors in children attending the emergency department.²⁵

The current study results showed a high incidence of DRPs that was due to drug dosing problems in children, which could be attributed to several factors. Increasing the number of medications prescribed, patients admitted for longer periods of time, or patients admitted to the emergency department were those more likely to receive inappropriate doses and use different dosing regimens of drugs. Other factors that we observed but were not adequately analyzed in our study include nursing staff unfamiliarity with drug dosing in the paediatric population (newly recruited nursing staff, new residents, or interns), different work shifts (duty in off-hours, night, evening, weekend occupancy, various rotating residents and interns) – were found to be causative factors of DRPs. We believed that the lack of specific paediatric CCDS (Computerized Clinical Decision Support) dosing in the institution's CPOE (Computerized Physician Order Entry) system was a major contributing factor to the high frequency of preventable drug dosing errors associated with DRPs that was preventable. Well-trained clinical pharmacologists and the active participation of the patient care team can play a major role in reducing the frequency of adverse drug events (ADEs) by two-thirds.²⁶ However, age and gender were found not to have significant association with DRPs, which is consistent with the findings in several previous studies.^{27,28}

To avoid any discrepancy in methodology, this study was conducted using standardized international terminologies and guidelines: the Anatomic Therapeutic Chemical (ATC) classification (WHO-ATC) for classifying drugs into various groups, the International Classification of Diseases version 10 (WHO-ICD 10) for classifying indication of drugs into various diagnoses, and standardized methods for data collection was used as per validated and the updated PCNE classification system for drug related problems, while the chart review system which was frequently used as part of main methodology in various similar studies has been well tested and verified in the United States and European countries.^{20,27,28} On the other hand, while interpreting the finding of our study, we came across several difficulties. The study's findings only represent the snapshot of single institute. Although the effect of the CPOE system in the prevention of occurrence of DRPs among hospitalized children, the current study results highlighted that incidence of DRPs that can be prevented is quite high (87.7%).



Our study has certain limitation. The outcome of preventable DRPs or the use of medicine in off-label pattern outside the indication was not investigated or analysed in paediatric patients. These parameters should be considered in future studies.

CONCLUSION

From the results of our study, it can be concluded that there is high incidence of preventable drug related problems which is generally ignored if not thoroughly investigated. Most of the DRPs are associated with dosing and drug choice problems. The findings of this observational study can be utilized in planning and establishing the most appropriate prevention strategies drug related problems. There is also a need for designing a specific, imbedded paediatric CCDS in the CPOE system, by using a unified dosing guide protocol for paediatric patients. Prevention of these DRPs is an important measure to ensure rational use of medicines among this vulnerable patient population.

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