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An Intensive Monitoring of Adverse Drug Reactions in Indoor Patients of Paediatric Department at Tertiary Care Teaching Hospital in Gujarat, India

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Abstract

Adverse Drug Reactions (ADRs) are a major source of concern in paediatric population as they differ from adults in pharmacokinetic and pharmacodynamics responses. ADRs reported in adults do not predict those in children. Thus, this study aimed to intensively monitor ADRs occurred in inpatients of paediatric department of tertiary care teaching hospital to assess the same in terms of incidence, causality, severity and preventability. A prospective observational single centre study was done in the paediatric department of SSG hospital, Vadodara over duration of 8 months. The ADRs were actively monitored and collected reports were analysed for ADR pattern, demographic profile, causality, severity, and preventability. A total of 66 ADRs were documented during the period of 8 months. Among these 53.03% ADRs occurred below the age of 1 year, 89.13% ADRs occurred due to antibiotics, 56.06% ADRs are of Diarrhoea and vomiting and 80.43% ADRs developed after receiving drug intravenously. As per WHO-UMC criteria, 46.96 % ADRs were of probable while 51.51% ADRs were of possible causality while as per Naranjo scale 60.61% ADRs were of probable and 39.39% ADRs were of possible category. As per severity scale 69.70% reactions were mild and 30.30 % reactions were moderate. Probably preventable ADRs were about 57.58%. ADRs occurred more among infants and antibiotics were more commonly implicated. Most of the reactions were of mild severity and were probably preventable. Certain Precautionary measures can lead to significant prevention of ADRs in paediatric patients.

Keywords : Adverse Drug Reactions, Inpatients, Paediatrics, Pharmacovigilance

Introduction

Drugs, no matter how safe and efficacious, are always coupled with inescapable risk of adverse reactions. Adverse Drug Reactions (ADRs) have been implicated as a leading cause of considerable morbidity & mortality.[1] ADRs are a major clinical problem, accounting for increased resources and also have an economic impact.[2] Incidence of ADRs varies with studies ranging from as low as 0.15% to high as 30% globally.[3,4] It has been suggested that patients who developed adverse effects during hospitalization, were hospitalised for an average of 1.2–3.8 days longer than patients who did not, with a substantial increase of the healthcare costs.[5] Up to 57% of the community acquired ADRs are not being recognized by the attending physician upon hospital admission, leading to inappropriate management of the adverse event and exposure of the patient to additional hazards

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of the drug and prolonged hospitalization.[6] The safety of drugs used in patients of an adult age group cannot be extrapolated to a paediatric age group. The pharmacokinetics and pharmacodynamics of many commonly used drugs vary significantly between these two age groups of patients[7] further, ADRs in children can have a relatively more severe effect when compared to adults. Thus, the ADRs can lead to significant morbidity among children.[8]

It has been observed that ADRs in children not only result in hospital admissions or prolonged hospitalization but also may lead to permanent disability or even death.[9] They constitute a reported incidence of 9.5%, including 2.1% of hospital admissions, with 39.3% of them being life-threatening.[10] The safety profile of a drug thus marketed with its testing done on adults can vary significantly when used in children.[11] This aspect of drug therapy is often difficult to predict for newer drugs. An active drug surveillance system is needed to capture risk information in children.[12]

Spontaneous reporting plays a major role in the identification of safety signals once the medicine is marketed and it may also provide important information on at-risk groups, risk factors (to a limited degree), and clinical features of known and serious ADRs. Also we cannot detect the incidence and the "spontaneous" part in prescribers is always lacking.[13] As a result, spontaneous reporting captures only a small fraction of the adverse events that actually take place (underreporting).[14] There are strong biases in reporting.[15]

The present study was carried out to study the incidence and the pattern of ADRs taking place in paediatric units including wards, PICU and NICU of a tertiary care teaching hospital named Sir Sayajirao General Hospital, Vadodara, Gujarat, India, a tertiary care teaching hospital over a period of eight months from January 2018 to August 2018. This intensive monitoring of ADRs was planned with the intention that the results obtained will be able to shed light on their extensiveness and pattern of occurrence in the tertiary care hospital.

Methods

This study involved intensive monitoring of ADRs in paediatric units including wards, Paediatric Intensive Care Unit (PICU) and Neonatal Intensive Care Unit (NICU) of a tertiary care teaching hospital named Sir Sayajirao General Hospital Vadodara, Gujarat, India. The data were collected for 8 months from January 2018 to August 2018. For Intensive monitoring of ADRs patient were observed and studied for any type of ADRs and various data about demographic details, past history, findings on general and systemic examination, laboratory investigation reports, diagnosis, and treatment were collected from prescription records.

The collected data were recorded in a predefined Case Record Form (CRF) and analysed using Microsoft Excel. This study was approved by Institution Ethics Committee for Human Research (IECHR), Medical College Baroda. Written informed consent was taken from parents before collection of data.

Inclusion Criteria

1. All patients of either sex or ≤ 12 years of age group.
2. Patients transferred from PICU and NICU to Paediatric wards.
3. Patients referred to higher centre, or discharged against medical advice but in whom the outcome of ADR was known were included in the study.

Table 1. Types of Adverse Drug Reactions

Type of ADRs	ADRs n (%)
Type A	49 (74.25%)
Type B	17 (25.75%)
Total	**66 (100%)**

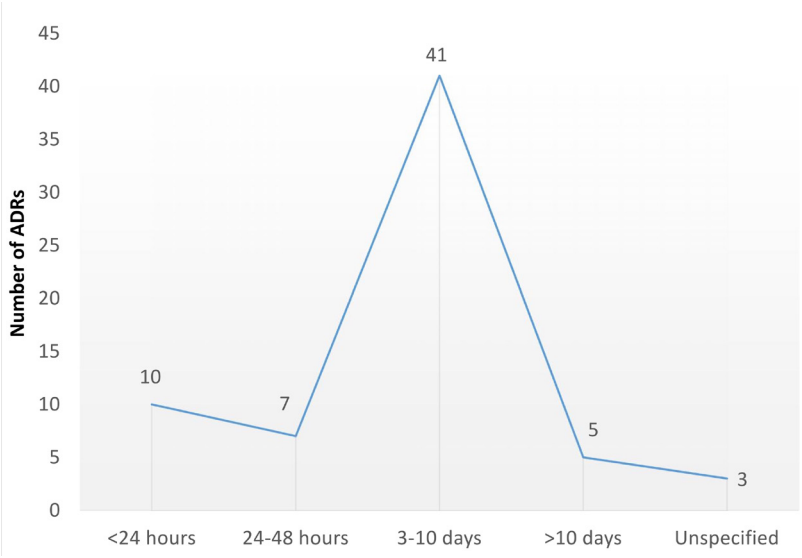

Figure 1. Onset of ADRs (n = 66)

Exclusion Criteria

1. >12 years of age groups patients
2. Patients referred to higher centre, or discharged against medical advice and in whom outcome of ADR was not known
3. Patients who developed an ADR during transfusion of blood or blood products and vaccines
4. Patients with intentional or accidental poisoning, drug abuse and patients with non-compliance

Statistical Analysis

Results were expressed in absolute number and percentages. Analysis of results were done after data were entered in Microsoft excel 2016.

Results and Discussion

A total number of 11632 patients were observed during the study period (11566 patients with no ADRs; 66 patients with ADRs) in the inpatients of paediatric departments in the study period of 8 months. Thus, the incidence of the ADRs in our study was 0.57 % (66/11632). Majority of ADRs were in aged 0-12 months (53.03%; 35/66). Out of total 66 patients, ADRs were reported in male patients as 59.09% (39/66) and in females as 40.90% (27/66). Total of 66 ADRs were subdivided as type A (Augmented) and type B (Bizarre). Most of the ADRs were type A (74.25%; 49/66) and related to the pharmacological reactions that usually subside with stoppage of drug/reduction in dose. A total of 25.75% (17/66) ADRs were of type B that were not dose related but immunologically mediated reactions, usually occurring in few susceptible patients.[16] (Table 1)

A study of correlation between the time of

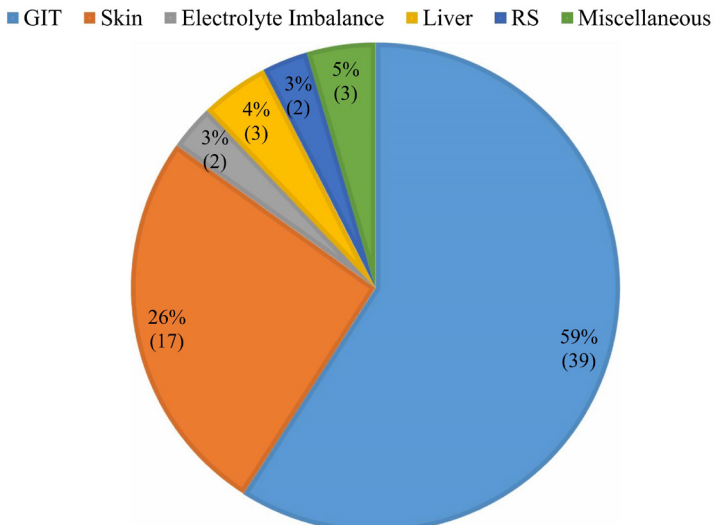

Figure 2. Organ System Categorization

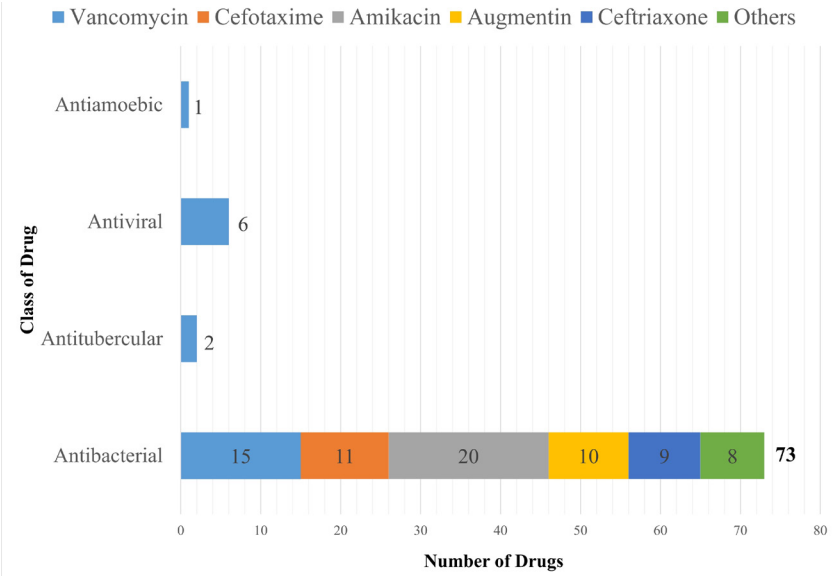

Figure 3. Suspected Antimicrobial Agents (n=82)

drug intake and the onset of ADRs showed that 62.12% (41/66) of the ADRs developed between 3 to 10 days of drug intake (Figure 1). On assessing outcome, all ADRs were completely recovered at the time of discharge. No ADRs associated with fatal outcome or led to any sequelae. A large number of ADRs 59.09% (39/66) belonged to gastrointestinal tract (GI) while skin consists of 25.75% ADRs (17/66) (Figure 2). Out of total 92 drugs suspected for these total 66 ADRs, in majority of the instances, it was antimicrobial agents (89.13%; 82/92) (Figure 3). Suspected medications were usually administered by intravenous route (80.43%; 74/92). Rest were given by oral route 19.56% (18/92).

A causality assessment carried out as per WHO-UMC criteria revealed that 46.96% (31/66) ADRs were probable while 51.51% (34/66) were possible (Figure 4). In Naranjo scale most of the causality assessments

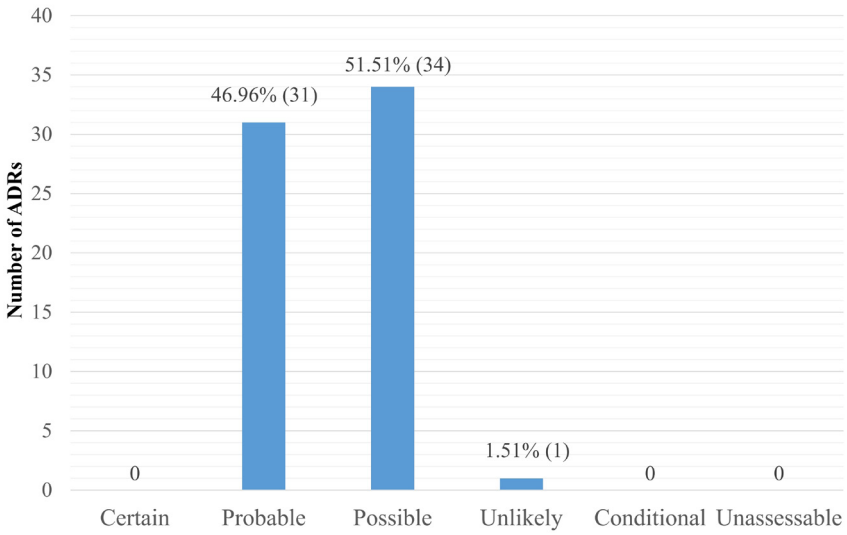

Figure 4. WHO Causality Assessment of ADRs (n=66)

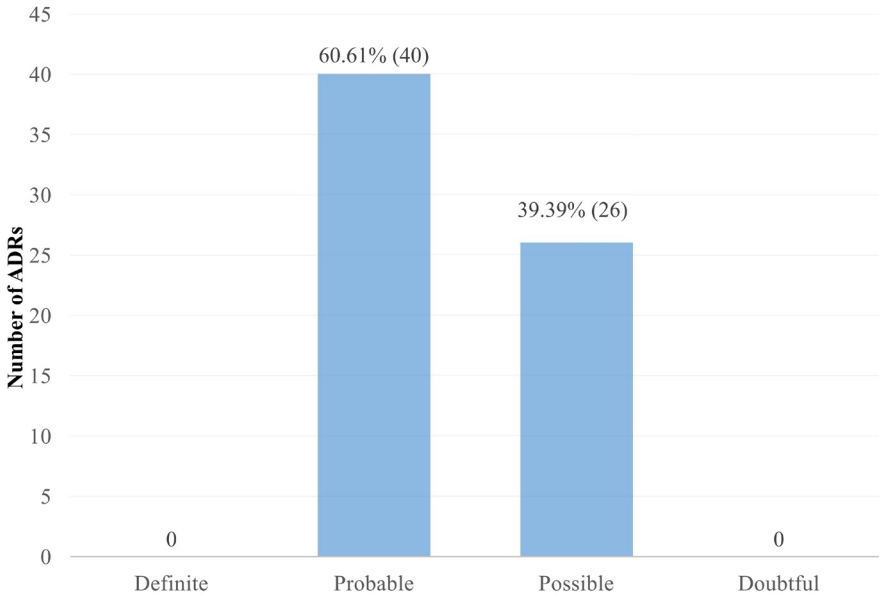

Figure 5. Causality assessment of ADRs as per Naronjo Scale (n=66)

were probable 60.60% (40/66) while 39.39% (26/66) were possible (Figure 5).

The analysis of the severity of ADRs was done according to Hartwig Siegel's scale. It was evident that ADRs mild in severity was 69.70% (46/66) while ADRs moderate in nature was 30.30% (20/66). According to Modified Schumock and Thornton preventability criteria, 57.58 % (38/66) ADRs were probably preventable, 19.70% (13/66) definitely preventable, and 22.72% (15/66) were not preventable.

Out of total number (11632) patients admitted in these 8 months, ADRs were reported in 66 patients, thus, the total incident rate of ADRs was 0.57% (66/11632). Majority of patients belonged to aged 0-12 months. This is in

agreement with study by R. Priyadharsini et al[17] who also observed that around 60% of the ADRs occurred in infants. Another study by Pramod Kumar Sharma et al; 2017-18[18] also has the same finding (ADRS in children less than 6 years of age out of which two third were in infants was 50% ADRs).

In our study, incidence of ADRs was higher in males. This result was similar to a study by Priyadharsini et al[17] in which 63% ADRs were reported in males (females: 37%). The present study has shown that 59.09% (39/66) reported ADRs were from gastrointestinal tract (GIT) system followed by skin 25.75% (17/66). This is in line with studies by Priyadharsini et al[17] and Pramod Kumar Sharma et al[18] where most common ADRs were from skin followed by GIT. One of the possible explanations for this observation could be that time relationship can be easily established in case of gastrointestinal adverse drug reactions and adverse effects on skin are easily noticeable and reported quickly by the patients.

The number of suspected medications were 92 that include ADRs due to antimicrobial agents (89.13%; 82/92). These findings were in agreement with several other studies conducted in India. Priyadharsini et al[17] study showed 67% of ADRs were due to antimicrobial agents while in that by Pramod Kumar Sharma et al[18] showed 60%. Antimicrobial drugs are the most frequently prescribed drugs in the hospital and to a great extent, the large amount of their use may be considered injudicious. Therefore, these agents are quite likely to be the most common offending group.

The causality assessment of the ADRs was carried out on the basis of two popular methods used for this purpose, namely WHO-UMC criteria[19] and Naranjo scale.[20] Based on WHO-UMC criteria, majority of the ADRs were 51.51% (34/66) were 'Possible' and 60.61% (40/66) were 'Probable'. Priyadharsini et al have reported that approximately 80% of the ADRs in their study were 'probable'[17], while in the study by Pramod Kumar Sharma showed 45%.[18] It shows that the pattern of causality is similar in most of these reports. Each of these two methods of causality assessment has their own peculiar characteristics, however, WHO-UMC method is simple and less time consuming. On the other hand, the Naranjo scale covers many more aspects of ADRs profile (Alternate causes, placebo effects, past history, blood concentration of drug etc).

The Naranjo criteria do not take into account drug-drug interactions. Drugs are evaluated individually for causality and points deducted if another factor may have resulted in the adverse event, thereby, weakening the causal association. Majority of the ADRs (69.70%; 46/66) reported were mild in nature according to the modified Hartwig and Siegel's severity scale.[21] In other similar studies, the major component of ADRs was moderate nature. In the study by Priyadharsini et al, 77% ADRs were moderate in nature[17], while Pramod Kumar Sharma et al found 90% ADRs were moderate as per severity assessment scale.[18]

The preventability assessment by Thornton and Schumock criteria[22] in the present study showed that most of ADRs 57.58% (38/66) were 'probably preventable'. Previous studies showed that 87% to 100% of ADRs were preventable and or probably preventable. This highlights was the most important part of study that on taking few precautionary measures like giving Vancomycin injection slowly over the period of time and minimising the use of multiple Antibiotics together can lead to significant prevention of ADRs in paediatric patients.

The present study has generated very useful data for our hospital as well as other tertiary

care teaching hospitals, particularly in the Indian context. The data generated in this study can be a guide which can help to prevent majority of undesirable drug effects observed by undertaking precautionary right steps in the right direction when treating with the same drugs in future.

Patients suffering from tuberculosis and HIV/ AIDS were very few in my study. All the same TB and HIV as well as their co-infections are a burning issue globally and require treatment using multiple drug regimens. Thus, these groups should be studied separately in terms of their ADRs profile and causality keeping in mind the increased chances of drug-drug interaction.

Conclusion

Our study has some limitations such as we studied only paediatric unit so same level of intensive monitoring can be done in other departments also. Other limitation is that patients were not followed after discharge so late in some patients late ADRs were remain undetected. Though the duration of the study was adequate, but not enough to be able to cover all the seasons in a year. So in our study we come to conclusion that ADRs occurred more among infants and antibiotics were more commonly implicated. Most of the reactions were of mild severity and were probably preventable. Certain Precautionary measures can lead to significant prevention of ADRs in paediatric patients.

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Conflicting of Interests

The Authors declare that there is no conflict of interest

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