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Research Article

ANALYSIS OF ADVERSE DRUG REACTIONS IN PEDIATRIC POPULATION: A RETROSPECTIVE STUDY

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ABSTRACT

Paediatrics is group of population in whom a wide range of pharmacokinetic and pharmacodynamic variations of the drug occurs because of diverse stages of development. Owing to this there are greater chances for the occurrence of adverse drug reactions in comparison to adults. The aim of this study is to assess, categorize and analyse the adverse drug reactions among the paediatric population. We performed a retrospective analytical study on the adverse drug reactions in paediatric patients reported by health care professionals to adverse drug reaction monitoring centre of Sri Venkateswara Medical College, Tirupati for a period of 12 months. The percentage of adverse drug reactions in total was found to be major among the male paediatric population (56%). Among the total adverse drug reactions, antibiotics (57.3%) were found to be the most common group of drugs associated with adverse drug reactions. Among antibiotics, majority of adverse drug reactions were due to cephalosporins (61.81%). As per World Health Organization causality assessment scale, majority of adverse drug reactions were found to be probable (74%). Majority of the adverse drug reactions under serious criteria of the reaction required intervention to prevent permanent impairment/damage (61.1%).

Keywords: Adverse drug reactions, Pediatrics, causality assessment, adverse drug reaction monitoring centre, antibiotics.

INTRODUCTION

Adverse drug reactions (ADRs) are responsible for the significant cause of increase for morbidity, hospital admissions and even death. It is also a cause for prolonged hospital stay and increased healthcare costs.[1,2,3] World Health Organisation (WHO) defined adverse drug reaction as "A response to a drug that is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis, therapy of disease, or for modification of physiological function".[4,5] According to American Academy of Paediatrics (AAP), "Paediatrics is the speciality of medical science concerned with the physical, mental and social health of children from birth to young adulthood". Early studies demonstrated high rate of adverse drug events (ADEs) in adult inpatients, and a later study documented threefold higher rate of potentially harmful medication errors in paediatric inpatients.[6]

Paediatrics is group of population in whom a wide range of pharmacokinetic and pharmacodynamic variations of the drugs occur because of diverse stages of development. Owing to this there are greater chances for the occurrence of adverse drug reactions when compared to adults. It is well known that delayed gastric emptying time in neonates and infants, results in longer absorption time and potentially increase the risk of ADRs. Volume of distribution, protein-binding capacity, phase I and II metabolic pathways and glomerular filtrate rate also varies in comparison to adults. Therefore, extrapolation of paediatric dosages from adult dosages should be avoided.[7]

Often, paediatric group are prescribed with medications in an off-label pattern, which can increase the risk of ADRs. Drug evaluation studies are seldom done in this patient population because of practical difficulties and ethical concerns. In addition, the paediatric population often represents a small percentage of the pharmaceutical market, so clinical trials do not yield large profit expectations for drug companies. Consequently, many medicinal products that have no paediatric marketing authorization are being prescribed, that lead to a potentially dangerous scenario for an ADR to occur.[8]

Other risk factors for ADRs are multiple medications, new drugs, conditions of hepatic / renal disease etc. Many of these ADRs are preventable. Prompt detection and identification of the ADRs helps to achieve substantial reduction in health care cost and unnecessary human suffering.[9]

ADRs account for 4.2-30% of hospital admissions in the USA and Canada, 5.7-18.8% in Australia, and 2.5-10.6% in Europe. Between 2.1% and 5.2% of ADRs in children lead to hospitalization, and up to 39% of ADRs in paediatric patients can

be life-threatening or fatal. ADRs may increase costs due to increased hospitalization, prolongation of hospital stay and additional clinical investigations in more serious cases.[10] The cost estimated for ADRs depends on the country where the study is being carried out as well as the level of care being taken and duration of the study period. Estimated cost of the studies range from a few million dollars at the institutional level to billions of dollars at the national level.[11] At least one ADR has been reported to occur in 10 to 20% of hospitalized patients.[12] Monitoring and documentation of ADRs are crucial to ensure the safe and rational use of medications.

In India, under the ageis of Ministry of Health and Family Welfare (MoHFW), the nationwide Pharmacovigilance Programme of India (PvPI) was initiated in the year 2010 and Indian Pharmacopoeia Commission (IPC), Ghaziabad, has been functioning as the National Coordination Centre (NCC) for PvPI since April 2011 [13]. The NCC and Adverse drug reaction monitoring centres (AMC) play significant role in creating awareness among healthcare professionals in monitoring and reporting of ADRs and thereby improve drug safety. The NCC-PvPI, excels in Pharmacovigilance and becomes a significant contributor for the global drug safety database. India is the world's sixth country recognized by the World Health Organization as a WHO Collaborating Centre for Pharmacovigilance in public health programme and regulatory services. [14, 15]

Extensive research has been carried out in India, Africa and Western population to study the ADR profile in adults. Whereas very scanty data is available in paediatrics population in India. Therefore safety monitoring of medicines is a vital element of healthcare and high-quality medical care in paediatrics. The objective of the present study is to analyse the spontaneously reported ADRs in paediatric population for their pattern, suspected medications, and to access causality and severity.

METHODS

This was a retrospective analytical study carried out based on the spontaneous reporting of adverse drug reactions by healthcare professionals to adverse drug reaction monitoring centre (AMC) of Sri Venkateswara Medical College (SVMC)/ Sri Venkateswara Ramnarain Ruia Government General Hospital (SVRRGGH), Tirupati, Andhra Pradesh, India. The reported ADRs in paediatric patients were evaluated, classified and assessed after approval from Institutional Ethics Committee SVRRGGH- SVMC, Tirupati, by maintaining a strict confidentiality about patient details.

Information regarding patient initials, age, gender, weight, adverse drug reaction, details regarding suspected drug, date of reaction started, date of recovery were captured in suspected adverse drug reaction reporting form. Further severity of ADRs and causality assessment were also evaluated. Causality was assessed as per the World Health Organization -The Uppsala Monitoring Centre (WHO-UMC) causality assessment scale, which classifies into certain, probable, possible, unlikely, conditional and unassessable ADR. Severity of the reaction was assessed using modified Hartwig and Siegel ADR severity assessment scale, which classifies ADR into mild, moderate and severe.

Study design

A retrospective analytical study was carried out for all adverse drug reactions in paediatric patients which were reported to AMC over a period of one year (July 2017-June 2018).

Statistical analysis

A descriptive analysis of the data was carried out using Microsoft Excel 2007 and results were expressed as numbers and percentages.

RESULTS

A total of 96 ADRs in paediatric patients were reported to AMC, SVMC during the period of July 2017-June 2018.

Demographic characteristics of patients with suspect ADR

Among these ADRs 42(44%) occurred in female where as 54(56%) occurred in male paediatric population as shown in Figure 1. Among 96 ADRs, 1(1.04%) ADR occurred in 0-30 days of age, 36(37.5%) occurred in 1 month- 2 years, 35(36.4%) occurred in 2-6 years and 24(25%) occurred in 6-12 years of paediatric population.

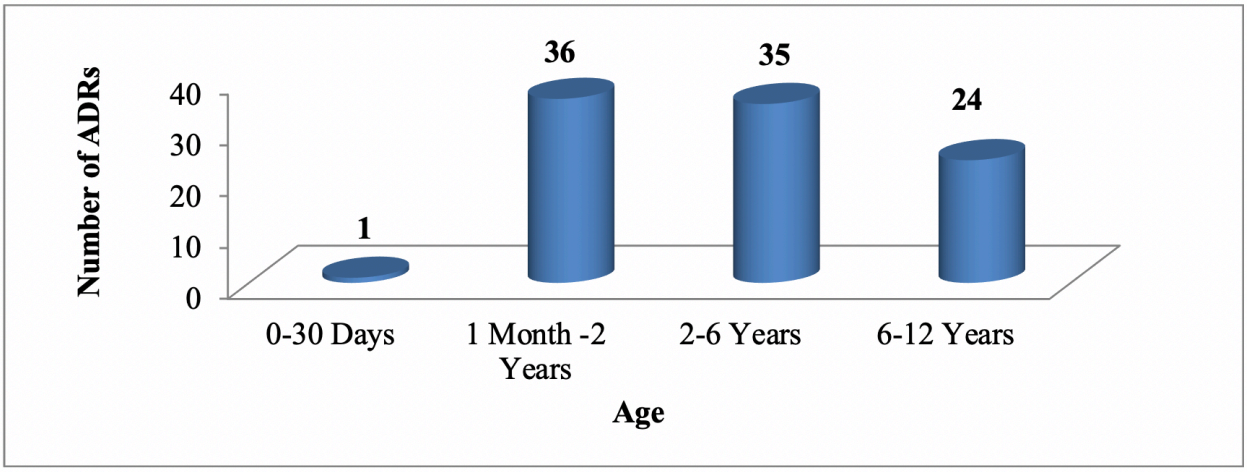

Figure 1: Age wise distribution of ADRs.

Major classes of drugs involved in suspect ADRs

Among 96 ADRs, antibiotics 55(57.3%) were implicated as most common groups of drugs associated with ADRs. Among antibiotics majority of ADRs were due to cephalosporins 34(61.81%) followed by penicillins 9(16.3%) and antiepileptics. And the least were caused due to other drugs such as 5HT3 receptor blockers 1(1.04%), proton pump inhibitor 1(1.04%) etc as shown in the Figure 2.

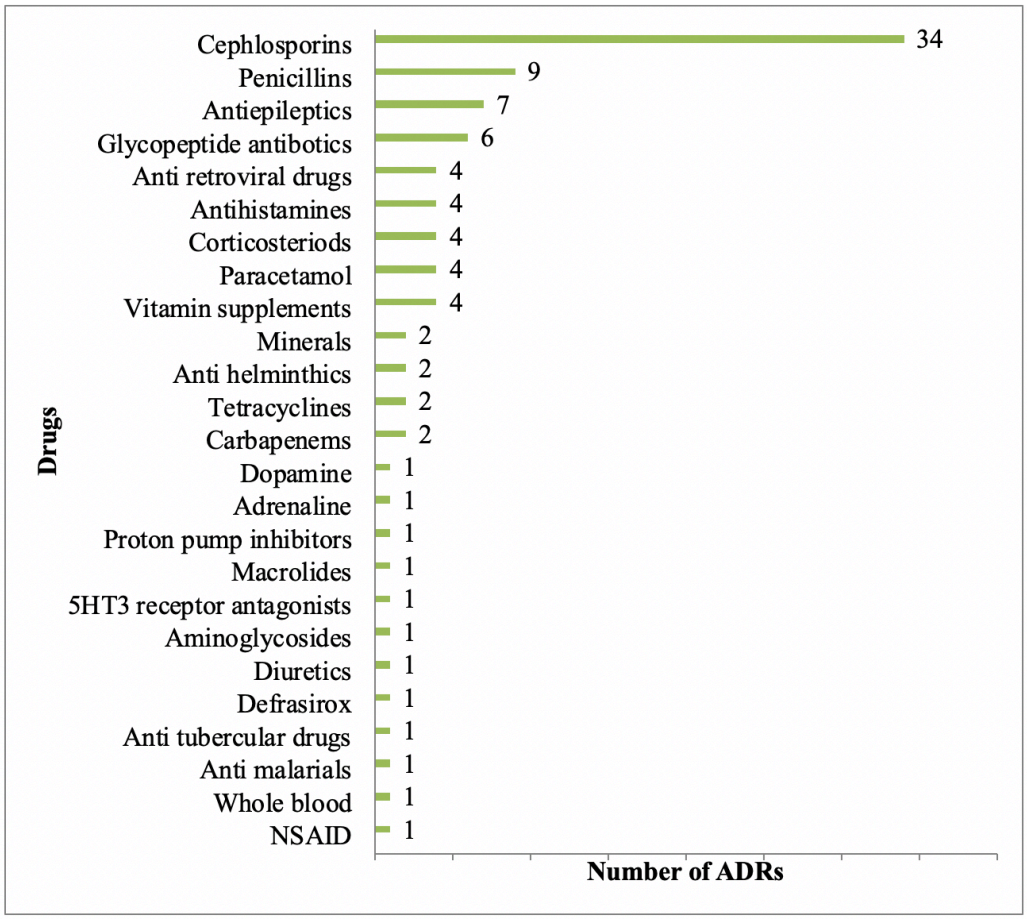

Figure 2: Classification of drugs involved in suspect ADRs.

Organ systems implicated in suspect ADR

Among 96 ADRs the highest number of ADRs affected gastro intestinal system 42(43.7%) followed by skin 24(25%) and the least corresponding to skeletal and musculoskeletal systems 1(1.04%) as shown in the Figure 3.

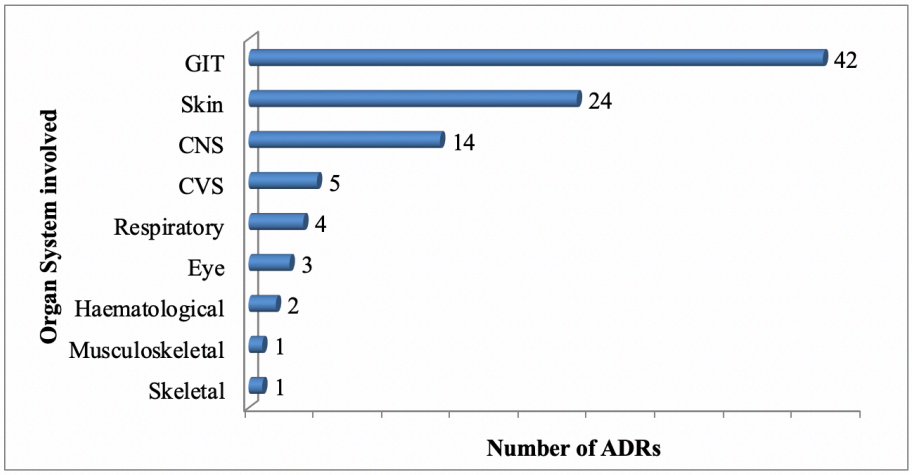

Figure 3: System wise distribution of ADRs.
***GIT- Gastrointestinal system, CNS- Central nervous system, CVS- Cardiovascular system**

Outcome of reaction

Among 96 ADRs, majority of the patients recovered from the ADRs 72 (75%), followed by recovering 16 (16.7%), unknown 5 (5.2%) and not recovered 3 (3.1%) as showed in Table 1.

Table 1: Outcome of reaction

S. no	Outcome of reaction	No of ADRs	Percentage (%)
1.	Recovered	72	75
2.	Recovering	16	16.7
3.	Unknown	5	5.2
4.	Not recovered	3	3.1
5.	Fatal	0	0
6.	Recovered with sequela	0	0

Causality Assessment of ADRs:

Table 2 represents the causality assessment of ADRs as per WHO-UMC causality assessment scale. 71 (74%) were found to be probable and 25(26%) were found to be possible.

Table 2: Causality assessment

S. no	Causality assessment	No of ADRs	Percentage (%)
1.	Certain	0	0
2.	Probable	71	74
3.	Possible	25	26
4.	Unlikely	0	0
5.	Conditional	0	0
6.	Unassessable	0	0

Severity of suspect ADRs

Among 96 ADRs, 68 (71%) ADRs were found to be mild and 28(29%) were moderate in nature as shown in table 3.

Table 3: Severity of suspect ADRs

S.no	Severity	No of ADRs	Percentage (%)
1.	Mild	68	71
2.	Moderate	28	29
3.	Severe	0	0

Seriousness of reaction

Among 96 ADRs, 18(18.75%) were found to be serious. Among these serious ADRs 11(61.1%) required intervention, 4 (22.2%) required hospitalization and 3 (16.6%) were responsible for prolonged hospitalization.There was no death reported due to the ADRs.

Table 4: Seriousness of reaction

S.no	Seriousness	No of ADRs	Percentage (%)
1.	Required intervention	11	61.1
2.	Required hospitalisation	4	22.2
3.	Prolonged hospitalisation	3	16.6
4.	Congenital anomaly	0	0
5.	Life threatening	0	0
6.	Disability	0	0
7.	Fatal	0	0

DISCUSSION

In our study a total of 96 ADRs from paediatric population were reported to AMC of SVMC, among these we found that there was male preponderance when compared to female, which is supported by a study carried by Divyalasya TVS[16] and Kalyani SSA[17]. Majority of ADRs occurred in the age groups of 1 month-2 years and 2-6 years followed by age group between 6-12 years. This may be due to increased usage of antibiotics in the age group of 1month-6 years to treat various infectious diseases. Majority of ADRs in the present study were due to antibiotics. This is consistent with the previous studies carried out by, Divya lasya TVS[16], Kalyani SSA[17], and Rebecca MDS [18]. Among antibiotics, highest ADRs were due to cephalosporins followed by penicillins, as these are broad spectrum antibiotics commonly prescribed in higher rate to treat infections in the children and the least were caused due to aminoglycosides and macrolides. Followed by antibiotics, more number of ADRs was caused due to antiepileptics. According to many studies carried out on ADRs, skin is the most common organ involved but contrast to those in the present study gastro intestinal system was the most common system involved, this may be due to delayed gastric emptying time in neonates and infants, resulting in longer absorption time and the least occurred in skeletal and musculoskeletal systems. Based on outcome of the reaction, most of patients recovered from the ADRs followed by recovering. According to WHO-

UMC causality assessment, it was found that majority of ADRs were probable and possible. Severity assessment was carried out by modified Hartwig and Siegel's scale, where most of the ADRs were mild and around one fourth were moderate. Among 96 ADRs around one fifth were found to be serious, among these majority of the ADRs required intervention to prevent further damage followed by ADRs that needed hospitalization. Certain problems have been identified, and necessary precautions have been taken to reduce the incidence of preventable ADRs. Health care professionals including nursing staff were also educated and several sensitization programmes were conducted to health care professionals on pharmacovigilance and adherence to rational use of medicines.

CONCLUSION

Children, being a vulnerable group, are prone to ADR related morbidity and mortality. Therefore, utmost care must be taken while prescribing the drugs. According to the present study, high level of caution should be exercised while prescribing antibiotics to the paediatric population, as they are responsible for causing more number of ADRs. Measures should be taken for the improvement of the detection and reporting of ADRs by all health care professionals. Therefore there is utmost need to continuously monitor the ADRs. To enhance the impact of understanding these reactions in children, strategies should be implemented for early detection of adverse drug reactions by targeting the specific drugs.

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