INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Research Article

Retrospective Study Of Adverse Reaction In Paediatric Patients

I. B. Deshmukh[1], S. R. Burute*[2], S. M. Pore[3], A. S.[4] , F. M.[5]

[1]*Junior resident, Government Medical College Miraj, Maharashtra.*
[2]*Associate Professor MD Pharmacology, Government Medical College Miraj, Maharashtra.*
[3]*Associate Professor MD Pharmacology, Government Medical College Miraj, Maharashtra.*
[4]*Senior Resident, MD Pharmacology, Government Medical College Miraj, Maharashtra.*
[5]*Senior Resident, MD Pharmacology, Government Medical College Miraj, Maharashtra.*

ARTICLE INFO

Received: 05 March 2024
Accepted: 07 March 2024
Published: 10 March 2024
Keywords:
Paediatric, Patients, Retrospective, Adverse
DOI:
10.5281/zenodo.10945158

ABSTRACT

Harmful, unintended reactions to medicines that occur at doses normally used for treatment are called adverse drug reactions (ADRs).1 Drugs may behave differently in children (different pharmacokinetics) compared to adults and may cause different effects (different pharmacodynamics) in children. 2 With Thalidomide tragedy emphasized children are particularly vulnerable to the impact ADRs and may suffer more severe consequences compared to adults.3 Post marketing studies are mostly done for adults and there is paucity of data in children thus reflecting need for study of ADRs in pediatric age group. Hence we carried out this study with aim to study profile of adverse drug reactions (ADRs) in pediatric patients during last five years at an Adverse Drug Monitoring (AMC) with objective to determine the most common adverse drug reactions reported and most common drug reported to cause ADR in pediatric patients at AMC.

Methodology:

Adverse drug reaction reported in pediatric patient reported to AMC during last 5 years will be analyzed and coded and considered for this study after permission from PvPI and Ethics committee. Data collected for most common ADR, most common drug causing ADR and profile of patients with ADRs.

Conclusion

Only 4% (59) of the 1430 ADR s reported to AMC were in children. Skin involvement as most common ADR reported and sera and vaccine was most common implicated drug

INTRODUCTION

Adverse drug reactions (ADRs) refer to negative and unintended responses to medications at their usual treatment doses. In the context of children, these reactions tend to be more severe than in adults1. Adverse drug reactions (ADRs) in

***Corresponding Author:** S. R. Burute
Address: *Associate Professor MD Pharmacology, Government Medical College Miraj, Maharashtra.*
Email ✉: shreyas.burute @gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

children can have a relatively more severe effect when compared to adults. 4Adverse drug reactions (ADRs) in children can have severe consequences, including hospital admissions, prolonged hospitalization, permanent disability such as growth impairment e.g excessive use of exogenous corticosteroids can inhibit normal childhood growth., and even death. Drugs may behave differently in children (different pharmacokinetics) compared to adults and may cause different effects (different pharmacodynamics) in children. 2 Children cannot be simply considered as miniaturized versions of adults when it comes to their medical conditions and disease processes, particularly neonates and infants. Therapeutics in children has come a long way but nothing comes for free. “Elixir of Sulphanilamide Tragedy” of 1937, in which more than 100 Americans mostly children died because of the use of diethylene glycol a potent nephrotoxin as a solvent for sulphanilamide.3,5 The increased awareness of adverse drug reactions in children came to the forefront after tragic incidents, highlighting a sorrowful aspect of healthcare that demands our attention and improvement.6Thus, exclusionary language “this drug is not labelled for use in patients under the age of 12”—became the norm. Shirkey coined the term "The Therapeutic Orphan" to highlight that 75% of prescription medications lacked approval for children.7. Since pre-marketing clinical trials primarily focus on adults, it is crucial to gather information on the frequency, severity, and types of drugs involved in adverse reactions specifically in the pediatrics population. This data holds significant importance.8 Recently post marketing studies about use of montelukast in children demonstrated that it is associated with sedation and neuropsychiatric symptoms, such as depression, aggression, nightmares, were significant in children.9 Further the spontaneous ADR reporting in children is not very common.10Hence it reflect the need the post marketing surveillance of ADRs in pediatrics population to detect specific ADRs to children to all the drug introduced to them. Hence with this aim we decide to analyze the profile of ADR observed in Pediatrics patients reported to AMC with objective to determine most common adverse drug reactions reported and most common drug reported to cause adverse drug reactions in pediatric patients .

METHODOLOY:

This was a retrospective report-based study. Adverse drug reaction reported were screened and only ADRs in children (age 12 year and less) were recorded and coded and considered for this study after permission from PvPI and Ethics committee.

Data regarding most common drug causing ADR and profile of patients with ADRs in predetermined format was collected and frequency was calculated.

RESULTS :

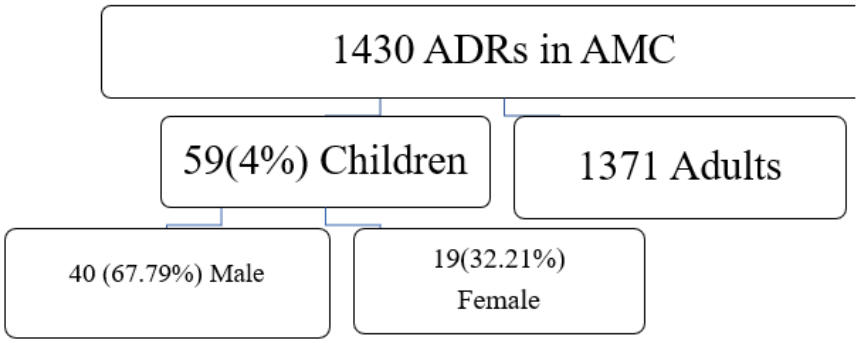

Figure 1 As per figure 1 only 4% (59) of the 1430 ADR s reported to AMC were in children

System	ADR (n=59)	Most common drugs implicated
Skin 42 (76.27%)	Rash generalized (13) 22.03%	Antirabies serum 12
	Urticaria (12) 20.33%	Inj. Vancomycin 4
	Pruritis (4) 6.77%	Injection Vancomycin 2
	Erythematous rash (4) 6.77%	Inj. Vancomycin 4
	Allergic reaction (3) 5.08%	Antirabies serum 3
	Angioedema (2) 3.39%	Antisnake venom serum 2
	Redman syndrome (2) 3.39 %	Inj. Vancomycin 2
	Papular rash (2) 3.39%	Antirabies serum 1
	Maculopapular rash (2) 3.39%	Antirabies serum 1
	Scaling (1) 1.69%	Abacavir+ Lamivudine+ Efavirenz

Figure 2A shows skin was most commonly affected (76.27%) in which generalized rash (22.03%) and urticaria (20.33%)were predominant and antirabies serum and injectable vancomycin being the most frequently implicated drugs.

Constitutional symptoms (15 .25%)	Fever with swelling (4) 6.77%	Inj. Pentavalent vaccine 3
	Fever with rash (1) 1.69%	Inj. Pentavalent vaccine 1
	Fever with breathlessness (1) 1.69%	Inj. DPT vaccine 1
	Fever with chills (1)1.69%	Inj. Amphotericin 1
	Fever with weakness (1)1.69%	Inj. Corbevax 1
	Fever with convulsion (1)1.69%	Inj. Pentavalent vaccine 1

Figure 2B As per figure 2B ,15.25% of ADRs were reported as constitutional symptoms most commonly seen after post vaccination.

GIT(6.78%)	Diarrhea (2) 3.38%	Tablet Albendazole 2
	Abdominal pain (1) 1.69%	Tablet Albendazole 1
	Vomiting (1) 1.69%	Antirabies serum 1
CNS(1.7%)	Convulsions (1) 1.69%	Inj. Phenytoin 1

Figure 2C From above figure 2c git (6.78%)and cns (1.7%) related ADRs were reported

DISCUSSION:

Adverse drug reactions (ADRs) in children are a significant concern for public health. Even though attempts are being made to decrease the occurrence of medication-related problems, the mortality and morbidity, particularly in the pediatric population due to drug-induced reactions, remain excessively high.11,12 Research has been conducted globally to explore ADRs among pediatric patients.8 The findings reveal that ADR is an important cause of mortality.13This underscores the ongoing challenge and emphasizes the importance of addressing and reducing the impact of ADRs in the pediatric demographic. In developed countries they find that about 5.8% of ADRs in children are reported spontaneously14. Our study shows a similar number, around 4%, when we compare the two. This means our findings are in line with what is observed in well-developed areas, highlighting that the issue of ADRs in kids is consistent across different regions. Our study found that 67.79% of ADRs were in males, while females comprised 32.21%, similar to Ratikanta Tripathy, Swarnalata Da etal study15: suggesting similar trend. This reflects two possibilities either male inherently develop more ADR or gender bias affects reporting of ADRs. A meta-analysis revealed that around 12.3% of cases involved severe adverse drug reactions (ADRs. 16 Our study similarly found a rate of 15%, indicating a close resemblance in the occurrence of severe ADRs between the two studies. The most ADRs observed in present study was related to skin (76.27% % of

ADRs) out of which urticaria(28.89%) and generalized rash (26.66%). Although studies by Priyadharsini R, Surendiran A et al 17 and and Dash M, Jena M, 18 and Tripathy R, Das S, Das P 15reveal a ubiquitous presence of cutaneous involvement in adverse drug reactions, they did not cite any ADR to vaccines and sera; Where as we observed 57.62 % reaction associated to vaccine and sera of which 33.89 % were due to Antirabies serum and were related to skin. One of the reasons skin could be the most common observed ADR could be the readily noticeable nature of skin symptoms unlike behavioral changes or abnormal laboratory findings . In our study, we found that constitutional symptoms, like fever with other symptoms was second most commonly (ADRs), like study done by Priyadharsini R, Surendiran A et al. In contrast Dash M, Jena M et al17 and Tripathy R, Das S, Das P18 cite gastrointestinal issues as the most frequently reported symptoms Fever is a well-known side effect after vaccination 19and all cases of fever to vaccination are not reported as ADRs to the ADR monitoring center due to a policy of counselling the mothers at time of vaccination and in our study, only those ADRs linked with other symptoms were reported. Most cases were associated with the use of the pentavalent vaccine. It's worth noting that our study observed one case of convulsion following a Pentavalent vaccination, highlighting a potential serious side effect. Although the present study cannot reflect prevalence in general population the findings are still significant for following reasons 1) vaccines are administered to healthy children20.2)Other ADR monitoring studies15 which included vaccines have not reported any ADRs to vaccines 3)Other ADR monitoring17,18 studies have not included vaccine in their study Tripathy et al 18 previously identified third-generation Cephalosporins as common cause of adverse drug reactions (ADRs) in children. However, our study found that Vancomycin is often associated with such reactions. While Vancomycin is approved for use in children, specific adverse effects related to children's use are not well-documented21.Available literature exhibits a notable scarcity of detailed information concerning specific adverse effects associated with children's use, indicating a lack of well-documented data on potential risks in this context. This could be due to difficulty in conducting clinical trials in children 22as a result most of the data regarding safety in children becomes available after post marketing surveillance .16 This highlights the importance of further understanding and closely monitoring the safety of drugs used in pediatric patients to ensure its rational use in this age group. Therefore, its crucial to ensure that pediatricians and caregivers are well-informed about Adverse Drug Reactions (ADRs) in children and report them. Implementing an active monitoring system for ADRs is essential.

Limitations:

It is a retrospective report-based study, therefore, we cannot ascertain the history and clinical profile of the patients.

ACKNOWLEDGEMENT:

We extend our sincere thanks to PVPI coordinator and PVPI India for their valuable support and collaboration. This concise acknowledgment expresses gratitude to PVPI India for their contribution to the project.

REFERENCES

1. https://www.who.int/docs/default-source/medicines/safety-of-medicines--adverse-drug-reactions-jun18.pdf?sfvrsn=4fcaf40_2
2. Digra KK, Pandita A, Saini GS, Bharti R. Pattern of adverse drug reactions in children attending the department of pediatrics in a tertiary care center: a prospective observational study. Clinical Medicine

Insights: Pediatrics. 2015 Jan;9: CMPed-S29493.
3. Weinshilboum RM. The therapeutic revolution. Clinical Pharmacology & Therapeutics. 1987 Nov;42(5):481-4.
4. Aagaard L, Hansen EH. Adverse drug reactions reported for systemic antibacterials in Danish children over a decade. Br J Clin Pharmacol. 2010 Nov 1;70(5):765-8.
5. Ballentine C. Sulfanilamide disaster. FDA Consumer magazine. 1981 Jun:5. Accessed on 9 April 2023
6. Burgio GR. The thalidomide disaster briefly revisited. European journal of pediatrics. 1981 Jul; 136:229-30.
7. Stiers JL, Ward RM. Newborns, one of the last therapeutic orphans to be adopted. JAMA pediatrics. 2014 Feb 1;168(2):106-8.
8. Chien JY, Ho RJ. Drug delivery trends in clinical trials and translational medicine: evaluation of pharmacokinetic properties in special populations. Journal of pharmaceutical sciences. 2011 Jan;100(1):53-8.
9. Haarman MG, van Hunsel F, de Vries TW. Adverse drug reactions of montelukast in children and adults. Pharmacology research & perspectives. 2017 Oct;5(5):e00341.
10. López-Valverde L, Domènech È, Roguera M, Gich I, Farré M, Rodrigo C, Montané E. Spontaneous reporting of adverse drug reactions in a pediatric population in a tertiary hospital. Journal of clinical medicine. 2021 Nov 26;10(23):5531.
11. Berry MA, Shah PS, Brouillette RT, Hellmann J. Predictors of mortality and length of stay for neonates admitted to children's hospital neonatal intensive care units. Journal of Perinatology. 2008 Apr;28(4):297-302.
12. 12Neubert A, Dormann H, Weiss J, Egger T, Criegee-Rieck M, Rascher W, Brune K, Hinz B. The impact of unlicensed and off-label drug use on adverse drug reactions in paediatric patients. Drug safety. 2004 Nov;27:1059-67.
13. Patel TK, Patel PB. Mortality among patients due to adverse drug reactions that lead to hospitalization: a meta-analysis. European journal of clinical pharmacology. 2018 Jun;74:819-32.
14. López-Valverde L, Domènech È, Roguera M, Gich I, Farré M, Rodrigo C, Montané E. Spontaneous reporting of adverse drug reactions in a pediatric population in a tertiary hospital. Journal of clinical medicine. 2021 Nov 26;10(23):5531.
15. Tripathy R, Das S, Das P, Mohakud NK, Das M. Adverse drug reactions in the pediatric population: Findings from the adverse drug reaction monitoring center of a teaching hospital in Odisha (2015-2020). Cureus. 2021 Nov 9;13(11).
16. Impicciatore P, Choonara I, Clarkson A, Provasi D, Pandolfini C, Bonati M. Incidence of adverse drug reactions in paediatric in/out-patients: a systematic review and meta-analysis of prospective studies. British journal of clinical pharmacology. 2001 Jul;52(1):77-83.
17. Priyadharsini R, Surendiran A, Adithan C, Sreenivasan S, Sahoo FK. A study of adverse drug reactions in pediatric patients. Journal of Pharmacology and Pharmacotherapeutics. 2011 Dec;2(4):277-80.
18. Dash M, Jena M, Mishra S, Panda M, Patro N. Monitoring of Adverse Drug Reactions in Pediatric Department of a Tertiary Care Teaching Hospital: A Hospital Based Observational Study. Int J Pharm. 2015;4(4):69-76.
19. Paramkusham V, Palakurthy P, sri Gurram N, Talla V, Vishwas HN, Jupally VR, Pattnaik S. Adverse events following pediatric immunization in an Indian city. Clinical and

Experimental Vaccine Research. 2021 Sep;10(3):211.
20. https://www.who.int/publications-detail-redirect/9789241516990 accessed on 13/01/2024
21. Martindale W, Martindale BR. the complete drug reference. 40th ed 2020 ,vol A ,395
22. Meng M, Zhou Q, Lei W, Tian M, Wang P, Liu Y, Sun Y, Chen Y, Li Q. Recommendations on off-label drug use in pediatric guidelines. Frontiers in Pharmacology. 2022 Jun 9;13:892574.

HOW TO CITE: I. B. Deshmukh, S. R. Burute, S. M. Pore, A. S., F. M., Retrospective Study Of Adverse Reaction In Paediatric Patients, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 4, 550-555. https://doi.org/10.5281/zenodo.10945158