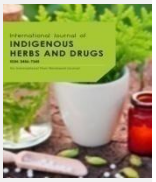
Review Article

International Journal of Indigenous Herbs and Drugs
Content Available at www.saap.org.in ISSN: 2456-7345



PHARMA COVIGILENCE IN PEDIATRICS

P. Akshitha*, M.Navya, B.Gayatri, Chandu Babu Rao
Priyadarshini Institute of Pharmaceutical Education and Research, 5th Mile, Pulladigunta, Guntur-522017, Andhra Pradesh, India

Article Info

Article History
Received on: 23-06-2025
Revised on: 07-07-2025
Accepted on: 01-08-2025

Abstract

Pharmacovigilance plays a pivotal role in paediatric care by monitoring and evaluating ADRs to improve patient safety and treatment outcomes. Children's physiological differences from adults necessitate targeted research to understand how they respond to medications, underlining the importance of this study: A systemic review of the previous 10 years (2010–2019) published studies were taken into consideration to describe observational studies on ADRs and to determine the incidence and characteristics of ADRs in paediatrics. Electronic relevant literature was searched in PMC, PubMed, Google Scholar, and Ovides'databases using MESH heading and text words. The titles, text, and abstracts were checked for patients below 18 years of age, nature of ADRs, observational studies (prospective or retrospective), and maximum information was recorded to count their frequency. The studies which discussed specific or particular drug exposures were not selected in this review. Of the 36,689 titles retrieved; 27 studies were selected for full-text review. Ten observational studies were added in the final review. Observational studies on paediatric were carried out in seven distinct nations.

Keywords: Pharmacovigilance, paediatrics, adverse drug reactions, teratogenic effects, clinical trials.

***Corresponding Author**
P. Akshitha

Production and Hosted By
www.saapjournals.org

Introduction

Extraction of base

All eligible studies were assessed to meet inclusion criteria. Any discrepancies at each stage of selection was discussed by a reviewer and resolved by consensus. All the investigators separately analysed by the methanoyl, results, criteria of every study by using standard data extracted proforma. The final results of the review were summarized narratively, and major characteristics of the study were arranged in a tabular form. Other information included in the analysis contains the country, year, mean age, studying population most commonly it is based on ADRs, and its drug formulations [1-4].

The lack of studies in paediatrics leads to mostly to on failing prescribing and to an increased frequency of adverse drug reactions. Off labelling refers to unapproved indication or in an unproved age of groups in dosing of a drug and route of administration. The main criteria for the extraction of the base for the pharmacovigilance that maintain the subsequent stability and some data paediatrics is a global issue and proper knowledge about of therapeutic agents. the ultimately, these issues have a major impact on public health due to imposing a significant economic load on society and already stretched healthcare systems [5,6].

This gap has been limited, leading to a paucity of specific data on paediatric drug safety and efficacy. The servility and type of ADRs can also vary widely across the paediatric age spectrum, further complicating the identification reporting, and management of these events. These clinical practices informing the risk assessment .it is a branch of pharmaceutical sciences which evaluated and monitor the adverse drug reactions or any other medication issues in their body [7]. Historically, the inclusion of paediatric populations in clinical drug trails has been limited, leading to a paucity of specific data. The severity and type of ADRs can also vary widely across the paediatric involves in the systematic review. Effective pharmacovigilance thus involves the systematic 'collection, elysian the type of science and activities related to the detection assessment. understanding and prevention of ADRs or any other drug related problems in this criterion, hence the present study was understanded to see the ADRs reactions in patients and drug related problems [8, 9].

To the detection assessment. understanding and prevention of ADRs or any other drug relatedproblems in this criterion, hence the present study was understanded to see the ADRs reactions in patients and drug related problems [8,9].

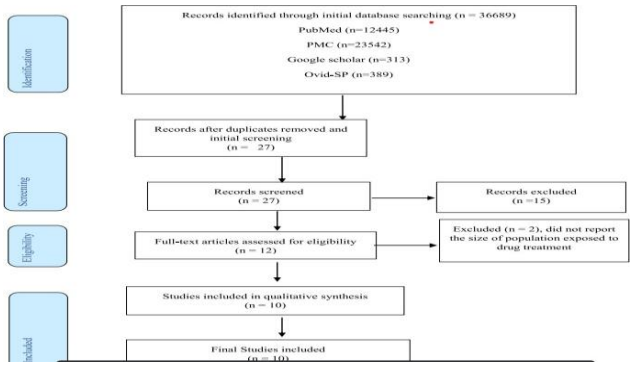


Table 1 Summary of observational studies (n=10) and ADRs incidence rate

Studies (year) (reference)	Country	Study design	Pediatrics population studied (n)	Duration of study	Incidence of ADRs % (n)
Gallagher RM et al. (2011) [22]	UK	Prospective	822	2 weeks	3.3% (27)
Gallagher RM et al. (2012) [23]	UK	Prospective	6821	1 year	3.6% (249)
Khan LM et al. (2013) [16]	Saudi Arabia	Retrospective-Prospective	1200	1 year	6.3% (76)
Dash M et al. (2015) [29]	India	Prospective cohort	500	1 year	25.4% (127)
Gholami K et al. (2015) [24]	Iran	Prospective	658	6 months	4.1% (27)
Rivas AB et al. (2016) [28]	Spain	Prospective cohort	313	1 year	17.2% (116)
Salas RdI et al. (2016) [30]	Colombia	Prospective cohort	772	6 months	20.2% (156)
Kurian J et al. (2016) [25]	India	Prospective	1082	6 months	5.9% (64)
Vázquez-Alvarez AO et al. (2017) [27]	Mexico	Prospective cross-sectional	1083	6 months	1.7% (19)
Sindhu AR et al. (2019) [26]	India	Prospective	200	6 months	7.5% (15)

The collates the data received from various AMCs and recommends regulatory interventions, besides communicating risks to health-care professionals and the public. These the study was conducted in accordance with ethical guidelines and standards. Informed

Consent was obtained from all participants. The study protocol was reviewed and necessary the study was conducted in accordance with ethical guidelines and standards. Informedconsent was obtained from all participants. The study protocol was reviewed and necessary prior permissions taken from concerned authorities' prior permissions taken from concerned

The term risk includes my treatment related problems based on their issues such as adverse effects and their reactions based upon their compliance, devices and their issues that may alter its reactions based upon their effects and its related problems [10]. pharmacovigilance aims to improve the understanding of known and potential risk and they identified as thebenefit of risk of management data collection and sequence of long-term effects [11]. The drugs most frequently reported with ADR's are those most commonly in paediatric age group are antibiotics, NSAIDs & vaccines. It is branch of pharmaceutical sciences which

evaluated and monitor the adverse drug reactions or any other medication related issue oflicenced drug to increase their safety in the market. Paediatrics are at risk of harm frommedications because of their organ immaturity and rapid developmental changes in their body [12].

Historical Background

To conduct a comprehensive analysis of adverse drug reactions (ADRs) in paediatric patients. The study retrospectively analysed medical records to identify adverse drug reactions (ADRs), categorizing them by age group, type, severity, and the drugs involved. This approach Facilitated the identification of patterns to inform safer prescribing practices and enhance clinical oversight. Pharmacovigilance is an identifying and responding process against a problem encountered in the drug administration [13] in [14 the past, children were rather often subject to serious harms caused by drugs which led to specific measures to improve the

safety of paediatric drug therapy [5]. In 1938, the Food, Drug, and Cosmetic Act was signed in the United States (US) following the death of107 patients, mainly children who had taken a new liquid form of thermal antibiotic sulphanilamide. The pharmaceutical company had intended to manufacture a special liquid formulation and used diethylene glycol as excipient to obtain an acceptable taste [14]. The first instance of safety related problem that led to a pharmacovigilance.

Pharmacokinetic characteristics in paediatrics

Paediatric growth is not a linear process. The pharmacokinetic parameters are

varied in paediatrics when compared to the adults they require the dosage adjustments and dose calculations Dose adjustments are required due to the metabolic immaturity ofreduced clearance and prolonged half-life explaining the need to space unit doses during the neonatal period. Paediatrics undergoes some organ developmental changes according to the EMA paediatric age classification [15].

Elimination

Glomerular filtration rate of neonate 2-3 ml / min and doubles by 1 week of age and reaches the adult GFR rate by the completion of the 1 year of the age. infants than in toddlers in relation to reabsorption. It is needed in reducing the predisposing factors of adverse drug reactions and medication related problems for increased susceptibility.

Systemic respiratory and antibiotics were the therapeutic groups mostly associated with theadverse drug reaction incidence and the most affected organ in neonates is hematologic Offlabelling is important in the public health services mainly in young children with rare diseases.[16]

Distribution

For most of the water-soluble drugs, the volume of distribution is increased in neonates. Distribution of drugs is affected in vascular perfusion, body composition, tissue binding & plasma protein binding.

Off-labelling is important in the public health services mainly in young children with rare diseases. However, the paediatrics labelling on drugs is seen in only 50% of the druglabelling's. Paediatric drug safety activities include the description of the paediatricsafetyspecification which is the basis for the development of paediatric pharmacovigilance and riskminimisation activities in clinical practice and clinical studies. an overview of therelationship between the

paediatric safety specification and paediatric pharmacovigilance and risk minimization [17].

Search strategy

A comprehensive and systematic search in different databases., PubMed, PMC, Google Scholar, and Ovides'-related published English literature was identifiedfrom 1 January 2010to 31 December 2019. These databases were searched to identify existed literature of Pharmacovigilance and ADR in hospitalized patients. Basic search terms were Pharmacovigilance drug therapy/adverse effects OR adverse drug reaction reporting system OR adverse effects/pharmaceutical preparations" AND "child OR paediatrics child- preschool"[18] AND "Observational studies.Changes in the pharmacokinetic and pharmacodynamic properties tin paediatric subjects to adults having an impact on the safety profile of the
medicine. ADR's preventable and by preventing them reduces potential readmission to the hospital and can improve the patient health.

Drugs mostly associated with ADRs

The evaluation of drugs implicated in ADRs identified antibiotics as the leading cause,responsible for 40% of ADRs, particularly penicillins and cephalosporins. Antipyretics andinflammatory drugs. Vaccines were linked to 15% of ADRs, mostly minor local or systemic reactions. The remaining 15% of ADRs were associated with other drugs, includinng and corticosteroids [19].

analgesics were associated with 30% of ADRs, primarily

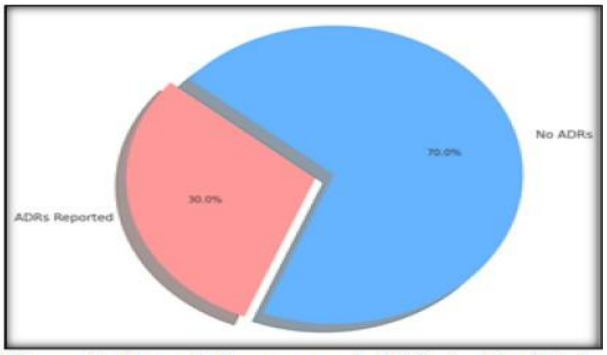
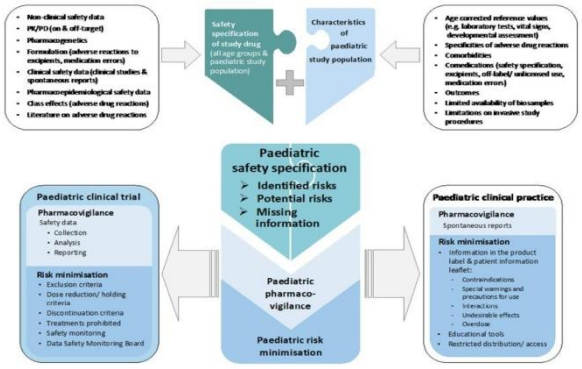


Figure 1: Overall frequency of ADRs in Paediatric Patients

involving non-steroidal anti-inflamatory. Vaccines were linked to 15% of ADRs, mostly minor local or systemic reactions. The remaining 15% of ADRs were associated with other drugs, including and corticosteroids [20].

The aim is to reduce the frequency and/or severity of known risks and to describe how any missing safety data will be collected or studied (e.g., risk factors and outcome for identified risk and additional data on potential risks). For each risk, a description of the risk and the corresponding risk minimisation activities are included.



- identified risks in children
- potential risks in children
- missing information (i.e., for identified or potential risks) in children.

Physiological changes	Characteristics
Absorption: Gastric pH	weak acids: lower bioavailability weak bases: higher bioavailability
Gastro intestinal motility	delayed absorption
Distribution: Body water	Hydrophilic drugs: higher Vt Hydrophobic drugs: lesser Vt
Metabolism: Phase I enzyme	less hepatic clearance
Elimination: Renal excretion	Low renal clearance

Results and Discussion

From a total of 20 paediatric patients (aged between3 months and 17 years), ADR reports were received by AMC until December 2016. The patients who had ADRs, 85% were males and 15% were females. Children, <6 years of age (50%), developed more ADRscompared to the higher age group [Figure 1]. Among children <6 years of age, almost two-thirds of them were infants. Polytherapy accounted for more than two-third of the ADRs received.

Conclusion

We may conclude that polytherapy probably is the major contributory factor in causing ADRs in children. Many of the patients, in fact, visited paediatric outpatient due to the problem of ADRs and were receiving more than one drug at the time of visit. Physicians should give polytherapy only when necessary, and the maximally tolerated doses of monotherapy are ineffectiveThe methods for ADR detection, evaluation, and monitoring should be strengthened, especially for the paediatric population as many of them may not directly communicate and one has to rely on parent description. The role of pharmacovigilance program in monitoring the safety of drugs in children should be evaluated for detection of newer and rarer ADRs. To improve spontaneous reporting of ADRs by HCPs, emphasis should be given to a regular educational workshop on pharmacovigilance. In addition, increasing awareness in general population to notify anything that they feel is unusual with medication use. motivation for voluntary reporting of

ADRs for preventing the morbidity and mortality in this vulnerable population could be of immense importance.

Author Contributions

All authors are contributed equally

Financial Support

None

Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

Acknowledgements

None

References

1. Rieder M. Adverse drug reactions across the age continuum: epidemiology, diagnostic challenges, prevention, and treatments. The Journal of Clinical Pharmacology. 2018 Oct;58:S36-47. **https://doi.org/10.1002/jcph.1115**
2. Bouuquet É, Star K, Jonville-Béra AP, Durrieu G. Pharmacovigilance in pediatrics. Therapies. 2018 Apr 1;73(2):171-80. **https://doi.org/10.1016/j.therap.2017.11.012**
3. Sandes V, Figueras A, Lima EC. Pharmacovigilance Strategies to Address Resistanceto Antibiotics and Inappropriate Use—A Narrative Review. Antibiotics. 2024 May 16;13(5):457. **https://doi.org/10.3390/antibiotics13050457**
4. Conroy S, McIntyre J, Choonara I, Stephenson T. Drug trials in children: problems and the way forward. British journal of clinical pharmacology. 2000 Feb;49(2):93. **https://doi.org/10.2165/00002018-200326080-00001**
5. Patsuree A, Krska J, Jarernsiripornkul N. Experiences relating to adverse drug reactions in the community: a cross-sectional survey among patients and the general public in Thailand. Expert opinion on drug safety. 2016 Mar 3;15(3):287-95. **https://doi.org/10.1517/14740338.2016.1135127**
6. levitzen S, Dubrall D, Toni I, Stingl J, Christ P, Köberle U, Schmid M, Neubert A, Sachs B. Adverse drug reactions in children: comparison of reports collected in a pharmacovigilance project versus spontaneously collected ADR reports. Pediatric Drugs. 2023 Mar;25(2):203-15 **https: //doi.org/10.1007/s40272-022-00540-z**
7. Khan Z, Karataş Y, Kıroğlu O. Evaluation of adverse drug reactions in paediatric patients: a retrospective study in Turkish hospital. Frontiers in pharmacology. 2021 Nov 12;12:786182 **https://doi.org/10.3389/fphar.2021.786182**
8. Impicciatore P, Choonara I, Clarkson A, Provasi D, Pandolfini C, Bonati 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. **https://doi.org/10.1046/j.0306-5251.2001.01407.x**
9. Liu M, McPeek Hinz ER, Matheny ME, Denny JC, Schildcrout JS, Miller RA, Xu H. Comparative analysis of pharmacovigilance methods in the detection of adverse drug reactions using electronic medical records. Journnformatics Aal of the American Medical Issociation. 2013 May 1;20(3):420-6. **https://doi.org/10.1136/amiajnl-2012-001119**
10. Dubrall D, Leitzen S, Toni I, Stingl J, Schulz M, Schmid M, Neubert A, Sachs B. Descriptive analysis of adverse drug reaction reports in children and adolescents from Germany: frequently reported reactions and suspected drugs. BMC Pharmacology and Toxicology. 2021 Dec;22:1-6. **https://doi.org/10.1186/s40360-021-00520-y1**
11. Dubrall D, Leitzen S, Toni I, Stingl J, Schulz M, Schmid M, Neubert A, Sachs B. Descriptive analysis of adverse drug reaction reports in children and adolescents from Germany: frequently reported reactions and suspected drugs. BMC Pharmacology and Toxicology. 2021 Dec;22:1-6. https://doi.org/10.1186/s40360-021-00520-y
12. Dubrall D, Leitzen S, Toni I, Stingl J, Schulz M, Schmid M, Neubert A, Sachs B. Descriptive analysis of adverse drug reaction reports in children and adolescents from Germany: frequently reported reactions and suspected drugs. BMC Pharmacology and Toxicology. 2021 Dec;22:1-6. **https://doi.org/10.1186/s40360-021-00520-y**
13. Neubert A. Pharmacovigilance in pediatrics: current challenges. Pediatric Drugs. 2012 Feb;14:1-5. https://doi.org/10.2165/11596590-000000000-00000
14. Scheiman M, Gallaway M, Coulter R, Reinstein F, Ciner E, Herzberg C, Parisi M. Prevalence of vision and ocular disease conditions in a clinical pediatric population. Journal of the American Optometric Association. 1996 Apr 1;67(4):193-202. **https://doi.org/10.1111/j.1755-3768.1980.tb04576.x**
15. Sharma PK, Misra AK, Gupta N, Khera D, Gupta A, Khera P. Pediatric pharmacovigilance in an institute of national importance: Journey has just begun. Indian Journal of Pharmacology. 2017 Sep 1;49(5):390-5. **https://doi.org/10.1186/s43054-020-00038-8**
16. Meibohm B. Knowledge gaps in the pharmacokinetics of therapeutic proteins in pediatric patients. Frontiers in Pharmacology. 2022 Feb 10;13:847021.7021. **https://doi.org/10.3389/fphar.2022.847021**
17. Meibohm B. Knowledge gaps in the pharmacokinetics of therapeutic proteins in pediatric patients. Frontiers in Pharmacology. 2022 Feb 10;13:847021.7021. **https://doi.org/10.3389/fphar.2022.847021**
18. Aagaard L, Strandell J, Melskens L, Petersen PS, Hansen EH. Global patterns of adverse drug reactions over a decade: analyses of spontaneous reports to VigiBase™. Drug safety. 2012 Dec;35:1171-82. **https://doi.org/10.1007/BF03262002**
19. Star K, Norén GN, Nordin K, Edwards IR. Suspected adverse drug reactions reported for children worldwide: an exploratory study using VigiBase. Drug

safety. 2011 May;34:415-28.
https://doi.org/10.2165/11587540-000000000-00000

20. Zyryanov SK, Butranova OI, Chenkurov MS. Chloramphenicol: new possibilities of the old drug. Obstetrics and Gynecology. 2021 Nov 15(11):81-94. **https://doi.org/10.18565/aig.2021.11.81-94**
21. Hwisa NT, Gindi S, Rao CB, Katakam P, Rao Chandu B. Evaluation of Antiulcer Activity of Picrasma Quassioides Bennett Aqueous Extract in Rodents. Vedic Res. Int. Phytomedicine. 2013;1:27.
https://www.researchgate.net/publication/248995990