

Critical Contribution of Pharmacists in Optimising Medication Safety among Children: A Narrative Review

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ABSTRACT

Paediatric patients are particularly vulnerable to medication errors and Adverse Drug Reactions (ADRs), with the incidence of adverse drug events being three times higher in children compared to adults. Given the complexity of paediatric care, it is essential that all healthcare professionals involved in paediatric medication management receive specialised training. Paediatric patients require individualised dosing, careful monitoring and age-appropriate formulations. The administration of the right drug to the right paediatric patient for the right indication, in the right amount, using the right route of administration, at the right time, and for the right duration forms the basis of rational therapeutics. The lack of availability of paediatric-appropriate medications necessitates urgent discussions among the health department, regulatory bodies, medical specialists and the pharmaceutical sector. The present review paper was aimed to identify the challenges associated with the development of paediatric formulations and Drug-related Problems (DRPs) faced by children, emphasising the critical role of pharmacists in addressing these issues, thus enhancing paediatric patient safety. Pharmacists, with their specialised knowledge and skills, are uniquely positioned to optimise medication therapy in paediatric care. They can significantly reduce medication errors by verifying dose calculations, identifying and mitigating potential drug interactions, and counselling caregivers on proper medication administration and storage. Additionally, pharmacists can serve as educators and communicators within the healthcare team, helping to minimise ADRs and improve their management and reporting. The present review study advocates for the increased involvement of pharmacists in paediatric care, recognising their potential to enhance therapeutic outcomes and safeguard paediatric patients from preventable medication-related harm.

Keywords: Adverse drug reactions, Drug-related problems, Medication error, Paediatric

INTRODUCTION

Ensuring the right medication is administered to the right patient, at the right time, in the right dose, by the right route, for the right disease by the healthcare team forms the basis of medication safety. The vast majority of currently available medications are designed for use in adults, making it particularly challenging to provide pharmacological care to paediatric patients. The percentage of drugs studied for the paediatric age group remains below 50% [1]. For this reason, many medications administered to paediatric patients are either not approved for use in this population or are utilised in ways other than those intended by the manufacturer. Together, these factors raise the risk of medication errors, which can diminish their effectiveness. Medication errors have been linked to a lack of knowledge and training among healthcare professionals, varying patient characteristics, environmental factors, prescribing errors and lack of communication [2].

Drug therapy in children is already challenging due to age-related differences in pharmacokinetics and pharmacodynamics. Not all drugs elicit the same response in infants, children, or adolescents, owing to differences in their pharmacokinetic processes, such as absorption and metabolism. It has been reported that 30-40% of paediatric patients experience at least one DRP, which may result in treatment failure, increased follow-up visits, the need for additional treatment, and increased costs [3]. Most of these DRPs can be prevented by including clinical pharmacists as medication experts. Paediatric populations are more vulnerable to ADRs than adults. There is a lack of information on clinical trials regarding ADRs in children, leading to a paucity of robust information on the ADR profiles of several drugs [3-5].

Therefore, a comprehensive, multidisciplinary and integrated approach is essential for ensuring the safe use of medications in children, and achieving improved patient outcomes. Pharmacists

have the opportunity to raise the standard of paediatric healthcare at multiple levels. Their expertise in dose calculations based on age and weight, attention to detail, strong communication skills, and deep knowledge of pharmacology, pharmacotherapeutics and pharmaceuticals make them invaluable in optimising medication safety for children. They can educate and counsel patients and their caregivers/parents, as well as provide evidence-based information and advice to healthcare workers to ensure the delivery of the correct, safest, and most effective medications to children [6-8]. The present review explores the major challenges in paediatric medication development and safety, and emphasises the critical role of pharmacists in addressing these issues to enhance paediatric patient care.

Challenges Associated with Development of Paediatric Medication

Traditionally, pharmaceutical research has concentrated on developing treatments for adults. Since there exists a non uniformity across various aspects within different age groups in children, the information provided for drug molecules is not readily suitable for direct application in the paediatric population. There is a scarcity of validated biomarkers that are appropriate for use in this population. Additionally, limited data is available to conduct paediatric studies; consequently, the number of drugs prescribed to the paediatric population has not been fully studied, especially in infants and neonates. Historically, clinical trials have predominantly included adults and rarely included children. Because of this, there is a demand for paediatric-labelled formulations and a market for children that is currently being neglected. Moreover, children represent a growing and changing population, even over the course of a single research study. Therefore, studies involving children are more difficult to plan and assess. Ethical concerns arise, in addition to the necessity of obtaining consent from both parents and subjects [9].

Due to the incomplete development of the Blood Brain Barrier (BBB) in newborns, certain lipid-soluble drugs, such as general anaesthetics, sedatives and narcotic analgesics, can have increased permeability. This is why neonates and infants are more sensitive to these drugs. Intravenous administration is preferred for seriously ill newborns. Drugs applied topically are readily absorbed, as the skin is well hydrated and the stratum corneum is thin.

Total body fat in preterm infants is about 1% of total body weight compared with 15% in full-term neonates [10]. Weight-related loading doses of aminoglycosides, aminophylline, digoxin and furosemide need to be larger for neonates than for older children. Another factor determining drug distribution is drug binding to plasma proteins [11]. Neonates have low protein binding capacity; hence, the fraction of free drug increases in plasma. For some drugs, the volume of distribution increases. For example, digoxin is distributed highly in the myocardium and in skeletal muscle in newborns. Additionally, salicylates are distributed in different body systems, such as the Central Nervous System (CNS), leading to salicylism. Some drugs compete with serum bilirubin for binding to albumin. Drugs given to neonates with jaundice can displace bilirubin from albumin, and this lipid-soluble bilirubin can cross the BBB to cause kernicterus; an example of this is sulfonamides [12].

Due to neonates' decreased ability to metabolise drugs, many drugs exhibit slow clearance rates and prolonged elimination half-lives. For instance, chloramphenicol-induced fatal gray baby syndrome in newborns occurs because of the decreased metabolism of chloramphenicol by glucuronyl transferase to the inactive glucuronide metabolite. Furthermore, infants have a greater capacity to carry out sulfate conjugation than adults. The increased metabolism by cytochrome P450 and enhanced sulfation explain its decreased hepatotoxic effects when given to children under six years of age. Phase II enzyme reactions mature between 3-6 months [13].

The renal excretory system matures over the first year of age. Drugs eliminated by the kidneys, such as aminoglycosides, penicillins and diuretics, require reduced doses. After six months of age, body weight and surface area-related daily doses are the same for all ages [13].

Technology requirements for drug delivery are also pressing issues when developing paediatric medicines [14]. As young patients often face swallowing difficulties, they may become non compliant; therefore, some medications need to be formulated as liquid orals, soluble films, or small-sized soluble tablets to make them more accessible. Some of these dosage forms require specialised methods, and it is possible that these technologies are not always readily available; instead, they may need to be developed locally or purchased from a third party, both of which can be expensive.

Excipients used in developing dosage forms are widely acknowledged as safe, and the vast majority are also non toxic, although not all of them are appropriate for use in paediatric dosages [15]. There is a lack of information on the usability and efficacy of excipients for children of varying ages and stages of development. In addition, factors such as age, weight, immature organ systems, the presence or absence of certain enzymes, and their fluctuating quantities all impact excipient metabolism in young patients. Hence, an additional difficulty not faced by adults is the possibility of unfavourable reactions in children caused by the excipients utilised in these medications.

Consideration of additional safety issues, including those related to growth and development, examination of alternative purposes, and the need for multicentric or even worldwide trials to enroll enough patients are just a few of the challenges that must be overcome [16,17].

Addressing the Challenges in Developing Paediatric Medications

For the very first time in India, guidelines for conducting clinical trials in the paediatric population were laid down and released as

the 'National Ethical Guidelines for Biomedical Research Involving Children' by the Indian Council of Medical Research (ICMR) [18]. These guidelines address the ethical issues of conducting research involving children, describe the assessment of benefits and risks in research, and outline informed consent, assent and general guidelines for research in children in special situations.

Such guidelines for the paediatric population are now also available in other countries, including the Institute of Medicine guidelines in the United States (U.S.), the Medical Research Council guidelines in the United Kingdom (U.K.) and the European Union (EU) guidelines [19].

The formulation for paediatric use should be bioequivalent to a product used for adults to reduce prescribing errors. The formulations for paediatric use must be appropriate in terms of the drug's dose, convenience and acceptability to children to ensure medication adherence. While formulating drugs for paediatric patients, the differences in physiology compared to adults must be considered to avoid any variations in the drug's pharmacokinetic profile. Important factors such as the child's age, ability to swallow and ease of administration should be taken into account when choosing medications for paediatric use. The characteristics of the formulation must be understood to select the right dosage form. Age-appropriate excipients should be chosen for paediatric use to minimise the risk of toxicity due to excipients [20].

The taste of medication is a very important parameter in paediatric use [20]. An unacceptable taste of a drug can be masked by mixing it with flavored syrups, such as acetaminophen syrup. The most preferred formulation for paediatric use is an oral liquid, due to its ease of swallowing and the ability to provide doses based on the child's weight [20]. Another property of liquid formulations is that they can be mixed with various flavors during administration, which can improve taste and mask the smell of a drug [21,22]. Oral liquid drops, such as those for the polio virus and rotavirus vaccines, can conveniently deliver small volumes of medicine to very young children. Small-sized dispersible and mouth-dissolving tablets are also accepted by paediatric patients [20].

Various other dosage forms used for paediatric patients include chewable tablets, powders, granules and pellets, due to the greater stability of solid dosage forms compared to liquid forms. Inhaled medicines are often prescribed to newborns and small children with asthma and cystic fibrosis. Airway size, respiratory rate, inspiratory and expiratory flow rates, and breathing patterns, as well as, lung sizes and capabilities, vary significantly throughout the early months and years of life. Dose modification is straightforward for the paediatric use of inhaled drugs since it is based on body weight; adult doses can be extrapolated to find suitable doses for patients aged 3-12 years [23]. For inhaled medications, the delivery mechanism impacts dosage, which is crucial for young patients [23]. Suppositories and other rectal dosage forms are considered appropriate for paediatric patients, such as diazepam, for those who may have difficulty swallowing pills and capsules [20].

Another suitable dosage form for the paediatric population is transdermal drug delivery systems, due to the avoidance of first-pass metabolism, regulated release and enhanced patient compliance [20]. Gummies are also preferred for formulating moisture-sensitive drugs in children [20-25].

Medication Errors in Paediatric Population

Paediatric patients are unique and should not be considered young adults when prescribing medicines. Mistakes made at any point in the medication use process, whether during prescribing, transcribing, dispensing, administering, or monitoring are considered medication errors [26]. The paediatric population is particularly vulnerable to these errors. Medication errors can result in significant harm, including morbidity and mortality, depending on their severity. In addition to affecting the patient, such errors also impact families and healthcare providers by increasing hospital expenditures, prolonging hospital

stays, and causing psychological distress. Available literature reports approximately 7.5 million preventable medication errors in paediatric patients in the United States alone each year [27]. A study in India reported one medication error for every 9.5 paediatric patients [28]. A systematic review conducted in 2019 for paediatric Intensive Care Units (ICUs) reported a median rate of paediatric medication errors as 14.6 per 1,000 medication orders [29]. According to the World Health Organisation (WHO), the global cost associated with medication errors has been estimated at 42 billion dollars annually [30]. If these mistakes are not avoided, they could lead to undesirable consequences.

Children in the ICU are at increased risk of such errors due to the complexity of their treatment plans. Treatment for many diseases requires intravenous administration, which typically involves diluting or reconstituting the drug. Antibiotics, electrolytes, fluids, analgesics, sedatives and proton pump inhibitors usually carry a higher risk of causing adverse effects in young patients [31]. Lack of communication between doctors and patients is also a major contributor to medication errors. Prescribing or administering an inappropriate dosage of drugs is one of the most common types of pharmaceutical errors reported in the literature. According to research, about 5% of all drug prescriptions contain an error, with wrong doses accounting for 28% of those cases [32].

A prospective observational study conducted in 2023 reported that in a paediatric Emergency Department, 218 medication errors were identified in patients under 16 years of age, and these were analysed by clinical pharmacists [33]. The most common error was the wrong dose, which accounted for 51.4%, while the wrong or inappropriate drug made up 46.8%. Serious ADRs were noted in 66.2% of cases, while wrong or improper drug errors comprised 29.7%, and drug or dose omission errors accounted for 13.5% [33]. Researchers in a Paediatric Emergency Room in the United States discovered that incorrect drug administration accounted for 30% of all medication mistakes [33]. In most cases, this was due to confusingly similar packaging or medicine names. Retrospective research conducted in the United Kingdom found that incorrect drug administration accounted for 12% of all prescription mistakes [2]. Premature infants and those younger than one year also appear to experience frequent medication errors. Such mistakes can prove to be particularly detrimental for premature infants and those under one year of age [29].

Pharmacist Intervention in Paediatric Medication Errors

Pharmacists are medication experts who bridge the gap between patients and physicians, providing optimal care to patients. A study conducted in a tertiary care hospital in Saudi Arabia reported 1,128 (68.2%) preventable medication errors identified by pharmacists in patients aged 1-6 years [33]. The order of medication errors was prescriber-related, followed by patient-related and finally drug-related [34]. A retrospective study evaluating electronic medical records in Riyadh showed 2,564 pharmacist interventions related to prescription errors, including dose adjustments (44.0%), restricted medication approvals (21.9%) and therapeutic duplications (11%) [35].

Clinical pharmacists play a significant role in the healthcare team due to their expertise and knowledge about drugs, as well as, their interactions with physicians, nurses and patients. Some intervention studies across the globe involving clinical pharmacists have significantly contributed to a decrease in medication errors and are listed below. Studies have reported that the introduction of computerised physician order entry has led to a decrease in medication errors [36,37]. Clinical pharmacists can play a crucial role in reviewing computerised physician order entries [36,37]. The participation of clinical pharmacists in ward rounds and the monitoring of patients' drug therapy in the Neonatal Intensive Care Unit (NICU) in Indian hospitals resulted in a 68.97% acceptance rate and changes in drug therapy [38]. Common errors included dose and frequency inappropriateness (40.22%), followed by

administrative errors (31.05%) and drug interactions (17.24%) [39].

A cross-sectional descriptive study carried out in a Paediatric Inpatient Department in Côte d'Ivoire showed that interventions by clinical pharmacists included 31.8% dose adjustments, 29.3% accuracy of drug administration modalities, and 27.6% proposed therapeutic choices, leading to significant clinical impacts in therapeutic optimisation [39]. A study in Pakistan reported a significant reduction in omission errors, which comprised 99.62% of all errors, through the education and training of nurses by clinical pharmacists [40-42]. In Malaysia, significant reduction in medication errors was reported, with the error rate decreasing from 44.3-28.6% by involving pharmacists in creating awareness among general medical ward staff members [43]. Interventions by pharmacists can play a significant role in reducing medication errors in the paediatric population [38-43].

The most common type of medication errors includes administration errors. Examples include incorrect administration, such as injectable amoxicillin/clavulanic acid given at the wrong amount or incorrect rate to children, dosing errors like carbamazepine given as 180 mg instead of 150 mg, and underdosing of digoxin and gentamicin [38-43]. A prospective, single-blinded study conducted in Jordan in 2017 showed that clinical pharmacist interventions in tertiary care hospitals, including patient care education, significantly improved asthma control and quality of life in children and adolescents [44]. Similarly, a cross-sectional study conducted from September 2017 to May 2018 in a tertiary care hospital in Iran reported that 54% of clinical pharmacist interventions occurred at the prescribing level, focusing on drug selection and dosing in hospitalised children [45].

Clinical pharmacist interventions played a vital role in identifying and mitigating the burden of medication errors, which included 59.3% prescription errors, 21% administration errors, 10.4% dispensing errors and 8.6% transcription errors, in a Paediatric ICU at a hospital in India [46]. Another study carried out in a teaching hospital in Iraq emphasised the role of clinical pharmacists in recognising, reporting and preventing 119 medication errors in infants and toddlers [47]. Clinical pharmacist-led interventions among cardiology patients in Palestine reported a 97.6% acceptance rate for interventions by cardiologists. Common DRPs were related to treatment effectiveness (50.8%) and safety (30.4%), with causes including errors in dosing instructions and improper combinations of drugs [48].

Adverse Drug Reactions (ADR) in Paediatric Population

Off-label use of drugs is a common practice in the paediatric population, even in the absence of strong supporting scientific evidence [49]. Off-label use refers to the prescribing or administration of drugs beyond the terms of their marketing authorisation regarding therapeutic indication, dose, frequency, age, or route of administration. In contrast, unlicensed use of drugs means modifying the formulation of licensed drugs, manufacturing drugs as extemporaneous preparations, importing or using drugs before a license is granted, or using chemicals as drugs due to a lack of such formulations [49]. The benefit-risk assessment for the use of off-label and unlicensed medications varies considerably between young and adult patients [50].

Moreover, children are especially prone to unwanted and harmful effects of drugs due to pathophysiological developmental changes, which result in marked effects on pharmacokinetics and pharmacodynamics. Unexpected adverse effects in children may differ from those seen in adults [51]. Chronic therapy with phenobarbital can significantly affect learning and behaviour in children [51], while children are at risk of delayed development and growth suppression with corticosteroid therapy [52]. Children under the age of two years are at a higher risk of hepatotoxicity from valproic acid than adults [53]. Long-term use of aspirin can lead to Reye's syndrome in patients with chickenpox [51]. The use of phenothiazines can cause extrapyramidal reactions, and

tetracyclines can result in discolored teeth in children. Additionally, the low level of P-glycoprotein transporters at birth can explain the increased sensitivity of neonates to opioids compared to older children [53].

ADRs in the paediatric patient population are a significant concern, as drugs that are safe for adult patients cannot be directly extrapolated to children [54]. Literature suggests that ADRs are both detectable and preventable. Pharmacists play a pivotal role in the detection, identification, prevention, management, evaluation, documentation and communication of ADRs [55].

Pharmacists can provide important care for inpatients by reviewing medication charts during ward rounds and managing medications in prescriptions. Several studies worldwide highlight that the off-label use of drugs, polypharmacy, and the irrational use of antibiotics in paediatric patients are responsible for the majority of ADRs [56]. An analysis of medical records for 301 paediatric patients in a university hospital in the Netherlands identified 132 cases of ADRs as a result of unlicensed and off-label drug use [57]. The study also emphasised that underreporting of ADRs is a significant issue among paediatric patients, finding that only an average of 513 ADR reports were made annually in the Netherlands [57].

Allen LV Jr, reported a retrospective study conducted at a teaching hospital in Odisha, India, from 2015 to 2020, where 105 ADRs were detected. Of these, 41% affected children in the age group of 0-5 years, and 21% of the cases were classified as serious [5]. The most common ADRs were cutaneous reactions (86.5%), primarily attributed to antibiotics (66%) [58].

A study by Leitzen S et al., analysed 20,854 spontaneous ADR reports from 2000 to 2019. The majority (86.5%) of the reports originated from healthcare professionals, while 12.2% came from non healthcare professionals. Additionally, 74.4% of the reports were classified as serious. Interestingly, only 3.5% of these reports involved off-label use [58]. Rani N et al., reported that out of a total of 14 ADRs detected in paediatric patients at a tertiary care hospital in Haryana, India, most of the ADRs were due to antibiotics affecting children between the ages of 3-5 years [59].

Role of Pharmacist in Adverse Drug Reaction (ADR)

Many studies have suggested that ADRs are detectable and preventable [55-60]. Pharmacists play a crucial role in the detection, identification, prevention, management, evaluation, documentation and communication of ADRs. Their interventions include reporting and managing ADRs and events, improving health-related quality of life,

addressing economic concerns, ensuring medication appropriateness and enhancing patient satisfaction and adherence [60].

Pharmacists can be pivotal in the care of inpatients by reviewing medication charts during ward rounds and managing the medications prescribed [54]. Development of ADR monitoring systems in hospitals can also be facilitated by pharmacists. Reporting ADRs is a critical aspect of monitoring and evaluating activities performed in hospital settings [60].

The role of pharmacists in paediatric patient care and safety has increased significantly. Clinical pharmacists have a greater role in NICUs and in managing patients diagnosed with chronic disorders, particularly regarding dose alterations and pharmacokinetic recommendations [61]. The incidence rate of 5.5 interventions per patient in paediatric ICUs has been shown to significantly impact patient health outcomes [61]. Pharmacists play a leading role in ensuring the right treatment, as well as, the safety and effectiveness of drugs [62].

Pharmacists also have an educational role, as they possess the necessary skills to address safety concerns related to patients and medications. DRPs encompass medication errors, ADRs, and adverse drug events. A prospective study conducted at a children's hospital in Vietnam demonstrated that pharmacist-led interventions significantly reduced DRPs, including inappropriate timing of administration and incorrect dosages, from 66.1-45.5% (p-value <0.001) [50].

Another prospective study conducted in three Paediatric Wards in Saudi Arabia involved clinical pharmacists, Paediatricians and interns analysing DRPs. A total of 596 DRPs were reported, with the highest incidence at 15.2% due to inappropriate drug choice, while 5.2% were classified as major DRPs. Additionally, 33.2% of DRPs were related to metabolism and the digestive system [63]. The predominant DRP was associated with dosing problems.

A study evaluating the prevalence and various DRPs led by clinical pharmacists found that out of 174 patients, one DRP was observed in 16% of the patients [64]. In total, 527 DRPs were identified, with drug-drug interactions found in 64.70%, therapeutic monitoring DRPs at 39%, and dosing issues at 1% [64].

The role of pharmacists has evolved and expanded in providing paediatric patient care, as well as, educating parents and healthcare professionals for effective reporting of ADRs. Some of the recent interventions by pharmacists that have led to a decrease in DRPs are listed in [Table/Fig-1] [65-72].

Sample size	Type of study	Intervention by pharmacist	Main findings
775 prescriptions	Randomised controlled trial [65]	Pharmacist's intervention was made for identifying and reporting DRPs. Two groups were made which were control and study groups and 31 physicians were randomly assigned to both the groups by pharmacist for identifying DRPs.	The pharmacist led study group had only 41% DRPs, whereas control group had 49%. Administration related DRPs decreased in study group from 31.3% to 25.3%.
1400 pharmacies	Non interventional observational study [66]	Clinical support system Electronic Expert Support (EES) was employed in pharmacies to evaluate prescriptions while dispensing.	High dose was found to be the most common DRP in 30.3% of paediatric patients. Therapy duplication was resolved in 4.6% of the alerts of DRP.
60 beds	Pre-post observational study [67]	Computerised Provider Order Entry (CPOE) system was implemented for reducing ordering and transcription errors.	After implementation of CPOE and utilising pharmacists, medication errors reduced from 133 to 109.
283 patients	Prospective observational cohort study [68]	Intervention by pharmacist as medication reconciliation service for children was carried out.	Pharmacist providing admission reconciliation resulted in reducing cost \$46,746.65 in 3 months which includes \$26,218 in preventing 8 major adverse drug events and \$20,528.65 for 54 minor adverse preventions.
195 patients	Prospective observational study [69]	Clinical pharmacists provided medication counselling to parents of paediatric patients in hospital and followed-up on call after few days of discharge of child.	Pharmacist's intervention led to increase in knowledge of parents by 28% after medical counselling. Administration of Drug-related Problems (DRP) faced by parent reduced by 67% and side-effects of drugs by 49% after pharmacist intervention.
2176 prescriptions	Retrospective study [70]	Trained pharmacists maintained the prescription pre-audit intelligent decision system for identifying and preventing drug-related medication errors in prescriptions.	The supervision of trained pharmacists identified 2176 errors that were associated with 35.2% drug dosage, 32.8% administration route, and 13.2% dose frequency errors. A 53.6% of errors were identified in infants' prescriptions.

100 patients	Retrospective Quasi-experimental interventional study [71]	Pharmacist-directed therapeutic drug monitoring service to optimise the correct prescribing of Initial Vancomycin doses and adjustments in dosing.	Post intervention cases with correctly prescribed Vancomycin significantly increased, (p-value <0.0001), there was increase in patients receiving correct dosage adjustments (p-value <0.05).
180 patients	Prospective interventional study [72]	Educational intervention including leaflets to reduce the inappropriate antibiotic use by clinical pharmacist in a 750 bedded hospital of south India.	The pre-intervention phase showed inappropriate use of antibiotic as the most commonly observed with wrong drug choice (23.3%), which was resolved by clinical pharmacist intervention in the post-intervention phase.

[Table/Fig-1]: List of recent interventions by pharmacists that led to decrease in DRPs [65-72].

CONCLUSION(S)

The heterogeneity of paediatric patients makes them more vulnerable to drug-related problems compared to adults, complicating their care. The development of medication for children is also a challenging process. Pharmacists are medication experts equipped with the necessary knowledge and skills to improve patient health outcomes. They can educate and counsel patients, caregivers/parents and healthcare workers, to provide optimised and safe medication use in paediatric patients. The role of pharmacists is crucial in reducing and managing medication errors and ADRs, as well as, in ensuring the delivery of the right medication in the right dose to children of all age groups.

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REFERENCES

- Hudgins JD, Bacho MA, Olsen KL, Bourgeois FT. Pediatric drug information available at the time of new drug approvals: A cross-sectional analysis. *Pharmacoepidemiol Drug Saf.* 2018;27(2):161-67.
- Mercer S, Furler J, Moffat K, Fischbacher-Smith D, Sancu L. Multimorbidity: Technical series on safer primary care. World Health Organization. 2016.
- Birarra MK, Heye TB, Shibeshi W. Assessment of drug-related problems in pediatric ward of Zewditu Memorial Referral Hospital, Addis Ababa, Ethiopia. *Int J Clin Pharm.* 2017;39(5):1039-46.
- Nguyen KT, Le VTT, Nguyen TH, Pham ST, Nguyen PM, Taxis K, et al. Effect of pharmacist-led interventions on physicians' prescribing for pediatric outpatients. *Healthcare (Basel).* 2022;10(4):751.
- 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;13(11):e19424.
- Bucci-Rechtweg C. Enhancing the pediatric drug development framework to deliver better pediatric therapies tomorrow. *Clin Ther.* 2017;39(10):1920-32.
- Keuler N, Bouwer A, Coetzee R. Pharmacists' approach to optimise safe medication use in paediatric patients. *Pharmacy (Basel).* 2021;9(4):180.
- Balakrishnan RP, Ravichandran R, Dillibatcha JS, Ravi AL, Sam NC, Nuthalapati R. Clinical pharmacists' role in paediatric patients' medical care. *Int J Contemp Pediatr.* 2020;7(12):2416-20.
- Truter A, Schellack N, Meyer JC. Identifying medication errors in the neonatal intensive care unit and paediatric wards using a medication error checklist at a tertiary academic hospital in Gauteng, South Africa. *S Afr J Child Health.* 2017;11(1):05-10.
- Ramel SE, Gray HL, Ode KL, Younge N, Georgieff MK, Demerath EW. Body composition changes in preterm infants following hospital discharge: Comparison with term infants. *J Pediatr Gastroenterol Nutr.* 2011;53(3):333-38. Available from: <https://doi.org/10.1097/MPG.0b013e3182243aa7>.
- Fernandez E, Perez R, Hernandez A, Tejada P, Arteta M, Ramos JT. Factors and mechanisms for pharmacokinetic differences between pediatric population and adults. *Pharmaceutics.* 2011;3(1):53-72. Available from: <https://doi.org/10.3390/pharmaceutics3010053>.
- Hulzebos CV, Tiribelli C, Cuperus FJC, Dijk PH. Kernicterus, bilirubin-induced neurological dysfunction, and new treatments for unconjugated hyperbilirubinemia in neonates. In: Buonocore G, Bracci R, Weindling M. (eds) *Neonatology.* Springer, Cham. (2016). Available from: https://doi.org/10.1007/978-3-319-18159-2_222-1.
- Lu H, Rosenbaum S. Developmental pharmacokinetics in pediatric populations. *J Pediatr Pharmacol Ther.* 2014;19(4):262-76. Available from: <https://doi.org/10.5863/1551-6776-19.4.262>.
- Golhen K, Buettcher M, Kost J, Huwyler J, Pfister M. Meeting challenges of pediatric drug delivery: The potential of orally fast disintegrating tablets for infants and children. *Pharmaceutics.* 2023;15(4):1033. Available from: <https://doi.org/10.3390/pharmaceutics15041033>.
- Rouaz K, Chiclana-Rodríguez B, Nardi-Ricart A, Suñé-Pou M, Mercadé-Frutos D, Suñé-Negre JM, et al. Excipients in the paediatric population: A review. *Pharmaceutics.* 2021;13(3):387. Available from: <https://doi.org/10.3390/pharmaceutics13030387>.
- Rishoej RM, Almarsdóttir AB, Christesen HT, Hallas J, Kjeldsen LJ. Medication errors in pediatric inpatients: A study based on a national mandatory reporting system. *Eur J Pediatr.* 2017;176(12):1697-705.
- Yin HS, Dreyer BP, Moreira HA, van Schaick L, Rodriguez L, Boettger S, et al. Liquid medication dosing errors in children: Role of provider counseling strategies. *Acad Pediatr.* 2014;14(3):262-70.
- Arora NK, Swaminathan S, Mohapatra A, Gopalan HS, Katoch VM, Bhan MK, et al. Research priorities in maternal, newborn, & child health & nutrition for India: An Indian Council of Medical Research-INCLIN Initiative. *Indian J Med Res.* 2017;145(5):611-22.
- Christiansen H, De Bruin ML, Hallgreen CE. Mandatory requirements for pediatric drug development in the EU and the US for novel drugs-A comparative study. *Front Med (Lausanne).* 2022;9:1009432. Available from: <https://doi.org/10.3389/fmed.2022.1009432>.
- Batchelor HK, Marriott JF. Formulations for children: Problems and solutions. *Br J Clin Pharmacol.* 2015;79(3):405-18.
- Fabiano V, Mameli C, Zuccotti GV. Paediatric pharmacology: Remember the excipients. *Pharmacol Res.* 2011;63(5):362-65.
- Baguley D, Lim E, Bevan A, Pallet A, Faust SN. Prescribing for children - taste and palatability affect adherence to antibiotics: A review. *Arch Dis Child.* 2012;97(3):293-97.
- Fink JB. Delivery of inhaled drugs for infants and small children: A commentary on present and future needs. *Clin Ther.* 2012;34(11):S36-S45.
- Salunke S, Giacoia G, Tuleu C. The STEP (Safety and Toxicity of Excipients for Paediatrics) database. Part 1-A need assessment study. *Int J Pharm.* 2012;435(2):101-11.
- Allen LV Jr. Basics: Excipients used in nonsterile compounding, Part 2. *Int J Pharm Compd.* 2019;23(5):393-96.
- Aronson JK. Medication errors: What they are, how they happen, and how to avoid them. *QJM.* 2009;102(8):513-21.
- Montastruc JL. Fatal adverse drug reactions in children: A descriptive study in the World Health Organization pharmacovigilance database, 2010-2019. *Br J Clin Pharmacol.* 2023;89(1):201-08.
- Bhusanpatnaik B, Varma CD, Sujatha NV, Satyasree TJ, Sreya A, Priyanka V. Clinical profile and outcome of snake bite in children. *Int J Pediatr Res.* 2019;6(3):107-12.
- Alghamdi AA, Keers RN, Sutherland A, Ashcroft DM. Prevalence and nature of medication errors and preventable adverse drug events in paediatric and neonatal intensive care settings: A systematic review. *Drug Saf.* 2019;42(12):1423-36.
- World Health Organization. Medication without harm [Internet]. [cited 2024 Dec 7]. Available from: <https://www.who.int/initiatives/medication-without-harm#:~:text=Unsafe%20medication%20practices%20and%20medication,of%20the%20medication%20use%20process>.
- Sanghera N, Chan PY, Khaki ZF, Planner C, Lee KK, Cranswick NE, et al. Interventions of hospital pharmacists in improving drug therapy in children: A systematic literature review. *Drug Saf.* 2006;29(11):1031-47.
- Sterling V. Minimizing medication errors in pediatric patients. *US Pharm.* 2018;44(4):20-23.
- Beatriz GC, José OM, Inés JL, Yolanda HG, Concha AD. Medication errors in children visiting pediatric emergency departments. *Farm Hosp.* 2023;47(4):141-47.
- Alanazi AA, Alomi YA, Almaznai MM, Aldwihi M, Aloraifi IAK, Albusalih FA. Pharmacist's intervention and medication errors prevention at pediatrics, obstetrics and gynecology hospital in East Province, Saudi Arabia. *Int J Pharm Health Sci.* 2019;8(2):122-28.
- Alzahrani AA, Alwhaibi MM, Asiri YA, Kamal KM, Alhawassi TM. Description of pharmacists' reported interventions to prevent prescribing errors among in hospital inpatients: A cross sectional retrospective study. *BMC Health Serv Res.* 2021;21(1):432.
- Liu KW, Shih YF, Chiang YJ, Chen LJ, Lee CH, Chen HN, et al. Reducing medication errors in children's hospitals. *J Patient Saf.* 2023;19(3):151-57.
- Satir AN, Pfiffner M, Meier CR, Caduff Good A. Prescribing errors in children: What is the impact of a computerized physician order entry? *Eur J Pediatr.* 2023;182(6):2567-75.
- Khan SN, Joseph SIBY, Sasidharan P, Faap A. A study of clinical pharmacist initiated intervention for the optimal use of medications in a neonatal intensive care unit (NICU) of a tertiary care hospital, South India. *Int J Pharm Pharm Sci.* 2016;8(1):23-26.
- Abrogoua DP, Békégánran CP, Gro BM, Doffou E, Folquet MA. Assessment of a clinical pharmacy activity in a pediatric inpatient department in Cote d'Ivoire. *J Basic Clin Pharm.* 2016;8(1):15-19.
- Ahmed T, Haq N, Rehman M, Nasim A. The impact of pharmacist intervention on medication errors in a teaching hospital Quetta, Pakistan. *Value in Health.* 2016;19(7):A630.

- [41] Smith L, Leggett C, Borg C. Administration of medicines to children: A practical guide. *Aust Prescr*. 2022;45(6):188-92.
- [42] Chua SS, Choo SM, Sulaiman CZ, Omar A, Thong MK. Effects of sharing information on drug administration errors in pediatric wards: A pre-post intervention study. *Ther Clin Risk Manag*. 2017;13:345-53.
- [43] Almomani BA, Mayyas RK, Ekteish FA, Ayoub AM, Ababneh MA, Alzoubi SA. The effectiveness of clinical pharmacist's intervention in improving asthma care in children and adolescents: Randomized controlled study in Jordan. *Patient Educ Couns*. 2017;100(4):728-35.
- [44] Jafarian K, Allameh Z, Memarzadeh M, Saffaei A, Peymani P, Sabzghabae AM. The responsibility of clinical pharmacists for the safety of medication use in hospitalized children: A Middle Eastern experience. *J Res Pharm Pract*. 2019;8(2):83-91.
- [45] Loni R, Charki S, Kulkarni T, Kamale M, Bidari LH. Utility of a clinical pharmacist in the pediatric intensive care unit to identify and prevent medication errors. *J Pediatr Crit Care*. 2020;7(5):249-54.
- [46] Al-Khyat M, Aladul M. Recognition and prevention of medication errors in pediatric inpatients: The role of clinical pharmacists. *Global Journal of Public Health Medicine*. 2021;3(2):438-46.
- [47] Elhabib MK, Yousif MA, Ahmed KO, Abunada MI, Almhari KI, Eldalo AS. Impact of clinical pharmacist-led interventions on drug-related problems among pediatric cardiology patients: First Palestinian experience. *Integr Phar Res Pract*. 2022;11:127-37.
- [48] Priyadharsini R, Surendiran A, Adithan C, Sreenivasan S, Sahoo FK. A study of adverse drug reactions in pediatric patients. *J Pharmacol Pharmacother*. 2011;2(4):277-80.
- [49] Meng M, Zhou Q, Lei W, Tian M, Wang P, Liu Y, et al. Recommendations on off-label drug use in pediatric guidelines. *Front Pharmacol*. 2022;13:892574. Available from: <https://doi.org/10.3389/fphar.2022.892574>.
- [50] van der Zanden TM, Mooij MG, Vet NJ, Neubert A, Rascher W, Lagler FB, et al. Benefit-risk assessment of off-label drug use in children: The bravo framework. *Clin Pharmacol Ther*. 2021;110(4):952-65. Available from: <https://doi.org/10.1002/cpt.2336>.
- [51] Kennedy GM, Lhatoo SD. CNS adverse events associated with antiepileptic drugs. *CNS Drugs*. 2008;22(9):739-60. Available from: <https://doi.org/10.2165/00023210-200822090-00003>.
- [52] Pal DK. Phenobarbital for childhood epilepsy: Systematic review. *Paediatr Perinat Drug Ther*. 2006;7(1):31-42. Available from: <https://doi.org/10.1185/146300905X75361>.
- [53] Meyers RS, Thackray J, Matson KL, McPherson C, Lubsch L, Hellinga RC, et al. Key potentially inappropriate drugs in pediatrics: The KIDS list. *J Pediatr Pharmacol Ther*. 2020;25(3):175-91. Available from: <https://doi.org/10.5863/1551-6776-25.3.175>.
- [54] Bushra R, Baloch SA, Jabeen A, Bano N, Aslam N. Adverse drug reactions: Factors and role of pharmacist in their prevention. *J Ayub Med Coll Abbottabad*. 2015;27(3):702-06.
- [55] Salazar A, Amato MG, Shah SN, Khazen M, Aminmozaffari S, Klinger EV, et al. Pharmacists' role in detection and evaluation of adverse drug reactions: Developing proactive systems for pharmacovigilance. *Am J Health Syst Pharm*. 2023;80(4):207-14. Available from: <https://doi.org/10.1093/ajhp/zxac325>.
- [56] Horen B, Montastruc JL, Lapeyre-Mestre M. Adverse drug reactions and off-label drug use in paediatric outpatients. *Br J Clin Pharmacol*. 2002;54(6):665-70. Available from: <https://doi.org/10.1046/j.1365-2125.2002.t01-3-01689.x>.
- [57] Dittrich ATM, Smeets NJL, de Jong EFM, Kämink JL, Kroeze Y, Draaisma JMT, et al. Quality of active versus spontaneous reporting of adverse drug reactions in pediatric patients: Relevance for pharmacovigilance and knowledge in pediatric medical care. *Pharmaceuticals (Basel)*. 2022;15(9):1148.
- [58] Leitzens S, Dubrall D, Toni I, Stingl J, Schulz M, Schmid M, et al. Analysis of the reporting of adverse drug reactions in children and adolescents in Germany in the time period from 2000 to 2019. *PLoS One*. 2021;16(3):e0247446.
- [59] Rani N. Pattern of adverse drug reactions among pregnant women and pediatric patients in a tertiary care hospital. *Curr Drug Saf*. 2023;18(2):190-95.
- [60] Alqurbi MMA, Atiah MAQ. The role of clinical pharmacists in reducing adverse drug reactions. *International Journal of Medicine in Developing Countries*. 2020;4(1):236-39.
- [61] Mathew AM, Sebastian J. Clinical pharmacy interventions in pediatric intensive care unit: A review. *Acta Scientifica Pharmaceutical Sciences*. 2021;5(7):164-70.
- [62] Rieder M. Adverse drug reactions in children: Pediatric pharmacy and drug safety. *J Pediatr Pharmacol Ther*. 2019;24(1):04-09.
- [63] Tawhari MM, Tawhari MA, Noshily MA, Mathkur MH, Abutaleb MH. Hospital pharmacists interventions to drug-related problems at tertiary critical care pediatric settings in Jazan, Saudi Arabia. *Hosp Pharm*. 2022;57(1):146-53.
- [64] Şahin Y, Nuhoglu Ç, Okuyan B, Sancar M. Assessment of drug-related problems in pediatric inpatients by clinical pharmacist-led medication review: An observational study. *J Res Pharm*. 2022;26(4):1007-15.
- [65] Nguyen PM, Nguyen KT, Pham ST, Thanh Le VT, Thi Le TC, Diep HG, et al. Pharmacist-led interventions to reduce drug-related problems in prescribing for pediatric outpatients in a developing country: A randomized controlled trial. *J Pediatr Pharmacol Ther*. 2023;28(3):212-21.
- [66] Abdulkadir SA, Wettermark B, Hammar T. Potential drug-related problems in pediatric patients-describing the use of a clinical decision support system at pharmacies in Sweden. *Pharmacy (Basel)*. 2023;11(1):35.
- [67] Liang MQ, Thibault M, Jouvett P, Lebel D, Schuster T, Moreault MP, et al. Improving medication safety in a paediatric hospital: A mixed-methods evaluation of a newly implemented computerised provider order entry system. *BMJ Health Care Inform*. 2023;30(1):e100622.
- [68] Hovey SW, Click KW, Jacobson JL. Effect of a Pharmacist Admission Medication Reconciliation Service at a Children's Hospital. *J Pediatr Pharmacol Ther*. 2023;28(1):36-40.
- [69] Solano M, Jeannin M, Anxionnat R, Vardanega J, Ridley A, Amsallem D, et al. Impact of pharmacist medication review for paediatric patients: An observational study. *Int J Pharm Pract*. 2022;30(5):420-26.
- [70] Wang G, Zheng F, Zhang G, Huang Y, Ye Q, Zhang X, et al. Intercepting medication errors in pediatric in-patients using a prescription pre-audit intelligent decision system: A single-center study. *Paediatr Drugs*. 2022;24(5):555-62.
- [71] Hussain K, Ikram R, Ambreen G, Salat MS. Pharmacist-directed vancomycin therapeutic drug monitoring in pediatric patients: A collaborative-practice model. *J Pharm Policy Pract*. 2021;14(1):100.
- [72] Azeez S, Panakkal LM, Meenpidiyil SS, Sulaiman N. Impact of clinical pharmacist intervention in promoting rational antibiotic use in pediatric patients. *Research J Pharm Tech*. 2020;13(11):5077-82.

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