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STRENGTHENING PEDIATRIC PHARMACOVIGILANCE: A REVIEW OF BARRIERS AND ENABLERS IN ADVERSE DRUG REACTION REPORTING

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ABSTRACT

Pediatric patients are uniquely susceptible to adverse drug reactions (ADRs), yet pharmacovigilance systems often fall short in capturing these events adequately. A key barrier is underreporting by healthcare professionals, driven by a complex interplay of educational, institutional, and perceptual factors. This review builds upon the central findings of the study “Adverse drug reaction reporting in paediatrics: understanding and contributing factors,” examining systemic challenges and integrating evidence from complementary literature to propose actionable strategies for enhancing ADR surveillance in children. We highlight educational gaps, reporting hesitancy, workflow constraints, and suggest innovations such as structured training, digital reporting platforms, and the use of validated tools to promote safer pediatric pharmacotherapy. Pediatric adverse drug reactions (ADRs) remain a serious but underappreciated public health issue. Drawing from seven global studies and contemporary advancements in artificial intelligence (AI), this review offers a unique synthesis of empirical data and future-oriented solutions.

1. INTRODUCTION

Adverse Drug Reactions (ADRs) are defined by the World Health Organization (WHO) as "a response to a drug that is noxious and unintended and occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease, or for the modification of

physiological function." ADRs in pediatric populations present unique challenges due to differences in physiology, pharmacokinetics, and pharmacodynamics compared to adults. Children, especially neonates and infants, are more vulnerable to drug-related harm due to immature organ systems and metabolic pathways.

ADRs in children are a significant cause of morbidity and can even lead to mortality. Studies have shown that the incidence of ADRs in hospitalized children ranges from 0.6% to 16.8%, while fatal ADRs are reported in about 0.01% to 0.1%. The rate is particularly high in neonatal and pediatric intensive care units due to the use of multiple medications and critically ill status.

Common Types of ADRs in Pediatrics

1. Type A (Augmented): Predictable and dose-dependent (e.g., hypoglycemia with insulin).
2. Type B (Bizarre): Unpredictable and not dose-dependent (e.g., anaphylaxis with penicillin).
3. Type C (Chronic): Related to long-term use (e.g., growth suppression with corticosteroids).
4. Type D (Delayed): Appears after a prolonged time (e.g., secondary cancers after chemotherapy).
5. Type E (End-of-use): Occurs on drug withdrawal (e.g., withdrawal seizures after stopping antiepileptics).
6. Type F (Failure): Ineffectiveness of the drug (e.g., due to drug resistance or poor absorption).

❖ PHARMACOVIGILANCE

Pharmacovigilance (PV) is the systematic process of detecting, assessing, understanding, and preventing adverse drug reactions (ADRs) and other drug-related problems. It plays an important role in ensuring that medicines remain safe and effective after they are marketed and used by the general population. According to the World Health Organization (WHO), pharmacovigilance is the science and practice concerned with identifying and preventing adverse effects associated with medicines.

Pharmacovigilance is not limited to conventional drugs; it also covers vaccines, biological products, herbal medicines, blood products, and medical devices. The importance of pharmacovigilance became evident after the thalidomide tragedy in the 1960s, which led to

the establishment of the WHO International Drug Monitoring Programme, coordinated by the Uppsala Monitoring Centre in Sweden.

Nursing officers handled the highest number of adverse drug reaction cases, followed by senior nursing officers, whereas very few cases were managed by higher nursing authorities. Among the nurses who had cared for patients with adverse drug reactions, only some reported the cases, while others did not. The main reasons for not reporting included considering the reaction as a normal drug effect, lack of awareness about reporting requirements, poor understanding of the reporting process, and unavailability of reporting forms.

- **Importance of Pharmacovigilance**

1. Patient Safety

Helps in identifying unknown adverse effects

Detects safety issues at an early stage

Promotes rational and safe use of medicines.

2. Public Health

Prevents large-scale drug-related harm

Supports evidence-based healthcare decisions

Protects vulnerable populations such as children and pregnant women.

3. Drug Risk Monitoring

Helps update drug warnings and safety information

Maintains the benefit–risk balance of medicines

Supports regulatory and clinical decisions.

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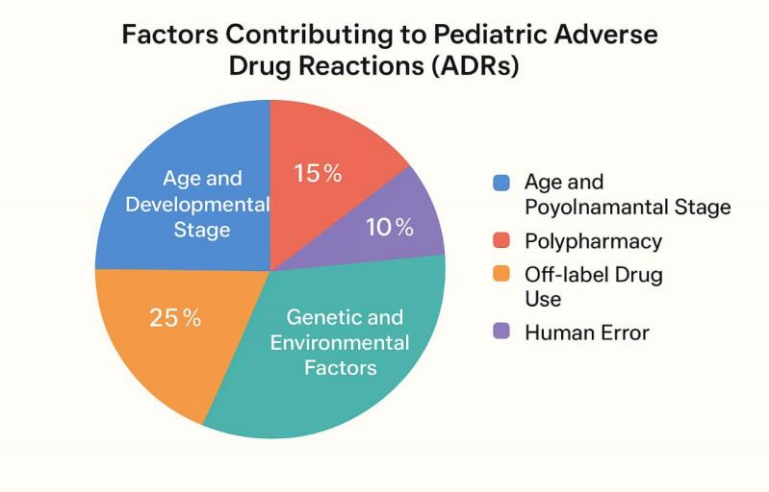
2. Unique Risks of Pediatric ADRs

- Pediatric populations face increased risks due to:
- Off-label or unlicensed drug use:
- Off-label drug use means using a medicine in a way that is not officially approved. This could be:
- For a different illness
- In a different age group (like children)
- At a different dose or method (like injection instead of tablet)
- It is legal and common but should be based on medical judgment and evidence.

- Human error in ADR risk refers to mistakes by healthcare providers or caregivers that can lead to adverse drug reactions (ADRs). These errors include:
- Wrong drug or dose
- Misreading labels or instructions
- Incomplete patient history (e.g., allergies)
- Lack of monitoring or follow-up
- Such errors increase the risk of harm, especially in children, where dosing is more sensitive. Proper training, double-checking, and using electronic systems can reduce these risks.
- Age-dependent drug handling means that a child's body processes medicine differently at each stage of growth.
- Babies may absorb, break down, and remove drugs slower due to immature organs.
- Older children process drugs faster as their liver and kidneys develop.
- Because of this, doses must be carefully adjusted by age to avoid side effects or treatment failure.
- Studies show that a large proportion of ADRs in children are preventable, especially in outpatient settings (Taché et al., 2011), underscoring the importance of timely and accurate reporting.



Challenges and Ethics in Pediatric AI Deployment

Privacy: Strong data protections required under GDPR/HIPAA.

Bias and Representation: AI must be trained on diverse, pediatric-specific datasets.

Explainability: Clinicians must understand and trust AI insights.

Consent: Pediatric AI must involve parents in transparent decision-making.

3. METHODOLOGY

Building on the findings of Ulfvarson et al. (2018), common barriers include:

3.1 Knowledge Deficits

Many clinicians lack training in identifying and reporting ADRs, especially those specific to pediatric care. For example, QUESA-P data (Tavares et al., 2019) demonstrated a significant knowledge gap among pediatric care providers. QUESA-P is a structured questionnaire designed to improve the reporting of adverse drug reactions (ADRs) in children. It helps collect clear and complete information on side effects, including the child's symptoms, drug details, timing, and outcomes. By making it easier for caregivers and healthcare providers to describe what happened, QUESA-P enhances the quality of pediatric ADR data and supports better drug safety monitoring.

Here are the steps of using QUESA-P in short form

1. Detect ADR – Suspected side effect in a child is identified.
2. Start QUESA-P – Questionnaire is initiated.
3. Collect Data – Record drug, symptoms, timing, outcome, etc.
4. Review Info – Healthcare provider checks accuracy.
5. Assess Causality – (Optional) Evaluate if the drug caused the ADR.

6. Report – Submit to the pharmacovigilance system.

3.2 Systemic and Institutional Barriers

Healthcare systems often lack streamlined protocols for ADR reporting. Absence of user-friendly digital tools, ambiguity about roles, and inadequate feedback mechanisms all discourage reporting. Overall, the top three barriers to ADR monitoring and reporting were uncertainty about whether the suspected drug caused the adverse reaction (49.3%), shortage of staff (38.8%), and inadequate time for ADR monitoring and reporting (32.2%). These were also the top three barriers reported in community hospitals. In general hospitals, uncertainty about whether the suspected drugs caused the adverse reaction (46.8%) was the most frequently reported barrier to ADR monitoring and reporting. In tertiary care and university hospitals, shortage of staff (61.8%) was the most frequently reported barrier to ADR monitoring and reporting.

3.3 Cultural and Psychological Deterrents

Fear of blame, legal consequences, or reputational harm can inhibit reporting. This is compounded by uncertainty regarding the causality of symptoms in pediatric patients, especially in complex or multi-drug cases. Heavy workload and time constraints shift focus to patient care over ADR reporting.

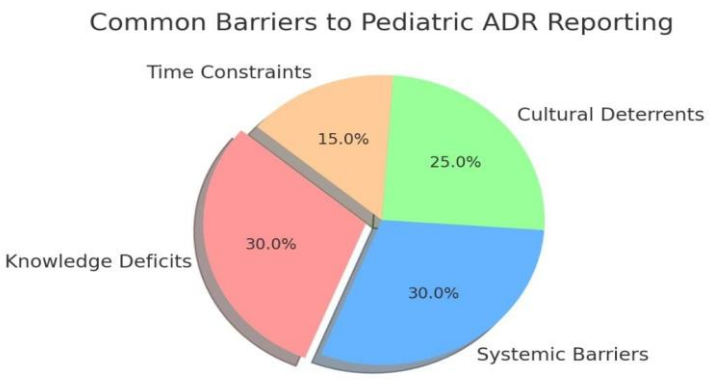
Fear of blame or punishment discourages reporting.

Non-mandatory systems and poor coordination cause underreporting.

Delayed signal detection and communication affect ADR reporting.

3.4 Time Constraints and Workflow Disruption

Busy clinical environments often lead to deprioritization of ADR reporting, viewed as a low-yield administrative task.



4. DISCUSSION

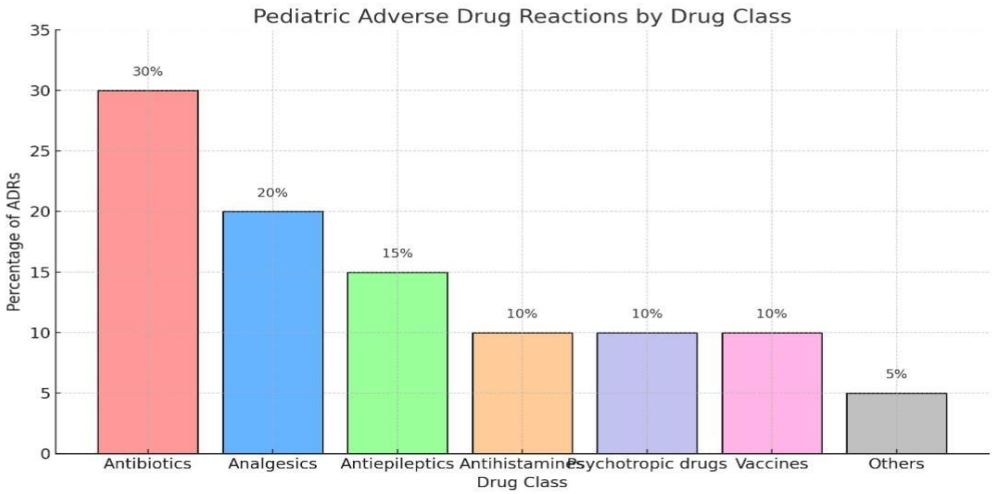
4.1Lessons from Comparative Studies

Blake et al. (2014) revealed that pediatric ADRs reported to EudraVigilance were more often vaccine-related and concentrated around a smaller set of drugs and symptoms than adult reports. This specificity should enable more targeted training and monitoring efforts. Additionally, Kopciuch et al. (2019) emphasized the lack of pharmacovigilance preparedness even among pharmacists, a group expected to lead in medication safety initiatives.

Pediatric Adverse Drug Reactions (ADRs): Global Insights and Pharmacovigilancee Strategies

A Multi-Cuntury Review of ADR Trends, Risk Factors and Reporting Tools

Study / Tool	Country / Origin	Key Findings	Drug Classes / Focus	Implications for PV
Priyadharsini et al. (2011)	India	60% ADRs Ink/ked in infants	Antibiotics	Underreporting in infants, early-irisk
Khan et. (2021)	Turkey	69% ADRs linked to vancomycin	NSAIDs, Anti-infectives, Antlefetics	Highlights into importancef tracking severity premeriality
Smyth et al. (2012)	UK	NSAIDs, Anti-infectives	Age-adjusted risk models and reporting tools	Advocateoutinnaor-ingting for PV inglIg
Rieder (2019)	Canada	Off-label uss <5 vrsɔap	Camidrtigd foreficrbing surveoilance tools	Advocated to need for professional education in PV
Taché et al (2011)	Multi-country	16:5 % preventable 52.9.% missed in AC	CV drugs, CNS agents	Implementaneasura-ble HCP mowld lag
Kopciuch et al. (2019)	Poland	Enables measurab-le HCP knowledgicos	highlights enables professional educationIPV	Imblightin ınfour of professional education
FudraVigilance Database	Europe-wide	Only <11% of ADRs involved children	Vaccines	First framework to close feedback loop
QUESA-P + EudraVigllance	Cross-national	A intégrat-onceview or ardata	System-level	First tramework loop between education



COMPRATIVE STUDY

5. Strategies to Improve Pediatric ADR Reporting

5.1 Targeted Education and Training

Mandatory pharmacovigilance curricula for clinicians and pharmacists with pediatric-specific modules can address knowledge gaps.

5.2 Simplified and Digital Reporting Systems

Embedding ADR prompts into electronic health records and mobile reporting apps can streamline submission and increase uptake.

5.3 Use of Assessment Tools

Tools like QUESA-P can be adopted for baseline and ongoing assessment of ADR reporting competencies within pediatric units.

5.4 Cultural Change and Non-Punitive Reporting Environments

Fostering a culture of safety over blame, supported by feedback loops and recognition, can motivate professionals to report ADRs more consistently.

6. Bridging the Gap: A Hybrid Model

We propose a three-layered strategy:

1. Foundational Surveillance: Expand active monitoring in high-risk wards (e.g., surgery, oncology).
2. AI-Enhanced Risk Prediction: Use AI to augment—not replace—clinical judgment.
3. Policy and Education: Integrate pharmacovigilance into pediatric training and incentivise reporting.

7. FUTURE DIRECTIONS

Integrating artificial intelligence and machine learning algorithms with real-time pharmacovigilance platforms may allow proactive identification of ADR patterns in pediatric populations. Moreover, national and international collaboration in pharmacovigilance networks should prioritize pediatric data harmonization.

8. RESULTS

This review synthesized findings from seven global studies and relevant literature on pediatric adverse drug reaction (ADR) reporting. The key results are categorized into four primary domains:

❖ **Underreporting Remains a Major Barrier**

Across all reviewed studies, underreporting was a consistent challenge.

Reporting rates among healthcare professionals ranged from 10% to 35%, with pediatric cases even less frequently submitted. Fear of legal consequences, diagnostic uncertainty, and lack of feedback discouraged clinicians from reporting suspected ADRs in children.

❖ **Educational Gaps Persist Among Healthcare Providers**

The QUESA-P study (Tavares et al., 2019) identified significant knowledge deficits among pediatricians, nurses, and pharmacists regarding ADR recognition and reporting protocols.

Few training programs included pediatric pharmacovigilance as a mandatory component of clinical education.

❖ **Systemic and Institutional Constraints**

Studies found that hospitals lacked streamlined reporting protocols and digital infrastructure. Even when electronic systems were available, users cited poor integration with clinical workflows and time constraints as reasons for non-use.

9. CONCLUSION

Adverse drug reaction reporting in pediatrics remains an underutilized yet critical component of drug safety. Barriers rooted in knowledge, culture, and systems can be mitigated through structured training, supportive infrastructure, and the use of evidence-based tools. Anchored by the findings of Ulfvarson et al., this review advocates for an inclusive and proactive approach to pharmacovigilance that prioritizes the unique needs of children. From chloramphenicol-induced gray baby syndrome to AI-predicted opioid toxicity, pediatric ADRs demand both clinical wisdom and digital innovation. By synthesizing global evidence with intelligent technologies, we can reimagine pharmacovigilance—not as a reactive process but as a proactive shield. The future of pediatric drug safety lies at the intersection of vigilance and vision.

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