Original Article

Clinical Profile and Short-Term Outcomes of Adverse Drug Reactions in Hospitalized Children at a Tertiary Care Centre in Central India: A Prospective Observational Study

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Abstract

Background: Adverse drug reactions (ADRs) pose a significant safety concern in pediatric populations, particularly within tertiary care settings where complex medications and polypharmacy increase vulnerability. Children face unique pharmacokinetic challenges due to immature organ systems and limited pediatric-specific clinical trial data, necessitating comprehensive evaluation of ADR patterns and outcomes in hospitalized patients. The objective is to assess the clinical profile and short-term outcomes of adverse drug reactions in pediatric inpatients at a tertiary care centre. **Material and Methods:** This prospective observational study was conducted over one year at the Department of Pediatrics of a government tertiary care centre in Central India, enrolling 125 children aged one month to 14 years who developed ADRs during hospitalization. Comprehensive clinical data, medication details, and ADR characteristics were documented using pre-structured proformas. Causality was assessed using WHO-Uppsala Monitoring Centre criteria, and outcomes were systematically tracked until discharge. Data were entered into Microsoft Excel and analysed using SPSS Version 22. **Results:** Among 125 patients, 38.4% were aged 1 month-5 years, with female predominance (58.4%) and 55% underweight. Antibiotics caused 32% of ADRs, followed by blood products (25.6%) and anticancer agents (21.6%). Cutaneous manifestations predominated (38.4%), with 56.8% of reactions occurring within one hour. Most ADRs were mild (67.2%) or moderate (32.8%), with 48.8% classified as "likely" causality. All patients achieved complete recovery, though 92.8% required hospitalization exceeding 72 hours. **Conclusion:** ADRs in pediatric inpatients predominantly affected younger children and manifested as acute hypersensitivity reactions, primarily caused by antibiotics. Despite favorable recovery outcomes, prolonged hospitalizations highlight the substantial healthcare burden, emphasizing the need for enhanced antibiotic stewardship and proactive pharmacovigilance in pediatric care.

Keywords: Adverse drug reactions, pediatric pharmacovigilance, antibiotic safety, tertiary care.

Received: 03 July 2025 **Revised: 02 August 2025** **Accepted: 15 September 2025** **Published: 27 September 2025**

Introduction

Adverse drug reactions (ADRs) are defined by the World Health Organization as 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function'.[1] In pediatric populations, ADRs pose a unique challenge due to developmental variations in drug absorption, distribution, metabolism, and excretion, which can alter pharmacokinetics and predispose children—especially neonates and infants—to toxicity.[2,3] Furthermore, the frequent reliance on off-label prescribing, driven by the lack of pediatric-specific formulations and clinical trial data, increases the risk of unforeseen adverse events.[4,5] In tertiary care settings, children often present with complex conditions requiring polypharmacy, further amplifying the potential for drug–drug interactions and immunologically mediated reactions.[6] Compounding these risks, the clinical presentation of ADRs in children may mimic common pediatric illnesses, leading to under-recognition and delayed management.[7] In resource-limited settings such as India, the high burden of malnutrition, infectious diseases, and restricted healthcare access alters drug metabolism and heightens children's vulnerability to adverse drug reactions. Moreover, widespread irrational use of antibiotics, corticosteroids, and other potent medications fuels both drug resistance and ADRs.[8,9] Underreporting of pediatric ADRs remains a significant barrier to robust pharmacovigilance, with Indian reporting rates falling below 1%, compared to a global average of 5%. Such delays in detection not only compromise patient safety but also hinder efforts to characterize the epidemiology and short-term outcomes of pediatric ADRs.[10,11] This prospective observational study aims to bridge

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DOI: 10.21276/amit.2025.v12.i3.96

How to cite this article: Singh NK, Biswas M, Channa U. Clinical Profile and Short-Term Outcomes of Adverse Drug Reactions in Hospitalized Children at a Tertiary Care Centre in Central India: A Prospective Observational Study. Acta Med Int. 2025;12(3):361-366.

this gap by systematically evaluating the incidence, clinical manifestations, causality, and short-term outcomes of ADRs in children admitted to a tertiary care hospital. By delineating the clinical profile and immediate consequences of these reactions, our findings will inform targeted strategies for early recognition, prevention, and management, ultimately enhancing pediatric drug safety in resource-limited settings.

Aim and Objectives

1. To study the clinical profile of adverse drug reactions in patients admitted to the Paediatric Department of a tertiary care centre.
2. To assess the short-term outcomes of these patients with adverse drug reactions.

Materials and Methods

This prospective, observational, single-centre study was conducted in the Department of Pediatrics at M.Y. Hospital and CNBC, Indore, Madhya Pradesh, India. The study spanned one year following approval from the Institutional Ethics Committee and Scientific Review Committee. The study enrolled pediatric patients aged between one month and 14 years admitted to the Pediatric Intensive Care Unit (PICU) who developed adverse drug reactions (ADRs) during hospitalization. Patients developing ADRs outside the hospital or whose guardians did not consent were excluded. Based on the expected ADR prevalence of 8.7% from a previous study, a final sample size of 125 was calculated using the formula $N=Z2\times P\times Q/d2$ (where Z=1.96 for 95% confidence interval, Q=100-P=91.3%, and margin of error d=5%).

Informed consent was obtained from parents or legal guardians. Detailed clinical histories, including comorbidities and allergies, were recorded. Medication details—such as drug name, batch number, expiry date, dilution, and duration—were documented. ADR characteristics including onset, type, and severity were captured using a structured proforma. Relevant laboratory and clinical investigations were performed as per hospital protocols. Causality was evaluated using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) scale, which classifies ADRs as Certain, Probable, Possible, or Unlikely based on temporal relationship, alternative explanations, dechallenge/rechallenge responses, and pharmacological plausibility. Primary outcomes included ADR incidence, causality, and severity. Secondary outcomes encompassed ADR types, implicated drugs, risk factors, hospital stay duration post-ADR, complications, recovery status, discharge outcomes, and interventions required.

Data were entered into Microsoft Excel and analyzed using IBM SPSS Version 22. Descriptive statistics were presented as percentages and counts; inferential statistics included p-values where applicable.

Operational Definitions

- Adverse Drug Reaction (ADR): A noxious and unintended response to a drug administered at normal doses for prophylaxis, diagnosis, or therapy, as defined by the World Health Organization (WHO).[1]
- WHO-UMC Causality Assessment Scale: The WHO-UMC scale is a structured, qualitative framework used in clinical practice to attribute adverse drug reactions (ADRs) to suspect medications. It evaluates temporal relationships, alternative explanations, dechallenge/rechallenge responses, and pharmacological plausibility to categorize causality.[12]

Causality Category	Key Assessment Criteria.[12]
Certain	- Clear temporal link to drug intake - No plausible alternative cause - Plausible improvement on drug withdrawal (dechallenge) - Confirmatory recurrence on re-administration (rechallenge)
Probable / Likely	- Reasonable temporal association - Unlikely to be explained by disease or other drugs - Clinically reasonable response on dechallenge - Rechallenge not required
Possible	- Temporal relation present - Could be due to underlying disease or concomitant therapy - Insufficient or unclear dechallenge information
Unlikely	- Temporal relationship makes causation improbable - Alternative explanations (disease or other medications) more plausible
Conditional / Unclassified	- Event reported but requiring additional data for definitive assessment - Further information under review
Unassessable/ Unclassifiable	- Report lacks sufficient or consistent information to permit judgment - Data cannot be supplemented or verified

- Severity of ADR: Classified based on clinical impact and intervention required, often using Hartwig's Severity Assessment Scale, simplified into mild (self-limiting or minimal treatment), moderate (requiring drug discontinuation or specific treatment), and severe (life-threatening or causing permanent harm).[13]
- Polypharmacy: Concurrent use of multiple medications, increasing risk for drug interactions and ADRs, particularly relevant in pediatric tertiary care settings.[14]
- Short-Term Outcome: Clinical status of the patient following an ADR during hospitalization, including recovery, complications, duration of hospital stay, and discharge status.[15]

Results

The study enrolled 125 pediatric inpatients who developed adverse drug reactions (ADRs). The results are organized to address the study's aims: characterization of ADR types, causality, and severity, and assessment of their short-term outcomes.

[Table 1] represents all age groups, with the largest proportion in the youngest cohort, i.e. 1 month–5 years. Over half of participants were underweight, and there was a female predominance.

More than half of ADRs manifested within the first hour of drug administration, indicating a predominance of acute hypersensitivity reactions as depicted in [Table 2].

Table 1: Baseline Socio-Demographic Characteristics and Nutritional Status of Study Participants (N= 125).

Characteristic	Category	Frequency (n)	%
Age (years)	1 month–5	48	38.4
	6–10	32	25.6
	11–15	45	36.0
Weight status	Underweight	69	55.2
	Normal weight	56	44.8
Gender	Female	73	58.4
	Male	52	41.6

Table 2: Time Interval to Adverse Drug Reaction Onset (N= 125).

Onset interval	Frequency (n)	%
<1 hour	71	56.8
1–6 hours	14	11.2
6–24 hours	11	8.8
>24 hours	29	23.2

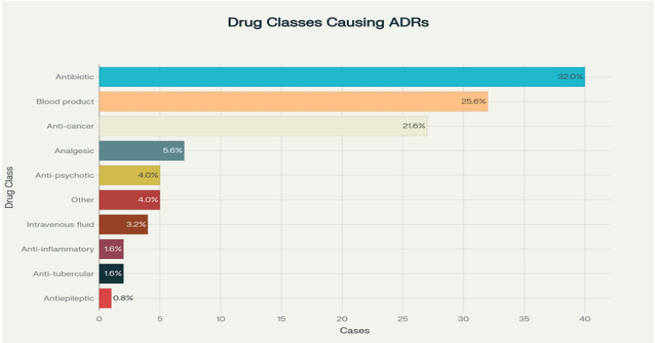

Figure 1: Distribution of Drug Classes Responsible for Adverse Drug Reactions in Pediatric Patients (N= 125).

[Figure 1] illustrates that antibiotics were the most frequently implicated agents in pediatric adverse drug reactions, accounting for 32.0% of cases, followed by blood products (25.6%) and anticancer drugs (21.6%). Less commonly involved were analgesics (5.6%), antipsychotics (4.0%), intravenous fluids (3.2%), anti-inflammatory and antitubercular agents (1.6% each), antiepileptics (0.8%), and other drug classes.

[Table 3] delineates that cutaneous manifestations (rashes/urticaria) were the most frequent presentation (38.4%), followed by systemic symptoms such as fever and chills.

Table 3: Clinical Manifestations of Adverse Drug Reactions

Clinical Manifestations	Frequency (n)	%
Rashes and urticaria	48	38.4
Fever	26	20.8
Chills and rigors	18	14.4
Mucosal involvement	8	6.4
Vomiting	7	5.6
Oliguria/anuria	6	4.8
Anaphylactic shock	1	0.8
Diarrhea	1	0.8
Others	36	28.8

Table 4: Severity Classification of Adverse Drug Reactions (Hartwig's Scale) (N= 125).

Severity Classification	Frequency (n)	%
Mild	84	67.2
Moderate	41	32.8
Severe	0	0.0

No severe reactions occurred; two-thirds were mild (67.2%), requiring minimal or no therapeutic change, while the remainder necessitated drug discontinuation or symptomatic treatment as depicted in table 4.

Table 5: WHO-UMC Causality Categories for Adverse Drug Reactions (N= 125).

Causality Categories	Frequency (n)	%
Certain	10	8.0
Likely	61	48.8
Probable	38	30.4
Possible	14	11.2
Unlikely	2	1.6

[Table 5] presents the causality assessment of adverse drug reactions using the WHO-UMC criteria. Nearly half of the reactions (48.8%) were classified as "likely," indicating a strong temporal and pharmacological link to the suspect medication, while 30.4% were deemed "probable," reflecting reasonable association without rechallenge. Reactions

judged as "certain" accounted for 8.0%, "possible" for 11.2%, and only 1.6% were classified as "unlikely," underscoring the predominance of clear drug–event relationships in this cohort.

[Figure 2] presents the total number of deranged laboratory parameters associated with each major drug category implicated in adverse drug reactions. Anti-cancer agents accounted for the highest burden of laboratory abnormalities (n = 12), predominantly electrolytes (n = 6), enzymes (n = 2), liver function tests (n = 2), and renal function tests (n = 2). Antibiotics were the next most frequent, with five derangements—four renal function test abnormalities and one case of decreased hemoglobin. All other drug classes showed no detectable laboratory abnormalities, underscoring the need for vigilant biochemical monitoring when prescribing anticancer therapies and antibiotics in pediatric inpatients. generate this figure as per this explanation.

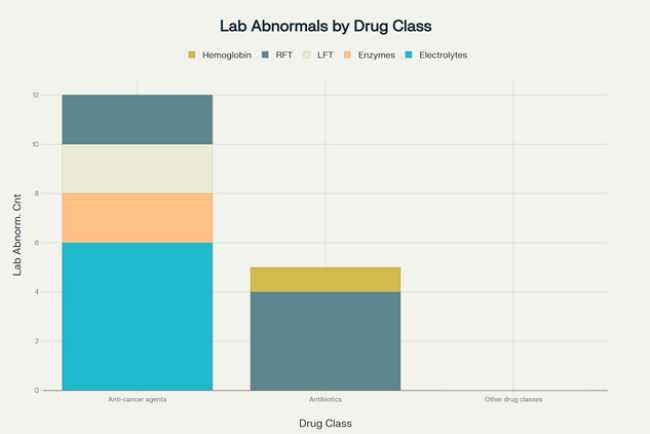

Figure 2: Laboratory Abnormalities Stratified by Implicated Drug Class (N= 125).

Table 6: Short-Term Outcomes and Clinical Management of ADR Cases (N= 125).

Outcome measure	Frequency (n)	%
Full recovery	125	100.0
Hospital stay >72 hours	116	92.8
Hospital stay <24 hours	9	7.2
Offending drug withdrawn	68	54.4
Dose modified	57	45.6

[Table 6] summarizes recovery, hospital stay, and interventions. All patients recovered fully. Most required prolonged monitoring (>72 hours), and over half had the culprit drug withdrawn, with the remainder managed by dose adjustment.

Discussion

This study investigated 125 pediatric inpatients who experienced adverse drug reactions (ADRs), revealing that the highest incidence occurred in children aged 1–5 years (38.4%), with a notable female predominance (58.4%) and over half of participants underweight (55.2%). Kurma et al. (2019) reported a similar age distribution, with 43.3% of ADRs in children under five years, and a male predominance of 60.8%.16 In contrast, Morales-Ríos et al. (2020) observed a slight female majority (52%) and an ADR frequency of 2.12%–8.07% in a Mexican tertiary pediatric hospital, underscoring geographic variations in demographic risk factors.[17]

Rapid-onset reactions predominated, with 56.8% occurring within one hour of drug administration. This aligns with Sugioka et al. (2020), who identified a significant association between polypharmacy and early-onset ADRs in Japanese children, reporting a 3.5% ADR-related hospital visit rate.[18] Birhane et al. (2021) similarly noted cutaneous reactions in over 75% of pediatric ADRs, with most occurring shortly after drug exposure in Ethiopian children.[19]

Antibiotics were the most implicated class (32.0%), followed by blood products (25.6%) and anticancer agents (21.6%). Khan et al. (2021) found that 40.8% of ADRs in Turkish pediatric inpatients were due to anti-infectives, predominantly antibiotics, with skin manifestations in 62.5% of cases.[15] Tripathy et al. (2021) also reported antibiotics as the leading cause in Odisha, India (66%), with serious ADRs in 21% of reports.[20]

Cutaneous findings dominated clinical presentations (rashes/urticaria, 38.4%), accompanied by fever (20.8%) and chills/rigors (14.4%). These proportions mirror Amaro-Hosey et al. (2021), who documented dermatologic toxicities in up to 67% of pediatric onco-hematology ADRs, and Alghamdi et al. (2022), who reported skin involvement in 67.7% of PICU adverse drug events, often preventable with early detection.[21,22]

Most ADRs were mild (67.2%) or moderate (32.8%), with no severe events recorded. Neininger et al. (2022) highlighted that 72% of German pediatricians perceived mild ADRs as common, yet only 4% reported them, suggesting under-recognition of moderate events.[23] Training interventions by Balsamo et al. (2022) increased ADR reporting and revealed a broader spectrum of non-serious reactions, decreasing vaccine-related ADRs from 83.3% to 55.1% after staff education.[24]

Laboratory derangements were uncommon; 86.4% of patients showed no abnormalities, while electrolytes and renal function tests each deranged in 4.8%. In contrast, Agarwal et al. (2023) identified hepatobiliary ADRs in 11.1% and gastrointestinal in 8.1% among malnourished children on antitubercular therapy, emphasizing nutritional status as a modifier of ADR risk.[25]

Causality assessment per WHO-UMC criteria classified 48.8% of reactions as "likely" and 30.4% as "probable." Tripathy et al. (2021) reported 70.6% of pediatric ADRs as probable, reflecting challenges in rechallenge-based confirmation, while Neininger et al. (2022) found that only 11% of German physicians were aware of pharmacovigilance tools, potentially affecting causality assignment.[20,23]

All patients recovered fully, mirroring Balsamo et al. (2022), who achieved complete resolution in 63.1% of vaccine ADRs post-training, and Amaro-Hosey et al. (2021), who reported

recovery rates of 83.6% in pediatric oncology ADRs.[21,24] The 100% recovery here underscores the impact of structured management protocols.

Overall, our findings corroborate and extend recent literature by highlighting the predominance of acute, immune-mediated ADRs in young, undernourished pediatric inpatients, chiefly driven by antibiotic exposure. The uniformly favorable recovery contrasts with the greater severity and mortality reported elsewhere, reflecting the benefits of proactive monitoring, prompt intervention, and educational initiatives.

Conclusion

In this prospective observational study of pediatric inpatients, ADRs predominantly affected children under five years, with antibiotics, blood products, and anticancer drugs as leading culprits. Clinical manifestations were chiefly cutaneous and febrile, with the majority of reactions classified as mild or moderate. Structured causality assessment and timely intervention achieved complete recovery in all cases, although most required hospitalization beyond 72 hours, underscoring the clinical and economic impact of ADRs. These findings advocate for enhanced antibiotic stewardship, vigilant post-administration monitoring, and integration of pharmacovigilance into pediatric care to minimize ADR burden.

Recommendations

Implementing focused antibiotic stewardship programs alongside structured post-administration observation—particularly during the first hour after high-risk medications—augmented by electronic ADR alert systems and ongoing pharmacovigilance training for multidisciplinary teams, will enhance early detection and prevention of adverse drug reactions.

Strengths and Limitations

The study's prospective, single-center design with standardized WHO-UMC causality assessment and complete in-hospital follow-up constitutes a major strength, ensuring thorough, real-time capture of clinical profiles and short-term outcomes. Limitations include its single-site scope, which may constrain external validity; the absence of preventability assessments and pharmacogenomic analyses; and potential underreporting of mild or delayed reactions that resolved before recognition.

Relevance of the Study

This study provides crucial insight into pediatric ADR profiles in a tertiary care setting, informing strategies for early recognition, prevention, and management to enhance medication safety in vulnerable children.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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