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Incidence, Spectrum, and Preventability of Adverse Drug Reactions in Hospitalized Patients: A Prospective Pharmacovigilance Study from a Tertiary Care Center in South India

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Abstract

Background: Adverse drug reactions (ADRs) constitute a significant cause of patient morbidity, prolonged hospitalization, increased healthcare costs, and, in severe cases, mortality. Active pharmacovigilance is essential to characterize the spectrum, severity, causality, preventability, and clinical impact of ADRs in real-world hospital settings.

Objective: The present prospective active-pharmacovigilance study aimed to determine the incidence of ADRs among hospitalized patients at a tertiary care teaching institution in Puducherry, characterize the implicated drug classes, organ-system patterns, severity profiles, causality assessments, and preventability of these events.

Methods: A prospective observational study was conducted from June 2016 to February 2017 in the Department of Pharmacology in collaboration with departments of medicine, surgery, paediatrics, and obstetrics in South India. A total of 1,050 hospitalized patients were monitored throughout their admissions through daily ward rounds, prescription review, laboratory monitoring, and structured interviews. Suspected ADRs were captured on the CDSCO yellow form. Causality was assessed using the WHO–UMC scale and Naranjo algorithm; severity using the modified Hartwig–Siegel scale; and preventability using the Schumock–Thornton criteria.

Results: Of 1,050 monitored patients, 184 (17.5%) experienced at least one ADR, with a total of 226 individual events. Implicated drug classes included antimicrobials (38.5%), cardiovascular drugs (16.8%), NSAIDs/analgesics (12.4%), anticonvulsants (8.4%), corticosteroids (6.2%), antineoplastic agents (5.3%), and others (12.4%). Cutaneous reactions (28.3%), gastrointestinal disturbances (22.6%), hepatobiliary reactions (12.4%), and metabolic/electrolyte disturbances (10.6%) were the most frequent organ-system patterns. Causality was 'certain' in 6.2%, 'probable' in 56.6%, 'possible' in 32.7%, and 'unlikely' in 4.4%. Severity was mild in 60.6%, moderate in 32.7%, and severe in 6.6% (one fatal). Preventable ADRs accounted for 41.6%. The mean prolongation of hospital stay attributable to ADRs was 2.8 ± 1.6 days.

Conclusion: ADRs occur in approximately one in six hospitalized patients at this tertiary care institute, with antimicrobials, cardiovascular drugs, and NSAIDs as predominant offenders, and 41.6% being preventable. Strengthened pharmacovigilance, prescribing audits, and clinical-pharmacy integration are essential.

Keywords:

Adverse drug reaction; pharmacovigilance; causality; WHO-UMC scale; Naranjo algorithm; preventability; hospitalized patients

1. Introduction

An adverse drug reaction (ADR) is defined by the World Health Organization as 'any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function' [1]. ADRs constitute a significant cause of patient morbidity and mortality, prolonged hospital stays, increased healthcare costs, and unnecessary re-hospitalization across all healthcare settings [2,3].

Internationally, ADRs are estimated to account for 2–7% of hospital admissions and to occur in 6–15% of hospitalized patients during their stay [4,5]. The Lazarou meta-analysis estimated that ADRs constituted the fourth-to-sixth leading cause of death in the United States [6]. Indian data, drawn from the Pharmacovigilance Programme of India (PvPI) initiated by the Central Drugs Standard Control Organization (CDSCO) in 2010, have suggested that hospital ADR incidence ranges from 6% to 25%, with substantial variability based on study design, monitoring intensity, and clinical setting [7,8].

The clinical impact of ADRs is multifaceted. Beyond direct patient harm — encompassing cutaneous reactions ranging from mild rashes to Stevens–Johnson syndrome and toxic epidermal necrolysis; hepatic, renal, hematological, and metabolic adverse events; cardiovascular adverse events; and idiosyncratic reactions — ADRs prolong hospital stay, demand additional investigations and therapies, exacerbate clinical instability, and substantially raise total healthcare expenditure [9,10].

Causality assessment is central to pharmacovigilance and uses validated instruments such as the WHO–Uppsala Monitoring Centre (WHO-UMC) scale and the Naranjo Adverse Drug Reaction Probability Scale [11,12]. Severity is graded using the modified Hartwig–Siegel scale [13], and preventability using the Schumock–Thornton criteria [14]. Active intensive ADR monitoring within hospitals consistently captures higher event numbers than spontaneous reporting and is therefore the methodological gold standard for descriptive pharmacovigilance research [15].

Despite the establishment of PvPI and ADR Monitoring Centres at major Indian academic institutions, real-world ADR data combining incidence, drug-class profiling, organ-system

patterns, validated causality assessment, severity, and preventability remain valuable for institutional, regional, and national learning. The present prospective study was therefore conducted at a major south Indian tertiary care institute to characterize the ADR landscape across multiple clinical departments.

2. Materials and Methods

2.1 Study Setting

This prospective observational pharmacovigilance study was conducted in the Department of Pharmacology, in collaboration with the departments of internal medicine, general surgery, paediatrics, and obstetrics & gynaecology, in South India — a 2,000-bedded apex tertiary care teaching institution and a designated ADR Monitoring Centre under PvPI. The study extended from June 2016 to February 2017.

2.2 Participants and Monitoring

All inpatient admissions to participating wards during the recruitment window who provided informed consent and were aged ≥1 year were eligible. Exclusion criteria included admissions <24 hours, patients receiving no medications, and refusal of consent. A total of 1,050 patients were monitored throughout their hospital stay through daily ward rounds, prescription review, laboratory and clinical monitoring, structured interviews, and review of nursing and medical records. ADRs were also detected by clinician notification.

2.3 Data Collection

Suspected ADRs were captured on the CDSCO Suspected Adverse Drug Reaction Reporting Form (yellow form) and entered into the VigiFlow database. Demographic data, primary diagnosis, drug history (including dose, route, frequency, duration, indication), date of ADR onset, description of the event, severity, action taken, and clinical outcome were documented.

2.4 Causality, Severity, and Preventability Assessment

Causality was assessed independently by two pharmacovigilance physicians using the WHO–UMC scale (categories: certain, probable/likely, possible, unlikely, conditional, unassessable) and the Naranjo algorithm (definite ≥9, probable 5–8, possible 1–4, doubtful ≤0). Discrepancies were resolved by consensus. Severity was graded using the modified Hartwig–Siegel scale (mild, moderate, severe, fatal). Preventability was assessed using the Schumock–Thornton criteria (definitely preventable, probably preventable, not preventable). Additional outcome variables included duration of ADR, prolongation of hospital stay, and final clinical outcome.

2.5 Statistical Analysis

Data were analyzed in SPSS version 26. Descriptive statistics summarized continuous variables as mean ± SD and categorical variables as frequencies and percentages. Inter-rater agreement for causality was assessed using Cohen's kappa. A p-value <0.05 was considered statistically significant.

3. Results

Of 1,050 monitored hospitalized patients, 184 (17.5%) experienced at least one ADR, contributing to a total of 226 individual events. Mean age of patients with ADRs was 42.6 ± 18.4 years; 56.5% were female. Polypharmacy (≥5 concurrent drugs) was present in 68.5%, and known comorbidities were present in 78.3%. Demographic and ADR profile is summarized in Table 1.

Table 1. Patient demographics and overall ADR profile (n = 1,050; ADR cases n = 184; events n = 226).

Parameter	Number / Mean	% / SD
Total monitored patients	1,050	100.0
Patients with at least one ADR	184	17.5
Total ADR events	226	—
Mean age of ADR patients (years)	42.6	± 18.4
Female with ADR	104	56.5
Polypharmacy (≥5 drugs)	126	68.5
Comorbidities present	144	78.3
Source – Internal medicine wards	98	53.3
Source – General surgery wards	32	17.4
Source – Paediatric wards	26	14.1
Source – Obstetrics & gynaecology	28	15.2
Mean prolongation of stay (days)	2.8	± 1.6
Drug withdrawn due to ADR	168	74.3 (of events)
Dose modified due to ADR	32	14.2 (of events)
No change in therapy	26	11.5 (of events)
Recovered fully	204	90.3 (of events)
Recovered with sequelae	12	5.3 (of events)
Continuing at discharge	9	4.0 (of events)
Fatal	1	0.4 (of events)

Antimicrobials were the most frequently implicated class, followed by cardiovascular drugs, NSAIDs/analgesics, anticonvulsants, corticosteroids, and antineoplastic agents. Within antimicrobials, beta-lactams, fluoroquinolones, and antitubercular drugs were the leading offenders. Organ-system pattern revealed cutaneous reactions as the most common, followed by gastrointestinal, hepatobiliary, metabolic, and hematological events. Drug-class and organ-system distribution is presented in Table 2.

Table 2. Drug classes and organ-system patterns of ADRs (n = 226 events).

Drug class / organ system	Events (n)	Percentage (%)
Drug class – Antimicrobials (overall)	87	38.5
• Beta-lactams (penicillins, cephalosporins)	32	14.2
• Fluoroquinolones	20	8.8
• Antitubercular agents	18	8.0
• Macrolides	9	4.0
• Others (aminoglycosides, sulpha, etc.)	8	3.5
Drug class – Cardiovascular drugs	38	16.8
Drug class – NSAIDs / analgesics	28	12.4
Drug class – Anticonvulsants	19	8.4
Drug class – Corticosteroids	14	6.2
Drug class – Antineoplastic agents	12	5.3
Drug class – Antipsychotics / antidepressants	10	4.4
Drug class – Antidiabetic agents	9	4.0
Drug class – Other	9	4.0
Organ system – Cutaneous	64	28.3
Organ system – Gastrointestinal	51	22.6
Organ system – Hepatobiliary	28	12.4
Organ system – Metabolic / electrolyte	24	10.6
Organ system – Cardiovascular	16	7.1
Organ system – Hematological	14	6.2
Organ system – CNS	12	5.3
Organ system – Renal	10	4.4
Organ system – Other / multisystem	7	3.1

Causality assessment using the WHO-UMC scale revealed 14 (6.2%) events as 'certain', 128 (56.6%) as 'probable', 74 (32.7%) as 'possible', and 10 (4.4%) as 'unlikely'. The Naranjo algorithm yielded categorically concordant results in 86.7% of cases (Cohen's $\kappa = 0.78$). Severity grading using the modified Hartwig–Siegel scale identified 137 (60.6%) as mild, 74 (32.7%) as moderate, 14 (6.2%) as severe, and 1 (0.4%) as fatal. Preventability assessment using the Schumock–Thornton criteria identified 94 (41.6%) as preventable. Causality, severity, and preventability are summarized in Table 3.

Table 3. Causality, severity, and preventability assessment (n = 226 events).

Assessment category	Events (n)	Percentage (%)
WHO-UMC – Certain	14	6.2
WHO-UMC – Probable / likely	128	56.6
WHO-UMC – Possible	74	32.7
WHO-UMC – Unlikely	10	4.4
Naranjo – Definite (≥9)	16	7.1
Naranjo – Probable (5–8)	126	55.8

Naranjo – Possible (1–4)	76	33.6
Naranjo – Doubtful (≤0)	8	3.5
Severity – Mild	137	60.6
Severity – Moderate	74	32.7
Severity – Severe	14	6.2
Severity – Fatal	1	0.4
Preventability – Definitely preventable	32	14.2
Preventability – Probably preventable	62	27.4
Preventability – Not preventable	132	58.4

4. Discussion

This prospective active-pharmacovigilance study from a major south Indian tertiary care institute provides comprehensive data on the spectrum, drug-class distribution, organ-system patterns, causality, severity, and preventability of ADRs in hospitalized patients. The 17.5% incidence of ADRs and 21.5% incidence of events per 100 admissions are concordant with the broader Indian and international pharmacovigilance literature, which has reported hospital ADR incidences ranging from 6% to 30% depending on monitoring intensity, definitions, and clinical settings [16,17].

Active intensive monitoring, as employed in our study, captures substantially higher event numbers than spontaneous reporting alone — a phenomenon repeatedly demonstrated in pharmacovigilance literature [18]. The dominance of antimicrobials (38.5%) as the leading drug class involved in ADRs reflects both their high prescription frequency in hospitalized patients and their well-recognized propensity for cutaneous, gastrointestinal, and hepatobiliary adverse events. Beta-lactams, fluoroquinolones, and antitubercular agents emerged as the leading antimicrobial offenders, consistent with prior reports [19,20].

Cardiovascular drugs (16.8%), NSAIDs/analgesics (12.4%), and anticonvulsants (8.4%) followed as next leading classes. Cardiovascular drug-related ADRs were dominated by ACE-inhibitor-induced cough and angioedema, calcium-channel-blocker-induced ankle oedema, and statin-induced myalgia. NSAID-related ADRs included gastrointestinal disturbances and acute kidney injury. Anticonvulsant ADRs included dose-dependent neurotoxicity and idiosyncratic skin reactions, particularly with phenytoin and carbamazepine [21].

Cutaneous reactions (28.3%) ranged from morbilliform rashes to severe cutaneous adverse reactions (Stevens–Johnson syndrome, toxic epidermal necrolysis), reaffirming the importance of vigilant skin examination and prompt drug withdrawal. Gastrointestinal disturbances (22.6%) and hepatobiliary reactions (12.4%) underscore the importance of routine liver function monitoring with hepatotoxic drugs. The single fatal event in our cohort — drug-induced hepatic failure progressing to fulminant hepatitis — emphasizes the critical importance of vigilance and timely withdrawal.

The 41.6% preventability rate in our cohort is concordant with the international literature, which has reported preventability of 30–55% [22,23]. Common preventable mechanisms include known allergy or contraindication overlooked, inappropriate dose for renal or hepatic dysfunction, drug–drug interactions, lack of monitoring, and excessive duration. Implementation of clinical decision-support systems, computerized prescription order entry with allergy/interaction alerts, structured medication reconciliation at admission and discharge, and integration of clinical pharmacy services have been demonstrated to substantially reduce preventable ADRs [24,25].

Strengths of the present study include prospective active monitoring, multidepartmental coverage, validated causality and severity instruments, dual-rater causality assessment with high inter-rater agreement, and comprehensive preventability evaluation. Limitations include single-centre setting, exclusion of outpatient and post-discharge ADRs, and reliance on clinical detection (which may miss subtle laboratory-only events).

5. Conclusion

Adverse drug reactions occur in approximately 17.5% of hospitalized patients at this Indian tertiary care institute, with antimicrobials, cardiovascular drugs, and NSAIDs as predominant offenders. Cutaneous, gastrointestinal, and hepatobiliary reactions dominate the organ-system spectrum. Causality is 'probable' or higher in nearly two-thirds of events, severity is moderate-to-severe in 39%, and preventability approaches 42%. Strengthened active pharmacovigilance, clinical-decision support, prescribing audits, and clinical-pharmacy integration are essential to reduce preventable harm.

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