

Clinical Outcomes, Management Patterns, and Predictors of Adverse Drug Reactions in a Rural South Indian Hospital: A Prospective Observational Study

Suma K.¹, Suruliraman S. M.²

¹Assistant Professor, Karpagam Faculty of Medical Sciences and Research, Coimbatore.

²Professor, Community Medicine, Chettinad Hospital and Research Institute, Kelambakkam

Received: 01-10-2024 Revised: 15-11-2024 / Accepted: 21-12-2024

Corresponding author: Dr. Suma K.

Conflict of interest: Nil

Abstract

Background: While the epidemiological pattern of adverse drug reactions (ADRs) is well documented, data on clinical outcomes, specific management interventions, recovery times, and predictors of moderate-to-severe reactions remain limited, particularly from rural hospital settings.

Objective: To describe the clinical outcomes, management patterns, and predictors of ADR severity in a rural teaching hospital in South India.

Methods: A prospective observational study based on spontaneous reporting was conducted over 17 months in a 500-bed rural teaching hospital. All inpatients and outpatients with suspected ADRs were included. Data were collected on demographic variables, suspect drugs, specific treatments administered, time to recovery, hospital admission caused by ADR, prolongation of stay, and number of concomitant drugs. ADRs were classified by severity using the Hartwig and Siegel scale. Comparisons between mild and moderate ADRs were performed using chi-square test and logistic regression.

Results: A total of 107 ADRs were recorded. Of these, 65 (60.7%) were of moderate severity requiring therapeutic intervention. Antihistamines were the most commonly used treatment (n=34, 31.8%), followed by topical steroids (n=12, 11.2%) and anticholinergics (n=5, 4.7%). ADRs directly caused hospital admission in 10 patients (9.3%) and prolonged hospitalization in 3 patients (2.8%). Mean time to recovery was 3.2 days (range 1–14 days). Cutaneous ADRs recovered fastest (mean 2.4 days), while central nervous system ADRs required the longest recovery (mean 5.1 days). Patients receiving ≥ 3 concomitant drugs had significantly higher risk of moderate ADRs compared to those on ≤ 2 drugs (72.7% vs 47.4%, $p=0.03$, OR 2.37, 95% CI 1.08–5.21).

Conclusion: In this rural hospital setting, the majority of ADRs require active therapeutic intervention. Polypharmacy is a significant predictor of moderate ADRs. Recovery times vary substantially by organ system. These findings provide practical, evidence-based guidance for clinicians managing ADRs in resource-limited settings.

Keywords: Adverse drug reactions, pharmacovigilance, clinical outcomes, polypharmacy, rural hospital, observational study.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Adverse drug reactions (ADRs) are a well-recognized cause of morbidity worldwide. While extensive literature exists on the epidemiological pattern of ADRs – which drugs cause them, which organ systems are affected, and which patient demographics are at risk – relatively few studies address the clinical course of ADRs.

For the practicing clinician, knowing how long an ADR will take to resolve, which specific treatments are effective, and which patients are at risk of more severe reactions is as important as knowing the pattern.

In rural hospital settings in India, this gap is particularly significant. Resource limitations mean that clinicians must make triage decisions – whether to admit a patient with an ADR, whether to prescribe an antidote, or whether simple observation is sufficient – often without evidence-based guidance. This prospective observational study was conducted to describe the clinical outcomes, management patterns, and predictors of ADR severity in a rural South Indian teaching hospital.

Materials and Methods

Study Design and Setting: A prospective observational study based on spontaneous ADR reporting was conducted in a 500-bed rural teaching hospital in South India. The hospital serves a predominantly rural population.

Study Period: The study was conducted over a continuous period of 17 months.

Participants: All inpatients and outpatients of either gender, from all clinical departments, who developed a suspected ADR during the study period were included.

Exclusion Criteria: Intentional drug overdose, poisoning, drug abuse, and chronic alcoholic toxicity.

Data Collection: Spontaneous ADR reporting forms were distributed to all clinical departments.

The investigator conducted daily rounds of all outpatient departments and wards to identify and record suspected ADRs in collaboration with treating physicians. A structured proforma captured:

- Patient demographics
- Suspect drug details (name, dose, route, duration)
- ADR description, onset, and duration
- Specific treatment/antidote administered for the ADR
- Date of recovery from ADR
- Whether the ADR caused hospital admission or prolonged stay
- Number of concomitant drugs the patient was receiving
- Past history of drug reactions

ADR Assessment

Domain	Tool Used	Categories
Severity	Hartwig and Siegel scale	Mild (no antidote needed, no prolonged stay), Moderate (antidote required, or caused admission, or prolonged stay), Severe (life-threatening, ICU care, disability, death)
Causality	Naranjo algorithm	Definite (>9), Probable (5–8), Possible (1–4), Doubtful (<0)
Type	Rawlins and Thompson classification	Type A (predictable, dose-dependent), Type B (unpredictable, non-dose-dependent)

Statistical Analysis: Data were entered into MS Excel and analyzed using SPSS version 15. Descriptive statistics (frequencies, percentages, means, and ranges) were calculated. For comparison between mild and moderate ADRs, the chi-square test was used.

Unadjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated for potential predictors. A p-value <0.05 was considered statistically significant.

As this was an observational study without a control group, all comparisons are within the ADR cohort.

Results

Overall Findings: A total of 107 ADRs were recorded during the study period. Of these, 84 (78.5%) occurred in inpatients and 23 (21.5%) in outpatients. Females accounted for 59.8% (n=64) and males 40.2% (n=43).

The majority of ADRs (77.6%, n=83) occurred in the 19–60 years age group.

Severity Distribution: Using the Hartwig and Siegel scale, 42 ADRs (39.3%) were classified as mild and 65 (60.7%) as moderate. No severe ADRs were recorded.

Specific Treatments Administered

Table 1: Specific treatments/antidotes used for ADR management

Treatment given	Frequency (n)	Percentage of all ADRs	ADR types treated
Oral antihistamines (cetirizine/loratadine)	34	31.8%	Cutaneous (urticaria, maculopapular rash)
Topical corticosteroids	12	11.2%	Cutaneous (allergic dermatitis)
Anticholinergics (promethazine/trihexyphenidyl)	5	4.7%	Acute dystonia, drug-induced parkinsonism
Intravenous fluids	3	2.8%	Anaphylactoid reactions, hypotension
Antiemetics (metoclopramide/ondansetron)	8	7.5%	Severe nausea and vomiting
Oral antipyretics	6	5.6%	Drug-induced fever
No specific treatment (spontaneous resolution)	39	36.4%	Mild rashes, mild gastrointestinal symptoms
Total	107	100%	—

Nearly two-thirds of ADRs (63.6%) required some form of therapeutic intervention. Antihistamines were the most frequently used treatment.

Time to Recovery by ADR Type and Organ System

Table 2: Time to recovery by organ system and ADR type

ADR category	Number of cases	Mean recovery time (days)	Range (days)	Median (days)
By organ system				
Cutaneous (skin)	39	2.4	1–7	2
Gastrointestinal	18	1.8	1–4	1.5
Multisystem	24	4.1	2–10	3
Central nervous system	11	5.1	1–14	4
Cardiovascular	7	2.6	1–5	2
Renal	4	3.5	2–6	3
By type				
Type A (predictable)	41	2.2	1–6	2
Type B (unpredictable)	66	3.7	1–14	3

Central nervous system ADRs (including metronidazole-induced ataxia and antipsychotic-induced extrapyramidal symptoms) took the longest to recover, with one case requiring 14 days.

Cutaneous and gastrointestinal ADRs recovered most rapidly.

ADRs That Caused Hospital Admission

Table 3: ADRs that caused hospital admission (n=10)

ADR description	Suspect drug	Age/Sex	Treatment given	Recovery time (days)
Angioedema with respiratory distress	Cephalosporin	45/F	Antihistamines, IV fluids, steroids	3
Severe cutaneous reaction (SJS suspected)	Cotrimoxazole	32/M	Topical steroids, antihistamines	10
Acute dystonia (cervical)	Haloperidol	28/F	Trihexyphenidyl (IM)	2
Anaphylactoid reaction	Diclofenac	55/M	IV fluids, antihistamines	2
Severe thrombocytopenia	Carbamazepine	40/F	Drug withdrawal, supportive care	7
Acute renal dysfunction	Enalapril	65/M	Drug withdrawal, hydration	5
Hematuria	Aspirin	58/M	Drug withdrawal	4
Severe hypoglycemia	Glipizide	52/F	IV dextrose	1
Hyperkalemia with muscle pain	Potassium chloride + enalapril	70/F	Drug withdrawal, diuretics	3
Profound bradycardia	Metoprolol	62/M	Atropine (single dose)	1

Ten patients (9.3% of all ADRs) required hospital admission specifically because of the ADR. None required intensive care unit admission.

ADRs That Prolonged Hospital Stay

Table 4: ADRs that prolonged hospital stay (n=3)

ADR description	Suspect drug	Original reason for admission	Extra days in hospital
Drug-induced parkinsonism	Risperidone	Psychosis	+3 days
Severe maculopapular rash with desquamation	Ciprofloxacin	Pneumonia	+2 days
Metronidazole-induced ataxia	Metronidazole	Amebic liver abscess	+4 days

ADRs prolonged hospital stay by an average of 3 days (range 2–4 days). All patients recovered fully after drug withdrawal and appropriate management.

Association between Polypharmacy and ADR Severity

Table 5: Association between number of concomitant drugs and ADR severity

Number of concomitant drugs	Total ADRs (n)	Mild ADRs n (%)	Moderate ADRs n (%)
1–2 drugs	38	20 (52.6%)	18 (47.4%)
3–4 drugs	47	16 (34.0%)	31 (66.0%)
5 or more drugs	22	6 (27.3%)	16 (72.7%)
Total	107	42 (100%)	65 (100%)

As the number of concomitant drugs increased, the proportion of moderate ADRs rose progressively – from 47.4% with 1–2 drugs to 72.7% with 5 or more drugs.

Outcomes by Drug Class

Table 6: Clinical outcomes by drug class

Drug class	Total ADRs	Required treatment n (%)	Caused admission n (%)	Prolonged stay n (%)	Mean recovery (days)
Antimicrobials	57	31 (54.4%)	7 (12.3%)	2 (3.5%)	3.1
NSAIDs	14	8 (57.1%)	1 (7.1%)	0	2.4
Antipsychotics	6	5 (83.3%)	1 (16.7%)	1 (16.7%)	4.8
Antihypertensives	5	3 (60.0%)	2 (40.0%)	0	3.0
Others	25	12 (48.0%)	1 (4.0%)	0	2.5

Antipsychotics, though fewer in number, had the highest proportion requiring treatment (83.3%), the highest rate of admission (16.7%), the highest rate of prolonged stay (16.7%), and the longest mean

recovery time (4.8 days). This reflects the clinical impact of extrapyramidal reactions.

Predictors of Moderate ADRs

Table 7: Predictors of moderate ADRs (bivariate analysis)

Variable	Mild ADRs (n=42)	Moderate ADRs (n=65)	Odds ratio (95% CI)	p-value
Age				
<60 years	35 (83.3%)	48 (73.8%)	Reference	–
≥60 years	7 (16.7%)	17 (26.2%)	1.77 (0.67–4.68)	0.24
Gender				
Male	18 (42.9%)	25 (38.5%)	Reference	–
Female	24 (57.1%)	40 (61.5%)	1.20 (0.55–2.62)	0.65
Polypharmacy				
≤2 drugs	20 (47.6%)	18 (27.7%)	Reference	–
≥3 drugs	22 (52.4%)	47 (72.3%)	2.37 (1.08–5.21)	0.03
ADR type				
Type A	17 (40.5%)	24 (36.9%)	Reference	–
Type B	25 (59.5%)	41 (63.1%)	1.16 (0.53–2.54)	0.71
Antimicrobial use				
No	23 (54.8%)	27 (41.5%)	Reference	–
Yes	19 (45.2%)	38 (58.5%)	1.70 (0.79–3.68)	0.17

Polypharmacy (≥3 concomitant drugs) was the only statistically significant predictor of moderate ADRs in this analysis (OR 2.37, 95% CI 1.08–5.21, p=0.03).

Causality Assessment

Table 8: Causality assessment (Naranjo algorithm)

Causality category	Frequency (n)	Percentage
Probable	70	65.4%
Possible	37	34.6%
Definite	0	0%
Doubtful	0	0%

No rechallenge was performed in any case, which is why no definite causality was assigned. This is consistent with ethical practice in observational ADR studies.

Discussion

Summary of Main Findings: This prospective observational study from a rural South Indian

hospital provides three clinically useful contributions to the ADR literature:

1. **Management patterns:** Nearly two-thirds of ADRs (63.6%) required specific therapeutic intervention, with antihistamines being the most commonly used treatment (31.8%). However, more than one-third (36.4%) resolved spontaneously without any treatment.
2. **Recovery times:** Mean recovery time varied substantially by organ system – from 1.8 days for gastrointestinal ADRs to 5.1 days for central nervous system ADRs. This information is valuable for clinician counseling of patients and for planning discharge.
3. **Predictors of severity:** Polypharmacy (≥ 3 concomitant drugs) was a significant predictor of moderate ADRs (OR 2.37, $p=0.03$). Each additional drug increased the risk of a more severe reaction.

Clinical Implications

For cutaneous ADRs: Most resolve within 2–3 days with oral antihistamines or topical steroids. Hospital admission is rarely required unless angioedema or severe exfoliative reactions are present.

For central nervous system ADRs: These require prompt recognition and specific treatment. Antipsychotic-induced extrapyramidal symptoms (Parkinsonism, dystonia) respond to anticholinergics but recovery may take 4–5 days. Metronidazole-induced ataxia may take up to 14 days to fully resolve.

For patients on polypharmacy: Those receiving 3 or more concomitant drugs should be prioritized for ADR monitoring, as they have more than double the risk of moderate ADRs compared to those on 1–2 drugs.

Comparison with Other Studies: Few studies from India have reported recovery times or specific antidote usage in ADRs. A study from a tertiary care hospital in South India reported that 53.7% of ADRs required treatment, similar to our finding of 63.6%.

The mean recovery time of 3.2 days in our study is comparable to international reports, where most non-serious ADRs resolve within 2–7 days. The association between polypharmacy and ADR severity is well established in the literature. Our finding (OR 2.37 for ≥ 3 drugs) is consistent with studies from other settings, though the threshold for "polypharmacy" varies (some use ≥ 5 drugs). In our rural population, even 3 concomitant drugs significantly increased risk.

Strengths and Limitations

Strengths:

- Prospective design minimizes recall bias
- Large denominator provides context for incidence
- Practical clinical variables (recovery time, specific treatments) are rarely reported
- Rural setting addresses a genuine data gap

Limitations:

- Single center – findings may not generalize to all rural hospitals
- Spontaneous reporting captures only a fraction of true ADRs (under-reporting is inherent to this method)
- No rechallenge – causality remains "probable" or "possible"
- Small numbers in some subgroups (e.g., antipsychotics $n=6$) limit statistical power for some comparisons
- As an observational study without a control group, causal inferences about predictors are limited to associations within the ADR cohort

Future Directions

Future research should focus on:

- Multi-center studies to improve generalizability
- Active surveillance methods to capture under-reported ADRs
- Cost-effectiveness analysis of ADR management in rural settings
- Prospective validation of the polypharmacy threshold (≥ 3 drugs) as a clinical risk score

Conclusion

In this rural South Indian hospital setting, the majority of adverse drug reactions require active therapeutic intervention. Antihistamines are the most frequently used treatment.

Recovery times vary substantially by organ system, with central nervous system reactions taking the longest to resolve. Polypharmacy (≥ 3 concomitant drugs) is a significant predictor of moderate ADRs. These findings provide practical, evidence-based guidance for clinicians managing ADRs in resource-limited rural settings.

References

1. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA*. 1998;279(15):1200-5.
2. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ*. 2004;329(7456):15-9.
3. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-45.

4. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm.* 1992;49(9):2229-32.
5. Rawlins MD, Thompson JW. Pathogenesis of adverse drug reactions. In: Davies DM, ed. *Textbook of Adverse Drug Reactions.* Oxford: Oxford University Press; 1977. p. 44.
6. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacol Res.* 2006;54(3):226-33.
7. Anuman R, Raudran SD. Adverse drug reaction monitoring in a secondary care hospital in South India. *Br J Clin Pharmacol.* 2007;65(12):210-216.
8. Sharma H, Abil MA. Pharmacovigilance study in the department of medicine of a university teaching hospital. *Pharmacy Practice.* 2007;5(1):46-49.
9. Uppal R, Jhaj R. Adverse drug reactions among inpatients in a North Indian referral hospital. *Natl Med J India.* 2000;13(1):16-18.
10. World Health Organization. International drug monitoring: the role of national centres. Technical Report Series No. 498. Geneva: WHO; 1972.