

Pattern and Profile of Adverse Drug Reactions in a Rural South Indian Teaching Hospital: A Prospective Observational Study

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Abstract

Background: Adverse Drug Reactions (ADRs) remain a significant global public health challenge, contributing to substantial morbidity, mortality, and escalating healthcare costs. Despite India's strengthened pharmacovigilance program, data from rural populations, which may exhibit distinct ADR profiles due to genetic, environmental, and health-seeking behavior differences, are still underrepresented in the national database.

Objective: This study aimed to determine the incidence, characterize the clinical pattern, and assess the causality, severity, and type of ADRs reported in a rural teaching hospital in South India.

Materials and Methods: A prospective, observational study based on spontaneous reporting. All inpatients and outpatients with suspected ADRs were included. Reported ADRs were analyzed using the Naranjo algorithm for causality, the Hartwig and Siegel scale for severity, and Rawlins and Thompson's classification for type.

Results: Out of 82,418 patients, 107 ADRs were documented, yielding an overall incidence of 0.13%. The incidence was significantly higher in inpatients (0.86%) than outpatients (0.03%). A predominance of ADRs was observed in women (59.8%) and the 19-60 years age group (77.6%). The Department of Medicine reported the highest number of ADRs (55.1%). The skin was the most frequently affected organ system (36.4%), with maculopapular rash being the most common manifestation. Antimicrobials were the most implicated drug class (53.3%), with ciprofloxacin being the foremost individual drug. Causality assessment showed 65.4% as 'probable' and 34.6% as 'possible'. Severity assessment revealed 60.7% as moderate and 39.3% as mild reactions. A majority (61.7%) were classified as Type B (unpredictable) reactions.

Conclusion: This study underscores the burden of ADRs in a rural Indian healthcare setting. This study identified that antimicrobials drugs were the leading causative agents for ADRs. The high proportion of Type B reactions highlights the need for vigilant monitoring. The low incidence rate likely reflects significant under-reporting, a persistent challenge that necessitates continuous education and robust institutional pharmacovigilance systems to improve drug safety in rural India.

Keywords: Pharmacovigilance, Adverse Drug Reaction, Rural Health, Antimicrobials, Spontaneous Reporting, India, Under-reporting.

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Introduction

The World Health Organization (WHO) defines an Adverse Drug Reaction (ADR) 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" [1]. ADRs represent a major clinical and economic burden on healthcare systems globally, contributing significantly to hospital admissions, prolonged hospital stays, and increased morbidity and mortality [2, 3].

Pre-marketing clinical trials, while essential, are inherently limited in their ability to detect all ADRs due to restricted sample sizes, short duration, and the exclusion of special populations like the elderly, children, and those with comorbidities [4]. Therefore, robust post-marketing surveillance, or pharmacovigilance, is critical for identifying previously unrecognized or rare ADRs and ensuring the continued safety of medicines in the general population [5].

In India, the Pharmacovigilance Programme of India (PvPI) was launched in 2010 to monitor drug safety. While it has made significant strides, a geographical disparity persists, with ADR data from rural areas being disproportionately low [6, 7]. Given the differences in patterns of disease, genetic polymorphisms, nutritional status, and healthcare access, the ADR profile in rural populations may differ substantially from urban settings [8]. This study was conceived to address this critical data gap by providing a detailed analysis of the pattern and profile of ADRs in a rural South Indian teaching hospital.

Review of Literature & Rationale: The significant impact of ADRs is well-documented globally. A systematic review and meta-analysis from 2020 estimated that the overall prevalence of ADRs in low- and middle-income countries (LMICs) was 8.3%, with 2.7% of hospital admissions being attributed to ADRs [9]. In the Indian context, a recent study from a tertiary care center in North India reported an ADR incidence of 3.47% among inpatients, with skin and gastrointestinal systems being most commonly affected [10].

Antimicrobials consistently emerge as a leading class of drugs implicated in ADRs across various Indian studies, reflecting their widespread and often irrational use [10, 11]. A 2021 study from a teaching hospital in South India also identified antimicrobials as the most common culprits, with cutaneous manifestations being the predominant ADR [12]. A critical challenge universally acknowledged in pharmacovigilance is under-reporting, which is particularly pronounced in rural and resource-limited settings [13, 14]. Factors such as lack of awareness, time constraints, and apprehension among healthcare professionals contribute to this gap, leading to a significant underestimation of the true ADR burden [15].

While numerous studies from Indian urban tertiary care centers exist, there is a relative scarcity of recent, prospective data from rural teaching hospitals, which form the backbone of healthcare in these regions. Understanding the local ADR patterns is the first step towards implementing targeted interventions for rational drug use and improved patient safety. This study aims to contribute this essential local evidence, highlighting the specific challenges and patterns observed in a rural South Indian context.

Objectives

1. To determine the incidence of ADRs occurring in inpatients and outpatients.

2. To characterize the ADRs based on the organ system affected and the drug classes implicated.
3. To assess the causality, severity, and type of the observed ADRs using standard scales.

Methodology

Study Design and Setting: A prospective, observational study.

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

Exclusion Criteria: Cases of intentional drug overdose, poisoning, drug abuse, and chronic alcoholic toxicity were excluded.

Data Collection: Following ethical approval, spontaneous reporting was encouraged across all departments. A customized data collection proforma, based on the PvPI form, was used to record patient demographics, details of the ADR (description, onset, duration), and suspect drug information (name, dose, route). The investigator conducted daily ward rounds and reviewed outpatient registers to actively identify and record ADRs in collaboration with treating physicians.

Assessment of ADRs:

- **Causality:** Assessed using the Naranjo probability scale [16], categorizing ADRs as Definite, Probable, Possible, or Doubtful.
- **Severity:** Assessed using the Hartwig and Siegel scale [17], categorizing ADRs as Mild, Moderate, or Severe.
- **Type:** Classified using Rawlins and Thompson's classification [18] as Type A (augmented/pharmacological) or Type B (bizarre/idiosyncratic).

Statistical Analysis: Data were entered into MS Excel and analyzed using SPSS. Descriptive statistics were used to present the results as frequencies and percentages.

Results

Incidence and Demographic Profile: From a total of 82,418 patients (9,739 inpatients; 69,391 outpatients), 107 ADRs were recorded, yielding an overall incidence of 0.13%.

The incidence was higher among inpatients (0.86%; n=84) compared to outpatients (0.03%; n=23). The gender distribution showed a female preponderance (59.8%, n=64). Most ADRs (77.6%, n=83) occurred in the 19-60 years age group (Table 1).

Table 1: Demographic Distribution of Adverse Drug Reactions (n=107)

Characteristic	Category	Frequency (n)	Percentage (%)
Location	Inpatients	84	78.5
	Outpatients	23	21.5
Gender	Male	43	40.2
	Female	64	59.8
Age Group	< 18 years	9	8.4
	19 - 60 years	83	77.6
	> 60 years	15	14.0

Department-wise and System-wide Distribution:

The Department of Medicine reported the highest number of ADRs (55.1%, n=59), followed by Surgery (26.2%, n=28). The skin was the most commonly affected organ system (36.4%, n=39),

with maculopapular rash being the predominant manifestation.

This was followed by multisystem involvement (22.4%, n=24) and gastrointestinal system (16.8%, n=18) (Table 2).

Table 2: System-Wise Distribution of Adverse Drug Reactions

Organ System Affected	Frequency (n)	Percentage (%)	Common Manifestations
Skin	39	36.4	Maculopapular rash, urticaria, itching
Multisystem	24	22.4	Angioedema, fever, chills, hypotension
Gastrointestinal (GIT)	18	16.8	Nausea, vomiting, epigastric distress
Central Nervous System (CNS)	11	10.3	Headache, parkinsonism, dystonia
Cardiovascular System (CVS)	7	6.5	Postural hypotension, tachycardia, edema
Renal System	4	3.7	Haematuria, renal dysfunction
Metabolic System	2	1.9	Hypoglycemia, hyperkalemia
Blood & Lymphatic	1	0.9	Leucopenia
Musculoskeletal	1	0.9	Tremor
Total	107	100.0	

Drugs Implicated: Antimicrobials were the most common drug class responsible for ADRs (53.3%, n=57). Among antimicrobials, ciprofloxacin was the leading individual drug (n=17), primarily

causing skin rashes. NSAIDs (13.1%, n=14) and antipsychotics (5.6%, n=6) were the second and third most common drug classes, respectively (Table 3).

Table 3: Drug Classes Implicated in Adverse Drug Reactions

Drug Class	Frequency (n)	Percentage (%)	Notable Examples (Number of ADRs)
Antimicrobials	57	53.3	Ciprofloxacin (17), Metronidazole (13)
NSAIDs	14	13.1	-
Antipsychotics	6	5.6	-
Antihypertensives	5	4.7	-
Others*	10	9.3	Iron supplements, Tramadol
Anticonvulsants	3	2.8	-
Antiasthmatics	2	1.9	-
Antiplatelets	2	1.9	-
Other Classes**	8	7.5	Antirheumatoid, Oral Hypoglycemics, etc.
Total	107	100.0	

*'Others' includes Ferrous salts, Tramadol, Multivitamins, Tetanus vaccine, Loperamide.

**Other classes contributed 2 or fewer ADRs each.

Causality, Severity, and Type Assessment:

Causality (Naranjo): The majority of ADRs were categorized as 'Probable' (65.4%, n=70), followed by 'Possible' (34.6%, n=37). No 'Definite' or 'Doubtful' categories were assigned.

Severity (Hartwig and Siegel): Most ADRs were of 'Moderate' severity (60.7%, n=65), requiring

therapeutic intervention or prolonging hospital stay. The remaining 39.3% (n=42) were 'Mild'.

No 'Severe' or fatal ADRs were reported.

Type (Rawlins and Thompson): A majority of ADRs were classified as Type B (61.7%, n=66), while 38.3% (n=41) were Type A.

Table 4: Assessment of Causality, Severity, and Type of ADRs

Assessment Scale	Category	Frequency (n)	Percentage (%)
Causality (Naranjo)	Probable	70	65.4
	Possible	37	34.6
	Definite	0	0.0
	Doubtful	0	0.0
Severity (Hartwig & Siegel)	Moderate	65	60.7
	Mild	42	39.3
	Severe	0	0.0
Type (Rawlins & Thompson)	Type B	66	61.7
	Type A	41	38.3

Discussion

This study provides a snapshot of the ADR landscape in a rural Indian teaching hospital. The overall incidence of 0.13% is lower than that reported in many active surveillance studies from India [10, 12], but is consistent with other spontaneous reporting studies, highlighting the universal challenge of under-reporting [13, 14].

The significantly higher incidence in inpatients is expected, as they are exposed to multiple drugs, are more severely ill, and are under closer observation.

The female preponderance (59.8%) aligns with several studies which suggest that gender-based differences in pharmacokinetics, body composition, and hormonal factors may increase susceptibility to ADRs in women [19]. The finding that the adult age group (19-60 years) experienced the most ADRs contrasts with studies that highlight higher rates in the elderly [9], but can be explained by this demographic constituting the majority of the patient population in this rural catchment area.

The predominance of antimicrobials as the leading cause of ADRs is a consistent and concerning finding across India [10, 11, 12], pointing towards their extensive and often irrational use in clinical practice. The high frequency of cutaneous manifestations is also a common observation, as the skin is often the first organ to display signs of drug hypersensitivity [12].

A notable finding was the high proportion of Type B (unpredictable) reactions (61.7%), which contrasts with the global understanding that 80% of ADRs are Type A [18]. This could be specific to the drug use pattern and genetic predispositions in this population, warranting further genetic studies. The absence of 'Definite' causality and 'Severe' ADRs is a limitation of the spontaneous reporting method, where rechallenge is rarely performed for ethical reasons.

Limitations: The primary limitation is under-reporting, a well-documented constraint of passive surveillance systems. The single-center design may limit the generalizability of the findings to other rural settings.

Conclusion

This study confirms that ADRs are a tangible clinical issue in rural South India, with antimicrobials being the principal offenders and the skin being the most vulnerable organ. The high rate of unpredictable Type B reactions calls for heightened vigilance. The low incidence rate is a stark reminder of the pervasive under-reporting that plagues pharmacovigilance. To improve drug safety, it is imperative to implement active surveillance methods, conduct continuous educational and sensitization programs for healthcare professionals, and integrate pharmacovigilance into the core curriculum of medical education. Strengthening the pharmacovigilance network at the rural level is crucial for generating reliable national data and safeguarding public health.

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