International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 1, January 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.1.2025.5

ORIGINAL RESEARCH

A prospective study of cutaneous adverse drug reactions at a tertiary care hospital in central India

[1]Dr. Raja Wasim Bakshi, [2]Dr. J L Marko, [3]Dr. Anand Dubey, [4]Dr. Stephen Nand, [5]Dr. Swapnil Mujumdar, [6]Dr. Saman Aatif Saulat, [7]Dr. Tarun Kumar, [8]Dr. Amruthadevi T S

[1]Post Graduate 3rd Year, [2]Professor, [4,8]3rd year PG resident, [5,6,7]Junior Resident, Department of Pharmacology, Gandhi Medical College/Hamidia Hospital Bhopal, MP, India
[3]Associate Professor, Department of Dermatology, Hamidia Hospital, Bhopal, MP, India

Corresponding author
Stephen Nand
3rd year PG resident, Department of Pharmacology, Gandhi Medical College/Hamidia Hospital Bhopal, MP, India
Email: stephennand@yahoo.com

Received: 21 November, 2024 Accepted: 26 December, 2024 Published: 06 January, 2025

ABSTRACT

Background: Cutaneous adverse drug reactions (CADRs) encompass a broad spectrum of clinical manifestations ranging from mild erythematous rashes to severe, life-threatening conditions such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). These reactions pose considerable challenges in clinical practice, particularly in resource-limited settings where early identification, causality assessment, and prompt management can mitigate morbidity and mortality. **Methods:** A 12-month prospective study was conducted at a tertiary care hospital in Central India. Patients from various departments with clinically suspected CADRs were enrolled after obtaining informed consent and Institutional Ethics Committee approval. Detailed histories—including drug, personal, and family histories—were recorded. Clinical diagnosis was established through expert dermatologist consultation and morphological criteria. Causality was assessed using both the WHO-UMC and Naranjo scales, while severity was analyzed by an adapted Hartwig rating scale. Statistical analysis was performed using descriptive statistics (mean, standard deviation, percentages). **Results:** A total of 188 patients were evaluated, of which 70 were included in the final analysis based on complete data and confirmed causality assessments. The prevalence of CADRs was slightly higher in males (57.2%). Fixed drug eruption (FDE) emerged as the most common clinical type, followed by erythematous drug eruptions and urticarial reactions. Analgesics/NSAIDs, antibiotics, and corticosteroids were frequently implicated drug groups. Most reactions were of moderate severity (89.9%), while 1.1% were severe. Drug withdrawal, along with appropriate adjunctive therapy, led to recovery or improvement in the majority of cases. **Conclusion:** CADRs represent a notable source of morbidity in clinical settings, underscoring the need for heightened vigilance, especially with commonly implicated drug classes. Early diagnosis, thorough history-taking, and systematic causality assessments can reduce the risk of severe outcomes. Further large-scale studies are recommended to better characterize CADRs and to improve preventive measures.

Keywords: cutaneous adverse drug reactions, fixed drug eruption, causality assessment, prospective study, Central India

INTRODUCTION

Cutaneous adverse drug reactions (CADRs) constitute a clinically significant subset of adverse events related to pharmacological agents. They can range from benign, self-limiting presentations—such as mild erythema or maculopapular rashes—to severe, life-threatening manifestations, including Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) [1-3]. The global incidence of CADRs varies widely, but they remain one of the most common reasons for drug discontinuation or switch in clinical practice [4]. CADRs not only pose a therapeutic challenge but also contribute substantially to healthcare costs through increased hospital stays, necessity for specialized care (e.g., burn units for TEN), and potential for fatal complications [2,5].

India, with its diverse population and frequent over-the-counter (OTC) medication use, is at high risk for CADRs [6]. Self-medication, suboptimal pharmacovigilance systems, and the availability of multiple drug combinations complicate the accurate identification of offending agents. Understanding the

DOI: 10.69605/ijlbpr_14.1.2025.5

local epidemiology of CADRs is therefore essential for clinicians to anticipate, diagnose, and manage these reactions efficiently. Moreover, identifying risk factors—such as underlying comorbidities, polypharmacy, and genetic predispositions—can facilitate targeted preventive strategies [2,7].

Despite growing awareness, systematic data on CADRs in Central India remain limited. Existing studies often focus on specific drug categories or specific reaction types, resulting in fragmented evidence. To address this gap, the present study aimed to prospectively evaluate CADRs in a tertiary care hospital setting, considering the broad spectrum of potential etiological factors and clinical presentations. Specifically, we sought to (1) characterize the demographic profile of patients presenting with CADRs; (2) determine the types and frequencies of cutaneous reactions; (3) identify the most frequently implicated drugs and drug classes; (4) assess the severity and probability of CADRs; and (5) evaluate the treatment outcomes, including hospitalization rates and clinical resolution [8].

The findings from this study have implications for both clinical practice and public health. By providing a systematic analysis of CADRs, healthcare providers will be better equipped to recognize early warning signs and adapt treatment regimens accordingly. Furthermore, the insights gained may serve as an evidence base for policy changes relating to pharmacovigilance and prescribing practices in resource-limited settings. Such improvements could ultimately reduce the burden of preventable CADRs and enhance patient safety.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective, observational study conducted over 12 months (from November 1, 2014, to October 30, 2015) at a tertiary care hospital in Central India. Institutional Ethics Committee approval was obtained prior to participant enrollment.

Study Population

Inclusion criteria

1. Patients of any age and sex presenting with or suspected of having a CADR.
2. Willingness to provide written informed consent.

Exclusion criteria

1. Patients with incomplete or unclear drug histories (e.g., unknown medications).
2. Patients unwilling to comply with study procedures.

A total of 188 patients were screened; 70 patients with confirmed CADRs (based on causality assessments) were included in the final analysis.

Data Collection

Detailed demographic data (age, sex, residence, religion) and clinical information (medical and drug history, including concomitant medications and comorbid conditions) were obtained. Patients underwent thorough dermatological examinations by expert dermatologists to establish the clinical type of CADR—e.g., fixed drug eruption (FDE), erythematous drug eruption (EDE), urticaria, acneiform eruptions, DRESS, among others. In cases of multiple suspected medications, the most likely offending agent was withdrawn sequentially to observe clinical improvement. Rechallenge was not performed due to ethical concerns.

Causality and Severity Assessment

Causality was evaluated using both the WHO-UMC scale (certain, probable, possible, unlikely, conditional/unclassifiable) and the Naranjo algorithm (definite, probable, possible, doubtful). Only "certain/definite," "probable," and "possible" cases were included in the final dataset. The severity of reactions was classified according to an adapted Hartwig rating scale as mild, moderate, or severe.

Laboratory Investigations

Routine hematological and biochemical tests (e.g., total leukocyte count, differential counts, absolute eosinophil count) were performed when clinically indicated or to aid in diagnosing severe or atypical presentations.

Follow-up and Outcome Measures

Severe cases (e.g., SJS, TEN, DRESS) were followed weekly after initial hospitalization until the resolution of lesions. Patients with mild-to-moderate reactions were followed for any persistent lesions, recurrence, or complications. Outcomes were categorized as recovered, recovering, not recovered, fatal, or recovered with sequelae.

Statistical Analysis

Data were recorded using Microsoft Excel 2007 and analyzed using descriptive statistics (mean, standard deviation, percentages). Differences in categorical variables (e.g., sex distribution) were examined using the z-test where appropriate. Tables and graphs were used to present the data succinctly.

RESULTS

Overview of Study Participants

A total of 70 patients met the criteria for confirmed CADRs. Males (57.2%) slightly outnumbered females (42.9%), although this was not statistically significant. Patients ranged from pediatric to geriatric age groups, with the most affected age bracket being 20–30 years. Urban residents constituted 64.3% of the sample, while 35.8% resided in rural areas. The majority of participants were Hindu (60%), followed by Muslim (35.8%), and a minority under "Others" (4.3%).

DOI: 10.69605/ijlbpr_14.1.2025.5

TABLE 1. BASELINE DEMOGRAPHICS OF STUDY POPULATION

Variable	N=70
Age Group (years)	0–70
Mean Age (±SD)	35.2 (±14.7)
Sex	Male 57.2%, Female 42.9%
Residence	Urban 64.3%, Rural 35.8%
Religion	Hindu 60%, Muslim 35.8%, Others 4.3%

(Data summarized from study findings; percentages are approximations.)

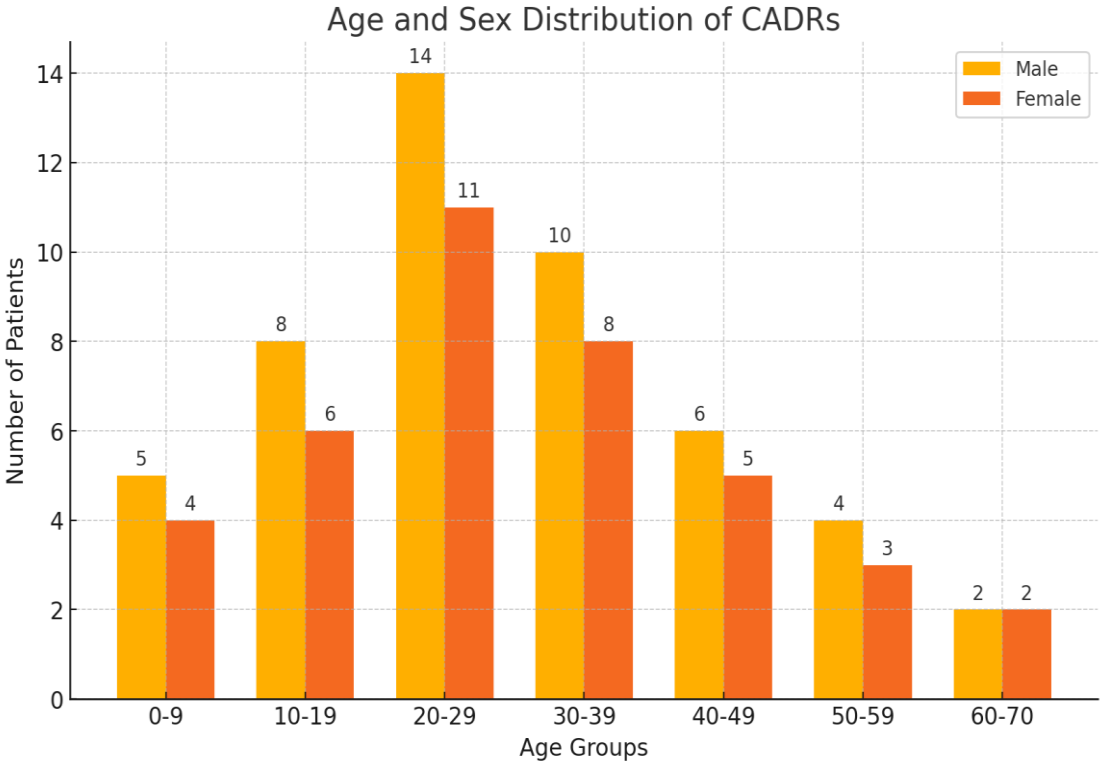

FIGURE 1. AGE AND SEX DISTRIBUTION OF CADRS

This bar chart shows the distribution of age groups and the number of male and female patients within each group.

Clinical Presentation

Pruritus and vesiculobullous lesions were common complaints. Some patients presented with more than one symptom (e.g., pruritus and edema). Fixed drug eruption (FDE) was the most frequently observed clinical pattern, accounting for about 29.8% of the cases, followed by erythematous drug eruptions (13.8%) and urticarial rashes (around 17%). Acneiform eruptions were also noted but mostly as exacerbations of pre-existing dermatoses.

TABLE 2. COMMON CLINICAL TYPES OF CADRS

Clinical Reaction	Frequency (%)
Fixed Drug Eruption (FDE)	29.8
Erythematous Drug Eruption	13.8
Urticaria	17.0
Acneiform Eruptions	~6–7
DRESS	~4
SJS / TEN	2.9
Others (e.g., angioedema)	remainder

(Percentages rounded for presentation.)

Causative Drugs

Among the implicated drugs, analgesics/NSAIDs (e.g., diclofenac, nimesulide) were most commonly responsible, followed by antibiotics (particularly beta-lactams and fluoroquinolones), corticosteroids, and antiepileptics. Polypharmacy

DOI: 10.69605/ijlbpr_14.1.2025.5

and self-medication practices were prevalent in a substantial subset of patients, complicating the identification of the offending agent. Oral administration was the most frequent route (around 64.9%), with topical applications accounting for roughly a quarter of cases.

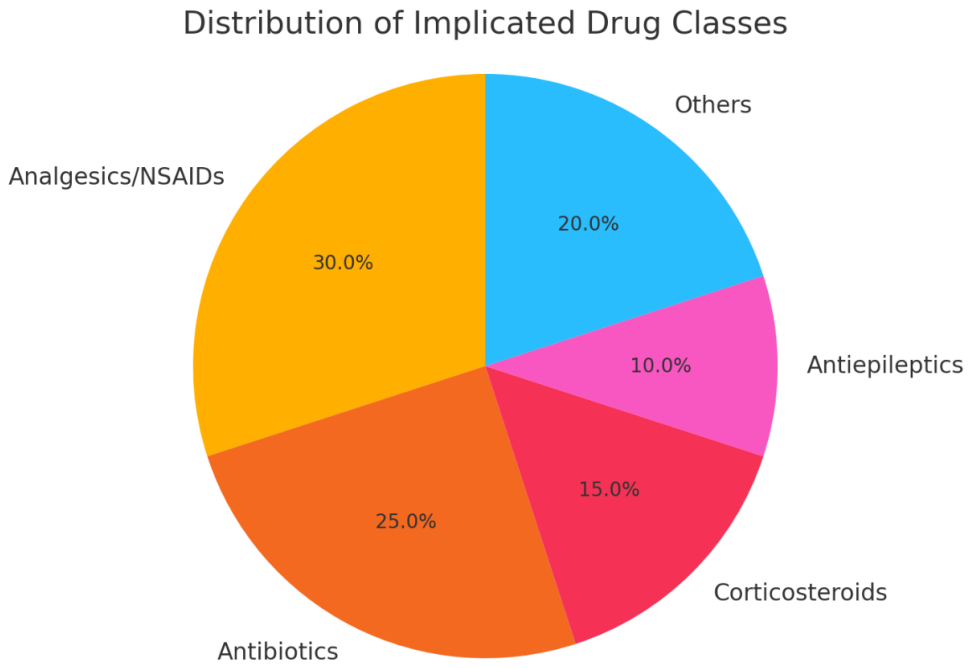

FIGURE 2. DISTRIBUTION OF IMPLICATED DRUG CLASSES

This pie chart illustrates the proportions of various drug classes implicated in the cases, including analgesics/NSAIDs, antibiotics, corticosteroids, and others.

Severity and Probability of Reaction

Most CADRs were moderate in severity (89.9%) according to the adapted Hartwig scale. Only 1.1% reached the severe category, necessitating intensive care. Probability assessments indicated that around 42.6% of reactions were categorized as “possible” and another 42% were “probable”; 29% were considered “certain/definite.”

Outcomes

Withdrawal of the offending agent was the primary intervention. In moderate cases, supportive care included antihistamines, topical and/or systemic corticosteroids, and other symptomatic treatments. Over 90% of patients either recovered or were in the process of recovering; 4.2% did not show significant improvement at the time of last follow-up, and 1.1% had a fatal outcome (observed in the severe spectrum of reactions like SJS/TEN). A small segment (up to 30.9%) had residual sequelae, predominantly hyperpigmentation.

TABLE 3. SUMMARY OF OUTCOMES

Outcome Category	Proportion (%)
Completely Recovered	~22.9
Recovering	~38.4
Not Recovered	~4.2
Fatal	~1.1
Recovered with Sequelae	~30.9

DISCUSSION

CADRs are recognized as significant contributors to patient morbidity and occasional mortality, especially in regions with frequent self-medication and less stringent pharmacovigilance [1,2]. In our study, the slight male predominance concurs with some previous reports [9], though other studies have noted female preponderance [10]. This discrepancy could be attributable to differences in health-seeking behavior, prescription practices, and local epidemiological factors.

The predominance of FDE aligns with prior literature indicating that it is among the most commonly observed CADRs in clinical practice, often triggered by sulfonamides, fluoroquinolones, and NSAIDs [2,4]. The second and third most frequent patterns—erythematous drug eruptions and urticaria—are also consistent with other regional data [11]. Notably, our cohort revealed that acneiform eruptions were

DOI: 10.69605/ijlbpr_14.1.2025.5

sometimes related to pre-existing dermatoses exacerbated by the offending drug, highlighting the complexity of diagnosing CADRs in patients with underlying skin conditions.

Analgesics/NSAIDs emerged as the most implicated drug class, followed by antibiotics and corticosteroids. These findings may reflect the widespread and often unregulated use of painkillers for various acute and chronic conditions, as well as the rampant prescription and self-administration of antibiotics in India [6,7]. Moreover, the frequent prescription of systemic corticosteroids for common inflammatory or allergic disorders explains their notable association with CADRs, such as steroid-induced acneiform eruptions [12].

Interestingly, most CADRs were of moderate severity, and only a small percentage (~1.1%) were classified as severe. The low rate of severe reactions may be attributed to increased awareness and more judicious use of known high-risk medications at our center. However, even moderate reactions can negatively impact patient quality of life and lead to the need for additional interventions [3]. Our results underscore the value of early detection, prompt withdrawal of the offending agent, and supportive care to avert progression to severe forms.

A substantial proportion of patients had a history of allergy or past drug reactions, suggesting that meticulous history-taking can help anticipate potential future events [10]. Furthermore, the presence of comorbid conditions such as diabetes or hypertension might predispose individuals to more severe outcomes or complicate the management of CADRs [1,11]. Implementing robust pharmacovigilance programs, encouraging rational prescribing, and promoting patient education about the risks of self-medication could collectively reduce the incidence and severity of CADRs [5,7].

The study's strengths include its prospective design and comprehensive approach to data collection and causality assessment. Nonetheless, the generalizability may be limited by the single-center setting and the relatively small sample size (n=70). Future multicenter trials with larger cohorts and longer follow-up periods could provide deeper insights into the pathophysiological mechanisms, genetic predispositions, and long-term sequelae associated with CADRs in similar populations.

CONCLUSION

CADRs remain a notable concern in clinical practice, particularly where self-medication and polypharmacy are prevalent. This study demonstrated that fixed drug eruptions, erythematous drug eruptions, and urticaria rank among the most frequent clinical types in Central India, with analgesics/NSAIDs and antibiotics being common culprits. While most cases are of moderate severity, the risk of severe outcomes persists, emphasizing the importance of vigilance. Systematic evaluation—encompassing clinical, laboratory, and causality assessments—facilitates early intervention and favorable outcomes. Strengthening pharmacovigilance, rational prescribing practices, and patient education can further mitigate the burden of CADRs in resource-limited settings.

REFERENCES

1. Nayak S, Acharjya B. Adverse cutaneous drug reactions. Indian J Dermatol. 2008;53(1):2–8.
2. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. N Engl J Med. 1994;331(19):1272–1285.
3. Pudukadan D, Thappa DM. Adverse cutaneous drug reactions: Clinical pattern and causative agents in a tertiary care center in South India. Indian J Dermatol Venereol Leprol. 2004;70(1):20–24.
4. Bigby M. Rates of cutaneous reactions to drugs. Arch Dermatol. 2001;137(6):765–770.
5. Chatterjee S, Ghosh AP, Barbhuiya J, Dey SK. Adverse cutaneous drug reactions: A one-year survey at a dermatology outpatient clinic of a tertiary care hospital. Indian J Pharmacol. 2006;38(6):429–431.
6. Patel TK, Barvaliya MJ, Sharma D, Tripathi C. A systematic review of the drug-induced Stevens–Johnson syndrome and toxic epidermal necrolysis in Indian population. Indian J Dermatol Venereol Leprol. 2013;79(3):389–398.
7. Suh KS. Advances in pharmacovigilance and patient safety. Korean J Intern Med. 2020;35(4):705–713.
8. Ardern-Jones MR, Friedmann PS. Skin manifestations of drug allergy. Br J Clin Pharmacol. 2011;71(5):672–683.
9. Hsu DY, Brieva J, Silverberg NB, Silverberg JI. Pediatric adverse drug reactions in the United States. Pediatr Dermatol. 2017;34(2):128–134.
10. Chatterjee S et al. Patterns of cutaneous drug reactions in a tertiary care outpatient setting. J Clin Pharmacol. 2010;50(11):1266–1275.
11. Sharma VK, Sethuraman G. Adverse cutaneous reactions to drugs: An etiological survey of 197 cases. Indian J Dermatol Venereol Leprol. 2001;67(1):2–4.
12. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006;54(1):1–15.