



Cutaneous Adverse Drug Reaction Profile in Tertiary Care Teaching institute: A Prospective Study

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Abstract

Introduction: Cutaneous adverse drug reactions (CADRs) are the most common type of drug sensitivity reactions, with a varied and diverse range of morphologies. Therefore, it is essential to be aware of them for diagnosis and prevention. **Aim:** To assess the cutaneous adverse drug reaction (CADR) profile of patients from the tertiary care teaching hospital in North India. **Methods:** A prospective, observational study was conducted over 6 months in the Department of Pharmacology & Therapeutics, Jammu in collaboration with the Dermatology department, SMGS Hospital, Jammu after obtaining permission from the institutional ethical committee. Patients with drug rash, of either sex and all age groups were included in the study. The WHO-UMC scale and Naranjo algorithm scale were used to determine the causality assessment. Details regarding drug intake, morphology of eruption, offending drugs, drug rechallenge/ de-challenge history, and treatment given to the patients were assessed. **Results:** Out of 100 patients enrolled, 42% had an exanthematous drug eruption, while 21% had fixed drug eruptions. Most reactions were caused by antimicrobials 64% followed by non-steroidal anti-inflammatory drugs (NSAIDs) in 15% of patients, with 9% experiencing severe cutaneous adverse drug reactions (SCADRs), like Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), caused by antituberculous drugs. **Conclusion:** The study findings show that reporting adverse drug reactions (ADR) can help identify the drugs most commonly associated with dermatological reactions. This leads to better patient treatment through early identification and management of these reactions.

Keywords

Cutaneous Adverse Drug Reactions, Antimicrobials, Exanthematous Drug Eruption

Introduction

Adverse drug reactions (ADRs) refer to harmful reactions to drugs under normal usage conditions. CADR, which stands for cutaneous adverse drug reactions, represents approximately 1/3-1/4 of ADRs and is characterized by skin-related symptoms. CADR represents a diverse spectrum of skin disorders induced by the administration of various pharmaceutical agents.

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As the human body's largest organ, the skin serves as a critical interface between the internal environment and the external world. Consequently, it is susceptible to the effects of drugs that are ingested, injected, or applied topically. Among all the medications, certain drug groups are more likely to cause a drug reaction. These groups include penicillin, sulfonamides, anticonvulsants, NSAIDs,

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fluoroquinolones, and angiotensin-converting enzyme inhibitors.^[1-3]

CADR encompasses a wide array of dermatological manifestations, ranging from mild and self-limiting eruptions to severe and life-threatening conditions. The incidence of CADR is a significant concern in clinical practice, given the widespread use of medications to treat various medical conditions.

Approximately 10-30% of adverse drug reactions (ADRs) have cutaneous manifestations out of which 2-3% are seen in patients who get admitted to the hospital.^[4,5] Understanding the underlying mechanisms and risk factors associated with CADR is essential for healthcare professionals to make informed decisions regarding drug therapy and to provide timely and appropriate interventions when adverse reactions occur. Patients can be educated to avoid re-administering offending drugs, reducing morbidity from CADRs.^[6]

It is crucial to report adverse drug reactions (ADRs) as it helps predict the type of drug reaction and the underlying causative agent in a particular population. This information is valuable in evaluating whether there is any underlying genetic or metabolic susceptibility to a particular drug reaction in a specific group of people. Additionally, it helps in taking necessary measures to reduce the harmful effects on patients and, in turn, improve public health. This study's objective is to assess the CADR patterns, including the causative drugs and causality and severity assessment.^[7]

Material and Method

This prospective, observational study was conducted over 6 months in the Department of Pharmacology & Therapeutics, Jammu in collaboration with the Dermatology department, SMGS Hospital, Jammu after getting permission from the institutional ethics committee (IEC/GMCJ/2022/1182). The period of study was from 1st October 2022 to 30th April 2023. 100 patients (in-patient) suspected to have CADR were examined. The study recorded a detailed history of the patient's age, gender, type of drug intake, dosage, duration, frequency, and type of cutaneous rashes. The time interval between drug intake and the appearance of cutaneous lesions and indications of drug intake were also noted. The

morphology of different cutaneous lesions was also noted, along with any history of similar eruptions and the number of episodes.

The causality assessment of ADRs was done by using the World Health Organization- Uppsala Monitoring Center (WHO-UMC) causality assessment scale as certain, probable, possible, unlikely, conditional/unclassified, and unassessable /unclassifiable and also by using the Naranjo algorithm scale.^[7] Descriptive statistics were used to analyze the data and values are expressed in numbers and percentages.

Results:

Out of 100 patients, 71 were males and 29 were females. So, the ratio was 2.44:1 (M:F). The most common age group affected was 21-40 years (35%) followed by the age group 41-60 years (27%) and the least common being less than 20 years (11%) as shown in *Table 1*.

The most common class of drugs implicated were cephalosporins (antimicrobials) with 65% of cases, followed by Diclofenac, a non-steroidal anti-inflammatory drug, NSAIDs (15%), and 11% of ATT resulted in Severe cutaneous adverse drug reactions (SCARs) as shown in *Fig 1*.

The most common cutaneous ADR seen was exanthematous drug eruptions (42%), [*Fig 2A*] followed by fixed drug eruptions FDE, (21%), [*Fig 2B, 2C*], 9% of SCAR's [*Fig 2D*] and 05% of miscellaneous CADRs were seen [*Fig 2E, and 2F*]. (*Table 2*,

Causality assessment was done using the WHO-UMC causality assessment scale, with most CADRs categorized as possible.

The time interval between drug intake and the appearance of CADRs ranged from a few minutes to one and a half months.

Discussion

Cutaneous adverse drug reactions have various morphological and distributional patterns. Exanthematous rashes, urticarial rashes, fixed drug eruptions, and erythema multiforme are common patterns observed in studies.^[7] In our study, exanthematous drug eruption was the most common drug eruption (42%) followed by fixed drug eruptions (21%) in accordance with the studies done by Saha *et al* (30.18%), Choon *et al* (42.3%), Nandha *et*

Table 1. Incidence of cutaneous adverse drug reactions in different age groups (n=100)

Age Group	Value	%
< 20 years	11	11
20-40 years	35	35
41-60 years	27	27
>60 years	25	25

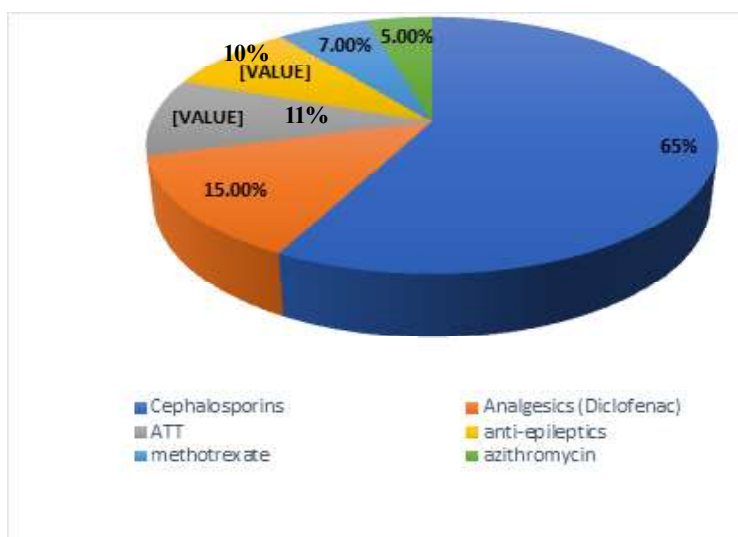
Table 2 Morphological types of drug eruptions (n=100)

Type of adverse Reaction	Value	%
Erythematous drug eruption	42	42
Fixed Drug eruptions	21	21
Urticaria	19	19
Severe cutaneous adverse drug reactions	09	09
Miscellaneous	05	05

Table 3: Causality assessment of inpatients to drugs by using the WHO-UMC scale

	Certain%	Probable%	Possible%	Unlikely%	Unassessable%
Anti-microbial	08.00	09.00	32.00	6.0	3.00
NSAIDs	05.00	10.00	28.00	0	0
Methotrexate	07.00	04.00	28.00	0	0
Anti-tubercular drugs	0	07.00	32.00	0	0
Prednisolone	0	18.00	23.00	0	0

Fig1: Pie Chart showing percentage (%) of offending drugs.



al (42.85%), Sharma *et al* (34.6%), Noel *et al* (35%), and Hiware *et al* (37.7%).^[5,8-12] AL Raaie and Banodkar found drug-induced urticaria (35%) whereas Pudukadan and Thappa found fixed drug eruptions (FDE) to be the

most common CADR in their respective studies.^[6,13-14] This variation in the observed results could be attributed to differences in drug utilization patterns, drug reaction rates, and the studied population's pharmacogenetic



Fig 2: The figures above illustrate the cutaneous adverse drug reactions in our study. (A) Erythematous drug eruption. (B) Fixed drug eruption. (C) Fixed drug eruption (Bullous). (D) Steven-johnson syndrome. (E) Erythema Multiforme secondary to phenytoin. (F) Erythema of Face.

traits.^[5]

The most common class of drugs implicated was antimicrobials (64%) followed by NSAIDs (15%) in our study. This is in concordance with other studies by Choon *et al* (77.1%), Pudukadan *et al.* (58.88%), and Nandha *et al* (48.3%).^[5,6,9]

In our study, we found that the most common group of drugs that caused exanthematous drug eruption was cephalosporins, accounting for 65% of cases. However, Amrinder *et al* reported that ampicillin was the most common drug responsible for exanthematous drug eruption. On the other hand, Saha *et al* and Noel *et al* found that antiepileptics were the most common drugs causing exanthematous type of CADR.^[8,11] SCADRs accounted for 09.00% of the total CADR which is much lower than the incidence noticed by Saha *et al* (32.04%).^[8]

While most studies have reported antiepileptics as the most common drugs causing Severe Cutaneous Adverse Drug Reactions (SCADRs), we have found that antituberculous drugs (11%) are the predominant agents causing SCADRs. This could be due to the increased burden of tuberculosis in the region.^[4,8,15-18] In a study by Cidhdavaduta *et al* the majority of CADR (92.5%) were probably caused by suspected medication, which contradicts the findings of the present study where the majority of the cases fell into the possible category (87%) of WHO-UMC category scale.^[19]

Our study showed a higher number of males (male: female = 2.44:1), which is consistent with the findings of Patel and Marfatia. However, some studies conducted by Pudukadan and Thappa and Nandha *et al* have reported a higher number of females.^[5,12]

The main limitation of our study was that the drug rechallenge test could not be performed due to ethical reasons. Rechallenge tests aid in identifying the causative drug for a specific reaction, improving reliability and reducing false positives. Our study highlights the importance of a stringent and effective pharmacovigilance system. Although adverse drug reactions are unavoidable, it's crucial to lower their incidence in clinical practice. With the introduction of new drugs every day, it's necessary to conduct more studies to alert clinicians and mitigate this problem. The changing trends in drug use further emphasize the need for such studies.

Conclusion:

In conclusion, our study underscores the prevailing role of antimicrobials in cutaneous adverse drug reactions (CADRs), with a notable prominence of antituberculous treatment in severe cases and a male predominance. CADRs represent a significant and often underestimated aspect of medication-related complications.

These reactions manifest in various forms, ranging from mild skin rashes to severe conditions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. In developing countries like India, self-medication and the use of over-the-counter drugs pose major obstacles to conducting studies on CADRs. These findings emphasize the imperative to mitigate CADRs and advocate for the judicious use of medications. The potential impact on patient health and well-being necessitates a concerted effort to understand, identify, and report CADRs, facilitating a proactive approach to minimize risks and enhance drug safety in clinical practice.

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Nil

Conflicts of Interest

There are no conflicts of interest.

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