International Journal of Basic & Clinical Pharmacology
Kalola AS et al. Int J Basic Clin Pharmacol. 2024 May;13(3):339-343
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20240989

Original Research Article

A study of cutaneous adverse drug reactions in the dermatology department of a tertiary care teaching hospital in Gujarat

Abhishek S. Kalola*, Shreya M. Shah, Chirag B. Mistry

Department of Pharmacology, Government Medical College Baroda, Gujarat, India

Received: 13 February 2024
Revised: 10 March 2024
Accepted: 11 March 2024

***Correspondence:**
Dr. Abhishek S. Kalola,
Email: abhi.kalola@gmail.com

ABSTRACT

Background: Various drugs are responsible for different cutaneous adverse drug reactions (CADRs). Considering variation in drug responses and the day-to-day increasing burden of ADRs, this study was done with emphasis on the need for effective evaluation and the reporting of the ADR reporting programme.
Methods: This was an observational cross-sectional study conducted for the duration of six months in the dermatology department to evaluate various clinical patterns of CADRs.
Results: A total of 60 CADRs were reported. Among them, 51.67% were present in males and 48.33% were present in females. The most common CADR was FDE (35%), followed by macula-papular rash (25%). Antimicrobials were most commonly responsible for CADRs, followed by NSAIDs, antiepileptic, anti-gout, and anti-hypertensive medications.
Conclusions: For better patient care, drug safety, and rational use of medicines, knowledge of various drugs responsible for CADRs can be useful for health care professionals to reduce mortality and morbidity by monitoring, reporting, and assessment of CADRs whenever detected.

Keywords: Cutaneous adverse drug reactions, Fixed drug eruption, Medicines, Urticaria

INTRODUCTION

Pharmacovigilance is defined by the WHO as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem."[1]

According to the World Health Organization (WHO), definition of an adverse drug reaction is "a response to a drug that is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis and therapy of disease, or modification of physiological functions."[2]

An adverse cutaneous reaction caused by a drug is any undesirable change in the structure or function of the skin, its appendages, or mucous membranes, and it encompasses all adverse events related to drug eruption, regardless of the etiology.[3]

Cutaneous adverse drug reactions (CADRs) are common among ADRs. They account for patients' suffering, hospitalization, and economic burden and may sometimes be fatal. The common CADRs are skin rash, urticaria, fixed drug eruption (FDE), angioedema, and contact dermatitis. Serious CADRs endangering patients' lives are Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reactions with eosinophilia and systemic symptoms (DRESS), and Acute Generalized Exanthematous Pustulosis (AGEP).[3] The common offending drugs are antimicrobials, non-steroidal anti-inflammatory drugs (NSAIDs), anti-epileptic drugs, and

anti-gout agents. The cutaneous reaction pattern and causative drugs may vary with prescribing habits and levels of health care. The majority of CADRs are diagnosed clinically. Recognition of the offending medicine enables early withdrawal and improved outcomes. Observational studies are tools to know the pattern of reactions and the causative drug.[3]

With the introduction of new drugs for patient care, the intake of multiple medications, self-medication, and the availability of over-the-counter medications, the incidence of ADRs is progressively increasing. Atopy, genetic variations in drug metabolism, HLA variation, co-morbidities, underlying disease, active viral infection, immune status of the patient, and concomitant intake of other drugs can alter the rate, presentation, course, and outcome of CADRs.[4] This study aimed to document various cutaneous adverse effects and reactions experienced by the patients and to study common drugs implicated in cutaneous adverse drug reactions. Also, to study patients characteristics presenting with cutaneous ADR.

METHODS

Study design and place

This was observational cross-sectional study. This study was carried out in outpatient Dermatology Department of a Tertiary care teaching Hospital of Sir Sayajirao General Hospital, Vadodara, Gujarat. After getting approval from the ethics committee, the study was done for a duration of six months, e.g., from 1st August 2022 to 31st January 2023.

Study population

All patients attending dermatology OPD, who present with cutaneous adverse drug reaction.

Sampling and sample size

Based on the data from the dermatology department, we were likely to get 2-3 adverse drug reaction per week. So, considering duration based study of 6 months period we has estimated sample size of 60 participants.

Inclusion criteria

Patients of any age and gender attending dermatology OPD for cutaneous drug reaction and willing to give informed written consent to participate voluntarily were included.

Exclusion criteria

If history or document of patient presenting with cutaneous adverse reaction but drug taken before reaction was not available.

Informed written consent was taken from the patient or parent/s for paediatric patient before obtaining the required information from the case history. Privacy and confidentiality of patients with data safety was maintained during all stages of research and publication.

Data collection procedure

Data of Patients attending OPD of Dermatology Department for any cutaneous adverse drug reaction was recorded in case record form (CRF). After getting clinical and treatment history of patient, adverse drug reaction/s experienced by the patients were recorded in CRF as well as ADR form and were analyzed.

Statistical analysis

The recorded qualitative data was entered in excel sheet and they were analyzed as a percentage and frequency distribution with the help of excel software. For all the CADRs obtained, causality assessment was done by WHO-UMC scale, while Severity assessment was done by using modified Hartwig and Siegel scale and preventability of CADRs were assessed as per Schumock and Thronton preventability scale.

RESULTS

As per analysis of this qualitative - case based observational study of six months duration, total 60 cutaneous adverse drug reactions (CADRs) were reported. Among them, 31 (51.67%) were in males and 29 (48.33%) were noted among females (Table 1).

Table 1: Age and gender-wise distribution of cutaneous adverse drug reactions (CADRs).

Age group of patients (years)	Male	Female	Total
0 to 10	0	1	1
11 to 20	5	1	6
21 to 30	13	6	19
31 to 40	9	10	19
41 to 50	4	9	13
51 to 60	0	2	2
Total	31	29	60

The most common CADR pattern seen in the present study was fixed drug eruption (35%), followed by maculo papular rash (25%), urticaria (23.33%), angioedema (8.33%), urticaria with angioedema (5%) and DRESS syndrome (3.33%) (Table 2).

Antimicrobials were most commonly responsible for CADRs, followed by NSAIDs, antiepileptic, anti-gout, and anti-hypertensive medications as mentioned in Table 3. Different antimicrobial groups like fluoroquinolones, cephalosporin, azole, nitroimidazole and tetracycline were responsible for CADRs.

Table 2: Distribution of various types of cutaneous adverse drug reactions (CADRs).

List of CADRs	Male	Female	Total (n=60)	Percentage ADR/ (n=60) %
Fixed drug eruption (FDE)	14	7	21	35.00
Maculopapular rash	9	6	15	25.00
Urticaria	6	8	14	23.33
Angioedema	1	4	5	8.33
Urticaria with angioedema	1	2	3	5.00
DRESS syndrome	0	2	2	3.33
Total	31	29	60	100.00

Table 3: Drugs responsible for cutaneous adverse drug reactions (CADRs).

Group	List of possible drugs linked with CADRs	No. of CADRs	Percentage
Anti-microbial drugs	Ofloxacin + ornidazole, ciprofloxacin, levofloxacin, ofloxacin, norfloxacin ornidazole, amoxicillin clavulanic acid, metronidazole, fluconazole, itraconazole, doxycycline, cefixime, ceftraiaxone, cefadroxyl, ivermectin	37	61.67
NSAIDs	Paracetamol, nimesulide, diclofenac, aceclofenac and ibuprofen.	18	30.00
Anti-epileptic	Phenytoin, carbamazepine and phenobarbitone	3	5.00
Anti-gout	Allopurinol	1	1.67
Anti-hypertensive	Losartan	1	1.67
Total		60	100.00

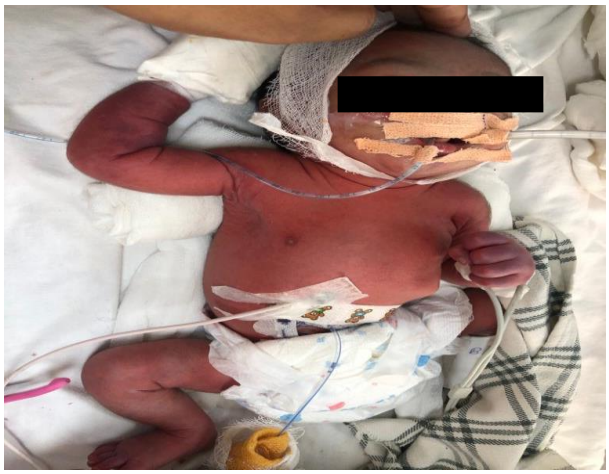

Figure 1: Urticaria after treatment of Phenobarbitone.

As shown in Figure 1, we have identified a case of urticaria after treatment of Phenobarbitone. Urticarial toxidermia, also known as "Urticaria and Quincke's Edema," typically presents in two distinct ways. Immediate urticaria occurs very quickly after the start of treatment, within 1 or 2 hours. Immediate reactions necessitate discontinuation of the drug due to the potential for the development of anaphylaxis.[5]

As shown in Figure 2, we have identified a case of Fixed Pigmented Erythema (FPE), also known as a Fixed Drug Eruption (FDE) that might occur 24 hours to a few days after administration of related medication. The classic form is characterized by single or multiple circular or oval-shaped, red to brown macules. These lesions have the potential to progress into plaques with vesicles or blistering.[5]

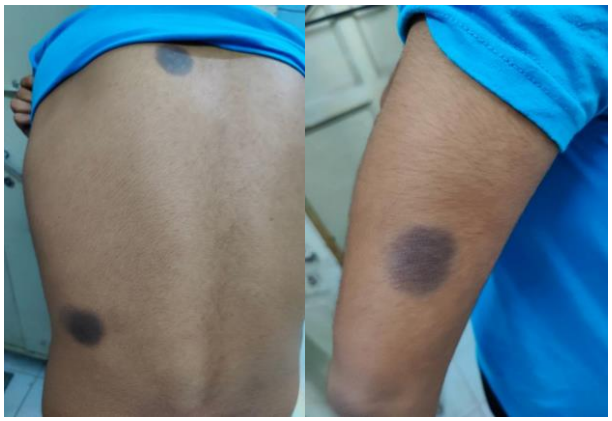

Figure 2: Fixed drug eruption after treatment of amoxicillin + clavulanic acid.

Overall, majority of CARDs came under probable causality assessment as per WHO-UMC criteria, while severity assessment using the modified Hartwig and Siegel scale has shown that majority of CADRs were moderate in nature. A total of 55 CADRs were not preventable as per the Schumock and Thronton Scale, on the other hand, for the CADRs due to NSAIDs, patients gave a history of self - medication with over the counter (OTC) drugs, so these

ADRs can be considered as a preventable cutaneous ADRS.

Table 4: Analysis of cutaneous adverse drug reactions (CADRs).

Causality assessment using WHO-UMC criteria		
Category	**No. of CADRs**	**Percentage**
Certain	0	0.00
Probable	53	88.33
Possible	7	11.67
Unlikely	0	0.00
Unclassifiable	0	0.00
Total	60	100.00
Severity assessment using modified Hartwig and Siegel scale		
Category	**No. of ADRs**	**Percentage**
Mild	2	3.33
Moderate	58	96.67
Severe	0	0.00
Total	60	100.00
Preventability assessment using Schumock and Thronton scale		
Category	**No. of ADRs**	**Percentage**
Definitely Preventable	5	8.33
Not preventable	55	91.67
Probably preventable	0	0.00
Total	60	100.00

DISCUSSION

Cutaneous Adverse Drug Reactions (CADRs) to drugs are common, affecting 2-3% of all hospitalised patients, and among them, approximately 2% of adverse cutaneous reactions are severe and very few are serious. The incidence of CADRs in developed countries ranges from 1 to 3% among in-patients, whereas in developing countries such as India, some studies project it to be between 2 to 5% of the in patients, however, there is still a need of comprehensive data among out-patients.[6]

In our study, total 60 CADRs were recorded. Out of them, 31 (51.67%) CADRs were observed in males and 29 (48.33%) were observed in females. In the study conducted by Gupta D et al, a higher number of CADRs were observed in females as compared to CADRs in males.[7]

In the present study, the most commonly observed CADRs were fixed drug eruptions in 35% of patients, followed by maculopapular rashes in 25% of patients. In the study conducted by Gupta et al., the most commonly observed reaction was maculopapular rash in 23% of patients. 5 On the other hand, in a study conducted in a hospital in central India, the most commonly observed CARD was fixed drug eruption followed by maculopapular rash.[8]

As per our study, CADRs were most commonly observed with antimicrobial agents (61.67%), while as per one study conducted in Western India, specific antimicrobial-antiretroviral drugs (38.5%) were responsible for the majority of CADRs.[9]

After analysis of CADRs, using WHO UMC criteria for causality assessment, a total of 53 CADRs were probable and 7 were possible. Similar finding was observed in one study conducted by Dhanani et al, which showed the majority (68%) of ADRs were in the probable group, 24% were in the possible group, and only 8% of ADRs were in a certain group.[10]

The severity assessment of CADRs was done using a modified Hartwig and Siegel scale, and it was found that the majority of ADRs were at a moderate level. A similar finding was observed in one study conducted by Torvi et al, showing that most of the CADRs-a total of 45 were in the moderate group.[10]

Preventability assessment using the Schumock and Tronton scale has shown that allergic types of idiosyncrasy reactions among 55 patients were not preventable ADRs. While self-medication-induced ADRs, among the five cases, can definitely be preventable. When a hypersensitivity reaction is detected, the immediate discontinuation of the possible drug is the safest option. The reaction itself can only be managed with supportive care like anti histaminic or glucocorticoids, as there is no causally directed treatment.

This study has some limitations. Considering only sixty participants from outpatient dermatology department developed CADRs during the six-month study duration, the results of this study may not be generalized to the entire population, so this study can be expanded by similar large-scale studies at various centers as a multi-centric study. This study was done for the duration of six months considering a cross-sectional study design, but a newer study by keeping the study duration for a year or more with prospective long-term annual follow-up might give confirmatory findings to differentiate dermatological disease recurrence versus cutaneous ADRs after looking at the most probable nature of CADRs on causality assessment.

CONCLUSION

In the outpatient department, whenever any cutaneous drug eruption has been diagnosed and treated, information provided to the patient regarding his or her drug rash in a card form or some other form can help patients in the future during emergencies for identification of drug allergies and/or intolerances, especially if they have had a severe reaction, and it can help physicians in choosing safer alternative drugs.

ACKNOWLEDGEMENTS

Authors would like to thank Doctors and staff of Dermatology Department for their support and help in identifying patient with various CADRs.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of Biomedical and Health Research. Approval No. IECBHR/ 116- 2022/Dated 19/07/2022

REFERENCES

1. Maiti R. Post graduation topics in pharmacology. 2nd ed. Paras medical publisher; 2015:291.
2. Aronson JK, Ferner RE. Clarification of terminology in drug safety. Drug Saf. 2005;2810:851-70.
3. Patel T, Thakkar S, Sharma D. Cutaneous adverse drug reactions in Indian population: A systematic review. Indian Dermatol Online J. 2014;56(Suppl2):76.
4. Jha N, Alexander E, Kanish B, Badyal DK. A study of cutaneous adverse drug reactions in a tertiary care center in Punjab. Ind Dermatol Online J. 2018;9(5):299-303.
5. Al Aboud DM, Nessel TA, Hafsi W. Cutaneous Adverse Drug Reaction. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK533000/ Accessed on 11th February 2024.
6. Nayak S, Acharjya B. Adverse cutaneous drug reaction. Indian J Dermatol. 2008;53(1):2-8.
7. Gupta D, Gairola B, Kumar B, Bharath M, Ansari MS. A study and evaluation of cutaneous adverse drug reaction in the patients attending dermatology department of tertiary care teaching hospital in Eastern Uttar Pradesh. Int J Basic Clin Pharmacol 2021;10:664-7.
8. Shende TR, Siddqui RA. A clinical study of morphological patterns of cutaneous adverse drug reaction and its causality assessment in tertiary care hospital of central India. Int J Basic Clin Pharmacol. 2020;9(10):1528-32.
9. Dhanani JG, Sukhlecha A. A study of adverse cutaneous drug reactions in the department of dermatology of a teaching hospital in Jamnagar, India. Int J Basic Clin Pharmacol. 2017;6(9):2259-64.
10. Torvi JR, Reddy VR SGS. An observational study to monitor cutaneous adverse drug reaction profile in Dermatology Department of tertiary care teaching hospital. Int J Basic Clin Pharmacol. 2019;8:442-5.

Cite this article as: Kalola AS, Shah SM, Mistry CB. A study of cutaneous adverse drug reactions in the dermatology department of a tertiary care teaching hospital in Gujarat. Int J Basic Clin Pharmacol 2024;13:339-43.