

## Original Research Article

# An observational study of cutaneous adverse drug reactions in tertiary hospital

Tejashwani, Dipti Patel\*, Neela Bhuptani

Department of D.V.L., P.D.U Medical College and Hospital, Rajkot, Gujarat, India

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**\*Correspondence:**

Dr. Dipti Patel,

E-mail: [drdiptikoradia@gmail.com](mailto:drdiptikoradia@gmail.com)

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### ABSTRACT

**Background:** Adverse cutaneous drug reactions include reactions due to overdose, side effects and idiosyncratic reactions. They pose a diagnostic challenge due to wide variety of causative agents and varied clinical manifestations. Our study aims to record various clinical patterns of adverse drug reactions, their offending drugs and to study the pattern of morbidity and mortality in patients with severe cutaneous adverse drug reactions especially in the HIV era.

**Methods:** 90 patients with adverse cutaneous drug reactions were included who came to Dept. of Dermatology, Venereology and Leprosy at P.D.U. Govt. Medical College and Hospital, Rajkot, Gujarat from October 2011 to November 2017. Thorough history with all routine haematological and biochemical investigations and septic screening was done. The morphology of skin lesions was noted. The offending drug was withdrawn in the patients and appropriate treatment was given.

**Results:** The most common age group observed was 31-40 years (24.44%) with male to female ratio being 1.2:1. Maculopapular rash was the most common clinical type (16.66%). NSAIDS were the most common offending drugs (16.66%). Among the individual drugs, carbamazepine was the most common offending drug (14.44%). Drug was prescribed by a medical practitioner in 86 cases (95.55%), while self administered in 4 cases (4.44%). History of some cutaneous drug reaction in the past was present in 17 patients (18.88%). Lesions were generalised in 76 cases (84.44%) and localised in 14 cases (15.55%).

**Conclusions:** Knowledge of the pattern and the offending drug helps in better management and reduced complications in these patients and also helps in preventing recurrences.

**Keywords:** Adverse drug reactions, Pattern of ADR, Offending drugs, Fixed drug eruptions, NSAIDS

### INTRODUCTION

An adverse drug reaction (ADR) may be defined as an untoward clinical manifestation resulting from administration of a particular drug; which may be due to drug overdose, predictable side effects and idiosyncratic reactions.<sup>1</sup> The overall incidence of CADR in developed countries as 1-3%, while the incidence in developing countries is thought to be higher between 2% and 5%.<sup>2</sup> Cutaneous drug reactions are responsible for

approximately 3% of all disabling injuries during hospitalization. Many of the commonly used drugs have reaction rates over 1%. Clinicians come across many instances of suspected CADR in their day to day practice. Therefore, not only the dermatologist, but the practicing physician should have a knowledge with these reactions to enable early diagnosis and prompt withdrawal of the causative drug and prevent mortality from severe reactions.<sup>3</sup> A cutaneous adverse drug reaction is termed severe if it is life threatening either in the form

of death or if it requires prolonged hospital stay or resulting in disability.<sup>4</sup> These reactions may vary from pruritus to life threatening skin conditions like toxic epidermal necrolysis. As CADRs could be seen across a wide spectrum of classes of drugs, clinical diagnosis may sometimes be difficult. The reasons for CADRs are multifactorial and include changes in drug metabolism, drug interactions, oxidative stress and various cytokines. The objective of our study is to ascertain the clinical spectrum of CADRs and the causative drugs and to find out any risk factors in a tertiary care centre.

## METHODS

The present study is a retrospective, open, observational study, carried out in the Department of Dermatology, Venereology and Leprosy at P.D.U. Government Medical College and Hospital, Rajkot, Gujarat during a period of 6 years from October 2011 to November 2017. All patients attending the Dermatology OPD with active and extensive lesions of cutaneous adverse drug reactions due to systemic drugs were included in the study. Thorough clinical history of all the patients was taken and recorded according to preformed proforma. Precise history of drug intake including allopathic, homeopathic, ayurvedic medicines along with its temporal correlation with initiation of the symptoms was elicited with an emphasis on whether it was prescribed or self administered. Careful history regarding relevant skin or systemic diseases, atopy, past and family history of drug eruption was noted. Final diagnosis was made after excluding other possible causes of similar clinical picture. Morphology of the eruption, duration of the rash, associated mucosal and systemic involvement and improvement on drug withdrawal was established. Rechallenge was attempted after recovery from drug reaction in mild reactions. In case of more than one drug suspected, the most likely offending drug was noted and the impression was confirmed by subsidence of the rash on withdrawing the drug. All routine investigations including complete blood count, urine routine and microscopic examination, renal function tests, liver function tests, serum protein and blood sugar, septic screening were done in all patients. HIV testing was done in cases of severe adverse drug reactions and in those with risk factors. CD4 count was recorded in all HIV reactive patients. The SCORTEN was calculated to assess the risk of mortality in all the patients.

Patients with severe reactions were hospitalized. Appropriate specific treatment was given to each patient and alternative drugs were prescribed after consultation from other departments. All patients were counseled and educated to avoid self-administration of the offending drugs. Each patient was given a list of drugs to be avoided in future. The patients were followed up regularly after treatment.

All the observations and proportions were inferred after analysing the data of all the cases and the results were calculated by information analysis done using microsoft excel.

## RESULTS

A total of 90 patients of Adverse Cutaneous Drug Reactions were studied. The male to female ratio was 1.2:1 with most common age group being 31-40 years (24.44%) (Table 1). Drug was prescribed by a medical practitioner in 86 cases (95.55%), while self administered in 4 cases (4.44%). History of some cutaneous drug reaction in the past was present in 17 patients (18.88%). Lesions were generalised in 76 cases (84.4%) and localised in 14 cases (15.5%). Maculopapular rash was the most common clinical types of drug reaction (16.66%) which was similar to the study by Sharma et al (34.6%) followed by drug reaction with eosinophilia and systemic symptoms (15.55%) and Steven Johnson syndrome (15.55%) (Table 2). Other types seen were fixed drug reaction, drug induced urticaria, drug induced lupus erythematosus, angioedema and acute generalized exanthematous pustulosis. Among the offending drugs for cutaneous drug reactions, NSAIDS were the most were the most common group (16.66%). Among the individual drugs, carbamazepine was the most common culprit drug (12.35%) overall (Table 3). The most common drugs causing morbilliform rash were carbamazepine, cotrimoxazole and antiretroviral drugs (14.28% cases each) (Table 4). Out of 90 patients, 21 (23.6%) were HIV reactive and morbilliform rash was the commonest pattern of drug reaction in them (28.56%) (Table 5). Oral mucosa was involved in 60(66.66%) of the cases, while ocular, anal and genital mucosa was involved in 55 (61.11%), 4 (4.44%) and 35 (38.88%) cases respectively (Table 6). 7 (7.77%) patients had 3% risk of mortality, 12 (13.33%) had 12% risk of mortality and 6 (6.66%) patients had 35% risk of mortality according to the SCORTEN (Table 7).

**Table 1: Age and sex wise distribution.**

Age (in years)	Male	Female	Total patients	% of patients
0-10	4	3	7	7.7
11-20	10	5	15	16.6
21-30	6	4	10	11.11
31-40	9	13	22	24.44
41-50	7	9	16	17.77
51-60	7	4	11	12.22
61-70	6	3	9	10
<b>Total patients</b>	49	41	90	100

**Table 2: Type of reaction wise distribution.**

S. no	Pattern of reaction	No.of case	% of cases
1	Maculo papular rash	15	16.66
2	DRESS syndrome	14	15.55
3	Steven johnson syndrome	14	15.55
4	Toxic epidermal necrolysis	13	14.44
5	Fixed drug reaction	12	13.33
6	Erythema multiforme	11	12.22
7	SJS-TEN overlap	6	6.66
8	Acute generalized exanthematous pustulosis	1	
9	Angioedema	1	1.11
10	Drug induced lupus erythematosus	1	1.11
11	Drug induced urticaria	1	1.11
12	Exfoliative dermatitis due to carbamazepine	1	1.11
	Total number of cases	90	100

**Table 3 :Commonest drugs causig cutaneous ADR.**

S. no	Offending drug	No of cases	% of cases
1	NSAIDS	15	16.66
2	Anti retroviral drugs	14	15.55
3	Carbamazepine	13	14.44
4	Other antileptic drugs(phenytoin, sodium valproate, phenobarbitone)	12	13.33
5	Fluconazole	6	6.66
6	Cotrimoxazole	6	6.66
7	Antitubercular drug	3	3.33
8	Griseofulvin	1	1.11

**Table 4: Most common drugs causing maculopapular rash.**

Name of drug	No of cases	% of cases
Carbamazepine	2	13.33
Cotrimoxazole	2	13.33
ZLN	2	13.33
Linezolid	1	6.66
Dapsone	1	6.66
Diclofenac	1	6.66
Antitubercular drugs	1	6.66
Nevirapine	1	6.66
Nimesulide	1	6.66
TLE	1	6.66
Not known	2	13.33
Total	15	100

**Table 5: Pattern of drug reactions in HIV patients.**

Pattern of drug reactions	No of cases	% of cases
Maculopapular rash	6	28.56
SJ syndrome	3	14.28
SJS-TEN	3	14.28
TEN	3	14.28
Erythema multiforme	3	14.28
DRESS syndrome	2	9.52
Angioedema	1	4.76
Total patients	21	100

**Table 6: Mucosal involvement.**

Mucosa	No of cases	% of cases
Oral	60	66.66
Ocular	55	61.11
Genital	35	38.88
Anal	4	4.44

**Table 7: Scorten in TEN patients.**

Scorten score	No of patients in this study (%)
0-1	7 (7.77)
2	12 (13.33)
3	6 (6.66)
4	-
≥5	-

**Table 8: Clinical patterns compared to other studies.**

	Pudukadan et al <sup>5</sup> (%)	Sharma et al <sup>8</sup> (%)	Present study (%)
Maculopapular rash	12.2	34.6	16.66
DRESS	-	-	15.55
Sj syndrome	18.8	4.8	15.55
TEN	-	6.6	14.44
Fixed drug reaction	31.1	30	13.33
Erythema multiforme	6.7	4.4	12.22
Urticaria	7.8	14	1.11

## DISCUSSION

Adverse cutaneous drug reactions differ in their patterns of morphology and distribution among various studies. In previous studies the most common morphologic patterns are exanthematous, urticarial, angioedema, fixed drug eruption and erythema multiforme.<sup>5</sup> In our study Maculopapular rash was the most common clinical types of drug reaction (16.66%) which was similar to the study by Sharma et al (34.6%) followed by Drug reaction with eosinophilia and systemic symptoms and Steven Johnson syndrome (15.55% each). This is in contrast with studies done by Pudukadan et al where most common pattern seen was fixed drug eruption in 31.1% cases (Table 8).<sup>5</sup> The incidence of erythema multiforme in our study was found to be 12.22% which is comparable to the studies done by Sharma et al (10%).<sup>3</sup> The incidence of cutaneous drug reactions was nearly equal in males and females with a slight preponderance of male sex (54.44%) in our study with male:female ratio being 1.2:1 which is again in contrast with 0.87:1 as observed by Pudukadan et al.<sup>5</sup> The mean age group of our patient was 31-40 years (24.44%) in contrast to the study by Pudukadan et al where maximum patients were in the group of 20-39 years.<sup>5</sup> Also, the mean age group in Marfatia et al study was 41-50 years and in the study by Manivannan et al was 36.20 years.<sup>6,7</sup> The youngest and oldest patients in our study were of 4 years and 70 years respectively however in both the studies the drug reactions are more common in

the middle age group. In majority of the cases the offending drug was prescribed (95.55%) by a medical practitioner. A past history was of some cutaneous drug reaction was found in 17 patients (18.88%). NSAID group of drugs were found to be the most common culprit (16.66%) in our study which is comparable to the study done by Marfatia et al. Carbamazepine was the most common individual culprit drug found in our study (14.44%) as opposed to cotrimoxazoles being the most common drug implicated by Pudukadan et al (22.2%) and Marfatia et al (29.5%) respectively as this drug is prescribed less often these days.<sup>5,6</sup> Morbilliform rash, in our study, was most commonly caused by carbamazepine, cotrimoxazole and antiretroviral drugs (14.28% each) in contrast to Marfatia et al and Sharma et al where fluoroquinolones and phenytoin were the commonest culprits respectively.<sup>6,8</sup> The common indications for drug intake included epilepsy, fever and URTI and HIV. One case of drug induced lupus erythematosus was reported. It was caused by Pyrazinamide. 38 (42.22%) patients had comorbidities of which 21 (22.22%) patients were suffering from HIV infection. There were 14 cases of SJ Syndrome, out of which 3 cases were HIV Reactive. All the cases recovered completely without any serious complications. Among the HIV reactive patients (22%), morbilliform rash was the most common clinical pattern (28.56%) followed by erythema multiforme and SJ Syndrome (14.28% cases each).

## CONCLUSION

Adverse drug reactions are distressing to both the patient and physician; when there are more effective and potent drugs being developed, it is inevitable in modern day practice. The pattern of cutaneous adverse drug reactions and the causative drugs is variable among all studies done by various authors due to non reporting of the cases to the institute and mainly the severe ones (those who needed hospitalization and observation) were taken into consideration. Knowledge of the pattern and the causative agents helps in prompt and early diagnosis of the condition, better management and reduced morbidity, mortality and consequences in these patients. Also proper counselling is required regarding further avoidance of the culprit and the related drugs so as to prevent further episodes of drug reactions. This study also takes into account the occurrence of pattern of drug reactions in HIV patients and its management. It is obvious that the cutaneous ADR patterns and the drugs causing various reactions are changing every year, which may be due to the emergence of newer molecules and changing trends in the use of drugs. Also cutaneous drug reactions should be reported to the manufacturer and the regulator agency especially if the skin eruption is rare, serious or unexpected. To conclude, every drug must be regarded as potentially hazardous. For each patient, the risk must be weighed against the expected therapeutic benefit.

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