

Clinical Profile of Adverse Cutaneous Drug Reactions

Dr. Nikita Sachdev¹, Dr. Kishor Singh², Dr. Shivanu Mathon³

¹(Department of Skin & V.D., National Institute of Medical Sciences and Research Centre, Jaipur, India)

²(Department of Skin & V.D., National Institute of Medical Sciences and Research Centre, Jaipur, India)

³(Department of Skin & V.D., National Institute of Medical Sciences and Research Centre, Jaipur, India)

Abstract:

Background: Adverse drug reactions have become more common in recent times. Among them cutaneous reactions have been steadily gaining importance and constitute a major proportion of all the adverse drug reactions. It is important to familiarize the clinician about the cutaneous adverse effects of various drugs which will in turn put a check on the mortality-morbidity related to cutaneous adverse drug reactions. (CADRs)

Aims & Objective: To evaluate clinical profile and clinical patterns of adverse cutaneous drug reactions (CADRs).

Materials & Methods: An observational, cross sectional study of eighteen-month duration conducted in the dermatology department at a tertiary care teaching hospital in north India in patients of all age groups, both gender, willing to participate with cutaneous adverse drug reactions. (CADRs)

Results: A total of 172 patients diagnosed with CADR, fulfilling the inclusion criteria were included in the study out of which 82 were males and 90 were females. Majority (23.55%) of the patients were in age group 31-40 and only 3.48% patients were in 71-80 age group. The most frequent CADR observed was maculopapular rash (48.83%). The other CADR included urticaria (12.79%), urticaria + angioedema (10.46%), EM (06.97%), FDE (5.81%), Erythroderma (5.23%), Acneiform eruptions (4.06%), Vasculitis (2.32%), SJS (1.79%), DRESS (1.16%) and TEN (0.58%) in that order. A total of 15 drugs were implicated in our cases of CADRs. Out of these, Amoxicillin group was the most common suspected drug with a total of 32 cases followed by Phenytoin in 28 cases, Cephalosporin in 24 cases, Diclofenac in 18 cases, Ibuprofen in 18 cases, Carbamazepine in 16 cases, Ciprofloxacin in 11 cases, Enalapril in 9 cases, Corticosteroid in 4 cases, Naproxen in 4 cases, Nimesulide in 3 cases, INH in 2 cases, Metronidazole in 1 case, Sodium Valproate in 1 case and Dapsone in 1 case. Route of administration of the suspected drug in majority of cases (77.90%) was oral followed by Intravenous (IV) (22.09%)

Conclusion: The most common class of drugs implicated to cause CADRs in our study were antimicrobials (39.53%) followed by anticonvulsant (26.16%), NSAIDs 43 (25%), ACE inhibitor (5.23%) and corticosteroid (2.32%)

Keywords: Cutaneous Adverse drug Reactions, Antimicrobials, Anticonvulsants, Maculopapular Rash, Urticaria.

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I. Introduction

A drug may be defined as a chemical substance, or combination of substances, administered for the investigation, prevention and treatment of a diseases or symptoms, real or imagined. WHO defined an adverse drug reaction as “a response to a drug that is noxious, unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function.^{1,2} In spite of a large database on CADRs, there continues to be a constant need for newer updates so as to develop a greater insight into these disorders.³

With an increase in the number of drugs, adverse drug reactions have become more common in recent times. Among them cutaneous reactions have been steadily gaining importance and constitute a major proportion of all the adverse drug reactions.⁴ Many epidemiological and clinical studies have highlighted the various aspects of cutaneous adverse drug reaction (CADRs). A large amount of data on cutaneous adverse drug reaction is being constantly updated.⁵

In spite of a large number of studies and case reports, the incidence of undesirable cutaneous adverse drug reactions (CADRs) is, at the best an approximation. In a large percentage of ambulatory patients, the CADRs are mild and transient, and therefore go unnoticed by the patient or the treating physicians. On the other hand, cutaneous symptoms of diseases that may appear to have a temporal relationship to drug therapy are often erroneously classified as CADRs.⁶

This study was undertaken as there is paucity of similar studies in the literature and also to familiarize the clinician about the cutaneous adverse effects of various drugs which will in turn put a check on the mortality-morbidity related to CADR⁷.

AIM AND OBJECTIVES

Aim: The aim of study was to evaluate clinical profile of CADR.

Objectives: To ascertain the various clinical patterns of CADR.

II. Materials And Methods

An observational, cross sectional study of eighteen month duration conducted in the dermatology department at a tertiary care teaching hospital in north India.

Selection criteria:

Patients of all age groups, both gender, willing to participate with cutaneous adverse drug reactions were included in the study.

Patients who had reactions where the drug implicated was not known and there was no temporal correlation between the drug intake and onset of rash, and dropout cases were excluded from the study.

III. Observation And Results

A total of 172 patients diagnosed with CADR, fulfilling the inclusion criteria were included in the study. The study population consisted of 82(47.67%) males and 90(52.33%) females.

In the present study, majority 40 (23.55%) of the patients were in age group 31-40 and only 6 (3.48%) patients were in 71-80 age group[Figure 1]. The youngest patient was 1 year infant, and the eldest patient was 80-year-old male.

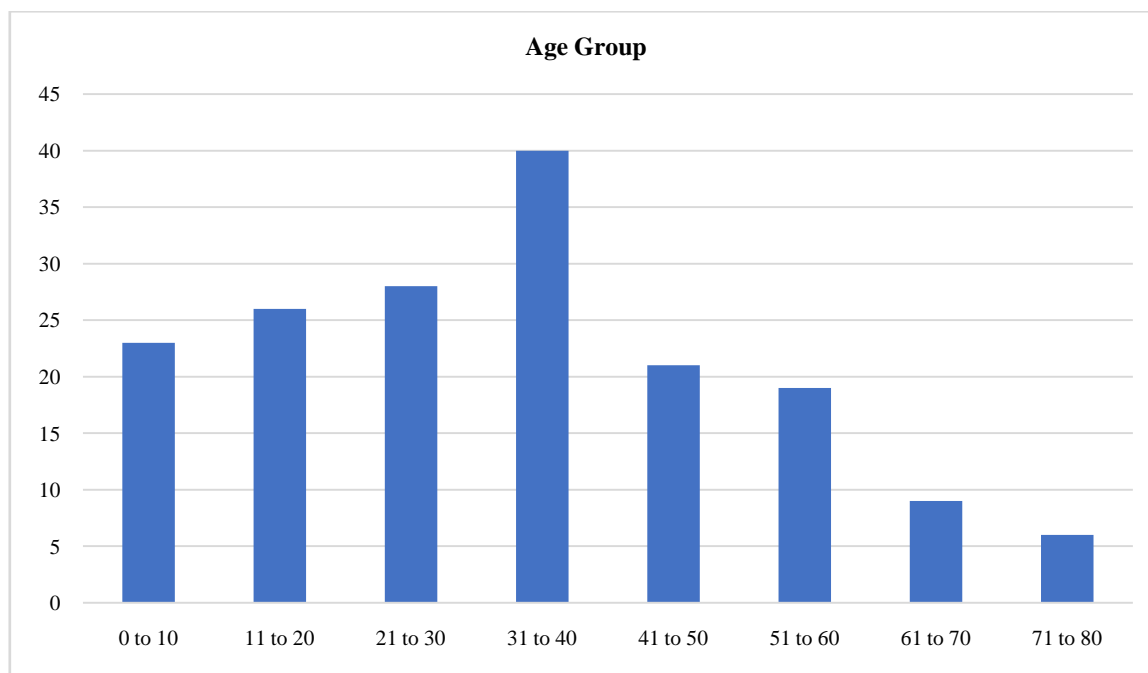


Figure 1: Frequency distribution according to age in patients with CADR

The most frequent CADR observed was maculopapular rash 84 (48.83%). The other CADR include urticaria 22 (12.79%), urticaria + angioedema 18 (10.46%), EM 12 (06.97%), FDE 10 (5.81%), Erythroderma 9 (5.23%), Acneiform eruptions 7 (4.06%), Vasculitis 4 (2.32%), SJS 3 (1.79%), DRESS 2 (1.16%) and TEN 1 (0.58%) in that order [Table 1 and Figure 2]

Sr. No.	Clinical types of drug eruption	Number	Frequency
1.	Maculopapular rash	84	48.83%
2.	Urticaria	22	12.79%
3.	Urticaria + Angioedema	18	10.46%
4.	EM	12	06.97
5.	FDE	10	05.81

6.	Erythroderma	9	05.23
7.	Acneiform Eruptions	7	04.06
8.	Vasculitis	4	02.32
9.	SJS	3	01.79
10.	DRESS	2	01.16
11.	TEN	1	00.58

Table 1: Frequency distribution according to types of cutaneous adverse drug reactions

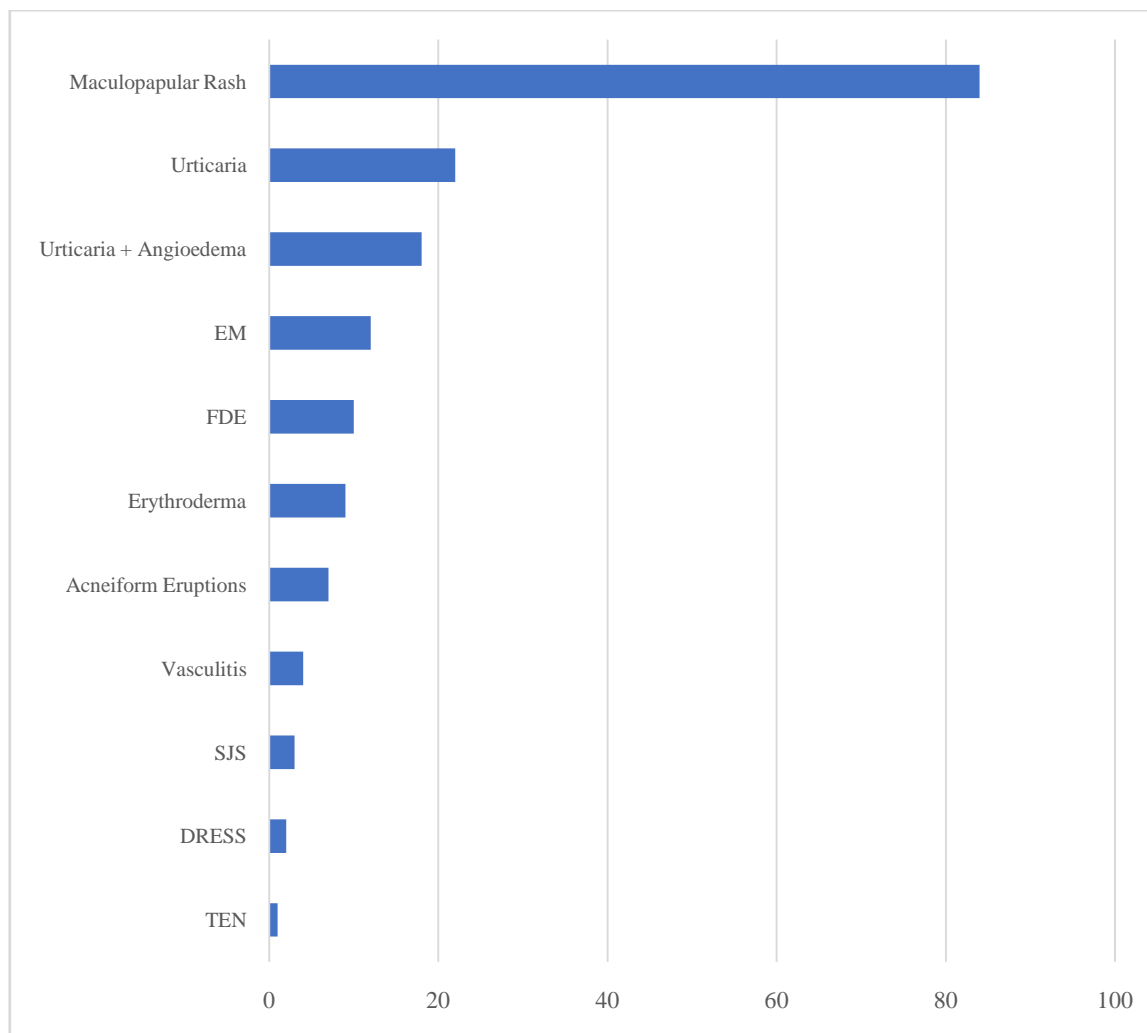


Figure 2: Frequency distribution according to types of cutaneous adverse drug reactions

A total of 15 drugs were implicated in our cases of CADR. Out of these Amoxicillin group was the most common suspected drug with a total of 32 cases followed by Phenytoin (28 cases), Cephalosporin (24 cases), Diclofenac(18 cases),Ibuprofen (18 cases) , Carbamazepine(16 cases), Ciprofloxacin(11 cases), Enalapril(9 cases), Corticosteroid(4 cases), Naproxen(4 cases), Nimesulide (3 cases), INH(2 cases), Metronidazole(1 case), Sodium Valproate(1 case) and Dapsone(1 case) [Table 2 and Figure 3].

Sr. No.	Drugs	Number	Frequency %
1.	Amoxicillin	32	18.60%
2.	Phenytoin	28	16.27%
3.	Cephalosporin	24	13.95%
4.	Diclofenac	18	10.46%
5.	Ibuprofen	18	10.46%
6.	Carbamazepine	16	9.30%
7.	Ciprofloxacin	11	6.39%
8.	Enalapril	9	5.23%
9.	Corticosteroid	4	2.32%
10.	Naproxen	4	2.32%
11.	Nimesulide	3	1.74%
12.	INH	2	1.162%

13.	Metronidazole	1	0.58%
14.	Sodium Valproate	1	0.58%
15.	Dapsone	1	0.58%

Table 2: Frequency of Drugs involved in CADR

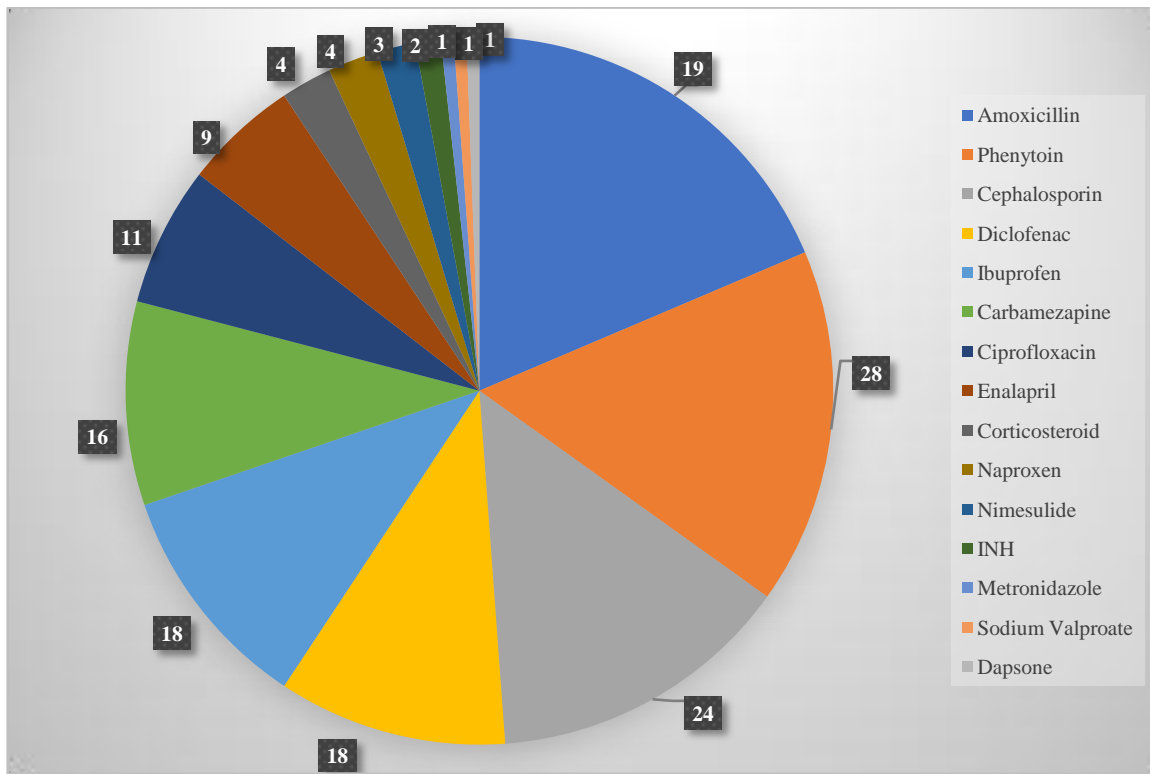


Figure 3: Frequency of Drugs involved in CADR

In our study, the majority of cases 134(77.90%) route of administration of the suspected drug was oral followed by Intravenous (IV) 38(22.09%)

Route of administration	Adult	Child	Total
Oral	109	25	134
IV	30	8	38
Total	139	33	172

Table 3: Frequency of route of drug administration among children and adults

IV. Discussion

Cutaneous Adverse drug reaction forms an important and common problem in both inpatient and outpatient setting. It is important for the clinician to keep them self updated on the latest trends in drug reaction with regards to newer drugs and newer manifestation of older drugs.

During the study period, 172 patients were diagnosed as CADR which constitute 1.1% of the total hospital attendance.

The male to female ratio of patients with CADR in our study was 0.9:1 almost similar to study by Padukadan et al with F:M ratio 0.87:1. The female patients appear to be slightly more conscious of any cutaneous eruption while on treatment whereas males tend to ignore minor cutaneous reactions.

In the present study the maximum number of cases were seen in the age group of 31-40 years (23.55%) followed in 21-30 years (16.27%) age group. These findings are at little variance with study by Sharma et al (2001). This may be due to polypharmacy along with altered drug metabolism in this age group and regional variation in health care system.

In our study, 33(19.19%) children were reported with CADR. It can be estimated that 2.5% of children treated with any drug, and up to 12% of children treated with an antimicrobial, may experience CADR as quoted in various other studies.^{8,9} This may be explained by the fact that children are exposed to a lesser number of drugs and the immune system is not yet well developed.

The commonest CADR in our study was Maculopapular rash 84(48.83%) followed by urticaria22(12.79%), urticaria+angioedema18(10.46%), erythema multiforme12(6.97%), fixed drug

reaction10(5.81%), erythroderma9(5.23%), Acneiform eruption7(4.06%), vasculitis4(2.32%), Steven's Johnson syndrome3(1.79%), DRESS2(1.79%), and TEN1(0.58%).

The most common class of drugs implicated to cause CADR in our study were antimicrobials 68(39.53%) followed by anticonvulsant 45(26.16%), NSAIDs 43(25%), ACE inhibitor 9(5.23%), corticosteroid 4(2.32%) and INH 2(1.162%). However various other studies also reported antimicrobials to be the most common cause of adverse drug reaction with followed by NSAIDs and anti-epileptics.^{10, 11}

Among the antimicrobials, amoxicillin was the most common offending drug whereas in NSAIDs, Ibuprofen was the most common drug.

In our study, urticarial CADR were mostly caused by NSAIDs, antibiotics, anticonvulsant, and ACE inhibitor. FDE's were caused by NSAIDs and anticonvulsant which is similar to other such studies.^{12, 13}

Most of the CADR encountered in our study were minor and only a small(4.16%) percentage were major life threatening reactions i.e. SJS, DRESS, TEN.

Majority of CADR were diagnosed clinically and there may be a possibility of heterogeneity in sample selection. In majority of the cases 134(77.90%) the route of administration of the suspected drug was oral followed by Intravenous(IV) 35(22.09%).

Prompt recognition of the offending drug enables the clinician for early withdrawal which leads to improved outcome of the cases.

Year after year newer and newer drugs are being added to our armamentarium. The spectrum of therapy for various diseases is also undergoing continuous change, so is adverse drug reaction including cutaneous adverse drug reactions.

Hence an up-to-date knowledge of ADR/CADR need no emphasis. Our study is an earnest effort to bring out aspects of CADR. Further studies are needed for continuous updating of our knowledge about CADR.

V. Conclusion

Clinician must always keep possibility of various ADR/CADR in the mind for prompt diagnosis, immediate discontinuation of offending drug and start appropriate treatment at the earliest. Doing so will go a long way in preventing morbidity, possible mortality, and litigations at times.

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