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Original Research

A Study Of Clinical Profile Of Adverse Cutaneous Drug Reactions At A Tertiary Care Centre

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ABSTRACT:
Introduction: A drug may be defined as a chemical substance, or combination of substances, administered for the investigation, prevention or treatment of diseases or symptoms, real or imagined. WHO defines an adverse drug reaction as "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function. **Aim :** To evaluate clinical profile of adverse cutaneous drug reactions. **Materials & Methods:** An observational, cross-sectional single centered study of eighteen-month duration at a tertiary care teaching hospital in north India. **Result:** A total of 172 patients diagnosed with CADR, fulfilling the inclusion criteria were included in the study. The most frequent drug eruption observed was maculopapular rash 84 (48.83%). The other drug eruptions included urticaria 22 (12.79%), urticaria + angioedema 18 (10.46%), Erythema multiforme 12 (6.97%), Fixed drug eruption 10 (5.81%), Erythroderma 9 (5.23%), Acneiform eruptions 7 (4.06%), Vasculitis 4 (2.32%), Steven's Johnson syndrome 3 (1.79%), DRESS 2 (1.16%) and Toxic epidermal necrolysis 1 (0.58%) in that order. **Conclusion:** Cutaneous adverse drug reaction profile in our study were analysed and compared with many other studies conducted earlier in various part of the country. Timely recognition of morphological patterns of cutaneous adverse drug reaction may be very helpful in identifying an offending drug in the setting of multiple drug therapy. Thus, limiting morbidity and mortality in patients.
Keywords: Adverse Cutaneous Drug Reactions, maculopapular rash, Urticaria.

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INTRODUCTION

A drug may be defined as a chemical substance, or combination of substances, administered for the investigation, prevention or treatment of diseases or symptoms, real or imagined. WHO defines an adverse drug reaction as "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological functions.1,2 Inspite of a large database on cutaneous adverse drug reactions, there continues 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 is on increase in recent times. Among them cutaneous reactions have been steadily gaining importance and constitute a major proportion of all the adverse drug reactions.4,5,6,7 A large amount of data on cutaneous adverse drug reactions is being constantly updated.

In spite of a large number of studies and case reports, the incidence of undesirable cutaneous adverse drug reactions (CADRs) is, at best an approximation. In a

large percentage of ambulatory patients, the CADRs are mild and transient, and therefore go unnoticed by the patient and 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 cutaneous adverse drug reactions.8,9,10 . Hence this study was undertaken in the Indian population with regards to causative drugs and appearance/ type of rash.

AIM

To evaluate clinical profile of adverse cutaneous drug reactions

MATERIALS & METHODS

An observational, cross-sectional single centered study of eighteen-month duration conducted in the department of dermatology with n=172 patients in a tertiary care teaching hospital of north India..

Selection Criteria of Patients:

Inclusion Criteria:

1. All age group
2. Both gender (male and female) and willing to participate.

Exclusion Criteria:

1. Reactions where the drug implicated were not known.
2. Cases where there is no temporal correlation between the drug intake and onset of rash and unwilling to participate

Procedure:

A detailed history and complete general physical examination, systemic examination and dermatological examination done with morphology and distribution of skin lesions, concomitant affection of mucosa, hair, nails, palms, soles, genital involvement was meticulously recorded and presence of any other associated diseases were noted.

For data analysis:

Data was compiled in excel sheet and statistically analyzed with the help of SPSS 22.0 found results in form of table, graph etc.

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 our study, there was a female preponderance. 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 years of age. The youngest patient was 1 year infant and the eldest patient was 80 year old. The study population consisted of 33(19.19%) children and 139(80.81%) adults. (Figure 1). The most frequent drug eruption observed in our study was maculopapular rash 84 (48.83%). The other drug eruptions included urticaria 22 (12.79%), urticaria + angioedema 18 (10.46%), Erythema multiforme 12 (06.97%), Fixed drug eruption 10 (5.81%), Erythroderma 9 (5.23%), Acneiform eruptions 7 (4.06%), Vasculitis 4 (2.32%), Steven's Johnson syndrome 3 (1.79%), DRESS 2 (1.16%) and Toxic epidermal necrolysis 1 (0.58%) in that order. (Figure 2 &3). Out of total 172 patients 141 (81.97%) cases had only cutaneous involvement and 30 (17.44%) cases had both skin and mucosal involvement and 1 (0.58%) case had only oral mucosal involvement.

In our study, recurrence was seen in 45 patients, maximum number of these recurrences were seen in cases of urticaria (11), urticaria with angioedema (9), FDE (8), maculopapular rash (8), EM (6) followed by vasculitis (3). A total of 15 drugs were implicated in our cases of CADRs. Out of these Antimicrobial was the most common suspected drug with a total of 68 cases followed by Anticonvulsants (45), NSAIDS (43), ACE Inhibitors (9) and corticosteroid (4) and sulpha drug (1). (Figure 4). In our study, in majority of the cases 134 (77.90%) route of administration of the suspected drug was oral followed by IV 38 (22.09%). (Table 1)

Table 1 – Table showing route of drug administration among children and adults

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

Figure 1- Table & pie diagram showing distribution of study population in children and adults

Figure 1

Category	Number	Frequency (%)
Children	**33**	**19.19**
Adult	**139**	**80.81**

Figure 2- Table & bar diagram showing types of cutaneous adverse drug reactions

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

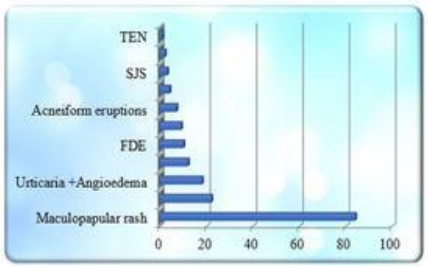
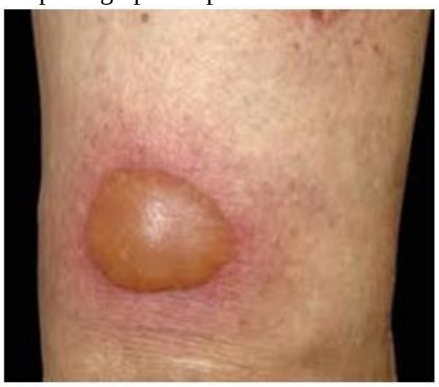
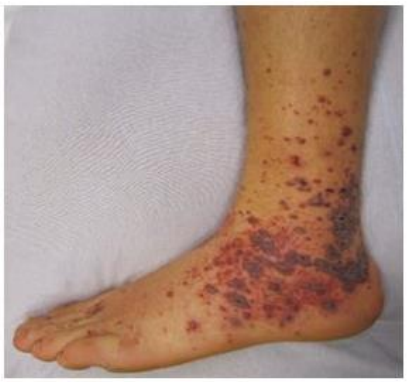


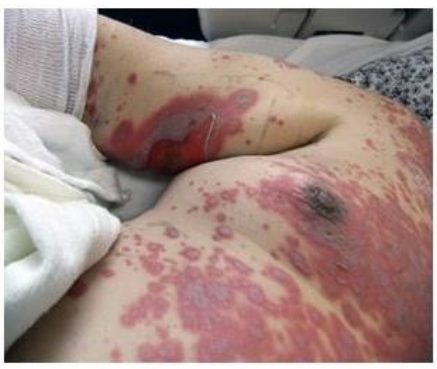
Figure 3- Clinical photographs of patients with various CADRs



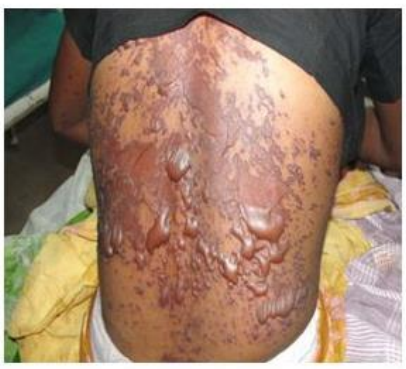
(a)Fixed drug eruption



(b)Vasculitis



(c) Steven Johnson syndrome

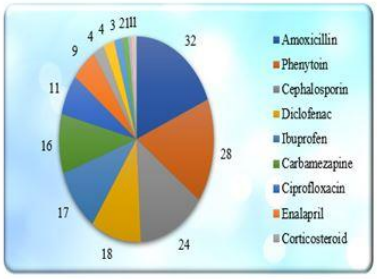


(d)Toxic epidermal necrolysis

Figure 4 – Table & pie diagram of drugs involved in CADRs

Figure 4

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.	Carbamezapine	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



DISCUSSION

Cutaneous Adverse drug reaction forms an important and common problem in both inpatient and outpatient setting. It is important to keep one-self updated with knowledge on latest trends in drug reaction with regards to the newer drugs, newer manifestation of older drugs as well as prompt diagnosis and management. At the same time, some of the older drug molecules are becoming obsolete and out of use. Newer insights have been developing in various factors affecting CADRs in Indian patients.

The male to female ratio of patients with CADR in our study was 0.9:1 almost similar to study by Pudukadan et al3 with F:M ratio of 0.87:1. However studies by Sharma et al4 reported M:F ratio (1.7:1.2) and Raksha et al5 reported M:F ratio (1.27:1) showed a male preponderance. This difference may be attributed to recent increased literacy as well as awareness among females. At the same time females are being more conscious of any cutaneous eruption while on treatment whereas males tend to ignore or not notice 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 and 33 (19.19%) were children. These findings are similar with study by Sharma et al4 who reported majority of cutaneous adverse drug reaction in age group 31-40 years (30.6%) followed by 1-30 years (26%). In a study by Raksha et al5 reported majority of CADR patients in the age group 41-50 years (22%) followed by 21-30 year (21%) and 31-40 years (20%) as opposed to our study. This may be due to polypharmacy in this age group along with altered drug metabolism and regional variation in health care seeking patients.

The commonest CADR in our study was Maculopapular rash [84,48.83%] followed by urticaria [22,12.79%], urticaria+angioedema [18,10.46%], erythema multiforme [12,6.97%], fixed drug reaction [10,5.81%], erythroderma [9,5.23%], Acneiform eruptions [7,4.06%], vasculitis [4,2.32%], Steven's Johnson syndrome [3,1.79%], DRESS [2,1.16%] and TEN [1,0.58%]. This was in concordance with various other studies which reported maculopapular drug reaction as most common CADR i.e. Nandha et al6 (39,42.85%) and MZ et al8.(38%). Out of total 172 patients 141 [81.97%] had only cutaneous involvement and 30[13.37%] cases had simultaneous skin as well as mucosal involvement.

In our study, recurrence was seen in 45 patients, majority of these recurrences were reported in patients of urticaria (11) followed by urticaria with angioedema (9), FDE (8), maculopapular rash (8), EM (6) and vasculitis (3). There is paucity of data reporting recurrence of cutaneous adverse drug reaction in similar studies. The most common class of

drugs implicated to cause CADRs 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%). Sharma et al4 and Nandha et al6 in their study reported antimicrobials to be the most common cause of adverse drug reaction with 40% and 48.3% cases respectively. Among the antimicrobials, amoxicillin was the most common offending drug in our study as opposed to previous studies by Pudukadan et al3 and Sharma et al4 in which sulphonamides were reported to be the most common drug. This may be because of decreasing use of sulphonamides in present day to day practice. We had 1.16% cases of DRESS in our study. The estimated incidence of DRESS ranges from 1 in1000 to 1 in 10000 drug exposure as quoted in a study by CY et al[11].

Most of the reactions encountered in our study were minor and a small percentage (SJS 3 (1.79%), DRESS 2 (1.16%), TEN 1 (0.58%) were major life threatening reactions. With proper care, mortality and morbidity was greatly reduced. In our study, in majority of the cases 134 (77.90%) the route of administration of the suspected drug was oral followed by IV 35 (22.09%). There is paucity of data regarding route of administration in various similar studies. . Gangaiah et al[12] reported only skin (58.7%) involvement in majority of their patients followed by simultaneous skin and mucosal involvement (17.4%) patients. Early recognition of various morphological patterns of cutaneous adverse drug reaction is very essential for each and every clinican so that culprit drug is promptly identified and stopped. At the same time, serious and life threatening cutaneous adverse drug reactions are one of the common reason for litigation. By warning the patient about potential adverse effect and not prescribing a drug or a cross reactive medication to which a patient have shown ADR/CADRs earlier go a long way in ensuring safe patient recovery.

CONCLUSION

Cutaneous adverse drug reaction profile in our study is to sensitize treating clinicans for timely recognition of morphological patterns of cutaneous lesions. It is very much helpful in identifying an offending drug especially in the setting of multiple drug therapy.

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