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Clinical spectrum of cutaneous adverse drug reactions (ADR) and to determine the causative drugs

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Abstract
Introduction: Cutaneous adverse drug reactions (ADR) can be caused by a wide variety of agents. The present study was conducted to assess clinical spectrum of cutaneous adverse drug reactions (ADR) and to determine the causative drugs.
Materials & Methods: The present study was conducted on 140 cases skin lesions of both genders. A subgroup analysis of causative drugs for common CADRs was performed.
Results: Authors found that most common drug reaction was maculopapular rash, urticaria, pruritis, angiodema, oral ulcer, acneiform eruption and lichenoid reaction and common drug involved was acelofenac.
Conclusion: 65 patients were elderly, 45 were adults, 30 were pediatrics. ADR was seen in 14 patients in elderly, 12 in adults and 6 in pediatrics. The difference was significant ($P< 0.05$). Common cutaneous adverse drug reactions was maculopapular rash in 4, urticaria in 5, pruritis in 7, angiodema in 5, oral cancer in 4, acneiform eruption in 2 and lichenoid reaction in 5 cases. Common drug causing ADR was ciprofloxacin in 6 cases, Amoxycillin in 5, fluoroquinolones in 4, acelofenac in 7, Cotrimoxazole in 3, paracetamol in 2, Phenytoin in 4 and Metronidazole in 1 case.

Keywords: Adverse drug reactions, Acelofenac, Urticaria

Introduction
Cutaneous adverse drug reactions (ADR) can be caused by a wide variety of agents. They are responsible for approximately 3% of all disabling injuries during hospitalisation and complications of drug therapy are the most common type of adverse event in hospitalised patients [1]. Many of the commonly used drugs have reaction rates above one percent. There is a wide spectrum of cutaneous ADR ranging from a transient maculopapular rash to fatal toxic epidermal necrolysis [2].
Skin is one of the major target organs for ADRs. An adverse cutaneous drug reaction is an undesirable change in the structure or function of the skin, its appendages, or mucous membranes and it encompass all adverse events related to drug eruption, regardless of the etiology [3]. The incidence of dermatological ADRs among indoor patients in developed countries ranges from 1–3%, whereas in developing countries such as India, it is 2–5% [4]. In many countries, ADRs rank among the top 10 leading causes of mortality and India is one of them. Drug eruptions are among the most common cutaneous disorders encountered by the dermatologist. There is a wide spectrum of cutaneous ADRs varying from transient maculopapular rash to toxic epidermal necrolysis [5]. The present study was conducted to assess clinical spectrum of cutaneous adverse drug reactions (ADR) and to determine the causative drugs.

Materials & Methods
The present study was conducted in the department of Dermatology. It comprised of 140 cases adverse drug reaction of both genders. The study protocol was approved by the Ethics Committee. All were informed regarding the study and written consent was obtained.
Data such as name, age, gender etc was recorded. A proforma was used to collect information such as investigations, adverse reactions, their clinical morphology and causative drugs. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table I: Distribution of patients

Total- 140		
Gender	**Male**	**Female**
Number	80	60

Table I shows that out of 140 patients, males were 80 and females were 60.

Table II: Incidence of cutaneous adverse drug reaction

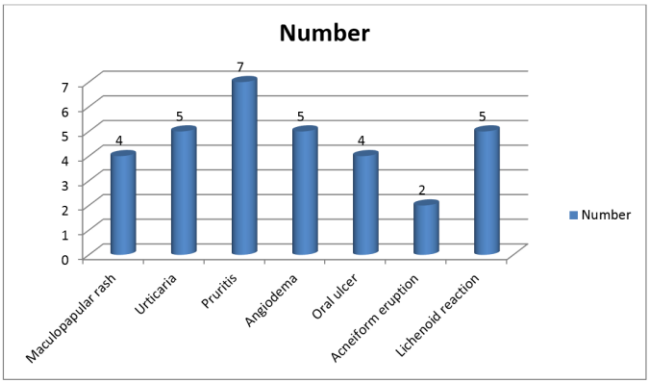
Variable	Number	ADR	P value
Elderly	65	14	0.01
Adult	45	12	
Pediatric	30	6	
Total	140	32	

Table II shows that 65 patients were elderly, 45 were adults, 30 were pediatrics. ADR was seen in 14 patients in elderly, 12 in adults and 6 in pediatrics. The difference was significant (P< 0.05).

Table III: Cutaneous adverse drug reactions

Variable	Number	P value
Maculopapular rash	4	0.01
Urticaria	5	
Pruritis	7	
Angiodema	5	
Oral ulcer	4	
Acneiform eruption	2	
Lichenoid reaction	5	

Table III, graph I shows that common cutaneous adverse drug reactions was maculopapular rash in 4, urticaria in 5, pruritis in 7, angiodema in 5, oral cancer in 4, acneiform eruption in 2 and lichenoid reaction in 5 cases.

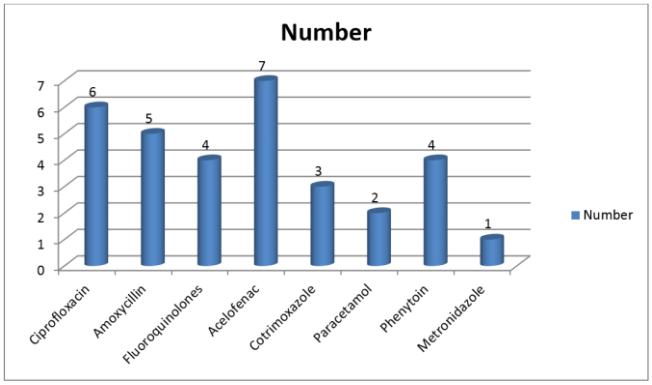


Graph I: Cutaneous adverse drug reactions

Table IV: Suspected drug causing ADR

Drug	Number	P value
Ciprofloxacin	6	0.05
Amoxycillin	5	
Fluoroquinolones	4	
Acelofenac	7	
Cotrimoxazole	3	
Paracetamol	2	
Phenytoin	4	
Metronidazole	1	

Table IV, graph II shows that common drug causing ADR was ciprofloxacin in 6 cases, Amoxycillin in 5, fluoroquinolones in 4, acelofenac in 7, Cotrimoxazole in 3, paracetamol in 2, Phenytoin in 4 and Metronidazole in 1 case.



Graph II: Suspected drug causing ADR

Discussion

According to the World Health Organization (WHO), an adverse drug reaction (ADR) is defined as "a response to a drug that is noxious and unintended and occurs at doses, used in man for prophylaxis, diagnosis, or therapy of a disease or for modification of physiological function." Skin is one of the major target organs for ADRs [6]. An adverse cutaneous drug reaction is an undesirable change in the structure or function of the skin, its appendages, or mucous membranes and it encompass all adverse events related to drug eruption, regardless of the etiology [7]. The present study was conducted to assess clinical spectrum of cutaneous adverse drug reactions (ADR) and to determine the causative drugs.

In present study, out of 140 patients, males were 80 and females were 60. We found that 65 patients were elderly, 45 were adults, 30 were pediatrics. 14 patients were seen in elderly, 12 in adults and 6 in pediatrics. Thakkar *et al*. [8] in their study a total of 171 CADRs were observed from 37,623 patients. The CADR incidence was 0.45%. The incidence did not significantly differ in different age groups and gender. Commonly observed CADRs were maculopapular rash (23.98%), urticaria (21.64%), and fixed drug eruptions (FDEs) (18.13%). Antimicrobials (35.18%) and nonsteroidal anti- inflammatory drugs (NSAIDs) were suspected in all common CADRs. Anti-infective and NSAIDs were most commonly suspected drugs in overall CADRs, maculopapular rash, urticaria, FDEs, and erythema multiforme. The exact nature of drugs remained inaccessible in one- fourth cases due to use of the over‐the‐counter self‐medications. The incidence of preventable and serious and fatal CADRs was 0.08% respectively.

Modi *et al*. [9] in their study found that out of 2171 ADRs reported during study period, 538 were cutaneous ADRs (24.78%). The most common clinical presentation was maculopapular rash (58.92%) followed by itching (10.59%), and Stevens–Johnson syndrome (4.83%). The time relationship of cutaneous ADRs to drug therapy revealed that they can develop within 1 week to 1 year of treatment. Most common causal drug groups were antimicrobials (46%), non-steroidal anti-inflammatory drugs (NSAIDs) (18%), and antiepileptics (10%). Polypharmacy was observed in 7% of the cases. Most of the cutaneous ADRs were non-serious (91%), however, 10 were

life-threatening and 1 was resulted in death due to the Stevens–Johnson syndrome. Causality category for majority of cutaneous ADRs was possible.

Anjaneyan *et al*. [10] study showed that antimicrobials, NSAIDs, and antiepileptic drugs were most prominent group of drugs responsible for cutaneous ADRs. Antimicrobial and NSAIDs are commonly prescribed by the physicians and general practitioners and sometimes irrationally used. Antimicrobials like antiretroviral and antitubercular drugs were more involved in developing cutaneous ADRs in the present study which was different finding from other studies. The integration of National Pharmacovigilance Program in Public Health Programs (Revised National Tuberculosis and Control Program and National AIDS Control Organization) has increased reporting of ADRs due to antitubercular and antiretroviral drugs.

Conclusion

Authors found that most common drug reaction was maculopapular rash, urticaria, pruritis, angiodema, oral ulcer, acneiform eruption and lichenoid reaction and common drug involved was acelofenac.

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