

## Original research article

# Study of drug induced-skin reactions in the patients attending outpatient department of dermatology

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## Abstract

**Introduction:** Drugs prescribed for medical illness can produce adverse drug reaction which are manifested differently according to the system involved.. Drug induced skin reactions ranges from macular rash to severe life threatening reaction. Non-steroidal anti-inflammatory drugs, antibiotics and antiepileptics are most common drug groups causing such reactions. AIM; This study was conducted to study the profile of different clinical manifestations of drug induced skin reactions in the patients attending outpatient department of dermatology in a tertiary care hospital.

**Methodology:** A descriptive cross sectional study was conducted from September 2011 to February 2013 in Dermatology Out-patient Department of Government Kilpauk Medical College, Chennai among 100 patients with drug induced skin reactions. Institutional ethics committee approval was obtained. All patients with drug induced skin reactions who attend the OPD of dermatology were included. Patients with other skin conditions and patients not willing to consent for participation in the study were excluded. . The clinical diagnosis of drug induced skin reaction was confirmed by the dermatologist.

**Results:** Majority (33%) of drug induced skin reaction was common in the age group years  $\leq 30$  years Drug induced skin reaction was found more in males compared to females. More number of cases was seen after 24 hours. Most common drug induced skin reactions was Drug Rash (44%). Nonsteroidal anti-inflammatory drugs was the most common suspected drug to cause adverse drug reaction (24%) .

**Conclusion:** Constant vigilance in detecting Adverse drug reaction is needed so that drug therapy is safe and effective.

**Key Words:** Adverse drug reaction, Drug rash, Nonsteroidal anti-inflammatory drugs.

## Introduction

The art of medicine is defined as a fine art of practice combining medical knowledge, intuition, and judgment in the care of patients.<sup>1</sup> The major tool of medicine is Drug prescribed. A Drug is an active chemical molecule used for diagnosis, prevention, and treatment of a disease.<sup>2</sup> These Drugs which are prescribed for medical illness can also produce adverse effects which are manifested differently according to the system involved. An Adverse drug Reaction is defined as ‘Any noxious change which is suspected to be due to a drug, occurs at doses normally used in humans, for prophylaxis, diagnosis and therapy of disease or for modification of physiological

function (WHO definition).<sup>3</sup> It excludes therapeutic failure, overdose, drug abuse, non compliance and medication errors.

Adverse drug reactions (ADR) cause deaths in 0.1% of medical and 0.01 % of surgical patients. Although only few patients are affected ADRs adversely affect the quality of life. The morbidity and mortality associated with adverse effects of drug often present as diagnostic problems because they involve every organ and system of the body. They are mistaken for signs of underlying disease, resulting in unnecessary investigations and delay in treatment. Treatment of ADRs increases the costs of patient care. Cutaneous drug eruptions are the most common type of adverse reaction to drug therapy, with an incidence rate of 2–6% .<sup>4</sup> Any medicine can induce skin reaction. Non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics and antiepileptics, have drug eruption rates approaching 1–5%.<sup>5</sup> The clinical presentation of drug related cutaneous eruption ranges from mild rash to severe rash besides causing life-threatening reactions. Serious reactions include angio-oedema, erythroderma, Stevens–Johnson syndrome and toxic epidermal necrolysis. Sometimes drug eruptions occur as part of a multiorgan involvement like drug-induced systemic lupus erythematosus.

Cutaneous drug reaction is suspected in any patient who is currently taking any medicine or recently been exposed to any medicine including the prescribed and over-the-counter medicines, herbal or homoeopathic preparations, vaccines or contrast media. In some patient's non-drug components of a medicine, i.e. the pharmaceutical excipients may also cause hypersensitivity reactions like cutaneous drug eruptions. 10-20 % of patients in hospital suffer from an adverse drug reaction. In the hospital 0.24-2.9 % deaths are due to adverse drug reaction.<sup>6</sup> 2-6% of hospital admissions are due to adverse drug reaction.<sup>7-9</sup> In England a study was conducted which showed that more than 40 % of patients undergoing drug therapy are upset by their treatment<sup>10</sup> due to drug reaction. 75% to 95 % of cutaneous drug eruption are Maculopapular rash/Drug Rash followed by urticaria.<sup>11</sup> 20% of emergency room visits for adverse event are due to antibiotics and Nonsteroidal anti-inflammatory drugs which causes reaction of about 1 in 2000.<sup>15</sup> The reaction rate for digoxin, lidocaine, prednisolone, codeine are less than 1 in 1000.

Hence this study was conducted to study the profile of different clinical manifestations of drug induced skin reactions in the patients attending outpatient department of Dermatology in a tertiary care hospital.

#### **Ethical consideration**

The study was approved by the Institutional Ethics Committee.

Confidentiality and anonymity of the patients' information were maintained during and after the study.

Treatment and care of the patient was not interfered during the study process.

#### **Methodology**

This is a descriptive cross sectional study conducted from September 2011 to February 2013 in Dermatology Out-patient Department (OPD) of Government Kilpauk Medical College, Chennai-10 among 100 patients with drug induced skin reactions. All patients with drug induced skin reactions who attend the OPD of dermatology were included in the study. Patients with other skin conditions and patients not willing to consent for participation in the study were excluded from the study. The patients were registered after obtaining informed consent. Patients with other skin reactions were excluded. All the details regarding patient's basic data, present illness, past medical history, co-morbidities, concomitant medications, and family history were collected and recorded in the proforma. Details of the drugs suspected to be causing ADR and the details of cutaneous lesions were recorded in the proforma. A detailed clinical history and physical examination was done. The prescription

details available with the patient were also collected. The clinical diagnosis of drug induced skin reaction was confirmed by the dermatologist.

The data was recorded in the Suspected Adverse Drug Reaction Reporting Form obtained from Central Standard Control Organisation.<sup>12</sup> The patient's initials but not the names were recorded to maintain the privacy and confidentiality. Basic data like age, gender, height, weight were recorded. Details of cutaneous reaction like date of start and recovery, type of cutaneous ADR were recorded. Details of suspected drug causing ADR, and details of concomitant medications were recorded. The relevant medical history and details of applicable test in relation to cutaneous reaction were recorded.

**Statistical Analysis**

Data collected were checked for completeness and consistency. Data was entered and analysed using SPSS software Version 22. Descriptive statistics like percentages were used.

**Results**

Table 1: Age wise distribution

Age in years	Frequency	Percent
<= 30	33	33.0
31-40	25	25.0
41-50	23	23.0
51-60	13	13.0
> 60	6	6.0
Total	100	100.0

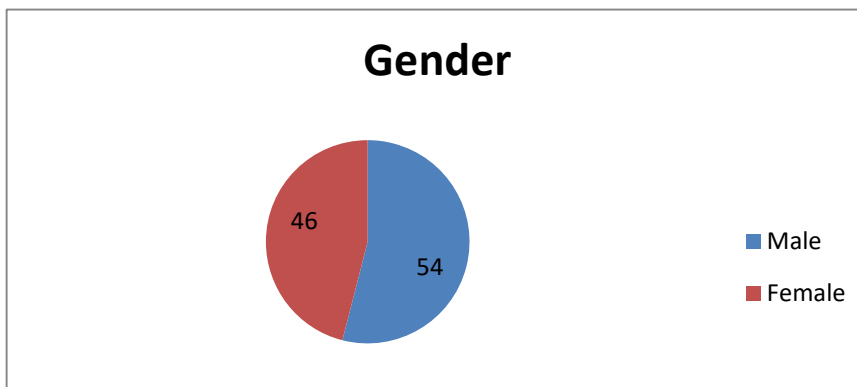


Fig 1 : Gender distribution of patients with ADRs

Table 2: Time interval between drug intake and onset of drug reaction

Time of onset	Number of cases
1 <sup>st</sup> day	13
2 <sup>nd</sup> day	23
3 <sup>rd</sup> day	18
4 <sup>th</sup> day	7
5 <sup>th</sup> day	8
6-14 <sup>th</sup> day	16
15 <sup>th</sup> -21 <sup>st</sup> day	5
22 <sup>nd</sup> -28 <sup>th</sup> day	2
28 <sup>th</sup> -35 <sup>th</sup> day	3
36 <sup>th</sup> -42 <sup>nd</sup> day	3
43 <sup>rd</sup> -49 <sup>th</sup> day	1
50 <sup>th</sup> -56 <sup>th</sup> day	1

Table 3: Frequency of different types of Drug induced skin reactions

Drug reaction	Frequency	Percent
Drug Rash	44	44.0
Erythema multiforme	14	14.0
Toxic epidermal necrolysis	4	4.0
Steven-Johnson syndrome	2	2.0
Fixed drug eruption	18	18.0
Urticaria	6	6.0
Urticarial vasculitis	7	7.0
Drug induced purpura	4	4.0
Drug induced Photo dermatitis	1	1.0
Total	100	100.0

Table 4: Frequency of various groups of drugs suspected to be the causative agents

Suspected drugs	Frequency	Percent
Antiepileptics	6	6.0
NSAIDs	24	24.0
Muscle relaxant	1	1.0
Antibacterial agents	32	32.0
Antileprotic drugs	3	3.0
Antiretroviral drugs	15	15.0
Antimalarial drugs	2	2.0
Antifungal	1	1.0
OHAs	2	2.0
Antihypertensive	1	1.0
Antiulcer agents	1	1.0
Antimetabolite	2	2.0
Vaccine	1	1.0
Unknown	4	4.0
Fixed drug combination	4	4.0
Hypolipaedemic drugs	1	1.0
Total	100	100.0

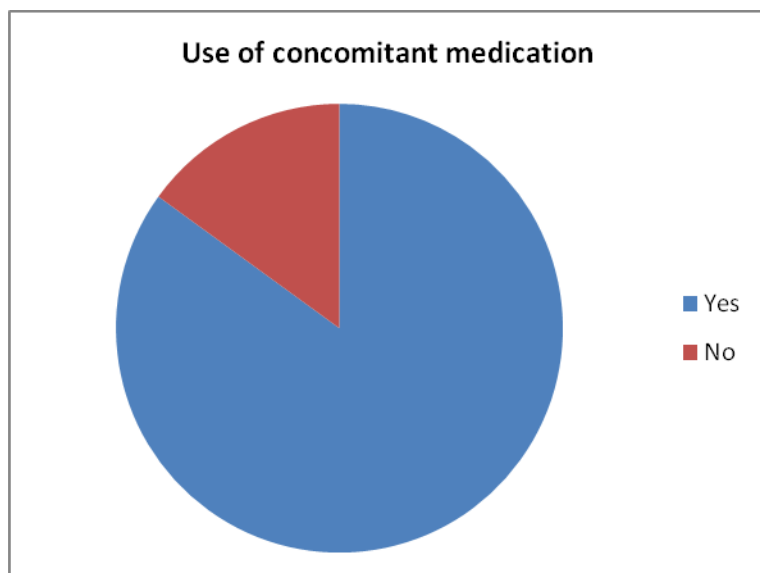


Fig 2: Pattern of use of Concomitant Medications

Table 5: Distribution of Seriousness of reaction

Seriousness of reaction	Frequency	Percent
1)Required Intervention to prevent permanent damage	87	87.0
2)Life threatening	9	9.0
3)Hospitalization	4	4.0
Total	100	100.0

Table 6: Distribution of outcome

Outcome	Frequency	Percent
Recovered	37	37.0
Recovering	62	62.0
Died	1	1.0
Total	100	100.0

Table 1 shows that Majority (33%) of drug induced skin reaction was common in the age group years  $\leq 30$  years and only 6% of ADR was seen above 60 years. Drug induced skin reaction was found more in males compared to females (Fig 1). Table 2 shows that on the day of drug intake 13 cases were affected by drug induced skin reaction. More number of cases was seen after 24 hours. Table 3 shows that most common drug induced skin reactions was Drug Rash (44%). NSAIDs was the most common suspected drug to cause adverse drug reaction (24%) (Table 4). Concomitant medications were used in 85% of Cases (Fig 2). Table 5 show that 87 % of cases required intervention to prevent permanent damage, and 9% of cases were life threatening required intensive monitoring. Regarding outcome One case died, 37 cases recovered and 62 cases were in recovery phase regarding outcome as shown in Table 6.

**Discussion**

In our study more reactions were seen in the age group  $\leq 30$  years. Sushma et al in their study found that drug induced skin reactions were mostly seen in third and fourth decades of life.<sup>13</sup> Hence more caution should be taken while prescribing medicines to this age group. Drug induced skin reaction was found more in males compared to females. Mahmood Farshchian et al<sup>14</sup> studied 308 patients with adverse cutaneous drug reaction from 2007–2009. They found that females (63%) were more commonly affected than males (37%)

The frequency of cases decreased as the time progresses but still the reaction has occurred. Even after 4 weeks interval the drug reactions occurred and was caused by antiretroviral drugs. Hence physician should be alert atleast upto one week. Noel, et al found that drug rash was the common the most common type of

cutaneous drug reaction.<sup>15</sup> Study performed by Souissi et al in 2007, found that the most common cutaneous clinical manifestation was maculopapular eruption followed by fixed drug eruptions, and antibiotics and NSAIDs were the most commonly causing agents.<sup>16</sup> In one study, Acute urticaria was the most common clinical presentation (59.2%) followed by fixed drug eruptions (18.5%), and maculopapular eruptions (14.9%). Results of our study were comparably similar to above mentioned studies.

Study of 464 case series reported by Kauppinen K found that 4% patients had Steven Johnson Syndrome.<sup>17</sup> In our study 2% of patients had Steven Johnson Syndrome. Ghosh, et al in Manipal found that Antimicrobials were the most common group causing cutaneous drug reaction.<sup>18</sup> In our study antibacterial agents have caused more drug induced skin reactions. Beta-lactam antibiotics was found to be the most frequent cause of adverse cutaneous drug reactions (42.7%), followed by non-steroidal anti-inflammatory drugs (16.5%). The study was done in a limited group of population. The concentration of drug in blood or other samples was not detected which may be helpful in preventing the lethal dose concentration. Rechallenge for drug reaction was not performed in the study due to ethical considerations. Hence the study gives a representative view about the drugs and ADRs among patients attending dermatology O.P in a tertiary care hospital.

### **Conclusion**

India is the fourth largest manufacturer of pharmaceutical products in the world and emerging as clinical trial hub. Hence constant vigilance in detecting ADRs is needed so that drug therapy is safe and effective. ADRs can also be reduced by using less medication so that drug interactions are avoided. Hippocrates admonition “at least do no harm” should be followed by all Health care professionals.

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