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# Severity, Preventability and Predisposing Factors Assessment of Adverse Cutaneous Drug Reaction: A Prospective Hospital Based Observational Study.

KEYWORDS: Severity, Preventability, Predisposing factors, Adverse cutaneous drug reaction.

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**ABSTRACT** *Adverse cutaneous drug reactions (ACDR) are the commonly reported type of ADR. 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.*

*Aims: Our objective was to assess severity, preventability and to identify any potential risk factor of reported ACDRs using suitable scales in the tertiary health care center.*

*Methods: fifty five patients with adverse cutaneous drug reactions were recruited for this study during 2013-2014.*

*Results: Assessing the severity of ACDRs is an essential component in Pharmacovigilance studies as an ACDR may require intervention. 87.27% patients had mild to moderate and 12.72% patients had severe ACDRs, 23.63% were considered definitely preventable & 52.72% patients had one or the other predisposing factors. polypharmacy was the most common predisposing factor observed in our study.*

*Conclusion: implementing the ADRs reporting and monitoring system, one can promote drug safety and better patient care, among health care professionals.*

## INTRODUCTION

There have been many drugs that were very successful and benefited thousands of patients, but were later found to have serious side-effects, resulting in their withdrawal.[1] The lack of awareness in society about the magnitude of drug-related problems is a mystery. One reason is probably that drug-related injuries are not always obvious, immediate and visible. They often manifest themselves gradually and with symptoms similar to those caused by common diseases.[2] The main responsibility of any drug regulatory authority is to ensure the quality, efficacy, and safety of all marketed products. The first two criteria can be established through data obtained from preclinical and clinical trials. It is a well-established fact that pre-marketing clinical trials do not have the statistical power to detect rare Adverse Drug Reactions (ADR) nor do they have significant follow-up to identify delayed ADRs or effects from long-term exposure. In view of this, Pharmacovigilance plays a prominent role in establishing the safety profile of marketed drugs.[3]Adverse cutaneous drug reactions (ACDR) are the commonly reported type of ADR.[4] 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.[5] The need for this study is for early diagnosis, to reduce the morbidity and mortality due to ACDR and to ensure safety of the patients.

## MATERIAL AND METHODS

The study was a prospective hospital based observational study. After getting approval from the institutional ethical committee, the study was jointly conducted in the Department of Pharmacology and Department of dermatology, NSCB medical college, Jabalpur over a period of one year (October 2013 to September 2014). The patients attending dermatology OPD with suspected ACDRs and the in- patients referred from other department with suspected ACDRs were enrolled. The participants had given the informed written consent before they were enrolled in the study. The diagnosis of the ACDRs was based on detail drug history and a thorough clinical examination done by consultant dermatologist, and pattern was recorded in form of maculopapular rash, urticaria, angioedema, fixed drug reaction, purpura, photosensitivity etc. The patient who consume medicines other than allopathic medications(like Ayurvedic/Homeopathic etc) & who are not able to recall the name of suspected medicine consumed(improper drug history) were excluded from the study. Detailed history of the patient including present illness, past or concurrent systemic illness & drug history were taken. Drugs used during the 3 weeks preceding the adverse reaction, route of administration, dosage, concomitant medical products if any including self-medication and herbal remedies, duration of treatment, improvement after discontinuation of drug, purpose of taking the drug, whether prescribed or over-the-counter drug were noted. Past history of drug allergy, family history of drug reactions and history of any skin disease was recorded.

To establish the etiologic agents for ACDRs, attention was paid to the drug history, temporal correlation with the drug, duration of the rash, pattern of lesion, improvement of lesion on withdrawal of drug & recurrence of lesion on rechallenge if possible. Rechallenge was not undertaken in any of our cases because of the possible associated risks. Finally data was recorded in CDSCO form.[6] and was compiled and analysed.

Severity of the ADRs was assessed by modified Hartwig and Siegel scale[7] which gives an overview of the severity of ADR whether it is mild, moderate, or severe in nature.

Preventability of the ADRs was assessed by modified Schumock and Thornton scale[8] This scale of preventability clas-

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sifies the ADRs as definitely preventable, probably preventable, and not preventable.

Each case of adverse cutaneous drug reaction was further assessed for presence of any predisposing factors which , include polypharmacy, increased potential for drug-drug interactions, age associated changes in pharmacokinetics and pharmacodynamics, altered homeostasis, multiple pathology and use of drugs with a narrow therapeutic margin.[9-11] Pre-existing diseases like impaired hepatic and renal function increase the risk of development of drug rashes.[12]

## RESULTS AND DISCUSSION

A total of 58 cases of adverse drug reactions were identified. Out of these 3 cases had to be excluded from the final because they failed to state the names of the offending drugs or the data was insufficient to make reliable analysis. The remaining 55 cases of ACDRs were analyzed further.

ACDRs were found relatively common in males than in females (ratio 1.75:1) Our study results are similar to the other Indian studies where male preponderance was observed.[13,14] Majority of the patients with ACDRs belonged to the age group of 21-30 years followed by 41-50 & > 50 yrs. The ACDRs were more common in adult patients (80%) as compare to the children(20%).The most common pattern observed was maculopapular rash (41.81%) followed by fixed drug eruption (20%), Erythema multiforme and SJS/TEN (10.90%), Other types of ACDRs that were seen in our study included 3.63% each of Exfoliative dermatitis, urticaria, Vasculitis and photosensitivity and 1.81% Serum sickness. Analysis of the data shows that NSAIDs were the most common drugs followed by antimicrobial agents for the same and two risk factors; multiple drug intake and history of allergy have been found to be significantly associated with the severity level of the reaction. On causality assessment, due to ethical issue rechallenge was not attempted hence maximum number of ACDRs were labeled as probable cases(72.72%).

Assessment of severity was done using Hartwig and Siegel scale.[7] Forty eight patients (87.27%) had mild to moderate ACDRs as they didn't require any specific treatment. They were simply managed by withdrawal of the suspected drug and supportive treatment. Seven patients (12.72%) had severe ACDRs and required immediate cessation of the suspected drug, hospitalization and intensive medical care (table1).

**Table 1: Assessment of severity using Hartwig and Siegel scale**

| Severity of reaction | No. of cases | Percentage |
|---|---|---|
| Mild-moderate | 48 | 87.27% |
| Severe | 7 | 12.72% |
| Total | 55 | 100 |

The results are complying with earlier studied. During our study 6 cases of SJS/TEN due to NSAIDs (66.66%), sulphonamide and penicillins(33.33%) & and one case of vasculitis due to ibuprofen were considered severe as they required immediate hospitalization and intensive medical care.(Table 1) Assessing the severity of ACDRs is an essential component in Pharmaco vigilance studies as an ACDR may require intervention including the stoppage of the suspected drug(s) and even hospitalization in severe cases.

**Table 2: Assessment of preventability by Schumock & Thornton criteria**

| Preventability | No. of cases | Percentage |
|---|---|---|
| Definitely preventable | 13 | 23.63% |
| Probably preventable | 02 | 3.63% |
| Not preventable | 40 | 72.72% |
| Total | 55 | 100 |

Preventability of the ACDRs was evaluated using the criteria of Schumock and Thomton, as modified by Leu et al. In our study 13 reactions (23.63%) were considered definitely preventable; 11 patients had history of similar reactions in the past; 2 had allergy. Two reactions (3.63%) were considered probably preventable as they involved poor patient compliance, potential drug interaction. The remaining 40(72.72%) were regarded as not preventable. Those definitely preventable cases have a previous history of similar reaction following same drug intake; which shows the lack of awareness. This would have been prevented by educating the patient.

**Table 3: Presence of predisposing factors**

| Predisposing factor | No. of cases | Percentage |
|---|---|---|
| Past history of ACDRs | 11 | 20% |
| Past history of allergy | 02 | 3.63% |
| Concomitant H/O systemic disease | 7 | 12.72% |
| Multiple drug therapy(≥ 3 drugs) | 9 | 16.36% |

Regarding predisposing factors, 52.72% had patients had one or the other predisposing factors (Table 3). Similarly, a study carried out in Manipal had 37% of predisposing factors.[15] It is accepted that patients taking more medications suffer more ADRs.[16-19] With this fact, polypharmacy was the most common predisposing factor observed in our study. One possible explanation for the polypharmacy was that many diseases require more than three drugs for treating the patient and this also shows the trend of prescribing number of drugs at a time where it actually not necessary to the patient.

Other predisposing factors observed in our study are past history of ACDRs, past history of allergy and past history of systemic illness or concurrent systemic disease like diabetes, hypertension, IHD, COPD, liver or kidney disease.

**Limitations:** Some minor drug rashes encountered by other departments could have been dealt with by treating doctors themselves and might not have been referred & Long term follows up and monitoring of the patients could not be done.

## CONCLUSION

To sum up, the occurrence of ACDRs in the present study was similar in many ways to other studies conducted in India. A wide clinical spectrum of ACDRs ranging from mild maculopapular rash to serious SJS/TEN was observed in age group of 21-30 years Slight male preponderance

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. Most of the reaction were mild to moderate in nature and could be managed by supportive treatment and withdrawal of culprit drug. Only 12.72% reaction was of severe grade that required hospitalization. Approximately 23.63% of ACDRs reported in this study were preventable.

***Certain recommendations to prevent such reactions:***

- Avoid polypharmacy cultivate habit of rational drug use in undergraduate and postgraduate students.
- Take a careful drug history beforehand exclude drug allergies and document all drugs already in use (including over the counter products).
- Individual drug therapy in situations like extremes of age, pregnancy, hepatic and renal insufficiency, immuno-compromised subjects etc.
- Instruct patient carefully on nature of drug and proper mode of use.
- Health professional should be periodically educated about ADRs and technical aspect of drug monitoring process through CME programme etc.

By implementing the ADRs reporting and monitoring system, one can promote drug safety and better patient care, among health care professionals.

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