

CLINICAL PROFILE OF ADVERSE CUTANEOUS DRUG REACTIONS AMONG PATIENTS VISITING DERMATOLOGY DEPARTMENT IN A TERTIARY CENTRE IN NORTH KERALA

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ABSTRACT

Background: Adverse Cutaneous Drug Reactions (ACDR) is a major issue with drug therapy. The main intention of our study was to know more about the cutaneous adverse effects of drug that are commonly prescribed. **Method:** A cross sectional, observational study was carried out over a period of six months at Department of Dermatology, in Pariyaram medical college hospital, Kannur. The suspected ADRs were collected in patient profile form and evaluated by using severity by Hartwig and Siegel scale. **Result:** Total 55 patients were enrolled with 55 suspected ACDRs. During the study, 34 (61.82%) were males and 21 (38.18%) were females. Maximum number of cases were seen in the age group 19 - 64 years (65.45%) followed by the age group 1-

12 years (16.36%), Maximum no. of cases occurred antibiotics (36.36%), NSAIDs (20%), anticonvulsant (14.54%), anticancer drugs (12.72%), antifungals, antiemetics (5.45%), PPIs, corticosteroids, Antiplatelets (1.81%). Maculopapular rash was the most common ACDR (n = 14, 25.45%), followed by fixed drug eruption (FDE) and Stevens- johnson syndrome (SJS) (n = 9, 16.36%), urticaria, acne, angioedema, Erythema multiforme were (n=3, 5.45%), hand

foot syndrome, purpura, ACD, rash, xerosis (n=2, 3.63%). Of all the 55 cases, 20% were classified as mild (n = 11), 60% as moderate (n =33) and 20% as severe (n =11). Among the 55 patients under the study, about 44 (80%) were cured, 11 (20%) were improved.

Conclusion: Adverse cutaneous drug reaction, more commonly occurred in patients taking medications such as antibiotics, NSAIDs, anticonvulsants, and anticancer drugs. Most common cutaneous drug reactions were maculopapular rash, followed by fixed drug eruption, Stevens - Johnson syndrome and urticaria.

KEYWORDS: Clinical profile Adverse cutaneous drug reactions.

1. INTRODUCTION

The skin(also known as the cutaneous membrane or integument covers the external surface of the body and is the largest organ of the body in both surface area and weight.^[1] Adverse Drug Reactions are a major problem of drug therapy. According to WHO, Adverse drug reaction is defined as “any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function”.^[2] The adverse skin reactions due to drug exposure are a common problem. The exact mechanism for many of the drug induced cutaneous disease is not fully understood and may result from both immune and non-immune mechanisms. Properties of a drug that increase the risk of drug induced hypersensitivity reactions are:

- a) Molecular weight.
- b) Presence of foreign protein or large polypeptides of non human origin.
- c) The ability of a parent drug or its active metabolite to bind to a carrier protein and form a complete antigen.

Drug induced skin disorders are often classified as either acute or chronic. Acute diseases include erythematous eruptions like maculopapular rash, urticaria, angioedema, and anaphylaxis, fixed drug eruptions, hypersensitivity syndromes, Stevens - Johnsons syndrome and toxic epidermal necrolysis, Warfarin – induced skin necrosis, vasculitis, serum sickness like reactions, acute generalized exanthematous pustulosis, and photosensitivity. Chronic disorders include drug induced lupus, drug induced acne and pigmentary changes.^[3]

Severity of illness and risk of disease manifested by patients is calculated based either on clinical data from the medical records or hospital discharge data. Severity of the reaction was

assessed by using the Modified Hartwig and Siegel Severity assessment scale and the severity is broadly categorized into "mild," moderate and "severe for each ADR.

Table no 1: Modified Hartwig's severity assessment scale.

Level 1	An ADR occurred but required no change in treatment with the suspected drug.
Level 2	The ADR required that treatment with the suspected drug be held, discontinued or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
Level 3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR An antidote or other treatment was required. No increase in length of stay (LOS).
Level 4	Any level 3 ADR which increases length of stay by at least 1 day. OR The ADR was the reason for the admission.
Level 5	Any level 4 ADR which requires intensive medical care.
Level 6	The adverse reaction caused permanent harm to the patient.
Level 7	The adverse reaction either directly or indirectly led to death of the patient.

Mild= level 1 & 2 Moderate =level 3 & 4 Severe = level 5, 6,7.^[4]

2. Literature Review

In a study by Surajit Nayak and Basanti Acharjya in Indian Journal of Dermatology, Adverse cutaneous reactions to drugs are frequent, a prevalence of 2-3% of all hospitalized patients. Only approximately 2% of adverse cutaneous reactions are severe and very few are fatal. About 3% Prevalence of drug induced cutaneous adverse reactions occurs in India.^[5] A study carried out by Dimple Gohel, in Indian Journal of Pharmacy Practice, shows incidence of dermatological ADRs among in-patients in developed countries ranging from 1–3% whereas in developing countries such as India it is 2–5%.^[6] Nandha R, et.al in a study in International Journal of Applied and Basic Medical Research, have found the incidence of CADR in developed countries as 1–3%, while the incidence in developing countries is supposed to be higher between 2 and 5%^[7] and similar results has been reported by Amrinder R, et.al in Journal of Pharmacovigilance.^[8]

3. Subjects and Methods

The study was carried out in patients visiting dermatology outpatient department with suspected drug induced skin disorders. *Inclusion:* All patients with cutaneous adverse drug reaction visiting dermatology Outpatient Department of Pariyaram medical college are included irrespective of their age and sex. *Exclusion:* All Patients visiting dermatology Outpatient Department with skin rash secondary to all causes other than drugs.

The study was approved by the Institutional Human Ethics Committee of Academy of Pharmaceutical Sciences, Pariyaram Medical College. In this study, patients who satisfied the inclusion criteria visiting dermatology department were included in the study. Prospective data was collected. A suitable data collection form was designed and with the help of the form patient's demographic data such as name, age, gender, past medication history, route of administration was recorded. Institutional review board and patient consent were obtained.

4. RESULT

A total of 55 patients who had satisfied the inclusion criteria were enrolled in the study. Of the total 55 cases reported during the study, 34 (61.82%) were males and 21 (38.18%) were females. The percentage distribution of sample is represented in Table 2 and Figure 1.

Table 2: Percentage of distribution of subject according to Gender.

Gender	Frequency	Percentage
MALE	34	61.82%
FEMALE	21	38.18%

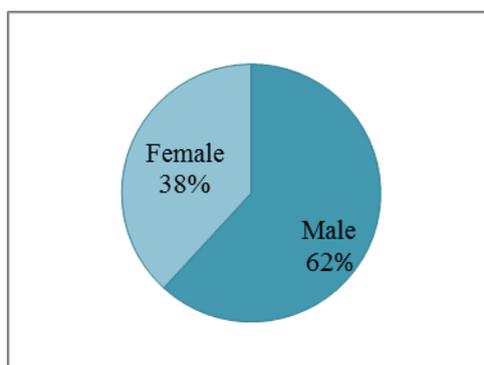


Figure – 1

4.1 Distribution of Class of Drug That Produced Adverse Drug Reaction

Maximum no. of cases occur in the class of drug were antibiotics (36.36%), NSAIDs (20%), anticonvulsant (14.54%), anticancer drugs (12.72%), antifungals, antiemetics (5.45%), PPIs, corticosteroids, Antiplatelets(1.81%). Percentage distribution of class of drug that produced adverse drug reaction is represented by figure 2.

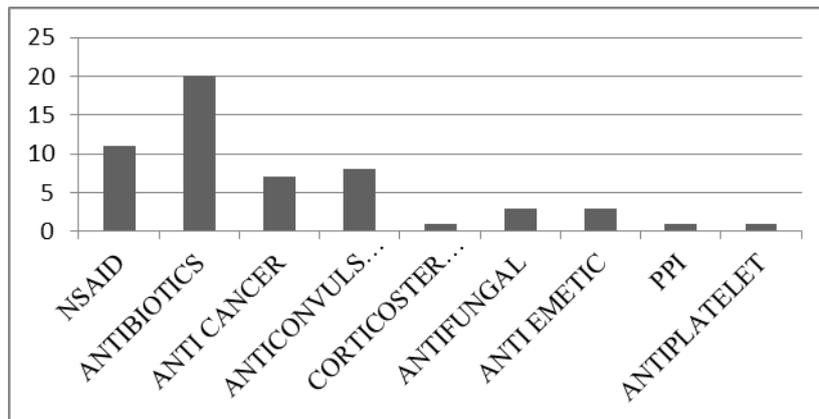


Figure – 2

4.2 Distribution of Type of Skin Reaction Produced By Drug

Maculopapular rash was the most common CADR ($n = 14$, 25.45%), followed by fixed drug eruption (FDE) and SJS ($n = 9$, 16.36%), urticaria, acne, angioedema, Erythema multiforme were ($n=3$, 5.45%), hand foot syndrome, purpura, ACD, rash, xerosis ($n=2$, 3.63%). Percentage distribution of type of skin reaction produced by skin is represented in Figure3.

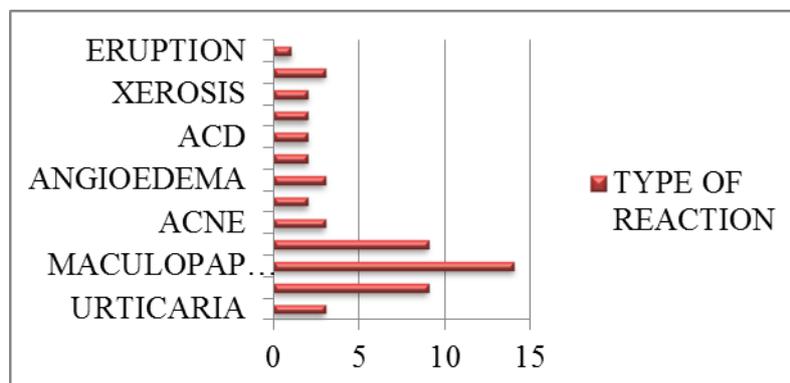


Figure – 3.

5. DISCUSSION

The study entitled “clinical profile of adverse cutaneous drug reactions among patients visiting dermatology department in a tertiary centre in North Kerala” was carried out in Dermatology Department, Pariyaram Medical College Hospital, Kannur. The study duration was for a period of six months from the date of approval from the Human Ethical Committee. During the study period, a total of 55 patients were enrolled in the study.

5.1 Gender of the population

The studies of Sudhaa Mahajan, et.al show that women tend to have higher risk of adverse drug reactions with a 1.5- 1.7-fold greater risk than men. Women are at more risk for

developing adverse drug reactions due to difference in pharmacokinetics and pharmacodynamics and also differ in their hormonal and physiological functions.^[9] The males in our study outnumbered the females. Study shows 62% were males and 38% were females. The male to female ratio was 1.61:1. There was a male predominance in our study which was in conformity with another study from Gujarat by Sushma *et al.*,^[10] and Dimple Gohel *et al.*^[6]

5.2 Class of drug that produced adverse drug reaction

The most common offending drug classes were antibiotics (36.36%), NSAIDs (20%), anticonvulsant (14.54%), anticancer drugs (12.72%), antifungals, antiemetics (5.45%), PPIs, corticosteroids, Antiplatelets (1.81%). Nandha, *et al.* showed the same higher incidence of suspected drug class with the drugs most commonly responsible for CADR being antimicrobials (48.30%), followed by non steroidal anti inflammatory drugs (NSAIDs) (21.90%) and anti-epileptics (13.20%)^[7]. In present study, beta lactum antibiotics were the highly suspected drug class followed by NSAIDs, and anticonvulsant. Among anticancer drugs major drug class was Tyrosine Kinase Inhibitors. Our study also shows paracetamol being a highly suspected drug followed by phenytoin. This could be due to common prescribing pattern of patient's disease condition.

5.3 Type of skin reaction produced by drug

In our study maculopapular rash was the most common cutaneous adverse drug reaction, followed by fixed drug eruption (FDE) and then Steven Johnson Syndrome, urticaria, acne, angioedema, Erythema multiforme, hand foot syndrome, purpura, ACD, rash, xerosis and eruption seen in patient population. According to Nandha, *et al.*, maculopapular rash was the most common CADR ($n = 39$, 42.85%), followed by fixed drug eruption (FDE) ($n = 19$, 20.87%), urticaria ($n = 11$, 12.08%)^[7]. This finding is similar to the result of our study. Maximum incidence of maculopapular rash was seen in cases of antimicrobial use, followed by NSAID use. Also SJS was not reported commonly in the population. But in our study, only 55 patients were enrolled and 9 cases of SJS reported. The chances of developing drug induced SJS was increasing found in our study.

5.4 Severity of ACDR

In present study, only 11 cases were of mild severity and the rest of all 33 cases were of moderate severity assessed by using Modified Hartwig's severity assessment scale. This was in accordance with studies of Dimple Gohel *et al.* and Shah SP, *et al.*^{[6],[11]}

5.5 Outcome

In present study about 44 cases were cured 44 (80%), 11 (20) improved. According to Nandha, et.al study shows outcome of CADR showed 65 (71.42%) patients cured, 25 (27.47%) improved.^[7]

6. CONCLUSION

From the study adverse cutaneous drug reaction (ACDR) more commonly occurred in male patients, who took medications such as antibiotics, NSAIDs and anticonvulsants. Most commonly occurred cutaneous adverse drug reaction was maculopapular rash and fixed drug eruption. Hence unwanted drug use should be avoided and prompt reporting should be promoted.

7. Limitation of the Study

1. Size of the study population available was very low because time of the study was too short and therefore results and conclusion made in this study can only be taken as a preliminary data and cannot be applied directly to general population.

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REFERENCES

1. Tortora G, Derrickson B. Principles of anatomy and physiology. 12th ed. Hoboken, N.J.: Wiley, 2009; 12(1): 154-159.
2. Sudershan V. Cutaneous adverse drug reactions in a tertiary care hospital. *Der Pharmacia Lettre.*, 2011; 3(6): 210-17.
3. Valerie clinard, Jennifer D. smith, Drug induced skin disorders. *US pharmacist.* 2012.
4. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm.*, 1992; 49: 2229-32.
5. Nayak S, Acharjya B. Adverse cutaneous drug reaction. *Indian J Dermatol*, 2008; 53: 2-8.
6. Dimple Gohel, Sandip Kumar Bhatt et.al. Evaluation of Dermatological Adverse Drug Reaction in the Outpatient Department of Dermatology at a Tertiary Care Hospital. *Indian Journal of Pharmacy Practice.*, 2014 Jul-Sep; 7: 42-50.
7. Nandha R, Gupta A, Hashmi A. Cutaneous adverse drug reactions in a tertiary care teaching hospital: A North Indian perspective. *Int J App Basic Med Res.*, 2011; 1: 50-3.

8. Amrinder R, Kaur I, Singh J, Kaur T (2016) Monitoring of Cutaneous Adverse Drug Reactions in a Tertiary Care Hospital. *J Pharmacovigilance*, 4: 207. doi:10.4172/2329-6887.1000207.
9. Sudhaa Mahajan. Women and risk for developing ADRs. *jk science editorial.*, january. march 2012; 14.
10. Sushma M, M. V. Noel, et.al. Cutaneous adverse drug reactions: a 9-year study from a South Indian Hospital. *Pharmacoepidemiol Drug Saf.*, 2005 Aug; 14(8): 567-70.
11. Shah S, Desai M, Dikshit R. Analysis of Cutaneous Adverse Drug Reactions at a Tertiary Care Hospital – a Prospective Study. *Tropical Journal of Pharmaceutical Research*, 2011; 10(4): 517.