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CUTANEOUS ADVERSE DRUG REACTIONS: CLINICAL PATTERN AND CAUSATIVE AGENTS IN A TERTIARY CARE CENTRE IN CENTRAL KARNATAKA

Dermatology

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ABSTRACT

Introduction: Cutaneous adverse drug reactions (CADRs) are the most common manifestations of drug sensitivity, exhibiting a wide range of morphologies. Thus, understanding these reactions is crucial for accurate diagnosis and prevention. **Objective:** The objective of the study was to study the most common aetiology, various clinical manifestations of adverse cutaneous drug reactions (CADR), and to assess the association of morphological cutaneous pattern of CADR and etiological group of drugs. **Methods:** A cross-sectional, observational study was carried out at dermatological department of a tertiary care center in Cental Karnataka. Written informed consent was obtained from all patients, and data were gathered using a pre-tested Performa that included a comprehensive clinical history, examination, and pertinent laboratory investigations. The results were analyzed using SPSS (Version 21.0). **Results:** This study included a total of 72 patients out of which 43 were females and 29 were males. Maximum CADR were observed in the age group of 20-30 years (31.9%), followed by 31-40 years (25.0%). The most common etiological group of drugs responsible for CADRs is antibiotics (33.3%) pointing toward its rampant use with and without prescription, NSAIDs (19.4%), antiepileptics (18.05%), and antitubercular therapy (5.55%) followed by antiretroviral therapy, antiprotozoals and antifungal agents (4.16% each). Majority of CADRs, that is, 52.7% comprised of probable CADRs as per "Naranjo's algorithm." The most common type of lesions observed were papules (30%), macules (20%), plaques (7%), and edema (7%). **Conclusion:** The significance of this study was to study the profile of CADR and to highlight the need for heightened vigilance among healthcare providers in monitoring and promptly reporting such reactions. Effective documentation and systematic oversight of adverse drug reactions (ADRs) can significantly reduce adverse events in patient care and contribute to more effective drug administration. Further research is crucial to enhance awareness of potential CADRs and to facilitate early detection, ultimately supporting the implementation of robust drug safety protocols.

KEYWORDS

Cutaneous adverse drug reactions; Morphological patterns of CADR

INTRODUCTION

The most common presentation of an adverse drug reaction (ADR) is a cutaneous adverse drug reaction (CADR). Adverse drug reactions (ADRs) are asignificant global health issue, affecting up to 0.1–1% of patients using systemic medications. They significantly influence patient care and quality of life and pose considerable financial burdens on healthcare systems.[1]

A CADR is defined as any undesirable change in the structure or function of the skin, its appendages, or mucous membranes caused by a drug, and it encompasses all adverse events related to drug eruption, regardless of the etiology.[2,3] Cutaneous adverse drug reactions (CADRs) can range from mild and temporary to severe, necessitating hospitalization and potentially causing morbidity and occasional mortality. CADRs constitute 10 to 45% of all adverse drug reactions (ADRs), and approximately 2–3% of hospital admissions are attributed to CADRs.[4,5]

The frequency of cutaneous adverse drug reactions (CADRs) ranges from 1 to 3% among adult patients, whereas approximately 2.5% of children treated with medications will encounter CADRs.[6,7]

Overall, CADRs affect up to 10% of all hospitalized patients. Fortunately, most CADRs are mild or self-resolving conditions; however, 2–6.7% of cutaneous reactions can develop into severe and potentially life- threatening clinical syndromes.

Objectives

1. To study the clinico-epidemiological pattern of various adverse cutaneous drug reactions.
2. To study the common drugs causing adverse cutaneous drug reactions.
3. To assess the association of morphological CADR and etiological group of drugs

MATERIALS AND METHODS

The study was conducted in the Outpatient department of Dermatology, venerology and leprosy of JJM Medical College, Davangere after the approval of institutional ethical committee.

All patients of suspected cutaneous adverse drug reactions who presented to the dermatology OPD over a period of 6 months (August 2023 to January 2024) were considered for the study. A detailed history (for drugs taken, their doses, frequency, skin lesions, associated prodromal symptoms, incubation period, any previous and present systemic illness, and improvement in symptoms on withdrawal of the suspected drug) was recorded, thorough clinical examination was performed and routine investigations were done in all cases.

All CADR patients were given appropriate treatment with antihistamines, topical, and oral steroids and other drugs, depending upon the severity of CADR and hospitalized when necessary.

At the end of the study, the data was analyzed, and inferences were drawn using Chi-square test.

The causality assessment of drug reaction was calculated according to the "Naranjo's algorithm" as- doubtful, probable, possible and definite adverse drug reaction. The Naranjo Algorithm is a questionnaire designed by Naranjo et al. for determining the likelihood of whether the adverse drug reaction is actually due to the drug rather than the result of other factors. The probability of CADR is divided as definite, possible and probable. The Naranjo score was obtained after answering pre-designed set of ten questions present in the Naranjo algorithm. A score of 9 and above was considered as a definite CADR, score of 5-8 was considered as a probable CADR and score of 1−4 was considered as a possible. CADR Master charts and graphs were prepared using MS-Excel 2007 and data were processed on SPSS (Version 21.0) to find frequency of variables. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Chi-square test was applied for qualitative variables to find the association.

RESULTS

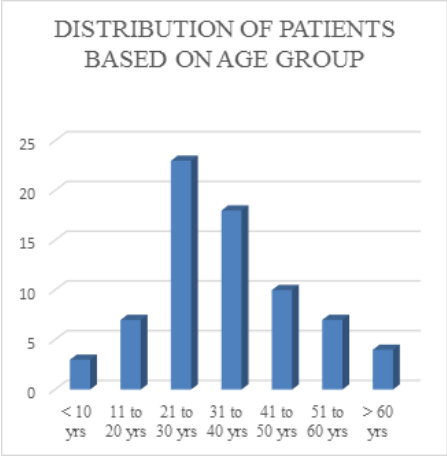
The study comprised 72 patients who had reported experiencing varied cutaneous medication responses. According to Naranjo's causality assessment, 52.7% (38 cases) CADRs were categorized as probable, 41.6% (30 cases) were possible whereas 5.5% (4 cases) of CADRs were categorized as definite.

This study included a total of 72 patients out of which 43 were females and 29 were males, which constituted 59.7% and 40.3% respectively.

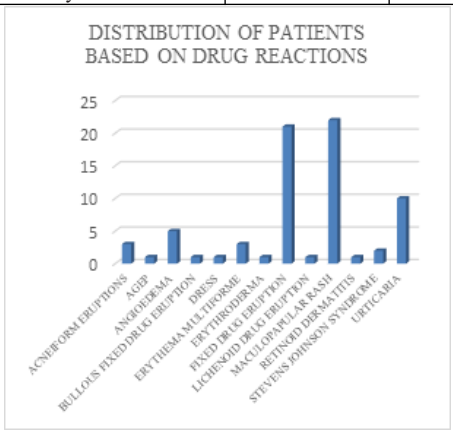
The youngest patient recorded was 3 years old and the oldest was 67 years old. The mean age distribution of the patients is 33.81 and

standard deviation is 13.84. Maximum CADR were observed in the age group of 20-30 years (31.9%), followed by 31-40 years (25.0%).

Gender	Number of patients	Percent
Females	43	59.7
Males	29	40.3
Recurrent episodes	**Frequency**	**Percent**
Absent	56	77.8
Present	16	22.2



Time period between the drug intake and onset of lesions	No. Of patients	Percent
<6 days	3	4.2
<6 hours	6	8.3
>3 weeks	5	6.9
1 day to 1 week	27	37.5
1 week to 3 weeks	14	19.4
6 hours to 1 day	16	22.2



Most common CADR noted was fixed drug eruption in 22 patients (30.6%) followed by maculopapular rash which was seen in 21 patients (29.2%). Angioedema was observed in 5 patients(6.9%), erythema multiforme in 4 patients (5.5%), acneiform eruptions in 3 patients (4.2%) and Stevens-johnson syndrome in 2 patients(2.8%).Lichenoid drug eruption, retinoid dermatitis, DRESS and AGEP accounted for 1 patient each(1.4%).

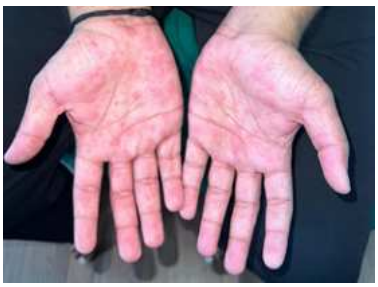
Among 72 cases recorded, recurrent episodes were noted in 16 cases (22.2%), which were most commonly seen in fixed drug eruptions.

The incubation period between the intake of the drug and the onset of skin lesions, in majority of the cases was between 1 day-1 week, seen in 37.5% of the cases (n=27) which was followed by 6 hours to 1 day, seen in 22.2% of the cases (n=16).

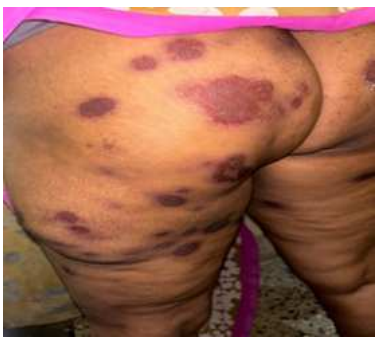
According to this study, the most common etiological group of drugs responsible for CADRs is antibiotics (33.3%), NSAIDs (19.4%), antiepileptics (18.05%), and antitubercular therapy (5.55%) followed by antiretroviral therapy, antiprotozoals and antifungal agents (4.16% each). Other drugs that were implicated in the causation of CADR in this study were corticosteroids, imipramine, isotretinoin, methylcobalamine and pregabalin. Among the class of drugs causing CADR, Antibiotics and NSAIDs caused significantly higher percentage of drug reactions pointing toward its rampant use with and without prescription. Among the Antibiotics, cotrimoxazole was noted to be the most common one responsible for CADR.

Other antibiotics significantly noted were amoxicillin, azithromycin, cefuroxime, ciprofloxacin, dapsone, doxycycline, levofloxacin, tetracycline and penicillin.After antibiotics, NSAIDs were the most common class of drugs responsible for CADR. Diclofenac was found be the most common NSAID followed by Paracetamol. Other drugs noted were aspirin, ibuprofen and piroxicam.

Maculopapular rash occurring secondary to antitubercular therapy



Erythema multiforme



Fixed drug eruption

Stevens-Johnson syndrome

Limitations And Discussion

The study was conducted over a brief period, providing a snapshot of cases at a specific point in time. Additionally, adverse cutaneous drug reactions reported in other departments were excluded from the study.

The risk of drug allergy is assessed by consideration of multiple factors. [8-11]

1) **Drug factors:** nature of the drug, dose, frequency, and duration of drug exposure, route of administration, and cross-sensitization;
2) **Host factors:** age, gender, genetic predisposition (e.g., human leukocyte antigen type and acetylation status), concomitant diseases (e.g., Epstein-Barr virus, human immunodefciency virus, and asthma), past drug reactions, and multiple allergic syndromes.

According to a systematic review on SJS and TEN in Indian population by Patel et al.,[12] antimicrobials and antiepileptics are the commonest drugs causing severe cutaneous adverse reaction (SCAR). Carbamazepine, phenytoin, fluoroquinolones, and paracetamol were the most commonly implicated drugs. Patients treated with polypharmacy are the most common association.

In a study conducted by N Sushma et al, the most common type of ADR was maculopapular rash (42.7%), followed by Stevens–Johnson syndrome (SJS) (19.5%) and fixed drug eruption (11.4%). The drug class implicated was antibiotics (45%), followed by antiepileptics (19%), NSAIDs (19%). [13]

According to a study conducted by Pudukadan D et al, the most common eruptions observed were fixed drug eruption (31.1%) and maculopapular rash (12.2%), and the most common causes were cotrimoxazole (22.2%) and dapsone (17.7%).[14]

CONCLUSION

Cutaneous drug eruptions are the common and easily identifiable clinical presentation of ADR. The CADR can be as mild and transient or severe, requiring hospitalization leading to morbidity and occasional mortality. Early diagnosis and treatment requires a vigilant mind and thorough understanding of common drugs causing CADR and their presentations. This article emphasizes the frequently encountered drugs that cause cutaneous adverse drug reactions (CADRs) and outlines the patterns of CADR presentations in our country.

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