Original Research Article

Prospective observational study of cutaneous adverse drug reactions at a tertiary medical college

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Abstract

Background: Adverse cutaneous drug reactions (ADR) are considered as one among the leading cause of mortality and morbidity. They cause 3-6% of hospital admissions at any age and up to 24% in elderly population. This study was done to analyze clinical pattern of ADR, mortality and morbidity of patients with ADRs. **Materials And Methods:** This study was a prospective observational study conducted at Department of DVL, Santhiram medical college and general hospital , Nandyal from August 2017- DECEMBER 2018 . All the patients who attended DVL OPD and those who are admitted in the wards with suspected ADR were included in the study. The patient's data was recorded in a prestructured proforma that includes detailed clinical history, general and cutaneous examination. Assessment of severity of adverse reaction was done using HARTWINGS severity assessment scale. **Results:** Total 101 were reported from AUGUST 2017- DECEMBER 2018. Maximum ADRs were reported in the age group of 31-40 (33.6%). Females were affected more than males. Mild ADRs were found in 44, moderate in 44 while severe ADRs were noted in 13. Patients reported with Fixed drug eruption – 50 (49.5%),Drug induced acne form eruptions - 16 (15.8%) , Maculopapular rash -7 (6.93 %) , Steven – Johnson syndrome – 5 (4.95%) , Erythema multiforme – 5 (4.95%) , Drug induced erythema nodosum - 5 (4.95%) , Toxic epidermo necrolysis -4 (3.95%) , Drug induced urticaria – 3 (2.9%) ,Drug induced pemphigus vulgaris – 2(1.9%) , Drug induced Exfoliative dermatitis - 2 (1.9 %) , Dapsone syndrome – 2 (1.9%) . The major drug group which was implicated in cutaneous adverse drug reactions was NSAIDs with frequency of 50.5%.

Key Word: Adverse cutaneous drug reaction,

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INTRODUCTION

According to the WHO, an Adverse drug reaction(ADR) is defined as any noxious, unintended or undesired effect of a drug, which occurs at doses which are used in humans for prophylaxis, diagnosis or therapy[1].They account for patients suffering, hospitalization and economic burden, and may sometimes be fatal. The commonly reported ADRs' are Fixed drug eruption , Drug induced acneform eruptions, maculopapular rash and Urticaria. A wide range of drugs can cause ADRs' and its patterns could change due to different prescribing patterns, use of newer drugs, self – medications, and referral bias. The studies conducted in this field from India are scarce. Hence, this study was undertaken at a tertiary care teaching hospital to assess clinical characteristics of ADRs' and pattern of their mortality and morbidity.[2]

AIMS AND OBJECTIVES

1. To study clinical patterns of Cutaneous Adverse drug reactions in patients attending Santhiram Medical College and General Hospital.
2. To study mortality and morbidity of Cutaneous Adverse drug reactions.

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MATERIALS AND METHODS

This study was an observational prospective study which was conducted at department of DVL, Santhiram Medical College and General hospital, Nandyal from AUGUST 2107 – DECEMBER 2018. All the patients who attended DVL outpatient department and those who were admitted in the wards with suspected ADR were included in the study.

Only those cases were included that satisfied the following criteria[3]:

1. Those in which the diagnosis of the cutaneous adverse reaction was in accordance with the definition of ADRs which was provided by WHO.
2. Those in which there was no alternate explanation for the reaction.
3. Those in which there was a plausible time relationship between the introduction of drug and onset of reaction.
4. Those in which there was improvement in the condition of the patient after dechallenge / withdrawal of suspected drug.

Adverse cutaneous drug reactions which were caused by the usage of topical medications were excluded from the study. Informed consent was obtained from each patient in our study. The study was undertaken after clearance certificate from institution ethics committee. The patient's data was recorded in a prestructured proforma that includes detailed clinical history, general and cutaneous examination. Assessment of severity of adverse reaction was done using HARTWINGS severity assessment scale[4]. Relevant investigations were done to rule out infectious etiology. The attributed drug was withdrawn and not rechallanged in our study.

RESULTS

Total 101 cases of adverse drug reactions were reported from AUGUST 2017- DECEMBER 2018 from our Santhiram medical college and general hospital, Nandyal. Out of 101 patients, 55 were females and 46 were males (Table 1). Predominance of patients were in the age group were 31-40. (Table 2) According to Hartwings severity assessment scale (Table 3) patients in level 3 were 30 (29.7%), level 4 were 14 (13.8 %) and level 5 were 13 (12.8%). In our study, Mild ADRs were found in 44, moderate in 44 while severe ADRs were noted in 13. No mortality was observed in our study. The maximum number of patients reported with Fixed drug eruption were 50 (49.5%), Drug induced acne form eruptions - 16 (15.8%) , Maculopapular rash -7 (6.93 %) , Steven – Johnson syndrome – 5 (4.95%) , Erythema multiformae – 5 (4.95%) , Drug induced erythema nodosum - 5 (4.95%) , Toxic epidermal necrolysis -4 (3.95%) , Drug induced urticaria – 3 (2.9%) ,Drug induced pemphigus vulgaris – 2(1.9%) , Drug induced Exfoliative dermatitis - 2 (1.9 %) , Dapsone syndrome – 2 (1.9%) . The major drug group which was implicated in cutaneous adverse drug reactions was NSAIDs with frequency of 50.5% (Table 5). The drugs implicated in fixed drug eruption were ibuprofen[27], diclofenac[15], metronidazole[5], cotrimaxozole[3]. The drugs implicated in acne form eruptions were isoniazid and rifampicin [10], carbamazepine[6]. The drugs implicated in maculopapular rash were cefadroxil[5], ampicilin[2]. The drugs implicated in erythema multiforme were carbamazapine[4], diclofenac[1]. The drugs implicated in steven johnson syndrome were ciprofloxacin[3], penicilins[2]. The drugs implicated in erythema nodosum were diclofenac[4], ampicilin[1]. the drugs implicated in toxic epidermo necrolysis were ciprofloxacin[2], phenytoin[1], cotrimaxozole[1]. the drugs implicated in drug induced urticaria were aspirin[3], drug induced pemphigus were Ramipril[1], aspirin[1], drug induced exfoliative dermatitis carbamazepine[1], phenytoin[1] and dapsone[2] in dapsone syndrome.(Table 6) . A single type of ADR was caused by different groups of drugs in different individuals. Similarly a single drug was responsible for different type of reactions in different individuals. In this way heterogeneity was observed.

Table 1: sex distribution

Gender	Number	Percentage
FEMALE	55	54.4
MALE	46	45.5

Table 2 - age and sex distribution

Age Group	Frequency	Male	Female	Percentage
21-30	29	12	17	28.7
31-40	34	19	15	33.6
41-50	10	4	6	9.9
51-60	13	5	8	12.8
61-70	9	3	6	8.9
>70	6	3	3	5.9

Table 3: Hart wings 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 the death of the patient

mild – level 1,2; moderate – level 3,4; severe – level 5,6,7

Table 4: Hart wings severity assessment scale

HARTWINGS SCALE	MALE	PERCENTAGE	FEMALE	PERCENTAGE
MILD	26	26.6	18	73.3
MODERATE	16	57.1	28	42.8
SEVERE	4	30.7	9	69.2

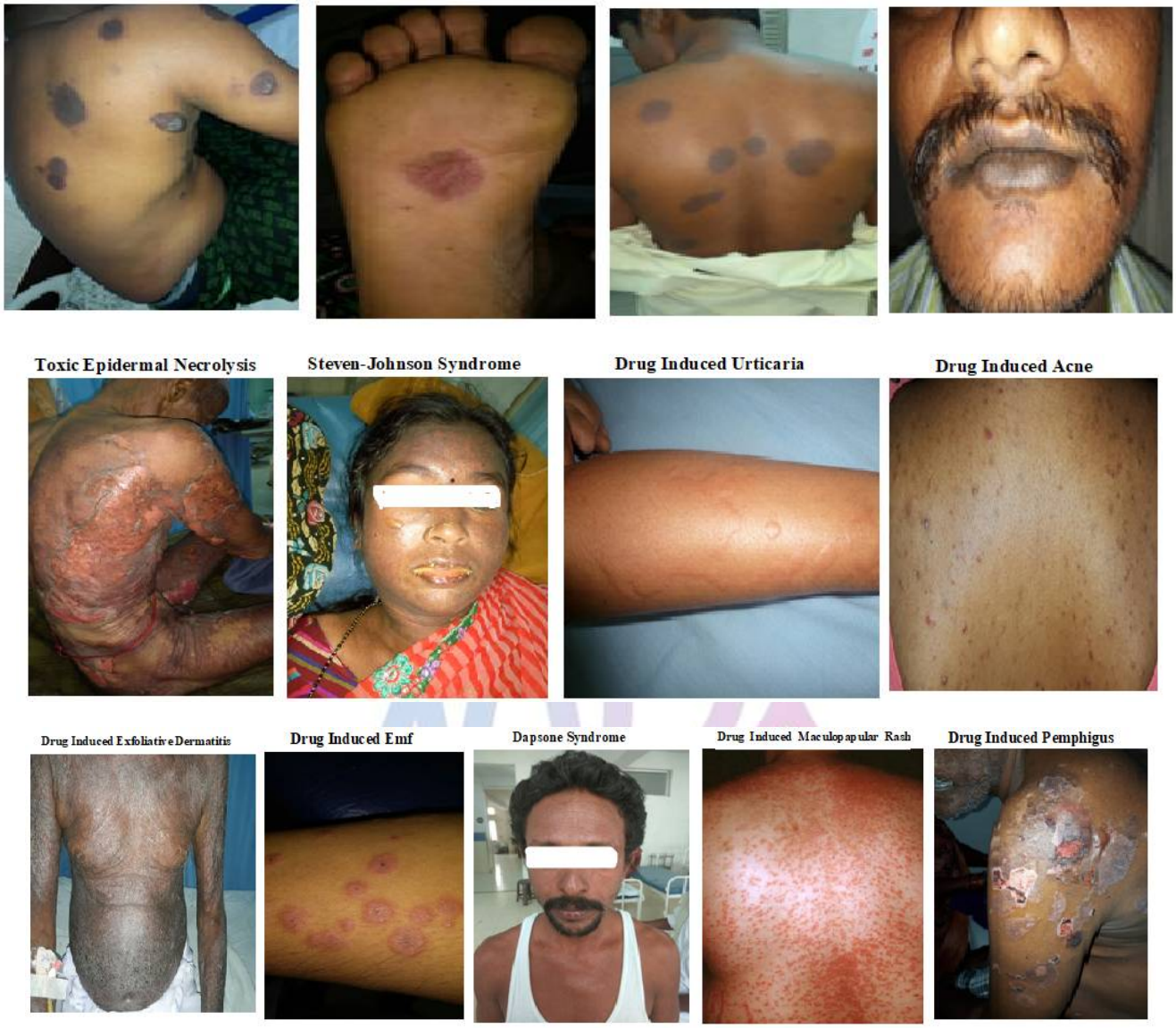
Table 5: drugs and frequency in cutaneous adverse drug reaction

drug involoved	frequency	total percentage	male	percentage	female	percentage
nsaids	51	50.5	20	39.2	31	60.8
antimicrobials	24	23.8	12	50	12	50
anti convulsants	15	14.8	8	53.3	7	46.7
anti tuberculosis drugs	10	9.9	5	50	5	50
antihypertensive	1	1	1	100	0	0

Table 6: pattern of ADR and drugs implicated

clinical pattern	frequency	drugs implicated	percentage
Fixed Drug Eruption	50	Ibuprofen (27) Diclofenac (15) Metronidazole(5) Cotrimoxazole(3)	49.5
Acne Form Eruptions	16	Isoniazid And Rifampicin(10) Carbamazepine(6)	15.8
Maculopapular Rash	7	Cefadroxil(5) Ampicillin (2)	6.9
Steven Johnson Syndrome	5	Ciprofloxacin(3) Carbamazepine(2)	4.9
Erythema Mulitiforme	5	Carbamazepine(4) Diclofenac(1)	4.9
Erythema Nodosum	5	Diclofenac(4) Ampicillin(1)	4.9
Toxic Epidermal Necrolysis	4	Ciprofloxacin(2) Phenytoin(1) Cotrimoxazole(1)	3.9
Drug Induced Urticaria	3	Aspirin(3)	2.9
Drug Induced Pemphigus Vulgaris	2	Ramipril(1) Aspirin(1)	1.9
Drug Induced Exfoliative Dermatitis	2	Carbamazepine(1) Phenytoin(1)	1.9
Dapsone Syndrome	2	Dapsone(2)	1.9

Fixed Drug Eruption



DISCUSSION

A wide spectrum of cutaneous manifestation ranging from exanthematous rashes to Toxic epidermal necrolysis can be produced by different class of drugs. There is no gold standard investigation for the confirmation of ADRs. The diagnosis of ADR involves the analysis of factors such as timing of the drug exposure and the reaction time, the course of reaction with drug withdrawal/discontinuation, the timing and nature of recurrent eruption on rechallenge and history of reaction with similar drug[5]. In our study, a total of 101 ADRs were reported. The majority of males were in the age group of 31-40 and females in the age group of 21-30. Leape LL *et al*[6], Hafner JW *et al*[7] noted that the elderly were more commonly affected. The differences in various studies may be due to variation in the health care seeking behavior of the population. Mild predominance of CADR was seen in females compared to males in concordance with studies done by Deepak Dimri *et al*[8], and Pudukandan K *et al*[9]. This disparity might be there because of more consciousness of females towards cutaneous reactions and its reporting than male counterpart. Another point is to consider the trend of selfmedication present in our society. Some of the drugs are easily available in General stores and females may be exposed to additional risk due to excess and unsupervised consumption of over the counter medicines. Over various types of ADRs seen in our study, Fixed drug eruptions was the most commonest followed by Acne form eruptions. Sulivan J *et al*[10], kauppin *et al*[11], Sharma *et al*[12] have noted exanthematous eruption to be the most common type of

eruption. This could be due to different patterns of drug usage and different ethnic group characteristics. Commonly attributed drugs in our study were NSAIDS followed by Antimicrobials. Sharma VK *et al*[13] Thapa *et al*[9], noted that antimicrobials were common in their study followed by NSAIDS. This difference may be due to increase in self medication with NSAIDS. Hartwig SC *et al*[14], characterized ADRs into seven categories based on severity. Level 1,2 fall under mild category, level 3,4 fall under Moderate and Level 5-7 fall under severe category. Patients under moderate and severe category require hospitalization. In our study, Mild ADRs were found in 44, moderate in 44 while severe ADRs were noted in 13. Systemic involvement was noted with SJS, TEN, Exfoliative dermatitis and Dapsone syndrome. Systemic involvement may predict poor outcome. But no mortality was reported in our study.

CONCLUSION

The commonest CADR was fixed drug eruption in our study. Commonest drug implicated was NSAIDS followed by antimicrobials. Mild and moderate ADRs were commoner than severe CADR. High morbidity was noted in SJS, TEN, Exfoliative dermatitis and Dapsone syndrome. The clinical pattern of CADRs and drugs causing them are different in our population implying that knowledge of various clinical patterns of drug reactions is required for a physician to identify the m early and manage accordingly. This study signifies the importance of strict pharmacovigilence. There is a need to sensitize the patients about the hazards of self medication.

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