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Research Article

Adverse Cutaneous Drug Reactions: Clinical Patterns & Its Impact on the Quality of Life. A Two Year Survey at Dermatology out Patient Clinic of Tertiary Care Hospital

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Abstract: Adverse cutaneous drug reactions (ACDR) are an important clinical entity seen in dermatology outdoor patient practice and it form a major cause of patient's morbidity & mortality. Our objective was to evaluate the different clinical spectrum of ACDR in dermatology outdoor department patients & to establish the impact of ACDR on the quality of life of patients. All 110 patients, more than 16 years of age, attended the dermatology outdoor department were enrolled. Morphological patterns of ACDR & their culprit drugs were recorded. Finlay & Khan's 10 questions were assessed in all 110 patients and DLQI score was prepared for each individual patient. The mean age of patients with ACDR was 34.09 years. Male to female ratio was 1.2:1. The most common ACDR observed were Fixed Drug Eruption (FDR) (30.9%) and maculo papular rash (20%). The most common causative agent was antimicrobial group of drug. Higher DLQI score (Dermatology Life Quality Index-impairment of quality of life) was observed in exfoliative dermatitis (29), Drug Rash with Eosinophilia & Systemic Symptoms (DRESS) (28.5) & severe Stevens-Johnson Syndrome (SJS) (27). Knowledge of different patterns of ACDR & their causative drugs is essential for a dermatology consultant, because it helps in reducing morbidity, mortality and health care cost of ACDR patients. Impairment of quality of life of ACDR patient can be measured by DLQI score. Knowledge of different patterns of ACDR & their DLQI score helps to reduce morbidity, mortality and health care cost of ACDR patients.
Keywords: Adverse cutaneous drug reactions (ACDR), Clinical patterns, Dermatology Life Quality Index (DLQI).

INTRODUCTION

Adverse cutaneous drug reactions (ACDR) are an important clinical entity in dermatology outdoor patient practice. ACDR form a major cause of patient morbidity and account for significant number of patient deaths [1] and also responsible for increased healthcare cost [2]. Many of the commonly used drugs in OPD can produce ACDR. A wide spectrum of cutaneous manifestations ranging from maculo papular rashes to severe Stevens-Johnson Syndrome (SJS) &Toxic epidermal necrolysis(TEN) can be produced by different classes of drugs [1]. A standardized method should be used to establish final decision of ACDR and causality of offending drug [3].

Many dermatological conditions frequently have a major impact on patient's psychological state, social relationship and everyday activities [4, 5]. DLQI scale was developed to assess the impact of skin conditions on patients psychological state and everyday activities [6]. Measure of DQL scale in ACDR helps to assist treatment decisions as well as to guide priority of health services among different social & cultural groups [7].

Comprehensive information about ACDR's incidence and ultimate health effects are often not available. This study was therefore designed to evaluate the clinical spectrum of all ACDR in dermatology outdoor department & to establish the impact of ACDR on the quality of life.

METHODOLOGY

The study was observational study carried in the dermatology OPD of our hospital. All patients who attended the dermatology OPD of hospital from 1st May, 2012 to 30th April, 2014 were screened & suspected cases of ACDR of more than 16 years of age were independently assessed. On the basis of WHO causality guidelines [8], causality of offending drug was finalized by our dermatology departments. Only cases of ACDR where causality was certain, probable/likely were included in study.

Detailed clinical history including drug history- all prescribed drugs before reaction, onset & duration of reaction, past history of drug sensitivity, routine laboratory investigation were recorded. Finally morphological pattern of ACDR with causality of offending drug was noted & recorded.

After taking written consent of all patients, Finlay & Khan's10 questions of DLQI were completed unaided by all 110 patients & all patients were more than 16 years of ages.

Each question was scored on 4 point Likert scale. Not at all & not relevant, unanswered question scored-0, a little scored-1, a lot scored-2, very much & question 7 prevented works or studying scored-3.

The DLQI was calculated by summing up score of each question resulting maximum of 30 and minimum of 0. The score was compiled and the impact of ACDR according to meaning of DLQI score was concluded.

Meaning of DLQI scores

0-1 score=No effect, 2-5 score= Small effect, 6-10 score=Moderate effect, 11-20 score=Very large effect, 21-30 score=Extremely large effect.

The domains assessed by DLQI were included psychosocial items (Q-2,5,6,8,9), physical items(Q-3,4,7) and symptoms items(Q-1,10) [2].

Psychological items

Q-2= embarrassed or self conscious
Q-5= effect on social or leisure activities
Q-6= effect on sport activities
Q-8= problem with partner, close friends or relatives
Q-9= difficulty in sexual activities

Physical activities items

Q-3= interfered with shopping, looking after home or gardening
Q-4= effect on wearing clothes
Q-7= prevented from working or studying

Symptoms items

Q-1= itchy, redness, rawness, scarring, swelling, bleeding, sore, painful or stinging
Q-10= problem facing because of treatment.

We created 3 types of scores using these 3 groups of questions. Psychosocial score was derived by adding scores of Q- 2, 5, 6, 8, 9; activity score was derived by sum up of scores of Q-3, 4, 7. Symptoms score was derived by sum up of Q- 1& 10.

RESULTS

The mean age of patients with ACDR was 34.09 Years (range 16-70years). We enrolled patients of more than 16 years of age only. Most of them 62 out of 110 were in the age group of 21-30 years, followed by 26 out of 110 in the 41-50 age groups.60/110 (54.54 %) were male and 50/110(45.45 %) were female. Male to female ratio was 1.2:1.

The mean duration of intake of drug prior to onset of drug rash was 9.68 Days. (range 1-67days). Out of 110 patients, 14 had given history of similar drug consumption previously. 12 patients had a past history of similar ACDR. All routine investigations including HIV antibody test (except eosinophil count higher in 38.2%) were within normal range.

Various types of drug reactions and the drugs implicated in these reactions with frequency of occurrence are enlisted in Table 1.

FDR is the most common type (30.9%) of drug reaction followed by maculo popular rash (20%). Number of female patients were higher indrug induced acneform eruptions & maculo papular rash ACDR patterns. In rest of ACDR patterns males were predominant. Most common offending drug group responsible for ACDR was antimicrobials (54.54%) followed by NSAIDS (18.18%).

Mean DLQIS (Table 2) was higher in exfoliative dermatitis (29) followed by DRESS (28.5) and SJS (27). Total DLQI score, independent of age was higher for patients with Exfoliative Dermatitis(29), DRESS (28.5), SJS (27) and lower for patients with Lichenoid eruption (14) followed by FDR (16.67). Mean psycho-social score was highest (15) for patients of exfoliative dermatitis followed by DRESS (14) & SJS (13.85). Lowest for patients for lichenoid eruptions (6). Mean activity score was higher in patients of DRESS (8.5) & SJS (8). This score was lowest for patients with macula-papular rash(4.59). Mean symptoms score was higher in exfoliative dermatitis (6.5). Lowest for patients of generalized pruritus (2.87). All patients were treated & the skin lesions subsided in all patients as a result of suspected drugs were withdrawn.

Table 1: Clinical patterns of drug reaction with frequency of offending drugs

Pattern of drug reaction	No. of patients			Percentage	Offending drug
	Total no.	Male	Female		
FDR (Fig. 1)	34	21	13	30.9	Ampicillin (2), Ciprofloxacin (2) Cotrimoxazole (4), Dapsone (3), Ibuprofen (4),Metronidazole (4), Ofloxacin (4), Tinidazole (3), Tetracycline (8)
Urticaria& angioedema (Fig. 2 D)	18	10	8	16.3	Amoxicillin (2), Ampicillin (1), Aspirin (1), Cephalexin (2), Cefadroxyl (2), Chloroquin (1), Enalapril (2), Ibuprofen (6), Phenytoin (1),
Maculo-papular rash (Fig. 2C)	22	9	13	20	Ampicillin (4), Amoxicillin (7), Ciprofloxacin (1), Carbamazepine (4), Cotrimoxazole (1), Ibuprofen (3), Phenytoin (2)
Erythema multiforme (Fig. 2A)	8	5	3	7.3	Amoxicillin-Clavulanate (1), Ciprofloxacin (1), Ceftazidime (1), Cotrimoxazole (2), Ibuprofen (2), Tetracyclin (1)
SJS (Fig. 2B)	7	4	3	6.3	Carbamazepine (2), Ibuprofen(3), Phenytoin (2)
DRESS (Fig. 3 A)	2	1	1	1.8	Dapsone (1), Nevirapine (1)
Acne form eruptions	7	2	5	6.3	Dexamethasone (2), Isoniazide (3), OC pills (2)
Exfoliative dermatitis (Fig. 3B)	2	2	0	1.8	Carbamazepine (1), Dapsone (1)
Generalized pruritus	8	4	4	7.3	Chloroquine (2), Dapsone (2), Ibuprofen (1), Isoniazide (2), Rifampicin (1)
Lichenoid eruption (Fig. 3C)	1	1	0	0.9	Amlodipine (1)
Acute generalized exanthematous pustulosis	1	1	0	0.9	Amoxicillin-Clavulanate(1)
Total	110	60	50		

Table 2: Mean DLQI scores of different conditions with its components

Pattern of ACDR	Mean psychosocial score	Mean activity score	Mean symptom score	Mean DLQI score
FDR	8.61	5	3.08	16.67
Urticaria& angioedema	8.83	6.11	5.05	20
Maculopapular rash	8.95	4.59	3.68	17.22
Erythema multiforme	11.12	7.125	5.25	23.5
SJS	13.85	8	5.57	27
DRESS	14	8.5	5.5	28.5
Acneform eruptions	8.85	5	3.71	17.57
Exfoliative dermatitis	15	7.5	6.5	29
Generalized pruritus	10.12	5.25	2.87	18.12
Lichenoid eruption	6	5	3	14
Acute generalized pustulosis	12	8	5	25

Table 3: Causative drug

Drug implicated for reaction	No. of cases (Percentage)
Amlodipine	1(0.90)
Ampicillin	7(6.36)
Amoxicillin,amoxicillin-clavulanate	11(10)
Aspirin	1(0.90)
Ceftazidime	1(0.90)
Cotrimoxazol	7(6.36)
Chloroquine	3(2.72)
Carbamazepine	7(6.36)
Cephalexin	2(1.81)
Cefadroxyl	2(1.81)
Ciprofloxacin	4(3.63)
Dexamethasone	2(1.81)
Dapsone	7(6.36)
Enalapril	2(1.81)
Isoniazide	5(4.54)
Ibuprofen	19(17.27)
Metronidazole	4(3.63)
Nevirapine	1(0.90)
Ofloxacin	4(3.63)
OC pills	2(1.81)
Phenytoin	5(4.54)
Rifampicin	1(0.90)
Tetacyclin	9(8.18)
Tinidazole	3(2.72)
Total	110

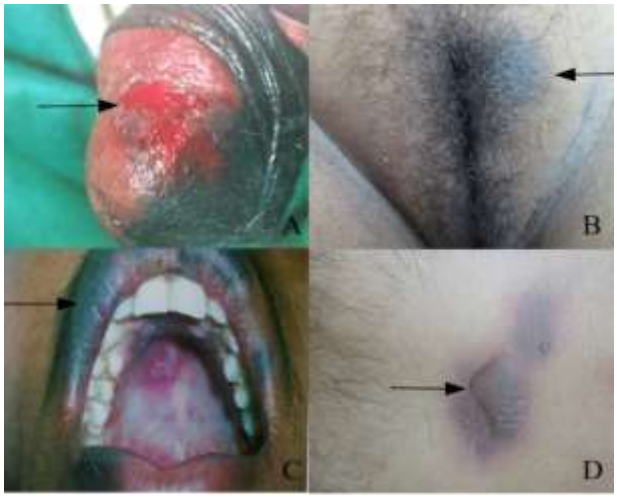

Fig. 1: (A) FDR on glans penis, (B) FDR on Vulva, (C) FDR on lip, (D) Bullous FDR

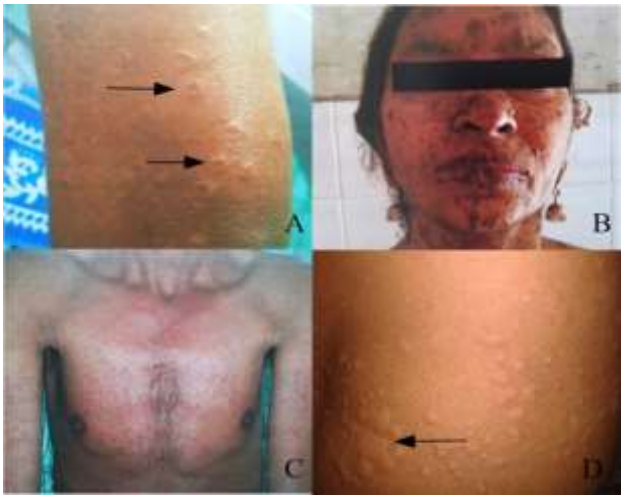

Fig. 2: (A) EM, (B) SJS, (C) Maculopapular Rash, (D) Urticaria

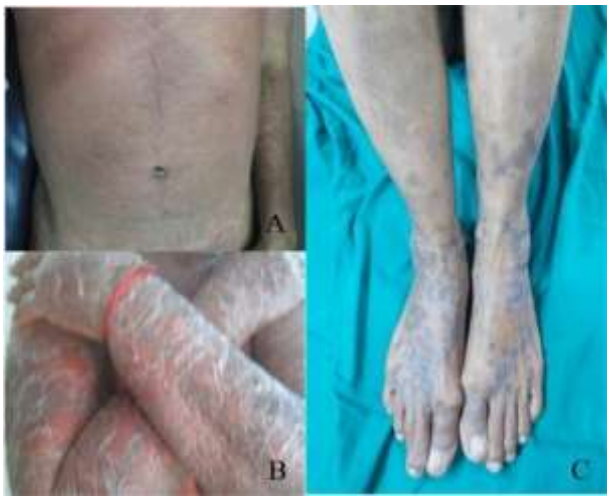

Fig. 3: (A) Dress, (B) Erythroderma, (C) Lichenoid eruption

DISCUSSION

Drug induced cutaneous eruptions(ACDR) are common & vary in their clinical patterns ranging from mild maculo papular rash to life threatening complications like SJS,TEN etc [1]. The incidence of ACDR in developed countries ranges from 1-3% [9, 10], while in developing countries like India, it is 2-5% of all hospitalized patients [11-14]. There is lack of comprehensive data of ACDR amongst outdoor patients. In present study only dermatology OPD patients were enrolled. The incidence of ACDR was 0.15% of total patients screened during study period of 2 years. In our study, the mean age of occurance was 34 years in males & 31 years in females. Males & Females constituted 54.54% & 45.45% of the total cases respectively. Male to female ratio was 1.2:1. A study conducted in tertiary care center in South India had revealed that the mean age of ACDR was 37 years & male to female ratio was 0.87:1 [13].

Most clinical manifestations of ACDR includes exanthematous, urticarial(and/or angioedema), pustular, bullous & fixed drug eruptions [1]. ACDR eruptions looking like other dermatological conditions like psoriasiform lesions, pityriasis rosea form eruptions, lichenoid eruptions, drug induced lupus, pseudolymphoma, pigmentary changes etc, are noticed less commonly. In our study various types of ACDR were seen. The most common type of ACDR was Fixed drug eruptions (30.9%) followed by maculo popular rash (20%).

A study from south India noticed that FDR (31.17%) was the most common type of ACDR followed by maculo papular rash (12.2%) [14]. Urticaria (27.19%) was most common followed by FDR (25.19%) & maculo papular rash (25.43%) reported by a study conducted in Kolkata [15]. A study from North India [16] & others found maculo papular rash to be the most common type [17, 18]. We noticed uncommon type of ACDR were 2 cases of DRESS, 1 case of AGEP & lichenoid eruption each. In our study we didn't find a single case of ACDR belonging to drug induced lupus, photosensitivity & pseudolymphoma. We excluded a pigmentary type of ACDR in patients taking clofazimine in anti leprosy treatment.

Almost any medicine can induce skin reactions and certain drug classes such as NSAIDs, antimicrobial and anti-epileptics have drug eruption rates approaching 1-5% [9]. Commonly offending drugs in our study were ibuprofen and amoxicillin. As our institute is located in poor socioeconomic class area, lots of patients are mostly restricted to drugs that are supplied free of cost from hospital and as a result, the suspected drugs were mostly from hospital OPD supply list.

Analysis of our study data (Table 3) showed that ibuprofen (17.27%)was the major culprit for ACDR followed by amoxicillin (10%).Among drug groups the anti bacterials formed the major group (54.54%), followed by NSAIDs (18.18%) & antiepileptic (10.9%). This is in concordance with an earlier report by Kauppien K *et al*. [18]. Antimicrobial followed by CNS depressants and NSAIDs were common implicated drugs reported by Pudukadan D *et al*. [14], Sharma VK *et al*. [16] & Chatterjee S *et al*. [15] Besides leprosy, dapsone is being used in many other dermatological conditions like LP,BP etc. This could possibly explain the number of cases of dapsone (6.36%) induced ACDR seen in our hospital.

DLQIS were developed to assess the impact of skin conditions on patient's psychological state, social relationship and everyday activities. Finlay & Khan's 10 questions of DLQIS are based on greater number of items, comprising psychosocial, physical activities and symptoms scales, and place considerable emphasis on the psychosocial impact of skin conditions which is measured directly in terms of psychological scale, and may also contribute to activity restrictions, such as going out, meeting friends [7] relatives, cloth wearing & other activities [6, 7].

This is the first study determining the impact of ACDR on the quality of life based on measurement of DLQIS of ACDR.

In our study total mean psychological score, sum of Q-2, 5, 6, 8, 9, independent of age was higher for patients with exfoliative dermatitis (15) type of ACDR pattern and lowest for patients for lichenoid eruptions (6) followed by FDR. Among psychological items, the effect on social & leisure activity domain showed higher DLQIS.

Total activities score, sum of Q-3, 4, 7, independent of age was higher for patients with DRESS (8.5) ACDR pattern followed by SJS(8), AGEP (8) and exfoliative dermatitis (7.5). Lowest for patients for maculo papular rash (4.59). Among activity items, the effect on wearing clothes domain showed higher DLQIS.

Total symptom score, sum of Q-1,10 independent of age was higher for patients with exfoliative dermatitis (6) followed by SJS (5.5), DRESS (5.5) and lowest for patients of generalized pruritus (2.87). Among activity items, the problems facing due to treatment domain showed higher DLQIs.

Total DLQIS score, independent of age was higher for patients with exfoliative dermatitis (29), DRESS (28.5) & SJS (27). Lowest for patient with lichenoid eruption (14) followed by FDR (16.67). It suggested exfoliative dermatitis; DRESS & SJS pattern of ACDR had maximum impairment of quality of life as compared to others ACDR.

The DLQI scales assist in informing treatment decisions by indentifying impact of different skin conditions. It also guides for providing priorities for services among different social and cultural groups [7]. The main emphasis of the present study was to produce a generalized measure (DLQIS) for assessing the impact of ACDR in terms of patient's psychosocial status & activity restrictions.

Finally our study concluded that the most common type of ACDR was Fixed drug eruptions (30.9%) followed by maculo papular rash (20%). Exfoliative dermatitis, DRESS and SJS patterns of ACDR had higher DLQI score that means quality of life was impaired in these patterns of ACDR and these patterns of ACDR required more attentions as compared to other ACDR. As a dermatologist one should have knowledge of different patterns of ACDR & their causative drugs, because it helps to reduce morbidity, mortality and health care cost of ACDR patients. Impairment of quality of life of ACDR patient can be measured by DLQI score .More research work should be required for above statement.

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