Cutaneous adverse drug reactions: A one year prospective study

Gurpoonam Jatana, MD [1]
Sunil Kumar Gupta, MD [1]
Sandeep Kaushal, MD [2]
Shobhna Kajal, MD [1]
Sandeep Kaur, MD [1]

1. Department of Dermatology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India
2. Department of Pharmacology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Corresponding Author:
Sunil Kumar Gupta, MD
Department of Dermatology, Dayanand Medical College and Hospital, Tagore Nagar, Civil Lines, Ludhiana, Punjab, India 141001
Email: vsunilgupta@rediffmail.com

Received: 13 February 2017
Accepted: 8 May 2018

Background: Adverse cutaneous drug reactions are unwarranted effects of modern medicine. These unfortunate events can assume any morphology from simple exanthem to full blown toxic epidermal necrolysis (TEN), and can simulate and mimic many diseases. Sometimes it is difficult to recognize the cause, but they may be due to polypharmacy or self-administration of medications. The analytical data from this study might help us to see certain patterns with various drugs and shed light on this problem. We performed this study at a tertiary hospital in Punjab, Dayanand Medical College and Hospital (DMCH), in order to determine the clinical patterns of cutaneous manifestations of adverse drug reactions (ADR).

Methods: The diagnosis was mainly based on detailed history and correlation between drug intake and the onset of rash along with laboratory investigations and skin biopsy results where possible. We assessed 695 patients (379 males and 316 females) who presented with cutaneous drug reactions over a 12-month period.

Results: The most common benign ADR observed was exanthem, which affected 199 (28.64%) patients followed by acute urticaria, including angioedema, which was seen in 126 (18.13%) patients, and fixed drug eruption (FDE) in 105 (15.11%) that included bullous FDE reactions. Other reactions included Stevens-Johnson syndrome (SJS) and TEN in 39 (5.61%) patients, erythroderma in 27 (3.88%), photosensitivity reactions, including phototoxic and photosensitive reactions, 31(4.46%), and lichenoid eruptions in 25(3.59%) patients.

Conclusion: Exanthems were the most common drug eruptions observed. Antibiotics and NSAIDS were the most common causes for benign drug eruptions, whereas antiepileptics were a major cause of severe cutaneous adverse reactions (SCARs).

Keywords: adverse cutaneous drug reactions, drug eruptions

Iran J Dermatol 2017; 20: 103-112

INTRODUCTION

Adverse drug reaction (ADR) is an unexpected, undesired, and unintended or toxic consequence of a drug administration [1]. ADRs are reportedly responsible for up to 7% of hospital admissions, and cutaneous ADRs (CADRs) alone contribute to 2%–3% of the overall hospital admissions [2]. ADR can mimic, disguise or appear in any morphology; therefore, a differential diagnosis of ADR should always be considered. The clinical spectrum and pattern of CADRs may vary from mild and transient maculopapular rash to severe and potentially fatal Stevens-Johnson syndrome (SJS) and toxic

epidermal necrolysis (TEN) [3]. Many patients with CADRs are lost to follow up, only to be found when they develop the same or another reaction to the same drug or a different drug. Hence, patient counseling, education, and guidance is of the utmost importance to decrease morbidity and mortality. The objectives of our study are to ascertain the pattern of cutaneous manifestations of ADRs and to determine their causality, severity, and preventability.

MATERIALS AND METHODS

This was a hospital-based cross-sectional, observational study conducted over a period of one year, from January 1, 2015 to January 1, 2016, in the Dermatology Outpatient Department of DMCH, Ludhiana Punjab, India. DMCH is a tertiary care teaching hospital. A total of 695 patients with CADRs were included in this study. We included all self-reporting patients, patients who referred from other departments of the hospital, and those who referred from peripheral health care facilities. All participants provided written informed consent. Detailed history (drug history, incubation period, route of administration, purpose of drug intake, any pre-existing or co-morbid diseases, past history of ADR), clinical examination (morphology of lesions, sites of involvement, any extracutaneous manifestations), and review of any available records were done. We used the Naranjo Adverse Drug Reaction Probability Scale for causality assessment and classified the ADRs as definite, probable, and possible. Based on a Modified Hartwig scale, drug reactions were graded from levels 1-7. Levels 1 and 2 were classified as mild, levels 3 and 4 were moderate, and levels 5-7 were severe. Preventability was assessed using the Schumock and Thornton scale and ADRs were classified as definitely preventable, probable, and not preventable. Investigations that included complete blood counts, blood sugar, liver, and renal function tests were done. When indicated, we ordered VDRL and HIV tests.

Based on history and clinical examination, the CADR were analyzed for demographic parameters, types of CADR, classes of drugs and individual drugs that cause CADR, any predisposing factors, systemic involvement and sites of involvement. Severe drug reactions included acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), erythroderma, and SJS/TEN. Descriptive statistics were used to analyze the data and the results

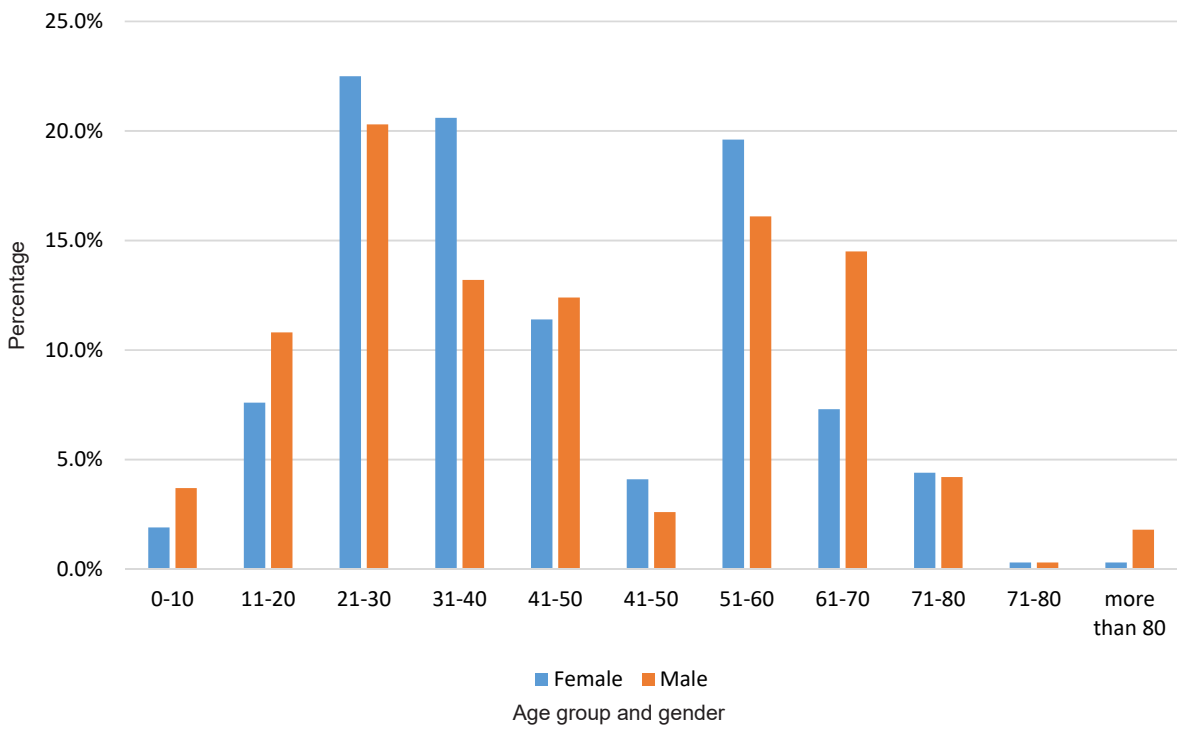

Figure 1. Age (years old) and gender distribution of the study population.

were expressed as mean ± standard deviation and percentages.

RESULTS

The total number of patients who attended the dermatology outpatient department during the one year study period was 43810, out of which 695 patients were found to suffer from CADRs, which accounted for an incidence of 1.6%.

Of the 695 patients, there were 379 (54.5%) males and 316 (45.5%) females. The male to female ratio was 1.2:1. Figure 1 shows the age and gender distribution.

The mean age of patients who developed CADRs was 42.01 years (range: 2 months to 90 years). The most common age group affected was 21-30 years, followed by 51-60 years, and 31-40 years. There were one third of the reactions in patients above the age of 50 years.

A total of 590 (84.89%)patients presented with only cutaneous lesions, 77 (11.08%) patients had both cutaneous and mucosal lesions, and 28 (4.03%) patients had mucosal lesions only. We documented a previous history of drug allergies in 65 (9.35%) patients. Co-morbidities noticed in the study population included hypertension (197, 28.35%), diabetes mellitus (125, 17.99%) and tuberculosis (72, 10.33%).

A total of 39.71% of patients presented with<10% of body surface area involvement, while 42.01% had 10%-30% body surface area involvement. More than 30% of body surface area involvement was present in 18.27% of cases.

Of the various types of CADRs seen in our study, exanthem was the most common drug eruption (28.63%) followed by acute urticaria (18.13%). Table 1 shows the frequency of various CADRs observed in this study. The drug reaction was benign in 87.05% cases while 12.95% patients had severe CADRs. Severe cutaneous adverse reactions (SCARs) included AGEP, DRESS, erythroderma, and SJS/TEN.

Exanthem

Exanthematous drug reactions showed a predilection for male gender (57.3%) in the present study. The age group most commonly affected was 51-60 years (20.1%). The majority of cases (78.9%) were due to a single drug, while 42 (21.1%) were because of multiple drugs.

Table 1. Cutaneous adverse drug reactions observed in this study.

Clinical diagnosis	Frequency	Percent
Exanthem	199	28.63
Acute urticaria	126	18.13
Fixed drug eruption (FDE)	95	13.67
Bullous FDE	10	1.44
Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)	39	5.61
Photosensitivity	31	4.46
Erythroderma	27	3.88
Lichenoid eruption	25	3.60
Drug reaction with eosinophilia and systemic symptoms (DRESS)	21	3.02
Vasculitis	20	2.88
Hyperpigmentation	20	2.88
Erythema multiforme	18	2.59
Acneiform eruptions	17	2.45
Generalized pruritus	14	2.01
Ichthyosis	6	0.86
Papulosquamous rash	6	0.86
Drug induced lupus erythematosus (LE)	5	0.72
Hand foot skin reaction	3	0.43
Acute generalized exanthematouspustulosis (AGEP)	3	0.43
Mucositis	2	0.29
Anaphylaxis with angioedema	2	0.29
Gingival hyperplasia	1	0.14
Onycholysis	1	0.14
Sweet`s syndrome	1	0.14
Petechiae	1	0.14
Bullous pemphigoid	1	0.14
Symmetrical drug related intertriginous and flexural exanthema (SDRIFE)	1	0.14
Total	695	100.00

Class and frequencies of drugs implicated in exanthema

The most common class of drug that caused exanthema was antimicrobial agents (37.2%) followed by NSAIDS (24.62%) as seen in Table 2.

Table 2. Frequency of different classes of drugs that caused exanthema.

Class of drug	Frequency	% of total
Antimicrobials	74	37.2
NSAIDS	49	24.62
Antiepileptics	12	6.03
Hypertensives	8	4.02
Antitubercular	5	2.52
Miscellaneous	13	6.53

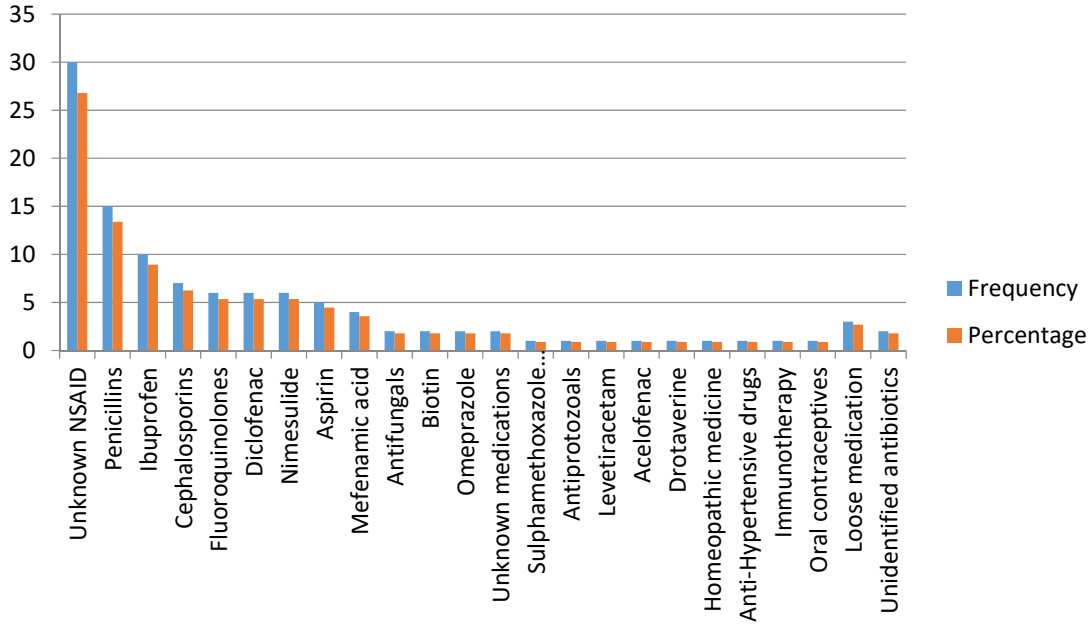

Figure 2. Frequency and percentage of individual drugs implicated in acute urticaria.

In the antibiotics, penicillins and cephalosporins were responsible for the maximum number of exanthematous reactions (Table 3).

Acute urticaria

Acute urticaria was the second most common morphology seen among adverse cutaneous reactions with equal affection of males and females. The age groups most commonly affected were 21-30 years, 31-40 years, and 11-20 years in decreasing order. The most common drug responsible for acute urticaria was NSAIDS (56.2%), followed by antibiotics (28.57%), and miscellaneous drugs that included antihypertensives, proton pump inhibitors, and biotin supplements. Amongst NSAIDS, the drug was unknown in 26.79% cases followed by ibuprofen in 9 (8.93%) patients, and diclofenac and nimesulide (5.36% each). Out of antimicrobials, penicillins were the offending agents in 13.39% of cases followed by cephalosporins(6.25%) and fluoroquinolones (5.36%).

Table 3. Frequency of type of antimicrobial agents implicated in exanthema.

Class of antimicrobial	Frequency	% in class
Penicillins	40	54.05
Cephalosporins	16	21.62
Fluoroquinolones	5	6.76
Sulfones	3	4.05
Nitroimidazoles	3	4.05
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	1	1.35
Polymyxin B	1	1.35
Tetracyclines	1	1.35
Unidentified antibiotics	4	5.41
Total	74	100

Fixed drug eruption (FDE)

FDE was the third most common reaction pattern, which showed a predilection for male gender with a M:F ratio of 1.76:1. The mostly affected age group was 21-30 years (28.6%), followed by 31-40 years (19.0%) and 41-50 years (15.2%). Bullous FDE was seen in 9.52% of patients. FDE was caused by NSAIDS in 44.76% patients, followed by antimicrobials in 25.70%, and antifungals in 4.76% cases. Figure 3 gives a detailed description of individual antimicrobial agents that caused FDE.

Photosensitive drug eruptions

Out of 31 photosensitive reactions, 17 (54.84%) were males and 14 (45.16%) were females. The most common age group was between 51-60 years followed by 21-30 years. The most common offending drugs were antibiotics (70%), out of which the most frequent culprits were tetracyclines and fluoroquinolones.

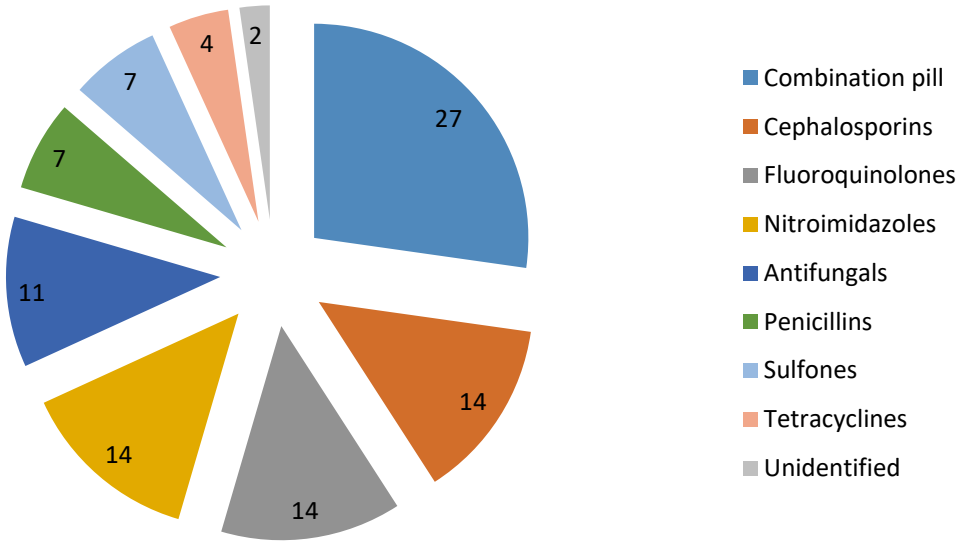

Figure 3. Percentage of antimicrobials that caused fixed drug eruption (FDE).

Figure 4 gives a detailed description of individual drugs that caused photosensitive eruptions.

Lichenoid drug eruptions

Lichenoid drug reactions were observed in 3.6% patients. There was no gender predilection seen (males 52% and females 48%). The most common age group was between 61-70 years (28%), which showed a predisposition for the elderly population. The most common drugs implicated in lichenoid reactions included oral contraceptive pills (OCPs), statins, NSAIDS, beta blockers, and thiazide diuretics as shown in Figure 5.

Vasculitis

The incidence of drug induced vasculitis in the

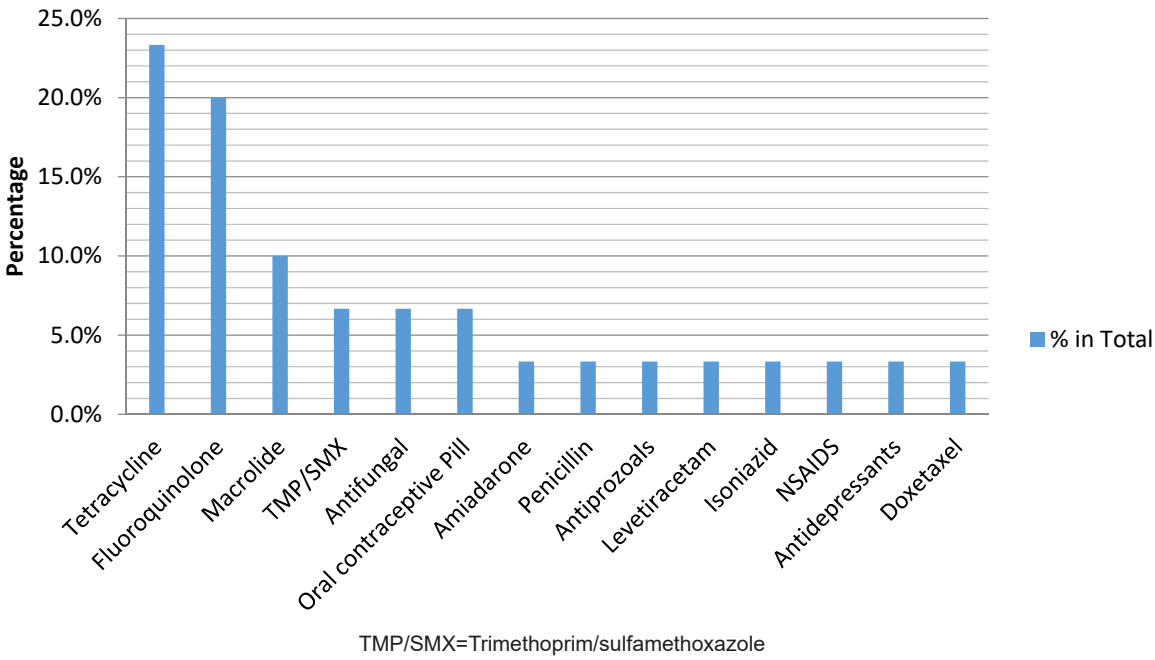

Figure 4. Individual drugs that caused photosensitivity.

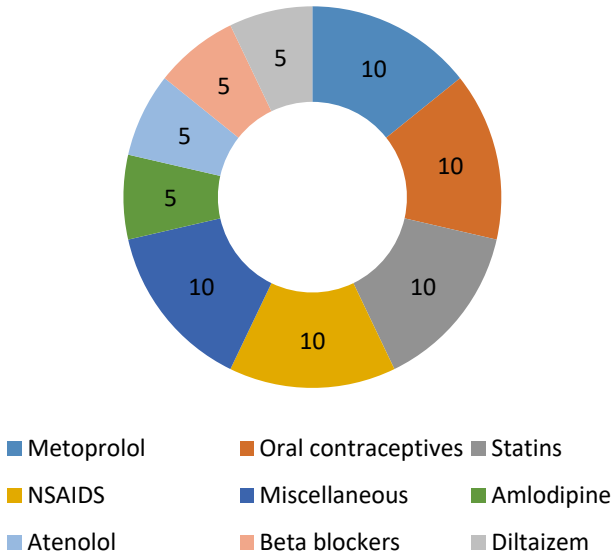

Figure 5. Individual drugs that caused lichenoid drug rash.

present study was 2.88%with an equal distribution among males and females, and a predilection for the 51-60 years age group. Vasculitis was seen in patients who took tetracyclines, rifampicin, NSAIDS, and allopurinol (13.33% each), while dapsone, thiazides, teicoplanin, carbamazepine, naproxen, and beta blockers each constituted 6.67% patients.

Severe cutaneous adverse reactions (SCARs)

SCARs were seen in 90 (12.95%) patients. A female preponderance was seen, with a M:F ratio of 0.7:1. The age group most commonly affected was 31-40 years (24.4%), followed by 21-30 years (14.4%) and 51-60 years (13.3%).The common causative drugs included antiepileptics (21.1%), a miscellaneous group that consisted of unknown drugs, indigenous medications and over-the-counter prescriptions (20.0%) followed by hypouricemics (11.1%). Figure 6 lists the details of individual drugs that caused SCARs.

Stevens-Johnson syndrome (SJS)/Toxic epidermal necrolysis (TEN)

The total number of cases of SJS and TEN reported were 39 (5.61%). The female to male ratio was 1.76:1. The most common age groups affected were 21-30 years and 31-40 years (7 patients in each age group). The most frequently offending drugs included phenytoin (28.1%), allopurinol (15.6%), NSAIDS (12.6%), lamotrigine (9.4%), penicillins (6.25%), nitroimidazole (6.25%), and indigenous medications (6.25%).

Assessment of causality

According to the Modified Hartwig severity classification, the ADR were mild in 133 (19.1%) patients, moderate in 520 (74.8%), and severe in 42 (6%).

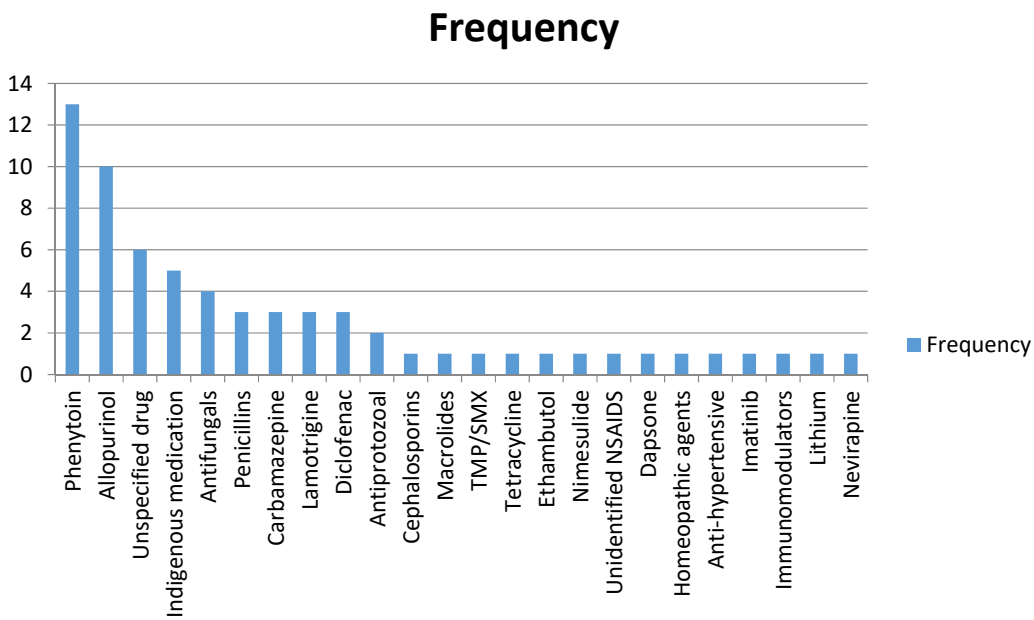

Figure 6. Individual drugs that caused severe cutaneous adverse reactions (SCARs).

Schumock and Thornton scale

Preventability criteria according to the Schumock and Thornton scale showed that 410 (59%) were not preventable, while 167 (24%) were definitely preventable, and 118 (17%) were probably preventable.

Naranjo adverse drug reaction probability scale

There were 692 probable reactions while 3 cases were possible drug rashes.

DISCUSSION

Adverse cutaneous drug reactions vary in their patterns of morphology and distribution. In previous studies, the most common morphologic patterns were exanthematous, urticarial and/or angioedema, FDE, and erythema multiforme [4].

Incidence

We have observed an incidence of 1.6% in our study. The incidence of CADRs in developed countries ranges from 1%-3% among inpatients, whereas in developing countries such as India, it varies from 2%-5% among inpatients [5,6]. Vijendra et al. have reported that CADRs occurred in 2%-3% of patients who received drug therapy for various reasons [3]. In a study conducted by Grover, ADRs were responsible for 7% of hospital admissions, out of which CADRS constituted 2-3% [2]. According to Pudukadan and Thappa, CADRs accounted for approximately 3% of all disabling injuries during hospitalizations and commonly used drugs had reaction rates of over 1% [7]. Ramakrisnaiah et al. have reported the incidence of ADRs in an Indian population that ranged between 1.8% and 25.1% [8]. This wide variation in the reported incidence of CADRs depends upon the diversity of the study population, pattern of drug prescription, and different clinical scenarios.

In this study, the incidence of CADRs among outpatients was 13.5/1000 while inpatients showed a lower incidence of 2.3/1000. Patel and Maratha reported rates of 8.72/1000 for outpatients and 82.59/1000 for inpatients [9]. The difference could be accounted to the fact that we only choose patients from the dermatology department and excluded cross consultations from the study. The total incidence of CADRs in our study was 1.6%, which was similar to that reported by Chatterjee et al. (2.6%) [10] and much higher than observed by Qayoom et al. (0.19%) [11]. This difference was attributed to the varying demographic features of the study population and whether the study was conducted in an outpatient department, inpatient department, or both.

Age and sex distribution

The mean age of patients that developed CADRs in our study was 42.01 years and the most common age group affected was 21-30 years (21.29%). This finding was similar to the studies conducted by Pudukadan and Thappa [7], Vijendra et al. [3], and Sharma et al. [12].

In our work, CADRs showed a predilection for the male gender, which was similar to findings observed by Sharma et al. [12] and Vijendra et al. [3] On the contrary, Pudukadan and Thappa [7] and Qayoom et al. [11] have reported a female preponderance. This difference may be due to different health care seeking patterns in various areas.

Mucosal versus cutaneous lesions

In this study, cutaneous lesions alone were present in 84.89%, both cutaneous and mucosal involvement in 11.08%, and 4.03% of patients had only mucosal lesions. Qayoom et al. [11] also reported cutaneous involvement in 49.33%, cutaneous and mucosal involvement in 46.66%, and only mucosal involvement in 4%. Patel and Marfatia [9] showed mucosal involvement in 16.26%. Only cutaneous involvement was predominant in these studies, which was similar to the pattern seen in the present study.

Body surface area

The majority of patients (81.7%) had less than 30% affected body surface area. In a study by Pudukadan and Thappa [7], 45.6% had 0-10% body surface area involvement; 31.4% patients had 31-90%, 16.6% had 11%-30%, and just 3 had more than 90% body surface area involvement. However, Patel and Marfatia [9], reported surface area involvement

of <10% in 58.57% of patients, 10%-30% in 20.95% of patients, and >30% in 20.48%. The higher percentage of involvement could be an observer bias or an interval lag of reporting a drug reaction at a tertiary hospital after primary care.

History of drug rash

A prior history of drug allergies was reported in 9.35% of cases. Similar observations were reported by Patel and Marfatia (10.84%) [9], Pudukadan and Thappa (14.4%) [7], and Qayoom et al. (13.3%) [11].

Clinical diagnosis

The most common benign ADR was exanthem in 28.64% of patients followed by acute urticaria in 18.13%, and FDE in 15.11%.Studies have shown variations in predominant morphological type of ADR. Sharma et al. [12] showed exanthem to be the most common clinical diagnosis, a finding similar to our study. Patel and Marfatia [9] and Sharma et al. [12] reported a higher incidence of FDE than urticaria in contrast to our observations. Jhaj et al. [13] found maculopapular rash to be the most common followed by urticaria, which was similar to our findings.

Exanthem

According to Rook's Textbook of Dermatology [14], exanthem is considered the most common cutaneous drug eruption that accounts for 40% of reactions. Similarly, we have observed that exanthem was the most common ADR, which was supported by Patel et al. study [15]. The most frequently implicated drugs were antibiotics that included semi-synthetic penicillin and trimethoprim sulfamethazole – a finding similar to our study. Hernandez-Salazar et al. [16] and Malhotra et al. [17] also reported that maculopapular rash was the most common morphological type and the penicillin group was the most common culprit. In contrast, Qayoom et al. [11] reported that antiepileptics were a major cause of reactions; however, exanthem was not the most common type of CADRs in their study.

Acute urticaria

Acute urticaria was the second most common type of CADRs seen in our study with no gender predilection. Acute urticaria was mostly caused by NSAIDS followed by antimicrobials. In Rook's Textbook of Dermatology [14], as well as studies done by Shipley and Ormerod [18] and Mathelier-Fusade [19], acute urticaria was found to be the second most common drug reaction. NSAIDS were the most common offending drugs, which agreed with our study. However, Andrews' Diseases of the Skin mentioned penicillins as the most common culprit. Chatterjee et al. [10] also found antimicrobials to be the most common cause of urticaria.

Fixed drug eruption (FDE)

FDE is characterized by recurrent well-defined lesions that occur at the same site each time the offending drug is taken [21,22]. Our study found a male preponderance for FDE. This observation was also reported by Pai et al. [23] and Sehgaland Srivastava [24], where as a study conducted in Singapore [25] found no sex predilection. This could be due to the differences in ethnicities of the study populations.

Pai et al. [23] reported that three fourths of the FDE cases were attributed to NSAIDS and antimicrobials, which was similar to our study. However, Pudukadan and Thappa [7] reported that sulfur based drugs like co-trimoxazole and dapsone were the main cause of FDE. Patel and Marfatia [9] and Hotchandani et al. [26] reported that co-trimoxazole was the main causative drug of FDE.

In the present study, bullous FDE was seen in 9.52% cases, which was much lower than reported by Pai et al. (33%) [23].

Photosensitive drug eruptions

There were photosensitive drug eruptions in 4.6% of patients, with no gender predilection noted and a predilection for the age group of 51-60 years. However, the incidence of photosensitive drug reactions was much higher (8%) in a study from Norway [27]. This could be explained on the basis of different climatic conditions that prevail in the study countries. Case reports have confirmed that antibiotics are a common cause of photosensitivity, a finding similar to our study [28,29].

Lichenoid drug eruption

Lichenoid drug reactions were observed in 3.6% patients in the present study. They were mostly caused by OCPs, statins, NSAIDS, beta blockers, and thiazide diuretics. Margo and Crowson reported that lichenoid drug eruptions occurred with antibiotics, ACE inhibitors, lipid lowering agents, beta blockers, H2 antagonists, NSAIDS, and hydroxycholoroquine [30].

Vasculitis

The incidence of drug induced vasculitis in the present study was 2.88%, which was comparable to studies by Vijendra et al. [3] (2.6%) and Lee et al. [25]

Severe cutaneous adverse reactions (SCARs)

SCARs were seen in 12.95% patients with a predilection for females. Lee et al. [25] found an incidence of 36.1% CADR. The most commonly implicated drugs were phenytoin (19.7%), allopurinol (15.5%), and unknown drugs (9.09%).

Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)

The incidence of SJS and TEN was 5.61% in the present study; however, other studies reported an incidence of 4% (Patel and Marfatia [9]), 22.2% (Malhotra et al. [17]), and 18.8% (Jhaj et al. [13]). The comparatively low incidence in present study could be due to the fact that patients were only included from the dermatology outpatient department.

Phenytoin was implicated in 28.1% patients, allopurinol in 15.6%, followed by lamotrigine (9.4%), diclofenac (12.6%), and penicillin (6.25%). Devi et al. [31] also reported antiepileptics to be the most common agent that caused SJS and TEN, which was similar to our findings. On the contrary, Patel and Marfatia [9] showed the main causative factor to be NSAIDS.

Schumock and Thornton scale

According to Qayoom et al. [11], 52 (69.3%) were not preventable, 17 (22.7%) were definitely preventable, and 6 (8.0%) were probably preventable. These observations were similar to our study.

Naranjo adverse drug reaction probability scale

This scale assesses the probability that a drug caused a certain reaction. Qayoom et al. [11] reported that 13.3% of the reactions were possible, 81.3% were probable, and 5.3% were definite. On the contrary, our study did not have any definite reactions because rechallenge was not attempted in our cases.

CONCLUSION

Most of the patients (84.89%) only presented with cutaneous lesions, whereas 11.08% patients presented with cutaneous as well as mucosal lesions, and 4.03% of cases only had mucosal lesions. Most of the drug reactions in the study were benign (87.05%), while SCARs were noted in 12.95% of patients.

Exanthems were the most common benign reactions followed by acute urticaria and FDE, whereas SJS was the most common reaction among SCARs. Antibiotics and NSAIDs were the most common culprits for benign drug reactions and antiepileptics were a major cause of SCARs. No rechallenge of any suspected drug was done in our study. Selection bias was present as only patients who presented to the dermatology outpatient department were enrolled in the study.

Conflict of Interest: None declared.

REFERENCES

1. Mahapatra S, Keshri U. Adverse cutaneous drug reactions in a tertiary care center patients: A prospective analysis. J App Pharm Sci.2012;2:96-8.
2. Grover S. Severe cutaneous adverse reactions. Indian J Dermatol Venereol Leprol.2011;77:3-6.
3. Vijendra R, Pundarikaksha HP, Gopal MG, et al. A prospective study of cutaneous adverse drug reaction in a tertiary care hospital. NJBMS. 2013;3:44-51.
4. Stern RS, Wintroub BU. Cutaneous reactions to drugs. In: Freedberg IM, Eisen AZ, Wolff K, et al (Eds). Fitzpatrick's dermatology in general medicine. New York: McGraw-Hill; 1999.1634-42.
5. Bigby M. Rates of cutaneous reactions to drugs. Arch Dermatol.2001;137:765-70.
6. Craig KS, Edward WC, Anthony AG. Cutaneous drug reactions. Pharmacol Rev. 2001;53:357-79.

7. Pudukadan D, Thappa DM. Adverse cutaneous drug reactions: clinical pattern and causative agents in a tertiary care centre in South India. Indian J Dermatol Venereol Leprol. 2004;70:20-4.
8. Ramakrisnaiah H, Krishnaiah V, Pundarikaksha HP, et al. A prospective study on adverse drug reactions in outpatients and inpatients of medicine department in a tertiary care hospital. Int J Basic Clin Pharmacol. 2015;4:515-21.
9. Patel RM, Maratha YS. Clinical study of cutaneous adverse drug eruptions in 200 patients. Indian J Dermatol Venereol Leprol. 2008;74:430.
10. Chatterjee S, Ghosh AP, Barbhuiya J, et al. Adverse cutaneous drug reactions: A one year survey at a dermatology outpatient clinic of a tertiary hospital. Indian J Pharmacol. 2006;38:429-31.
11. Qayoom S, Bisati S, Manzoor S, et al. Adverse cutaneous drug reactions – a clinico-demographic study in a tertiary care teaching hospital of the Kashmir Valley, India. Arch Iran Med. 2015;18:228-33.
12. Sharma VK, Sethuraman G, Kumar B. Cutaneous adverse drug reactions: clinical pattern and causative agents – a 6 year series from Chandigarh, India. J Postgrad Med. 2001;47:95-9.
13. Jhaj R, Uppal R, Malhotra S, et al. Cutaneous adverse reactions in in-patients in a tertiary care hospital. Indian J Dermatol Venereol Leprol. 1999;65:14-7.
14. Ardern-Jones MR, Lee HY. Benign cutaneous adverse reactions to drugs. In: Griffiths C, Barker J, Bleiker T, et al (Eds). Rook's textbook of dermatology. Chichester, West Sussex: Wiley-Blackwell; 2016. 118.1-17.
15. Patel TK, Thakkar SI, Sharma D. Cutaneous adverse drug reaction in Indian population: A systemic review. Indian Dermatol Online J.2014;5:S76-86.
16. Hernandez-Salazar A, Rosales SP, Rangel-Frausto S, et al. Epidemiology of adverse cutaneous drug reactions. A prospective study in hospitalized patients. Arch Med Res. 2006;37:899-902.
17. Malhotra S, Chopra SC, Dogra A, et al. Cutaneous adverse drug reaction-one year pharmacovigilance study in a tertiary care hospital. Indian J pharmacol. 2004;36:S41-2.
18. Shipley D, Ormerod AD. Drug-induced urticaria: Recognition and treatment. Am J Clin Dermatol.2001;2:151-8.
19. Mathelier-Fusade P. Drug-induced urticarias. Clin Rev Allergy Immunol.2006;30:19-23.
20. James W, Berger T, Elston D. Contact dermatitis and drug eruptions. In: James W, Berger T, Elston D (Eds). Andrew's diseases of the skin. Philadelphia, PA: Elsevier Saunders;2011. 108-54.
21. Ozkaya E. Fixed drug eruption: state of the art. J Dtsch Dermatol Ges.2008;6:181-8.
22. Rahman MH. Fixed drug eruption in Bangladeshi population: confirmed by provocative test. Int J Dermatol.2014;53:255-8.
23. Pai VV, Kikkeri NN, Athanikar SB, et al. Retrospective analysis of fixed drug eruptions among patients attending a tertiary care center in Southern India. Indian J Dermatol Venereol Leprol. 2014;80:194.
24. Sehgal VN, Srivastava G. Fixed drug eruption (FDE): changing scenario of incriminating drugs. Int J Dermatol.2006;56:897-908.
25. Lee HY, Tay LK, Thirumoorthy T, et al. Cutaneous adverse drug reactions in hospitalized patients. Singapore Med J. 2010;51:767-74.
26. Hotchandani SC, Bhatt JD, Shah MK. A prospective analysis of drug-induced acute cutaneous reactions reported in patients at a tertiary care hospital. Indian J Pharmacol. 2010;42:118-9.
27. Selvaag E. Clinical drug photosensitivity. A retrospective analysis of reports to the Norwegian Adverse Drug Reactions Committee from the years 1970-1994. Photodermatol Photoimmunol Photomed. 1997;13:21-3.
28. Domagala JM. Structure-activity and structure-side effect relationships for the quinolone antibacterials. J Antimicrob Chemother. 1994;33:685-706.
29. Fish DN. Fluoroquinolone adverse effects and drug interactions. Pharmacotherapy. 2001;21:253S-72S.
30. Margo CM, Crowson AN. Lichenoid and granulomatous dermatitis. Int J Dermatol. 2000;39:126-33.
31. Devi K, George S, Narayanan B. A study of severe cutaneous adverse reactions to drugs with special reference to treatment outcome. Indian J Dermatol Venereol Leprol. 2016;82:239.