National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Cutaneous adverse drug reactions from a teaching hospital in Bengaluru: An observational study to determine the spectrum and outcome

Jayanthi C R, Ankita Bedwal, Kavitha Rajarathna

Department of Pharmacology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India

Correspondence to: Ankita Bedwal, E-mail: anky.995@gmail.com

Received: December 06, 2016; **Accepted:** December 25, 2016

ABSTRACT

Background: Cutaneous adverse drug reactions (CADRs) are frequent manifestations of drug reactions that can lead to discontinuation of treatment, impaired quality of life and increased economic burden. Knowledge of drugs causing CADRs help in choosing safer drugs. **Aims and Objectives:** To determine the clinical spectrum, causality, severity, and preventability of CADRs. **Materials and Methods**: An observational study conducted from 2012 to 2016 to analyze the CADRs reported from Dermatology Department, of Bangalore Medical College and Research Institute to adverse drug reaction (ADR) Monitoring Center. Patient's demographics, clinical and drug data, details of ADRs were collected as per CDSCO form. Causality, severity, and preventability were assessed using relevant scales. **Results:** Out of 809 ADRs reported, 230 were CADRs. Male preponderance (56%) was seen. Age group of 21-40 years (57%) was most affected. Maximum CADRs were seen with beta-lactam class of drugs (20%), followed by nonsteroidal anti-inflammatory drugs (17.4%) and antiepileptics (13.5%). Maculopapular rash (26%) was the most common CADR. Stevens–Johnson syndrome (SJS) contributed to the majority of severe CADRs. Causative drug was withdrawn in 90% of cases. Causality assessment indicated 80.4% as probable and 19.6% as possible cases. 81% of CADRs were of moderate severity, and only 6% were severe like SJS. 11% were "definitely preventable" CADRs. **Conclusion:** Wide clinical spectrum of CADRs was observed. Definitely preventable CADRs were due to improper recording of history of drug allergy and wrong choice of self-medication by the patients. Inconsistent with the previous literature, the incidence of diclofenac-induced SJS was found high.

KEY WORDS: Cutaneous Adverse Drug Reactions; Causality; Severity; Preventability

INTRODUCTION

Adverse drug reaction (ADR) has been defined by the World Health Organization (WHO) 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."[1] It has been estimated to be fourth or sixth leading cause of death among hospitalized patients.[2] It also leads to increased financial burden as the ADR-related costs, such as hospitalization, surgery and lost productivity, often exceed the cost of the medications.[3] Cutaneous ADR (CADR) is any undesirable change in the structure or function of the skin, its appendages or mucous membrane and encompasses all adverse events related to drug eruption, regardless of the etiology.[4]

CADR is the most frequent of all manifestations of drug sensitivity.[4] It is recognized to be a major health problem worldwide having an incidence of 1-3% in developed countries and 2-5% in developing countries.[5,6] There is a wide spectrum of CADR ranging from a transient maculopapular rash to fatal toxic epidermal necrolysis (TEN).[7]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.1235625122016	

Drugs, no matter how safe and efficacious, are always associated with risk of adverse reactions.[8] Development of a skin eruption frequently leads to discontinuation of the treatment, impairment of quality of life and increasing costs of patient care.[4] Commonly used drugs implicated in CADRs are penicillins, sulfonamides, anticonvulsants, nonsteroidal anti-inflammatory drugs (NSAIDs), etc.[4] Early recognition and withdrawal of the offending drug improves outcome in the management of CADR. Knowledge of drugs that can cause CADR can help physicians in choosing safer drugs.[4]

Pharmacovigilance is "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems." In 1968, the WHO established the International Drug Monitoring Programme to collect data on ADRs and to issue public warnings when warranted. The monitoring and reporting of an ADR is an integral part of drug therapy but is still at infant stage in India.[9] As new drugs are being introduced every year, every health-care professional must have knowledge about the importance of pharmacovigilance.[1]

As the pattern of CADRs is changing every year with the introduction of new medications and evolving prescription practices, understanding its precise nature may help narrow down the search for the offending drug.[4,10] Bangalore Medical College and Research Institute (BMC and RI) is one of the ADR Monitoring Centre under Pharmacovigilance Programme of India (PvPI). This study has been undertaken to assess the clinical spectrum, causality, severity, and preventability of various CADRs reported from BMC and RI to the PvPI.

Aims of the Study

1. To determine the clinical spectrum of CADRs and the drugs associated with it
2. To assess the causality, severity, and preventability of CADRs.

MATERIALS AND METHODS

An observational study was conducted from January 2012 to May 2016 to analyze the CADRs reported spontaneously from Dermatology Department of BMC and RI to ADR Monitoring Centre, under PvPI. Patient's demographics, clinical and drug data, details of ADR, onset time, causal drug details, outcome, and severity were collected as per CDSCO form. Causality was assessed using WHO-ADR probability scale; severity was assessed using modified Hartwig and Siegel severity scale and preventability were assessed using modified Schumock and Thornton scale. The data were analyzed using descriptive statistics to study the characteristics of the ADRs. The results were expressed as percentages, odds ratio, etc.,

RESULTS

A total of 809 ADRs were reported, of which 230 (28.4%) were CADRs. Male patients constituted 56% of the total cases. The age group of 21-40 years (57%) was most affected followed by 41-60 years (22.6%) (Table 1). The age range was 4-79 years.

Antimicrobial agents accounted for the highest number of CADRs (37.8%), followed by NSAIDs (17.4%) and antiepileptic drugs (13.5%) (Table 2). Ceftriaxone (12.6%) was the most common offending drug. Other commonly implicated drugs were phenytoin (10.9%), nevirapine (10.9%), and diclofenac (10.4%) (Table 3).

Among the various known patterns of CADRs, the most common was maculopapular rash (26%), followed by fixed drug eruptions (FDEs) (21.7%), and erythematous rash (21.3%) (Figure 1). The offending drugs commonly associated with maculopapular rash were nevirapine (35%), phenytoin (17%), ceftriaxone (15%), and diclofenac (5%). FDEs were mainly caused by NSAIDs (30%) and fluoroquinolones (10%).

The most common severe CADR reported was Stevens–Johnson syndrome (SJS) (Figure 2), phenytoin (45.5%) and diclofenac (18.2%) being the most common causative agents (Table 4). The odds of developing SJS were 2.75 times more with phenytoin compared to diclofenac. Other severe CADRs

Table 1: Demographic details

Variables	Characteristics	Number of CADRs *N*=230 (%)
Age (years)	0-20	32 (13.9)
	21-40	131 (57)
	41-60	52 (22.6)
	>60	15 (6.5)
Gender	Male	129 (56.1)
	Female	101 (43.9)

CADR: Cutaneous adverse drug reactions

Table 2: Therapeutic classes of drugs causing CADRs

Therapeutic classes of drugs	Number of CADRs *N*=230 (%)
Antimicrobial agents	87 (37.8)
NSAIDs	40 (17.4)
Antiepileptic drugs	31 (13.5)
Antiretroviral agents	31 (13.5)
Corticosteroids	12 (5.2)
Antifungal agents	4 (1.7)
Gastrointestinal agents	4 (1.7)
Miscellaneous	21 (9.13)

CADR: Cutaneous adverse drug reactions, NSAIDs: Nonsteroidal anti-inflammatory drugs

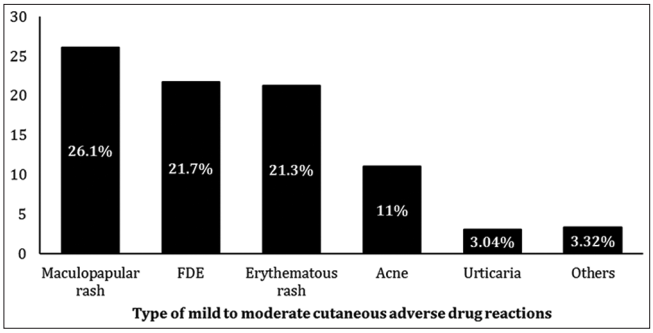

Figure 1: Mild-to-moderate cutaneous adverse drug reactions

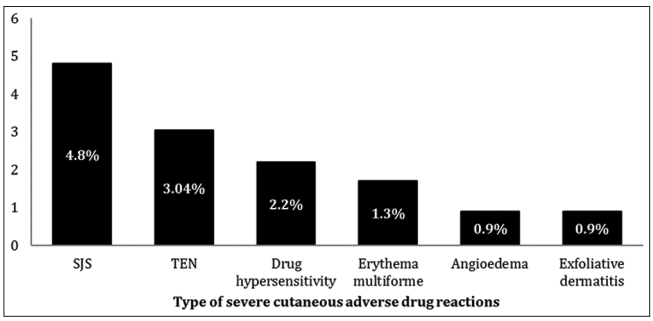

Figure 2: Severe cutaneous adverse drug reactions

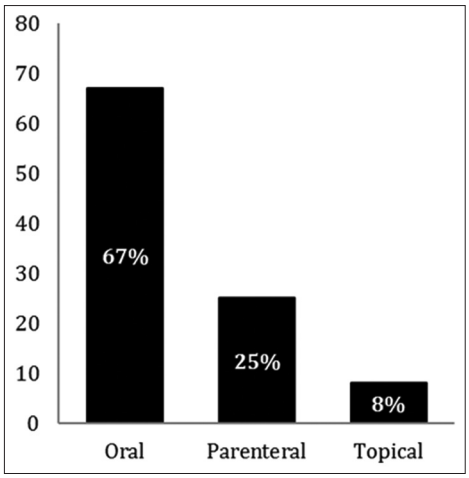

Figure 3: Routes of administration

encountered were erythema multiforme, TEN, angioedema, etc. Some rare CADRs, such as ambroxol-induced exfoliative dermatitis and dapsone hypersensitivity syndrome (DHS), were also noted.

The oral administration of drugs was associated with a maximum number of CADRs (67%) followed by parenteral route (25%) (Figure 3). Interval between drug intake and first appearance of cutaneous lesions (reaction time) varied from 10 min to 108 days. Most of the CADRs occurred between 1 and 10 days of drug administration (55%).

The causative drug was withdrawn in 90% of cases. 86% of cases were managed with additional treatment, and no mortality was noted. According to WHO-UMC probability scale, 80.4% had probable causality and 19.6% had possible

Table 3: Antimicrobial agents causing CADRs

Class of antimicrobials	Antimicrobial agents	Number of CADRs (*N*=87)
Beta-lactams	Ceftriaxone	29
	Cefixime	5
	Cefotaxime	5
	Amoxicillin-clavulanic acid	5
	Piperacillin-tazobactum	3
	Cefuroxime	1
Fluoroquinolones	Ofloxacin	14
	Ciprofloxacin	10
	Levofloxacin	1
Antitubercular drugs	Rifampicin	8
	Isoniazid	1
Macrolides	Azithromycin	1
	Erythromycin	1
Sulfa drugs	Cotrimoxazole	1
	Dapsone	1
Antiamoebic drugs	Metronidazole	1

CADR: Cutaneous adverse drug reactions

Table 4: Drugs causing severe CADRs

Severe CADRs	Drugs
SJS (11)	Phenytoin (5), diclofenac (2), ceftriaxone (1), cefuroxime (1), nevirapine (1), carbamazepine (1)
TEN (3)	Phenytoin (2), aceclofenac (1)
Drug hypersensitivity (5)	Phenytoin (3), dapsone (1), carbamazepine (1)
Erythema multiforme (4)	Paracetamol (1), clobazam (1), diclofenac (1), phenytoin (1)
Angioedema (2)	Efavirenz (1), ceftriaxone (1)
Exfoliative dermatitis (1)	Ambroxol (1)

SJS: Stevens–Johnson syndrome, TEN: Toxic epidermal necrolysis

(Figure 4). The majority of the CADRs (81%) was of moderate severity (Figure 5). Severe CADRs were 6% such as clobazam-induced erythema multiforme and DHS. Preventability scale indicates 86.5% to be "not preventable" and 11% to be "definitely preventable (Figure 6)."

DISCUSSION

CADRs are distressing to both the patients and physicians. It may lead to poor quality of life due to hospitalization, prolonged hospital stay, increased morbidity, and even mortality in cases of severe reactions.[4] Not warning a patient about potential adverse effects, prescribing a medicine to a previously sensitized patient, and prescribing a related medication with cross-reactivity are common medicolegal pitfalls.[4] In this study, a total of 230 CADRs were reported from January 2012 to April 2016. The majority of the patients

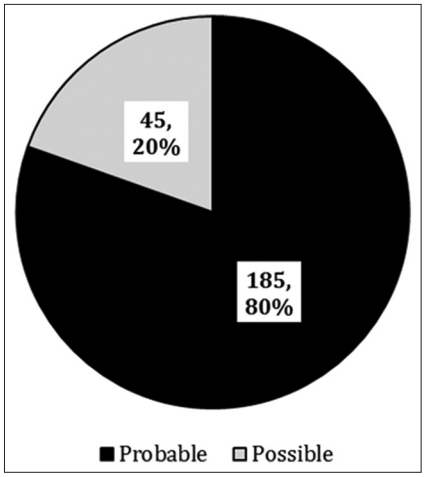

Figure 4: Causality assessment of cutaneous adverse drug reactions

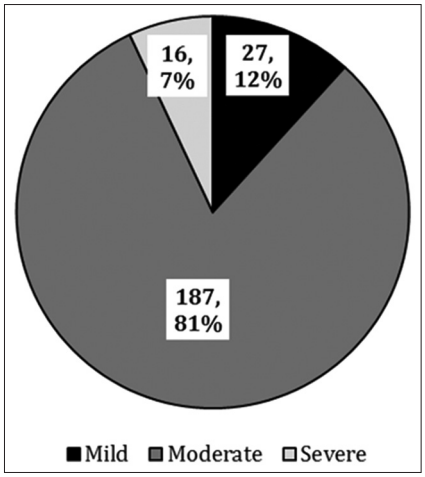

Figure 5: Severity assessment

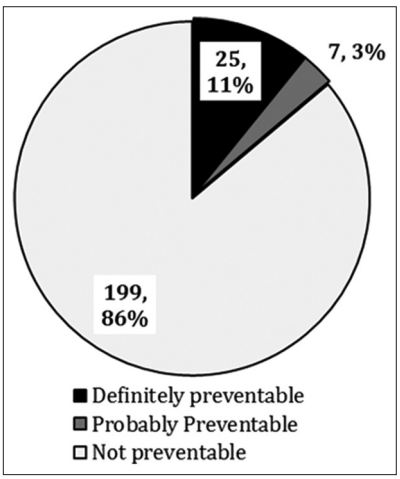

Figure 6: Preventability assessment

belonged to the age group of 21-40 years which is similar to the previous studies. Kongkaew et al. reported that higher number of CADRs in elderly could probably be due to polypharmacy and altered pharmacokinetics in them.[5,11] In our study, elderly constituted only 6.5% of the total CADRs. The youngest patient was 4-year-old, whereas the oldest patient was of 79 years. This shows that no age is exempted from CADRs. Our study showed that males (56%) were affected more than the females, which is similar to the study conducted by Sharma et al. in Jammu where male to female ratio was found to be 1.7:1.2.[5] Moulya et al. also observed a male preponderance (54.5%),[9] whereas Pudukadan and Thappa in South India showed men and women to be equally vulnerable (0.87:1).[12] As all these studies were institution based, the difference in demographic profile may be due to the regional variations in health-care seeking behavior of the patients.

This study showed maculopapular rash as the most common reaction (26.1%) followed by FDEs and erythematous rash. These findings are comparable to the study by Saha et al. in which maculopapular rash, FDE, and severe bullous eruptions were the most common.[4] Sushma et al. also reported maculopapular rash as the most common CADR followed by SJS and FDE.[13] In our study, nevirapine was the most common drug associated with maculopapular rash, followed by phenytoin. Nevirapine is most commonly used non-nucleoside reverse transcriptase inhibitor as part of first-line antiretroviral therapy (ART) as it is well tolerated and effective. With revision of ART initiation guidelines, the incidence of nevirapine-induced CADRs has also increased.[14] Nevirapine-induced rash is related to the 12-hydroxylation of nevirapine and is presumed to be due to the conversion of 12-hydroxy metabolite to a reactive quinone methide in skin.[15] FDE was the second most common CADR reported in our study, the main offending agents being diclofenac and ofloxacin. Acneiform eruptions contributed to 4.8% of the total cases, and topical steroids were common causative agents. In this study, severe CADRs constituted 6% of the total number, the most common being SJS (4.7%). SJS is an acute life-threatening mucocutaneous reaction characterized by extensive necrosis and detachment of the epidermis from skin. Its incidence is estimated to be 0.4-1.2/million person-years and has a mortality rate of nearly 1-5%.[16] It is a delayed type hypersensitivity reaction involving CD8+ cytotoxic T cells leading to keratinocyte apoptosis.[17] Cytolytic molecules FasL and granulysin also play a role in the pathogenesis of SJS/TEN.[17] This study showed phenytoin, diclofenac, and carbamazepine to be frequently associated with SJS. This finding was similar to the study conducted by Sasidharanpillai et al. in Kerala, who also found antiepileptic drugs to be the most common class of drugs associated with SJS.[18] Epilepsy is one of the most common neurological diseases, affecting about 50 million people worldwide, and antiepileptic drugs are the mainstay of treatment.[19] Antiepileptic drugs are metabolized to toxic substances that are subsequently detoxified in most individuals, but due to a genetic defect in some individuals, the metabolites may bind to the proteins and trigger an immune response leading to SJS.[17] Studies have also shown an association between HLA-B*1502 and SJS induced by carbamazepine and

phenytoin. Thus, identification of genetic polymorphisms offers the possibility of avoiding these high-risk drugs in genetically susceptible individuals.[20,21] Five cases of drug hypersensitivity reactions were reported in this study that included a case of DHS. Dapsone is used for treatment or prophylaxis of several infections and dermatological conditions such as bullous dermatoses, cutaneous vasculitis, and dermatitis herpetiformis. It is one of the commonly implicated drugs in drug-induced systemic hypersensitivity syndrome, apart from anticonvulsants, sulfonamides, etc. DHS is a rare dose-independent adverse effect that can develop several weeks to months after treatment initiation and the incidence reported ranges from 0.5% to 3%.[22] The proposed mechanism of DHS-metabolites of dapsone form haptens with the production of anti-dapsone antibodies. Differences in dapsone metabolism affect the production and detoxification of its reactive metabolites, and this might be responsible for differential susceptibility of people to the adverse effects of dapsone. Mortality of 12-23% has been reported in severe cases and thus early diagnosis, along with prompt treatment is essential to prevent fatalities.[22]

The most common class of drugs implicated in causing CADRs was antimicrobial agents. Beta-lactam antibiotics and fluoroquinolones were the major offending antimicrobials, with ceftriaxone being the most common beta-lactam, whereas ofloxacin was the most common fluoroquinolone. A possible mechanism for the development of drug-related exanthematic reaction is proposed to be an interaction between infection and drug exposure.[23] According to the study by Pudukadan and Thapa, sulfonamides were the most common offending antimicrobials, whereas Sharma et al. in Jammu showed Tinidazole to be most frequently associated with CADRs. This disparity may be due to the difference in pattern of drug use in different hospitals. In our study, NSAIDs accounted for a high number of the total CADRs and were next only to antimicrobials. Diclofenac, followed by ibuprofen, were the major offending NSAIDs. Diclofenac was frequently associated with moderate CADRs, most common being FDEs. The previous studies have shown that diclofenac-induced severe cutaneous reactions are very rare. In a study of 373 cases of TEN/SJS conducted by Mockenhaupt et al., the oxicam NSAIDs (piroxicam and tenoxicam) were shown to have the highest risk while the relative risk with diclofenac was low.[24,25] Inconsistent with the previous literature; the incidence of diclofenac-induced SJS was high in this study. This could be attributed to the increasing use of diclofenac as an over the counter drug for pain relief and inadequate recording of history of drug allergy in our set up.

The time interval between drug administration and the first appearance of cutaneous lesion varied with the type of CADR and the drug. In this study, it ranged from 10 min to 108 days. Most of the drug reactions occurred between 1 and 10 days of drug administration. Considering the different drugs and their respective reaction times, it appears that some of the drugs such as antimicrobial agents and analgesics have short reaction time, whereas antiepileptic drugs and antiretroviral drugs tend to take more time to develop the reaction.[4] This implies that physicians need to be vigilant about recent as well as remote drug history, which may be helpful in identifying the offending drug, and will prevent unnecessary withdrawal of innocuous medication.[4] According to the WHO-UMC causality assessment, the majority of the CADRs in our study had a probable causal relationship with the implicated drug. The causality could not be established as "Certain" because rechallenge was not done due to ethical considerations. Some of the CADRs had a possible causality, mostly owing to the concurrent use of other medications. 11% of the CADRs were definitely preventable, common reasons being the improper recording of the previous drug reaction history, and wrong choice of self-medications by the patients. Inappropriate use of topical steroids was a common cause of rashes and acneiform eruptions. The majority of the CADRs were not preventable according to Modified Schumock and Thornton scale. Modified Hartwig and Siegel severity scale showed most of the CADRs to be of moderate severity. Mild CADRs were less (11%) which could be a result of underreporting of mild and self-limiting cases. Severe CADRs (6%) such as SJS-TEN and exfoliative dermatitis required prolonged hospitalization and intensive care monitoring but no mortality was reported. The study highlights the importance of timely diagnosis and prompt withdrawal of the offending drug as it can be lifesaving. This study had some limitations. It was a retrospective study based on the analysis of the reported ADRs, so the patients follow-up was not possible. Furthermore, it did not provide a reliable estimate of reaction rate. Most of the patients attending the outpatient department of this hospital belong to low socioeconomic status, so the pattern of drug use among them is mainly restricted to the drugs supplied from the hospital pharmacy. Therefore, the generalizability of drug data generated from this study was not possible. Despite the above limitations, the study had strengths too. As it was a 5 years retrospective analysis of 809 spontaneously reported ADRs, it revealed some important aspects of CADRs. Some rare reactions such as DHS and ambroxol-induced exfoliative dermatitis were noted. It is evident that there is a need to create awareness among physicians as well as patients regarding CADRs so as to reduce the morbidity and mortality. A robust ADR monitoring system is the need of the hour and regional centers could play a role in the education of health-care providers in pharmacovigilance.

CONCLUSION

A wide clinical spectrum of CADRs was observed. Definitely preventable CADRs were found to be due to the absence of recording previous history of drug allergy and wrong choice of self-medication by the patients. Inconsistent with the previous literature, incidence of diclofenac-induced SJS was high in this study. Although the mortality reported for DHS

is high, it was prevented by early diagnosis and management in our center. Diligent and timely reporting of drug reactions are required as the most common offending drugs vary with the general prescription practices in a region and an early recognition of various morphological patterns can lead to timely intervention with better outcomes.

ACKNOWLEDGMENTS

The authors would like to thank the faculty and Postgraduate students from the Department of Pharmacology and Department of Dermatology, BMC and RI, Bengaluru, for their support in conducting the project work.

REFERENCES

1. Srinivasan R, Ramya G. Adverse drug reactions - Causality assessment. Int J Res Pharm Chem. 2011;1(3):606-12.
2. Devi P, Kamath DY, Anthony N, Santosh S, Dias B. Patterns, predictors and preventability of adverse drug reactions in the coronary care unit of a tertiary care hospital. Eur J Clin Pharmacol. 2012;68(4):427-33.
3. Raut AL, Patel P, Patel C, Pawar A. Preventability, predictability and seriousness of adverse drug reactions amongst medicine inpatients in a teaching hospital: A prospective observational study. Int J Pharm Chem Sci. 2012;1(3):1293-9.
4. Saha A, Das NK, Hazra A, Gharami RC, Chowdhury SN, Datta PK. Cutaneous adverse drug reaction profile in a tertiary care out patient setting in Eastern India. Indian J Pharmacol. 2012;44(6):792-7.
5. Sharma R, Dogra D, Dogra N. A study of cutaneous adverse drug reactions at a tertiary center in Jammu, India. Indian Dermatol Online J. 2015;6(6):168-71.
6. Hoetzenecker W, Nägeli M, Mehra ET, Jensen AN, Saulite I, Schmid-Grendelmeier P, et al. Adverse cutaneous drug eruptions: Current understanding. Semin Immunopathol. 2016;38(1):75-86.
7. 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(2):95-9.
8. Ghosh S, Acharya LD, Rao PG. Study and evaluation of the various cutaneous adverse drug reactions in Kasturba hospital, Manipal. Indian J Pharm Sci. 2006;68(2):212-5.
9. Moulya MV, Dinesh R, Nagesh G. Pattern of adverse drug reaction in teaching care hospital in Southern India: A retrospective study. World J Pharm Res. 2015;5(6):1429-39.
10. Pang JY, Pang SM, Koh HY. Cutaneous adverse drug reactions in a tertiary hospital in South-East Asia. Hong Kong J Dermatol Venereol. 2015;23(3):105-12.
11. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: A systematic review of prospective observational studies. Ann Pharmacother. 2008;42(7):1017-25.
12. Pudukadan D, Thappa DM. Adverse cutaneous drug reactions: Clinical pattern and causative agents in a tertiary care center in South India. Indian J Dermatol Venereol Leprol. 2004;70(1):20-4.
13. Sushma M, Noel MV, Ritika MC, James J, Guido S. Cutaneous adverse drug reactions: A 9-year study from a South Indian Hospital. Pharmacoepidemiol Drug Saf. 2005;14(8):567-70.
14. Lokhande AJ, Sutaria A, Shah BJ, Shah AN. Changing incidence of nevirapine-induced cutaneous drug reactions: After revised guideline Nov 2011. Indian J Sex Transm Dis. 2013;34(2):113-8.
15. Popovic M, Shenton JM, Chen J, Baban A, Tharmanathan T, Mannargudi B, et al. Nevirapine hypersensitivity. Handb Exp Pharmacol. 2010;196:437-51.
16. Prabhu VA, Doddapaneni S, Thunga G, Thiyagu R, Prabhu MM, Naha K. Phenytoin induced Stevens–Johnson syndrome exacerbated by cefepime. J Pharmacol Pharmacother. 2013;4(4):291-3.
17. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. Orphanet J Rare Dis. 2010;5:39.
18. Sasidharanpillai S, Riyaz N, Khader A, Rajan U, Binitha MP, Sureshan DN. Severe cutaneous adverse drug reactions: A clinicoepidemiological study. Indian J Dermatol. 2015;60(1):102.
19. Santhosh NS, Sinha S, Satishchandra P. Epilepsy: Indian perspective. Ann Indian Acad Neurol. 2014;17 Suppl 1:S3-11.
20. Man CB, Kwan P, Baum L, Yu E, Lau KM, Cheng AS, et al. Association between HLA-B*1502 allele and antiepileptic drug-induced cutaneous reactions in Han Chinese. Epilepsia. 2007;48(5):1015-8.
21. Locharernkul C, Loplumlert J, Limotai C, Korkij W, Desudchit T, Tongkobpetch S, et al. Carbamazepine and phenytoin induced Stevens-Johnson syndrome is associated with HLA-B*1502 allele in Thai population. Epilepsia. 2008;49(12):2087-91.
22. Vinod KV, Arun K, Dutta TK. Dapsone hypersensitivity syndrome: A rare life threatening complication of dapsone therapy. J Pharmacol Pharmacother. 2013;4(2):158-60.
23. Naldi L, Conforti A, Venegoni M, Troncon MG, Caputi A, Ghiotto E, et al. Cutaneous reactions to drugs. An analysis of spontaneous reports in four Italian regions. Br J Clin Pharmacol. 1999;48(6):839-46.
24. Ameen KH, Pinninti R, Jami S. Aceclofenac induced Stevens-Johnson/toxic epidermal necrolysis overlap syndrome. J Pharmacol Pharmacother. 2013;4(1):69-71.
25. Mockenhaupt M, Kelly JP, Kaufman D, Stern RS; SCAR Study Group. The risk of Stevens-Johnson syndrome and toxic epidermal necrolysis associated with nonsteroidal antiinflammatory drugs: A multinational perspective. J Rheumatol. 2003;30(10):2234-40.

How to cite this article: Jayanthi CR, Bedwal A, Rajarathna K. Cutaneous adverse drug reactions from a teaching hospital in Bengaluru: An observational study to determine the spectrum and outcome. Natl J Physiol Pharm Pharmacol 2017;7(5):476-481.

Source of Support: Nil, **Conflict of Interest:** None declared.