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Original Article

Pattern of Cutaneous Adverse Drug Reactions in a Tertiary Care Hospital of Bihar

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ABSTRACT

Introduction: CADRs are one of the most frequently reported adverse drug reactions (ADRs). Cutaneous reactions (CADR) of the skin can range from mild discomfort to life-threatening conditions. Reporting of ADRs can lead to heightened public vigilance and influence drug use recommendations by regulators. However, cutaneous adverse drug reactions vary according to geographic and socioeconomic factors, and very few researches of cutaneous adverse drug reactions have been conducted in eastern India.

Aims/ objective: To determine the clinico-epidemiological pattern of various cutaneous adverse drug reactions in patients attending Outpatient Department of skin and venereal diseases (VD) in a tertiary care hospital of eastern India.

Materials and Method: This was an observational and prospective study done on patients of all age group and gender who visited out-patient Department of the of Skin & VD and diagnosed clinically as a case of cutaneous adverse drug reaction. The WHO definition of ADR was considered. CADR was identified through patient interviews, pre-ADR drug use history, clinical examination, case record review, and dechallenge (effect of drug withdrawal on response). All patients were followed until recovery from her CADR.

Results: A total 13878 patients visited outpatient department of skin and VD during the study period. 147 cases of cutaneous adverse drug reactions with certain, probable, or possible causality relation with any drug according to WHO-UMC causality criteria were reported. The overall incidence of CADRs was 1.06 % (95% CI: 0.90–1.24). The most commonly observed CADRs were maculopapular rash, urticaria, and Fixed Drug Eruptions. The mean lag period in maculopapular rash, urticaria, and Fixed Drug Eruptions was 2.91, 1.83, and 1.04 day, respectively.

Conclusion: Our study observed lower incidence than other Asian and European studies. Age and gender do not affect the incidence of CADRs in our population. There is a need to sensitize the patients and clinicians about importance of past history of cutaneous adverse drug reactions.

Keywords: Cutaneous Adverse Drug Reaction, Skin, Pharmacovigilance, Incidence.

INTRODUCTION

Cutaneous adverse drug reactions (CADR), also known as toxidermia, are cutaneous symptoms resulting from systemic drug administration. These reactions range from mild erythematous skin lesions to further severe reactions such as Lyell's syndrome. They represent a heterogeneous field containing diverse clinical patterns with no specific features indicative of drug causality. It is important to look for causative agents. [1,2]

CADRs are one of the most frequently reported adverse drug reactions (ADRs). [3] Cutaneous reactions (CADR) of the skin can range from mild discomfort to life-threatening conditions. [4] They adversely impact patients in the form of prolonged hospitalization, systemic complications, mortality, morbidity and economic burden. [5, 6] Disabilities such as blindness from severe CADR can affect employment and quality of life. [7] Commonly reported CADRs are maculopapular rash, fixed drug eruption (FDE), and urticaria. [6] A wide range of drug groups can cause CADRs, and this pattern can vary with different prescribing patterns, new drug use, self-medication, and referral bias. [8, 9]

Most systemic drugs are potential causes of cutaneous adverse drug reactions. Contrast agents and certain classes of drugs, such as antibiotics, anticonvulsants, antineoplastics, nonsteroidal anti-inflammatory drugs, and allopurinol, are known to be common culprits. Antibiotics and antiepileptic drugs develop toxic complications in 1% to 5% of treatments. [10, 11]

Determining the cause of CADRs clinically requires a logical approach based on clinical features, chronological factors, and the establishment of a focused differential diagnosis. If the drug in question is a newly launched drug or has an unusual association with skin reactions, it is important to report serious suspected CADRs to the pharmacovigilance network. [12]

Thousands of people develop CADRs each year, and a few die. Cutaneous reactions are the most common type of ADR and can be difficult to diagnose. Healthcare professionals, including nurses and pharmacists, need to

be vigilant because CADR can occur in any patient at any time and can present with a wide variety of symptoms. Skin reactions can confuse even the most experienced clinicians.

Polypharmacy, or use of multiple drugs, can make identification of the problem even more difficult. In addition, there are genetic variants associated with skin reactions usually associated with antiepileptic drugs.

Reporting of ADRs can lead to heightened public vigilance and influence drug use recommendations by regulators. A study conducted in Pondicherry, India found that the most common CADR was fixed drug eruption (43.9%) and the most common causative drug was surprisingly found to be paracetamol. Antibiotics were the most common causative drug group, and two important associated risk factors were multiple drug use and a history of allergy. [13] However, cutaneous adverse drug reactions vary according to geographic and socioeconomic factors, and very few researches of cutaneous adverse drug reactions have been conducted in Bihar. Therefore, this study was done to determine the clinico-epidemiological pattern of various cutaneous adverse drug reactions in patients attending Outpatient Department of skin and venereal diseases (VD) in a tertiary care hospital of eastern India.

MATERIALS AND METHODS

Study Site: Department of Pharmacology, IGIMS, Patna.

Site of Collection of Data: Outpatient Department of Department of skin and venereal diseases (VD), Indira Gandhi Institute of Medical Sciences, Patna.

Study Duration: 24 months from September 2020 to March 2022.

Study Design: Observational and Prospective Study.

Ethical Consideration: The study protocol was approved by the institutional ethics committee of IGIMS, Patna and complied with International Conference on Harmonization Guideline for Good Clinical Practice and the Declaration of Helsinki. Informed consent was taken from patients in OPD of skin and VD. Participant Information Sheet (PIS) was provided and explained to patients in their local language. Thereafter, consent was approved by taking their signature or thumb impression on the informed consent form.

Inclusion criteria:

- All patients of all age group and gender who visited OPD of the Department of Skin & VD, IGIMS Patna (Bihar).
- Diagnosed clinically as a case of cutaneous adverse drug reaction.

Exclusion criteria:

- No or insufficient information about causality analysis.
- "Doubtful", "unlikely", and/or "unclassifiable" type of reactions based on WHO UMC causality criteria
- Patients with any skin disease
- Patients unable to give proper history of drug intake
- CADRs from locally applied drugs

Sample size calculation: With 14000 expected patients visiting department of skin and VD and anticipated 1% of patients presenting with cutaneous adverse drug reaction, minimum sample size required with 95% confidence level and 5% margin of error was calculated and found to be 144. Assuming 25% attrition rate, we planned to recruit 185 patients with CADR in our study.

185 patients with CADR were recruited in our study. Out of these, 22 patients were lost to follow-up. Relevant data were taken from these remaining 163 patients. Out of these, 16 patients were excluded from our study as per our exclusion criteria. So, final analysis was done on 147 patients.

Methodology

Identification of cutaneous adverse drug reactions and suspected drugs: The WHO definition of ADR – "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function" – was considered.[14] Active surveillance was used to identify CADR, and all patients attending the dermatology outpatient clinic and admitted to the inpatient ward were referred to the dermatology department with findings indicative of CADR.

CADR was identified through patient interviews, pre-ADR drug use history, clinical examination, case record review, and dechallenge (effect of drug withdrawal on response). For ethical reasons, rechallenge (reintroduction of the suspect drug after improvement) was avoided. However, when possible, information on accidental rechallenges was used to identify suspected medications. All patients were followed until recovery from her CADR. Follow-up was also performed in patients who did not have a prescription or a record of the medications they had taken prior to the onset of the reaction.

Outcome Measures:

- The primary outcome measure was incidence of CADRs.
- The secondary outcome variables were pattern of CADRs (their types, presenting features, lag period, and site of lesion), age and gender distribution of different CADR.

Statistical Analysis:

Data were entered in a Microsoft Excel sheet version 2019. Data entry was cross-checked by two investigators to ensure accuracy. Incidence was estimated using the number of CADR patients as the numerator and the total

number of dermatology outpatients as the denominator. We also performed subgroup analyses of incidence based on study population characteristics (age group, sex) and CADRs (individual types, preventable, serious and fatal). The patients of less than 12 years old were considered as paediatric with respect to ICH E11 guideline of clinical investigation of medicinal products in paediatric population and patients greater than 65 years old were considered as elderly population with respect to ICH E7 (R1) guideline of studies in support of geriatric population. [15,16] A chi-square test was used to compare the incidence of different subgroups. P < 0.05 was considered a statistically significant difference. Statistical tests were performed using SPSS ver-23.

OBSERVATION AND RESULTS

A total 13878 patients visited outpatient department of skin and VD during the study period. 147 cases of cutaneous adverse drug reactions with certain, probable, or possible causality relation with any drug according to WHO-UMC causality criteria were reported. [Table 1]

Table 1: Incidence of Cutaneous Adverse Drug Reactions

	Population	Number of CADR	Incidence in % (95% CI)
Overall	13878	147	1.06 (0.90 to 1.24)
Male	7709	78	1.01 (0.80 to 1.26)
Female	6169	69	1.11 (0.87 to 1.41)
Paediatric (<12 years)	1494	11	0.7 (0.37 to 1.31)
Adult (12-65 years)	11697	129	1.11 (0.92 to 1.31)
Elderly (>65 Years)	687	7	1.02 (0.4 to 2.10)

The overall incidence of CADRs was 1.06 % (95% CI: 0.90–1.24). There was no significant difference in the incidence of CADRs between male and female patients. Incidence in paediatric population was comparatively lower as compared to other age groups. [Table 1]

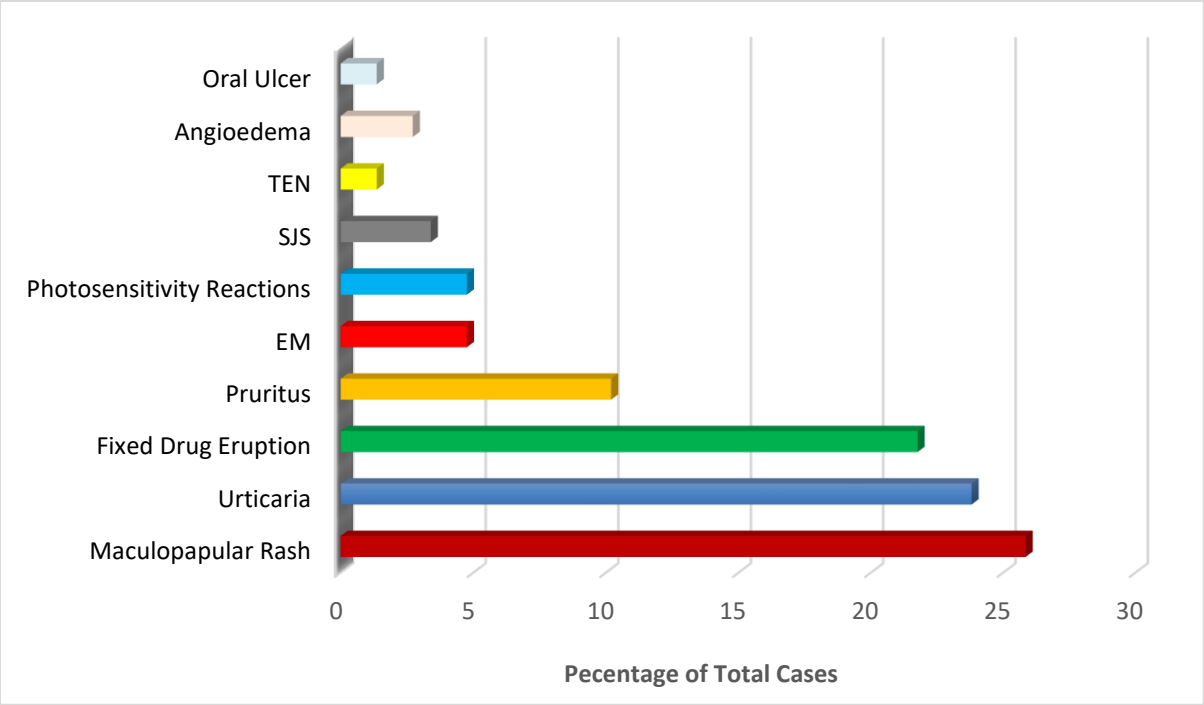

Figure 1: Incidence of Various Types of Cutaneous Adverse Drug Reactions

The most commonly observed CADRs were maculopapular rash, urticaria, and Fixed Drug Eruptionss. Their incidence ranged from 0.23 to 0.27/100 patients. There was no significant difference in incidence among maculopapular rash, urticaria, and Fixed Drug Eruptions. [Figure 1]

Serious CADRs like steven Johnson syndrome and toxic epidermal necrolysis were common in elderly. Maculopapular rash, urticaria and fixed drug eruptions were frequently reported CADRs in paediatric population.

Fixed drug eruptions, erythema multiforme, photosensitivity reactions, Steven Johnson Syndrome and Toxic Epidermal Necrolysis were more common in males while pruritus and angioedema were commonly reported CADRs in females.

Table 2: Incubation Period of Various Types of Cutaneous Adverse Drug Reactions

Type of CADRs	Incubation Period in Days (Mean ± SD)
Maculopapular Rash	2.91 ± 0.75
Urticaria	1.83 ± 0.51
Fixed Drug Eruptions	1.04 ± 0.23
Pruritus	2.13 ± 0.67
Erythema Multiforme	3.09 ± 1.02
Photosensitivity Reactions	7.98 ± 1.49
Steven Johnson Syndrome	3.31 ± 1.12
Toxic Epidermal Necrolysis	3.76 ± 3.21
Angioedema	0.78 ± 0.15
Oral Ulcer	0.93 ± 0.65

The mean lag period in maculopapular rash, urticaria, and Fixed Drug Eruptions was 2.91, 1.83, and 1.04 day, respectively. The angioedema and photosensitivity reactions showed shortest and longest lag period, respectively. [Table 2]

The common causative agents were of anti-infective, anti-parasitic, musculoskeletal, and nervous system class. Commonly suspected antimicrobial pharmacology groups were fluoroquinolones and penicillins. Commonly suspected nonsteroidal anti-inflammatory drugs (NSAIDs) were diclofenac and aceclofenac. [Figure 2]

Table 3: Site of Various Cutaneous Adverse Drug Reactions

Site	Number of CADRs	Percentage of CADRs (n=147)
Trunk	58	39.46
Upper Limb	39	26.53
Face	41	27.89
Lower Limb	25	17.01
Genitalia	4	2.72

The most common presenting symptoms of CADRs were itching, burning sensation, and pigmentation. The most commonly involved sites in CADRs were trunk and extremities, upper limb, and face. [Table 3]

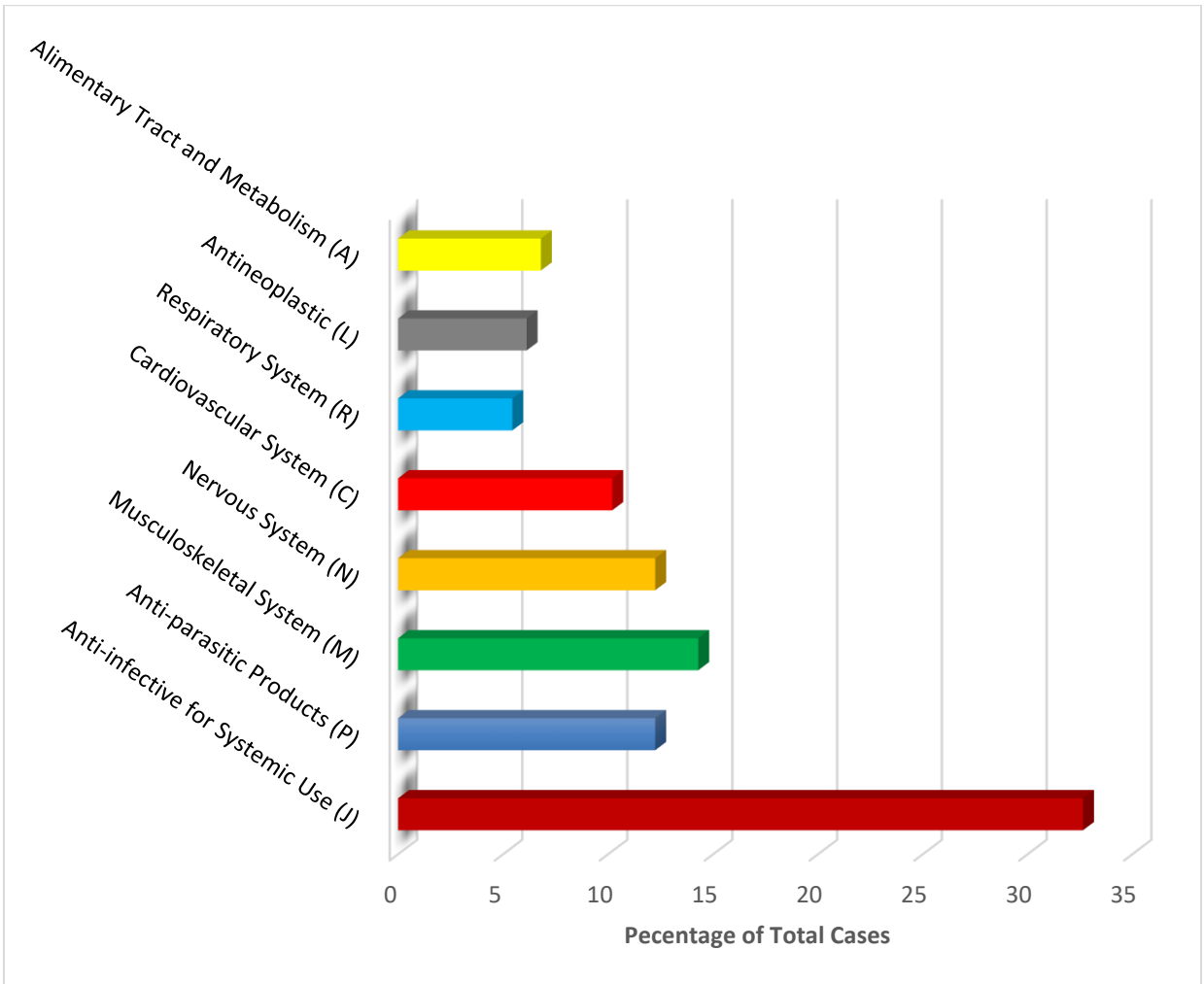

Figure 2: Distribution of Various Types of CADRs with respect to Suspected Drugs of Different ATC Group

DISCUSSION

This study analyzed the incidence, patterns, causative agents, and other characteristics of CADR. Many studies on CADR have been conducted in India with the main aim of explaining the pattern of CADR and the causative agents.[5,9,17-19] Previous Indian studies have descriptively interpreted the effect of demographics on CADR. In our study, we evaluated the impact of CADR on patients in terms of incidence through a one-year intensive study.

The observed incidence (1.06%) was lower than previous Denmark study (1.38%). [20] This was consistent with results from large studies showing a low incidence of CADR. [21,22] Choon and Lai et al. reported that the incidence of CADRs was 0.86% over a period of 10 years in a tertiary care hospital of Malaysia. [23]

In subgroup analysis, it was found that patients from India (0.35%) had significantly lower rates of CADR than those from Malay (0.89%) and Chinese (1.07%). [23] This suggests that the ethnic characteristics of the study population must be taken into account when interpreting the incidence of CADR. Based on a literature review, Svensson et al. mentioned that the incidence of CADR in hospitalized patients ranged from 1% to 3%.[4] Incidence rates in this study represent data from OPD patients only.

This study shows that gender and age had no significant effect on the incidence of allergic skin reactions. Incidence in the paediatric population was relatively low compared with other age groups. This may also be due to the lesser importance of age-related pharmacokinetic- and pharmacodynamics-mediated diversity in the intensity of the pharmacological response in the case of allergic CADR. Severe CADRs such as Steven-Johnson syndrome and toxic epidermal necrolysis were more frequent in the elderly. Maculo-papular rash, urticaria, and fixed drug eruptions were commonly reported as his CADR in children and adolescents.

Previous Indian study highlighting drug use in elderly patients has reported that most frequently prescribed drugs were for alimentary tract and metabolism, cardiovascular system, and blood and blood-forming organs.[24] Other Indian studies reported antihypertensive, antidiabetic, and antiplatelet agents as most commonly used drugs in elderly patients. [25] These drugs mainly lead to augmented type reactions (hypotension, hypoglycaemia, and bleeding) in the older people. Literature suggests that they are not common drugs to cause CADRs. [5,9,17-19] The incidence of CADR with these agents was also low in this study.[5,9,17-19] Thus, in contrast to augmentation-type reactions, the elderly population was not at undue risk of CADR and had similar incidences to non-elderly groups.

The most frequently observed CADRs were maculopapular rash, urticaria, and fixed drug eruption. Their incidence ranged from 0.23 to 0.27/100 patients. Combined macular papular rash, urticaria and FDE accounted for 7 out of 10 CADRs in our study, consistent with a previous systematic review in India.[6] Early Indian studies reported macular papules [9, 17] and FDE [5, 18, 19] as the most common CADRs.

The mean lag period in maculopapular rash, urticaria, and Fixed Drug Eruptions was 2.91, 1.83, and 1.04 day, respectively. The angioedema and photosensitivity reactions showed shortest and longest lag period, respectively.

Anti-infectives and NSAIDs were frequently suspected groups, consistent with previous studies. [9, 17, 19] Other studies have reported anti-infectives and anti-epileptic drugs as commonly suspected groups. [5, 8, 23] Among anti-infective drugs, CADRs due to fluoroquinolones were more common than cotrimoxazole [2, 5, 8, 9] and penicillins [7, 23] in contrast to earlier studies. Among NSAIDs, aceclofenac was the most common cause as compared to aspirin [3, 5] and mefenamic acid [23] in previous studies. This may be due to the widespread use of penicillin and aceclofenac in our setup.

Consistent with previous studies, anti-infectives caused all patterns of CADR. [3, 9] Anti-infective drugs were responsible for 3 out of 10 cases of maculopapular rash and FDEs and 7 out of 10 cases of EM. Individual anti-infective groups were causally related to specific pattern of CADRs. The fluoroquinolones mainly caused urticaria and FDEs while penicillins commonly caused the maculopapular rash. Fluoroquinolones, penicillins, and sulfa drugs have all been implicated in causing EM. Previous studies have reported that sulfonamides were the most common antibiotics causing macular papular rash and FDE, and penicillin causes urticaria. [9] Antiepileptic drugs were suspected to cause rashes, primarily macular papules.

The most common symptoms of CADR were itching, burning, and hyperpigmentation. The most commonly affected sites for CADR were the trunk and extremities, upper extremities, and face.

CADR management has been largely supportive and withdrawal of suspicious agents. Antihistamines are often used to relieve itching. Mild topical steroids and moisturizing lotions are helpful in the later stages of desquamation. [26] CADR requires hospitalization for severe reactions such as SJS/toxic epidermal necrolysis and DRESS. Suspicious drugs were discontinued in 93.58% of cases.

None of the patients in our study had a positive family history whereas according to a recently published study of CADR during a 5-year period by Fernandez et al, it was found that the risk for developing CADR to drugs in patients with a positive family history for these reactions was 14% compared to 1.2% for those without a family history. In his study, only 23% of the patients with CADR had a positive personal or family history. [27]

Limitation of the Study

Observer and statistician were not blinded in our study. Compliance of patients to the pharmacotherapy cannot be assessed with our study design. Drug interaction with OTC medicine, herbal product or food ingredients was not

checked in our study. Rechallenge was not possible in several cases due to ethical concerns. Most of the rechallenges were historical. Retrospective data was only taken from patients past medical history and was not correlated with previous laboratory reports. Long term follow up of the cases couldn't be done due to limited study period.

CONCLUSION

Our study observed lower incidence than other Asian and European studies. Age and gender do not affect the incidence of CADRs in our population. Data of this study confirm the earlier studies about the pattern of common CADRs and their incriminated drugs. There is a need to sensitize the patients and clinicians about importance of past history of cutaneous adverse drug reactions. Large-scale multi-centric Indian study is recommended to confirm the findings of this study. Ethnic characteristics should be considered while interpreting the incidence and pattern of CADRs.

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REFERENCES

1. Schifano F, Chiappini S. Is there such a thing as a 'lope' dope? Analysis of loperamide-related European Medicines Agency (EMA) pharmacovigilance database reports. PLoS One. 2018;13(10):e0204443.
2. Getova VI, Georgiev SR, Stoimenova AH, Petkova-Georgieva ES. Bulgarian Experience with Adverse Drug Reaction Reports from Patients and Consumers - Retrospective Data-base Study. Folia Med (Plovdiv). 2018 Sep 01;60(3):447-453.
3. 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;48:839–46.
4. Svensson CK, Cowen EW, Gaspari AA. Cutaneous drug reactions. Pharmacol Rev. 2001;53:357–79.
5. 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;70:20–4.
6. Patel TK, Thakkar SH, Sharma D. Cutaneous adverse drug reactions in Indian population: A systematic review. Indian Dermatol Online J. 2014;5:S76–86.
7. East-Innis AD, Thompson DS. Cutaneous drug reactions in patients admitted to the dermatology unit at the university hospital of the West Indies, Kingston, Jamaica. West Indian Med J. 2009;58:227–30.
8. Ding WY, Lee CK, Choon SE. Cutaneous adverse drug reactions seen in a tertiary hospital in Johor, Malaysia. Int J Dermatol. 2010;49:834–41.
9. 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.
10. Niebel D, Wenzel J. [Immunopathology of cutaneous drug eruptions]. Pathologe. 2018 Nov;39(6):563-570.
11. Graudins LV, Trubiano JA, Zubrinich CM, Elliott AS, Aung AK. Medication-related anaphylaxis treated in hospital: Agents implicated, patient outcomes, and management lessons. Pharmacoepidemiol Drug Saf. 2018 Sep;27(9):1029-1033.
12. Zhao Y, Wang T, Li G, Sun S. Pharmacovigilance in China: development and challenges. Int J Clin Pharm. 2018 Aug;40(4):823-831.
13. S P, K M, S A. Causality, severity and preventability assessment of adverse cutaneous drug reaction: a prospective observational study in a tertiary care hospital. J Clin Diagn Res. 2013;7(12):2765-2767. doi:10.7860/JCDR/2013/7430.3753
14. Edwards IR, Aronson JK. Adverse drug reactions: Definitions, diagnosis, and management. *Lancet.* 2000;356:1255–9.
15. ICH E11 Guideline: Clinical Investigation of Medicinal Products in the Pediatric Population. [Last accessed on 2020 Aug 08]. Available from: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E11/Step4/E11_Guideline.pdf
16. ICH E7 (R1) Guideline: Studies in Support of Special Populations: Geriatrics. [Last accessed on 2020 Aug 08]. Available from: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E7/Q_As/E7R1_Final_Concept_Paper.pdf
17. Nandha R, Gupta A, Hashmi A. Cutaneous adverse drug reactions in a tertiary care teaching hospital: A North Indian perspective. *Int J Appl Basic Med Res.* 2011;1:50–3.
18. Patel RM, Marfatia YS. Clinical study of cutaneous drug eruptions in 200 patients. *Indian J Dermatol Venereol Leprol.* 2008;74:430.
19. 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;6:168–71.
20. Borch JE, Andersen KE, Bindslev-Jensen C. Cutaneous adverse drug reactions seen at a university hospital department of dermatology. *Acta Derm Venereol.* 2006;86:523–7.
21. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): A meta-analysis of observational studies. *Pharm World Sci.* 2002;24:46–54.
22. Miguel A, Azevedo LF, Araújo M, Pereira AC. Frequency of adverse drug reactions in hospitalized patients: A systematic review and meta-analysis. *Pharmacoepidemiol Drug Saf.* 2012;21:1139–54.
23. Choon SE, Lai NM. An epidemiological and clinical analysis of cutaneous adverse drug reactions seen in a tertiary hospital in Johor, Malaysia. *Indian J Dermatol Venereol Leprol.* 2012;78:734–9.

24. Jhaveri BN, Patel TK, Barvaliya MJ, Tripathi CB. Drug utilization pattern and pharmacoeconomic analysis in geriatric medical in-patients of a tertiary care hospital of India. *J Pharmacol Pharmacother.* 2014;5:15–20.

25. Upadhyay J, Joshi Y. Observation of drug utilization pattern and prevalence of diseases in elderly patients through home medication review. *Asian J Pharm Clin Res.* 2011;4:143–5.

26. Criado PR, Criado RF, Vasconcellos C, Ramos RO, Gonçalves AC. Severe cutaneous adverse reactions to drugs – Relevant aspects to diagnosis and treatment – Part I: Anaphylaxis and anaphylactoid reactions, erythroderma and the clinical spectrum of Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's disease) *An Bras Dermatol.* 2004;79:471–88.

27. Nayak S, Acharjya B. Adverse cutaneous drug reaction. *Indian J Dermatol.* 2008;53:2–8.

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