Section: Dermatology

Original Research Article

PHARMACOVIGILANCE OF CUTANEOUS ADVERSE DRUG REACTIONS: A CLINICO-EPIDEMIOLOGICAL STUDY IN MEDICAL COLLEGE AND HOSPITAL, KOLKATA

Debalina Kanjilal[1], Suhena Sarkar[2], Dr Sangeeta De[3], Quazi Shabnam Waheed[4], Md.Faisal Rahmani[5], Abanti Saha[6]

[1]Post Graduate Resident, Department of Dermatology, Venerology and Leprosy, Medical College & Hospital, Kolkata, West Bengal, India
[2]Associate Professor, Department of Pharmacology, Medical College & Hospital, Kolkata, West Bengal, India
[3]Assistant professor, Department of Pharmacology, PKG Medical College & hospital , Newtown , Kolkata
[4]Postgraduate Resident, Department of Pharmacology, Medical College & Hospital, Kolkata, West Bengal, India
[5]Postgraduate Resident, Department of Pharmacology, Medical College & Hospital, Kolkata, West Bengal, India
[6]Associate Professor, Department of Dermatology, Venerology and Leprosy, Medical College & Hospital, Kolkata, West Bengal, India

Received : 05/10/2025
Received in revised form : 01/12/2025
Accepted : 17/12/2025

Keywords:
anatomy; medical education, class attendance, assessment, performance.

Corresponding Author:
Dr. Suhena Sarkar,
Email: suhena.m@gmail.com

DOI: 10.47009/jamp.2025.7.6.194

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

Int J Acad Med Pharm
2025; 7 (6); 743-748

ABSTRACT

Background: Cutaneous adverse drug reactions (CADRs) represent a significant challenge in clinical practice, impacting patient safety and healthcare outcomes. This study aims to evaluate the pattern, causality, and epidemiological factors associated with CADRs in a tertiary care hospital in Eastern India. The aim of this study is to evaluate the epidemiological trends, clinical manifestations, and causative factors of cutaneous adverse drug reactions (CADRs) in a tertiary care hospital to enhance pharmacovigilance and patient safety. The objectives include assessing the demographic and clinical profiles of affected patients, identifying common CADR types and implicated drugs, evaluating hospitalization rates and systemic involvement, and analyzing causality using the WHO-UMC scale. Additionally, the study aims to highlight challenges in ADR reporting and propose strategies for improving early detection, reporting, and prevention of CADRs through better pharmacovigilance and public awareness. **Materials and Methods:** A cross-sectional, observational study was conducted from June 2023 to May 2024 at the Department of Dermatology, Medical College, Kolkata. A total of 95 patients presenting with CADRs were enrolled. Data were collected on demographic details, drug history, clinical presentation, and causality assessment using the WHO-UMC scale. Statistical analysis was performed using MedCalc software. **Result:** The mean age of participants was 38.25 ± 14.58 years, with a female predominance (52.7%). Fixed drug eruption (51.6%) was the most common CADR, followed by Stevens-Johnson syndrome/toxic epidermal necrolysis (12.6%). Antibiotics (40%) and nonsteroidal anti-inflammatory drugs (26.3%) were the leading culprits, with metronidazole being the most frequently implicated agent. The majority of reactions (57.9%) were localized, and 21.1% required hospitalization. Causality assessment categorized 86.3% of reactions as probable. **Conclusion:** CADRs are a prevalent and clinically significant issue, often associated with commonly prescribed drugs like antibiotics and NSAIDs. Enhanced pharmacovigilance efforts and clinician awareness are crucial for early detection, prevention, and management of CADRs.

INTRODUCTION

A drug has both pharmacodynamic effects and side effects. Pharmacodynamic effects are of interest in treating diseases; which are first documented in animal studies then in Phase 1 and Phase 2 studies in humans and finally in Phase 3 clinical trials. Clinically relevant pharmacodynamic effects are used by regulatory agencies to define the clinical

ISSN (O): 2687-5365; ISSN (P): 2753-6556

indications of the drug. On the other hand side effects are pharmacological properties of the drug that exist along with the pharmacodynamic effects. These can be beneficial as well as deleterious.[1] WHO has defined adverse reaction to a drug as 'any response to a drug which is noxious and unintended that occur at doses used in man for prophylaxis, diagnosis or therapy' and it has been in use for more than 30 years.[2] Adverse reactions are classified into six types: Dose-related (Augmented); non-dose related (Bizzare); dose related and time-related (chronic); time-related (Delayed); withdrawal (End of use) and failure of therapy (Failure).[3] An adverse cutaneous reaction caused by a drug is affecting structure, function, or mucous membranes, regardless of an etiology.[4]

Pharmacovigilance (PV) focuses on detecting, assessing, and preventing adverse drug reactions (ADRs), medication errors, and drug interactions, ensuring patient safety through systematic monitoring and reporting of drug-related issues.[5] Pharmacovigilance faces challenges as most reports involve suspected adverse drug reactions without specific diagnostic tests or ethical rechallenges. Various causality assessment systems exist, but none provide precise relationship estimates. The WHO-UMC system, developed with National Centres, offers a practical tool, considering clinical-pharmacological aspects and documentation quality for case report evaluation.[6]

An important task of the PV centres is to evaluate the causal relationship between unwanted events and drugs. Documented ADRs are recorded in the national pharmacovigilance database, which communicates the data to the world health organization.

Advancements in computer technology have enhanced pharmacovigilance (PV) by improving data collection and drug safety signal detection, which is a potential or new association between drugs and adverse reactions, requiring further investigation which arise from spontaneous reports, literature reviews, and active surveillance, influencing public health strategies.[7]

Spontaneous Reporting System (SRS) enables healthcare professionals, drug companies, and patients to report ADRs, improving drug safety. It detects new, rare, or serious reactions beyond clinical trials. While applicable to all drugs, SRS faces challenges like underreporting and low-quality reports, requiring active participation from healthcare professionals for effectivenes. A health care professional's knowledge about and access to local ADR reporting system, clinical skills in detecting an ADR and attitude towards reporting ADR are the main determinants of ADR reporting.[5]

Aims and objectives:

1. To describe the pattern of occurrence of CADR
2. To assess the recent clinical pattern of CADRs and find association with epidemiological epidemiological and clinical factors if any
3. To determine the causality assessment by using WHO-UMC scale to support pharmacovigilance programmes in India.

MATERIALS AND METHODS

The study was an institution-based, descriptive, cross-sectional study conducted in the Dermatology Department, Medical College, Kolkata, from June 2023 to June 2024. Patients with cutaneous adverse drug reactions (CADRs) meeting the inclusion criteria were recruited. The sample size was calculated using the formula $n = 4pq/l^2$, resulting in 81 subjects, accounting for a 10% attrition rate.

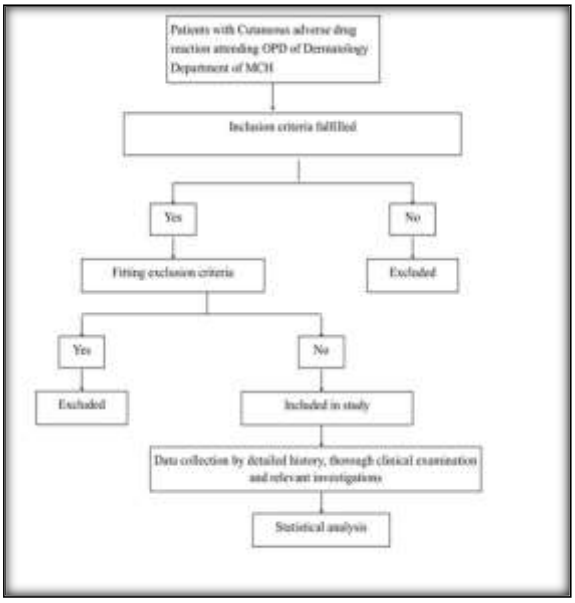
Consecutive sampling included all dermatology OPD and admitted patients. Patient details such as age, sex, weight, occupation, symptoms (pain, itching, burning, discharge), and history of drug use (causative drug, indication, dosage, route, frequency, and time to reaction) were recorded. Lesions were documented based on number, size, shape, color, and site.

Study tools included: OPD admission registers, informed consent forms, adverse drug reaction reporting forms, journals, textbooks, and digital imaging. Data collection and literature review spanned from June 2023 to May 2024.

Statistical Analysis: Descriptive statistical techniques will be used. Continuous efficacy variables will be compared between groups by independent samples t test. Mann Whitney U test will be used for unpaired non-parametric data. Categorical data will be compared between groups by chi-squared test. Data will be entered in Microsoft Excel and analysis will be done with the help of Microsoft Excel and statistical software Med Calc (latest version).

P-value ≤ 0.05 will be considered significant.

Road Map of Study



ISSN (O): 2687-5365; ISSN (P): 2753-6556

IEC Approval Reference no : MC/KOL/IEC/NON-SPON/1912/05/2023

RESULTS

Demographic Profile: The study included 95 patients, with a mean age of 38.25 ± 14.58 years. The majority (65.3%) belonged to the 30-59 age group, and 52.7% were female.

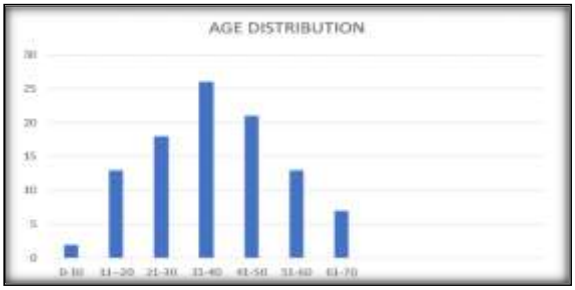


Chart 1: Bar Chart Showing Age Distribution

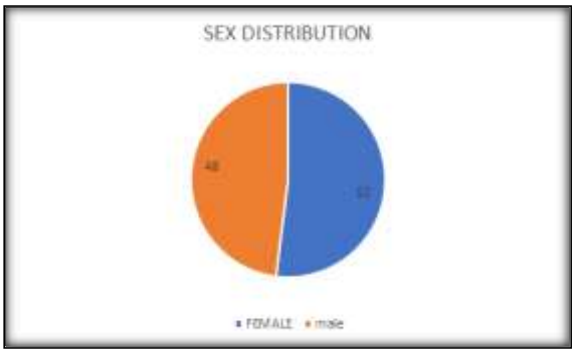


Chart 2: Pie Chart Showing Sexdistribution

Clinical Presentation:

1. Fixed drug eruption (51.6%) was the most common CADR.
2. Stevens-Johnson syndrome/toxic epidermal necrolysis was observed in 12.6% of cases.
3. Other reactions included morbilliform eruptions (8.4%), urticaria (8.4%), and erythroderma (3.2%).

Distribution of the study participants according to type of adverse reaction: Fixed drug eruption occurred in more than half of the participants (51.6%).

Type of adverse drug reaction	Frequency (%)
Morbiliform / exanthematous	8 (8.4)
Fixed drug eruption	49 (51.6)
TEN / SJS	12 (12.6)
Urticaria / Angioedema	8 (8.4)
Exfoliative dermatitis / Erythroderma	3 (3.2)
Miscellaneous	15 (15.8)
Total	95 (100.0)

Causative Drugs:

1. Antibiotics (40%) were the leading cause, with metronidazole being the most implicated.
2. NSAIDs accounted for 26.3% of cases, with paracetamol being the most common agent.
3. Other causative drugs included chemotherapeutic agents (5.3%) and proton pump inhibitors (3.2%).

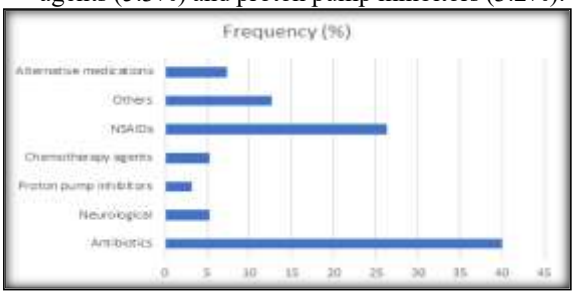


Chart 3: Bar Chart Showing Distribution Of Participants According To Type Of Offending Drugs

Hospitalization and Systemic Involvement

1. 21.1% of cases required inpatient management.
2. Systemic involvement was noted in 15.8% of cases.

Distribution of Participants Requiring Hospital Admission: 78.9% adverse drug reaction cases did not require hospital admission

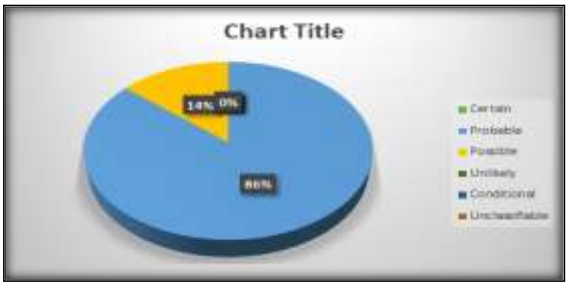
Hospital admission	Frequency (%)
Needed	20 (21.1)
Not needed	75 (78.9)
Total	95 (100.0)

Distribution According to Systemic Involvement of Adverse Drug Reactions: Systemic involvement of adverse drug reactions

Systemic involvement	Frequency (%)
Present	15 (15.8)
Absent	80 (84.2)
Total	95 (100.0)

Causality Assessment:

1. 86.3% of cases were classified as "probable" according to the WHO-UMC scale.
2. No cases fell into the "certain" category due to the absence of rechallenge.



Pie chart showing cases of cutaneous adverse drug reactions by WHO- UMC Standardized case causality assessment scale.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Chi-square test showing correlation:

Correlation of severity of adverse drug reaction with elevated serum IgE levels					
			elevated serum IgE levels		Total
			1	2	
Severity of adverse drug reaction	SCAR	Count	4	17	21
		% within Severity of adverse drug reaction	19.0%	81.0%	100.0%
	Not so severe CADR	Count	47	27	74
		% within Severity of adverse drug reaction	63.5%	36.5%	100.0%
Total		Count	51	44	95
		% within Severity of adverse drug reaction	53.7%	46.3%	100.0%

Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	13.008a	1	.000		
Continuity Correctionb	11.281	1	.001		
Likelihood Ratio	13.619	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	12.871	1	.000		
N of Valid Cases	95				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 9.73.					
b. Computed only for a 2x2 table					

INFERENCE: 81% of participants with severe adverse reaction had elevated serum IgE levels as compared to 36.5% participants with non-severe adverse reaction. This association was found to be statistically significant ($\chi 2=13.008$, $p<0.001$)

DISCUSSION

We have taken a total of 95 cases of adverse drug reactions out of which a history of definite drug was identified in 84 cases. Rest 10 cases had a history of an unknown drug intake or patient could not recall about any drug intake. We had 1 patient who had a history of taking homeopathic medications before developing Toxic epidermal necrolysis. No other drug history could be elicited in these patients. Till date there has been no reports where homeopathic medications were the cause of ADRs.

The maximum age of the study participants was 70 years and the minimum age was 10 years. The mean age of the study participants was 38.25± 14.58 years. Most of the study participants were in the age group of 30 – 59 yrs (65.3%) similar to the study done by Patel et. Al.[8]

Males(47.3%) and females(52.7%) were almost equal in number. There was no gender predilection which is in sharp contrast to the study by Pistone et. al where the female to male ratio of adverse reactions were 1.7:1.[9] According to a study done by Alomar et al.[10] females are anatomically and physiologically more predisposed to develop adverse drug reactions.

None of the patients had any family history of adverse drug reactions and past history was present in 43.2% which is in contrast to the study done by Deepthi P et. al where family history was present in 8.1% and past history in 22% patients.[11]

The average duration of illness of the patients was 15.32 ± 33.59 days. The maximum was 180 days for severe cutaneous adverse drug reactions and minimum was 1 day for mild reactions which is almost similar to the study by Deepthi P et. Al.[12]

Most common complaint of the patients was skin rash (43.2%) followed by itching (32.6%). The other symptoms were pain, discharge, acneiform eruption, oral and genital ulceration which is similar to the study of Inbaraj SD et. al where the most frequent complaint was skin rash as well.[13]

The average duration from drug intake to onset of reaction is 5.37 days. The maximum duration was 60 days and the minimum was 1 day in our study while in one study done by Nandha et al,[14] the minimum duration was less than 2 days and maximum was 30 days.

Most of the study participants (62.1%) had no comorbidities. Among the 37.9% who had co morbidities 63.9% had type 2 diabetes mellitus and 55.5% had hypertension which differs from a study done by Sasidharanpillai S et al,[15] where hypertension was the most common comorbidity. Other previous studies,[16] have also identified hypertension as the most commonly associated comorbidity. The fact that diabetes mellitus was the most common comorbidity in our study might reflect the rising cases of diabetes mellitus in a developing country like India. All these 37.9% of the patients were adequately controlled with medications which were started long before the patient had any cutaneous manifestation and were apparently fine before taking the causative drug.

The most common group of drug causing cutaneous adverse drug reactions were antibiotics (40%) followed by NSAIDs (26%) which is similar to the study by Jadhav et al,[17] since these are the drugs that are commonly sold over the counter and are easily available. Among the group of antibiotics, Nitroimidazoles, particularly Metronidazole was found to be the most common causative agent which is in contrast to the study done by Sinha S et al,[18] where fluoroquinolones were the most common causative drug . However both of these drugs are extensively sold over the counter for any cause of gastrointestinal upset.

Among NSAIDs, paracetamol was the most commonly identified one but there were at least 9 cases where the exact NSAID could not be identified

ISSN (O): 2687-5365; ISSN (P): 2753-6556

since many times they were bought over the counter for treatment of fever or pain.

Alternative medications were responsible for 7.4% cases. There are a few studies which have reported SCARs as well as casualties due to cutaneous adverse reactions from traditional medicine such as the one done by Marvaliya BJ et al.[19] This sharply contradicts the popular myths regarding alternative medications among the general population who often resort to these drugs for their treatment thinking they are devoid of adverse effects.

The most common indications for taking these drugs were gastrointestinal upset and fever (25.3% each) which is in contrast to a study done by Salam A et. al where headache was most common cause.[20]

Antitubercular drugs were responsible for 3.2% cases which is similar to the findings of Anamika G et al.[21]

The most common type of adverse drug reaction observed was fixed drug reaction (51.6%) which is similar to the study done by Pudakan et al, but different from the study done by Jha et al,[22] where the most common type of adverse reaction was exanthematous drug reactions. Exanthematous/ morbilliform eruptions were the third most common type of reaction in our study.

Life threatening severe cutaneous adverse reactions(SCAR) like TEN/SJS were seen in 12.6% and erythroderma was seen in 3.2% cases. Total SCARs were 15.8% in our study which was less than the severe cases seen in a study done by Saha et. al.[23]

The most common route of drug intake was enteral (93.7%) which is similar to the study done by Sharma S. et al,[8] although they had 46.7%(majority) taking the drug orally.

57.9% of patients developed localized reactions which is almost identical (55.65%) to the study done by Sharma S et. al.[8] Hospital admissions were needed in 21.1% of our patients as compared to 28.2% of hospital admissions with no fatality observed when compared to the same study.[24]

The mean eosinophil count of all patients was 280.9 ± 189.1/cumm. The maximum value was 987/cumm and minimum was 69/cumm. 14.7% of our patients had eosinophlia (absolute eosinophil count >500) which is almost similar to a study done by Rana S et al,[25] where eosinophilia was 20.6%.For 86.3% of the study population the drug reaction belonged to the probable category of causality assessment(WHO-UMC criteria) while remaining belonged to possible category. There were no cases in the certain category as re challenge was not done due to ethical reasons and unlikely, unclassified or unclassifiable cases were not included in our study. These findings were similar to the findings of Sharma S et al.[24]

Cutaneous adverse drug reactions (CADRs) were classified into severe (SCARs), including Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, DRESS, AGEP, and Erythroderma, and non-severe reactions.

Limitations: The study's limitations include its single-center design, restricting generalizability. Reliance on retrospective self-reported medication histories introduces recall bias, while incomplete documentation may affect data accuracy. The inability to perform rechallenge procedures limits definitive causality assessment. A cross-sectional design precludes long-term follow-up, and pharmacogenomic variability was not analyzed. Underreporting in spontaneous reporting systems may have affected incidence estimates. Future research should incorporate multicentric, prospective designs with genetic analysis and objective diagnostics.

CONCLUSION

Fixed Drug Eruption (FDE) is the most common cutaneous adverse drug reaction (CADR), occurring most frequently in the 3rd to 5th decade, with no sex predilection. Awareness of CADRs is low, as most patients have only secondary-level education. Family history does not predict CADR occurrence. Skin rash and itching are the most common symptoms, often with a sudden onset. Type 2 diabetes mellitus is the most common comorbidity. Antibiotics, particularly Nitroimidazoles like Metronidazole, are the leading cause, typically taken orally for fever or gastrointestinal issues. Most reactions are localized and resolve within a month without hospitalization, though severe cases may become systemic. Symptoms usually appear within 5–6 days. Serum IgE and absolute eosinophil counts are typically normal but can be elevated. Most CADRs fall under the "Probable" category in WHO-UMC causality assessment. Severe CADRs (SCARs) are most associated with chemotherapeutics and elevated serum IgE levels (>300 mg/dL).

REFERENCES

1. Sommet A, Lacroix I, Olivier P, Durrieu G, Damase-Michel C, Lapeyre-Mestre M, Bagheri H. Pharmacovigilance for evaluating adverse drug reactions: value, organization, and methods. Joint Bone Spine. 2006 Dec 1;73(6):629-32.
2. Venulet J, Borda MH. WHO's international drug monitoring—the formative years, 1968–1975: Preparatory, pilot and early operational phases. Drug safety. 2010 Jul;33(7):e1-23.
3. Ralph E. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356:1252.
4. Nayak S, Acharjya B. Adverse cutaneous drug reaction. Indian Journal of dermatology. 2008 Jan 1;53(1):2-8.
5. Hadi MA, Neoh CF, Zin RM, Elrggal ME, Cheema E. Pharmacovigilance: pharmacists' perspective on spontaneous adverse drug reaction reporting. Integrated Pharmacy Research and Practice. 2017 Mar 22:91-8.
6. Center UM, World Health Organization. The use of the WHO-UMC system for standardised case causality assessment. Accessed August. 2018;30:2021.
7. Bihan K, Lebrun-Vignes B, Funck-Brentano C, Salem JE. Uses of pharmacovigilance databases: an overview. Therapies. 2020 Nov 1;75(6):591-8
8. Lobo MG, Pinheiro SM, Castro JG, Momenté VG, Pranchevicius MC. Adverse drug reaction monitoring: support for pharmacovigilance at a tertiary care hospital in Northern Brazil. BMC Pharmacology and Toxicology. 2013 Dec;14:1-7.
9. Montastruc F, Sommet A, Bondon-Guitton E, Durrieu G, Bui E, Bagheri H, Lapeyre-Mestre M, Schmitt L, Montastruc JL. The importance of drug–drug interactions as a cause of adverse drug reactions: a pharmacovigilance study of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

serotoninergic reuptake inhibitors in France. European journal of clinical pharmacology. 2012 May;68:767-75.
10. de Vries ST, Denig P, Ekhart C, Burgers JS, Kleefstra N, Mol PG, van Puijenbroek EP. Sex differences in adverse drug reactions reported to the National Pharmacovigilance Centre in the Netherlands: An explorative observational study. British journal of clinical pharmacology. 2019 Jul;85(7):1507-15.
11. Alomar MJ. Factors affecting the development of adverse drug reactions. Saudi pharmaceutical journal. 2014 Apr 1;22(2):83-94.
12. Cliff-Eribo KO, Sammons H, Choonara I. Systematic review of paediatric studies of adverse drug reactions from pharmacovigilance databases. Expert Opinion on Drug Safety. 2016 Oct 2;15(10):1321-8.
13. Chindhalore CA, Gupta AV, Dakhale GN, Srivastava A. Analysis of Cutaneous Adverse Drug Reactions (ADR) Reported at an ADR Monitoring Center of a Tertiary Care Teaching Institute in Central India. Cureus. 2024 Feb 6;16(2).
14. Mulchandani R, Kakkar AK. Reporting of adverse drug reactions in India: A review of the current scenario, obstacles and possible solutions. International Journal of Risk & Safety in Medicine. 2019 Feb;30(1):33-44.
15. Tandon VR, Mahajan V, Khajuria V, Gillani Z. Under-reporting of adverse drug reactions: a challenge for pharmacovigilance in India. Indian journal of pharmacology. 2015 Jan 1;47(1):65-71.
16. Irujo M, Beitia G, Bes-Rastrollo M, Figueiras A, Hernandez-Diaz S, Lasheras B. Factors that influence under-reporting of suspected adverse drug reactions among community pharmacists in a Spanish region. Drug safety. 2007 Nov;30:1073-82.
17. Smith MP, Webley SD. Pharmacovigilance teaching in UK undergraduate pharmacy programmes. Pharmacoepidemiology and drug safety. 2013 Mar;22(3):223-8.
18. Patel TK, Barvaliya MJ, Sharma D, Tripathi C. A systematic review of the drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Indian population. Indian journal of dermatology, venereology and leprology. 2013 May 1;79:389.
19. Pistone G, Gurreri R, Alaimo R, Curiale S, Bongiorno MR. Gender differences in adverse drug reactions in dermatological patients in west Sicily: an epidemiological study. Journal of dermatological treatment. 2014 Dec 1;25(6):510-2.
20. Alomar MJ. Factors affecting the development of adverse drug reactions. Saudi pharmaceutical journal. 2014 Apr 1;22(2):83-94.
21. Deepthi P, George S, Sanker A, Asokan N. A cross-sectional study of adverse cutaneous drug reactions with special reference to reaction time. Muller Journal of Medical Sciences and Research. 2022 Jul 1;13(2):98-102.
22. Inbaraj SD, Muniappan M, Muthiah NS, Amutha A, Josephine G, Rahman F. Pharmacovigilance of the cutaneous drug reactions in outpatients of dermatology department at a tertiary care hospital. Journal of clinical and diagnostic research: JCDR. 2012 Oct 15;6(10):1688.
23. Nandha R, Gupta A, Hashmi A. Cutaneous adverse drug reactions in a tertiary care teaching hospital: A North Indian perspective. International journal of Applied and Basic medical research. 2011 Jan 1;1(1):50-3.
24. Lee AY. Immunological Mechanisms in Cutaneous Adverse Drug Reactions. Biomolecules & Therapeutics. 2024 Jan 1;32(1):1.
25. Sasidharanpillai S, Riyaz N, Khader A, Rajan U, Binitha MP, Sureshan DN. Severe cutaneous adverse drug reactions: a clinicoepidemiological study. Indian Journal of Dermatology. 2015 Jan 1;60(1):102.

ISSN (O): 2687-5365; ISSN (P): 2753-6556