International Journal for Research in Biology and Pharmacy

GREEN PUBLICATION

ISSN (Online): 2208-2093
Volume 10 Issue 01 March 2024
Available on-line at: https://ijrbp.com/index.php/bp/issue/view/490

DOI:*https://doi.org/10.69980/bp.v10i1.2484* *Received: 14-Dec-2023 Accepted: 24-Feb-2024*

ASSESSMENT OF CUTANEOUS ADVERSE DRUG REACTIONS ASSOCIATED WITH COMMON THERAPEUTIC AGENTS

Dr. Blanca R. Del Pozzo-Magaña[1], Dr. Carmen Liy-Wong[2], Dr. Young-Min Son[3], Dr. Joo-Young Roh[4]

[1] Department of Pediatrics, Division of Pediatric Clinical Pharmacology, Children's Hospital of Western Ontario, Western University, London, Ontario, Canada
[2] Department of Pediatrics, Division of Dermatology and Rheumatology, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Ontario, Canada
[3] Department of Dermatology, Gachon University Gil Medical Center, Incheon, South Korea
[4] Department of Dermatology, Gachon University of Medicine and Science, Gil Hospital, Incheon, South Korea

Corresponding Author
Email: jyroh1@gilhospital.com

Abstract
Cutaneous adverse drug reactions (CADRs) are among the most frequently reported adverse drug reactions and represent an important clinical concern in pharmacotherapy. These reactions can range from mild skin eruptions to severe and potentially life-threatening conditions, affecting patient safety and treatment adherence. Understanding the patterns and drug classes associated with CADRs is essential for improving pharmacovigilance and ensuring safe medication use. A retrospective observational study was conducted in a tertiary care hospital to evaluate the occurrence and patterns of CADRs. Data were collected from previously documented medical records and pharmacovigilance reports of patients diagnosed with CADRs. A total of 80 patients were included in the study. Information regarding demographic characteristics, suspected drug classes, types of cutaneous reactions, time of onset, and severity of reactions was extracted and analyzed. Descriptive statistics, including frequencies, percentages, mean, and standard deviation, were used to summarize the data, and correlation analysis was performed to examine relationships between selected clinical variables. CADRs were observed among patients of different age groups and both genders. Antibiotics were the most frequently implicated drug class, followed by non-steroidal anti-inflammatory drugs and antiepileptic medications. Maculopapular rash was identified as the most common clinical manifestation, followed by urticaria and fixed drug eruption. The results also indicated positive associations between selected clinical variables, including age, onset time, and severity of reactions. The study highlights the clinical significance of CADRs and the need for effective monitoring of adverse drug reactions in healthcare settings to enhance patient safety and optimize therapeutic outcomes.

Keywords: *Cutaneous adverse drug reactions, Pharmacovigilance, Drug safety, Antibiotics, Adverse drug reactions, Dermatological reactions.*

1. Introduction

The World Health Organization (WHO) has defined Adverse Drug Reactions (ADRs) as any adverse and unforeseen reaction in relation to a drug and that is experienced at dosages otherwise used in humans to prevent, diagnose or treat disease. ADRs are a significant health issue of concern since they cause morbidity, hospitalization and health expenditures. Research in the hospital environment has shown that ADRs are commonly documented in patients who have been undergoing pharmacological treatment, which is why it is always crucial to implement systematic monitoring and assessment of the safety of the drug in clinical practice (Adhikari et al., 2017). Some treatment regimens, especially those ones applied in chronic pathologies like tuberculosis, are characterized by increased probability of adverse reactions because of the long-term contact with medications and complicated treatment regimens (Amalba & Bugri, 2021). A cutaneous adverse drug reactions (CADR) are among the most prevalent types of ADRs witnessed in the medical practice. The variety of dermatological reactions to drug administration is truly impressive, and CADRs may start with mild skin eruption and end with severe and life-threatening manifestations. Dermatological side effects have been described as adverse reactions to many pharmacological agents (psychotropic and other systemic drugs) (Bangwal et al., 2020). On the same note, the prolonged use of antifungal agents and other systemic drugs has also been linked with dermatologic and systemic adverse effects which further underlines the importance of patient monitoring in patients on such treatments (Benitez & Carver, 2019). CADRs can be clinically presented in a variety of forms, including maculopapular rashes, urticaria, fixed drug eruption, and more severe diseases, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Though being relatively uncommon, these severe reactions are linked to a high level of morbidity and mortality and should be immediately recognized and treated (Copaescu & Trublano, 2022). The development of the pharmacovigilance research has also brought forth new analytical and predictive solutions like computational models and data-driven solutions to enhance ADR detection and prediction using clinical and pharmacological data (Dey et al., 2018). Although these progress has been made, severe cutaneous adverse reactions are a significant issue in dermatology and pharmacology, as they are unpredictable and may be acute (Duong et al., 2017). Recent studies have also been able to emphasize on the genetic predisposition in the occurrence of some drug induced reactions. HLA alleles have been associated with the high risk of hypersensitivity response to specific drugs, which is why pharmacogenetics represent a significant issue that could determine individual predisposition to CADRs (Fan et al., 2017). Moreover, there are standardized instruments like the Common Terminology Criteria of Adverse Events (CTCAE), that have been created to categorize and severity grade the adverse events, which give clinicians structured ways to evaluate and record the drug-related complications (Freites-Martinez et al., 2021). Clinical practice further supports the evidence that different therapeutic agents applied to chronic diseases may contribute to serious adverse drug reactions that influence the treatment tolerability and adherence of the patient (Galli et al., 2017). Therefore, to enhance patient outcomes, drug safety, and improve healthcare settings, the pharmacovigilance systems and continuous monitoring of ADRs are needed.

Even though there are pharmacovigilance programs and ADR monitoring systems in most healthcare institutions, a number of challenges exist in the documentation and assessment of adverse drug reactions. According to the hospital-based research, ADR reporting systems are not actively used, which leads to the incomplete reporting of ADR and a poor perception of drug-related complications in clinical practice (Giardina et al., 2018). Moreover, most pharmacological researches concentrate on the systemic toxicities and the treatment effects, whereas the dermatological expressions of adverse reactions are relatively less discussed in clinical reporting and research (Goncalves et al., 2019). It has been demonstrated in epidemiological researches that CADRs constitute a considerable percentage of all adverse drug reactions reported but their distribution and patterns are highly diverse in populations and healthcare facilities (Mockenhaupt, 2017). Immune-related cutaneous adverse events have also been on the rise in recent years, which is another indication of the intricacy of drug-induced dermatological conditions (Muntyanu et al., 2021). In spite of such increased awareness, there is still a dearth of data in most healthcare facilities in terms of the nature of drug causing CADRs and their severity trends and demographic distribution among patients. Systematic review of patient records has been proposed as a good approach to offer meaningful information about the epidemiology and clinical manifestation of CADRs, but these studies have not been conducted in most regions (Murthy et al., 2022).

Cutaneous adverse drug reactions are a significant clinical issue in that they may be mild or serious life threatening reaction that needs urgent medical attention. Going forward, the ADRs need to be effectively identified and managed in order to enhance patient safety and optimize therapeutic outcomes (Patton & Borshoff, 2018). In numerous instances, dermatological adverse events can have a strong impact on the treatment choice, discontinuation or adjustment of the offending medication that can eventually impact disease management and quality of life of patients (Phillips et al., 2019). In addition, the growing scope of immune-mediated adverse reactions, with a significant number of them being skin and mucous membrane related, has been linked to the increasing use of modern pharmacological therapies, such as targeted agents and immunotherapies (Ramos-Casals et al., 2020). Drug-related adverse event management has become a critical element of patient care and thus, has to be carefully observed, diagnosed on time, and necessitated by therapeutic interventions, which can ensure a minimum of complications and better treatment outcomes (Rimassa et al., 2019). In this regard, a retrospective review of hospital reports can be a useful source of information in defining trends of CADRs, identifying frequently used medications, and gaining demographic information related to these responses.

Research Objectives

1. To assess the incidence and clinical patterns of cutaneous adverse drug reactions among patients receiving therapeutic agents.

2. To identify the commonly implicated drug classes associated with CADRs.
3. To evaluate the demographic characteristics and severity patterns of CADRs in the study population.

2. Methodology

2.1 Study Design and Setting

The research was done in the form of a retrospective observational study at the dermatology department and pharmacovigilance unit of a tertiary care hospital. The previous clinical records were discussed to measure the incidence and trends of cutaneous adverse drug reactions (CADRs) due to commonly used therapeutic agents. The retrospective design allowed the study of the existing records of patients without affecting treatment practise and gave an idea of how often, which drugs are associated, and have clinical features CADRs in the hospital environment.

2.2 Study Population and Sample Size

Patients diagnosed with a cutaneous adverse drug reaction during the study period, whose cases were reported in the hospital medical records or pharmacovigilance reports were included in the study population. These were clinical diagnosed cases by the dermatologists and documented in patient case sheets or ADR monitoring forms. Eighty patients with various ages and both sexes were selected with the recorded CADRs to assess demographic tendencies, reaction types, and CADRs-related drug classes.

2.3 Inclusion and Exclusion Criteria

The population of the study included patients of both genders and any age provided that the medical records of their hospital stays or pharmacovigilance reports contained adequate clinical and drug-related information to be used in the analysis. The patients whose records were not complete or were incomplete and could not provide any information that was valuable concerning drug exposure or clinical manifestations were not included in the study. Furthermore, the cases of skin reactions that are not dependent on drug exposure (i.e., skin diseases related to infection, autoimmune disorders, etc.) were also discarded to make sure that the analysis considered only the actual drug-induced cutaneous reactions.

2.4 Data Collection

The retrospective data was gathered, based on patient medical records, case sheets on dermatology department, and pharmacovigilance reporting forms stored in the hospital. The relevant information was collected in a structured form of data extraction including the demographic characteristics of the patient like age and sex, suspected drug causing the reaction and the drug class, the nature of the cutaneous reaction, the period of time since the drug administration and the severity of the reaction as reported in the clinical records. This was critically analyzed and recorded in a manner that will result in accuracy of data and data consistency that will be analyzed.

2.5 Data Analysis

The data obtained were typed into Excel. Demographic data were summarized with frequencies and percentages and the pattern of cutaneous reaction classes based on drug classes linked to CADRs and the clinical trends of these reactions. The variables, which were used to compute the mean and standard deviation, included age, the time of reaction onset, and the severity score. Correlation analysis was also done to check the relationship between the age, time of onset and the severity of reactions. Tables and percentages were used to provide the results with easy interpretation.

3. Results

3.1 Demographic profile of Patients with CADRs

Table 1 shows the demographic makeup of the cutaneous adverse drug reactions in patients. There were 80 patients who participated in the study, including both males and females of rather equal gender balance. The responses were noted to be observed in various age groups which means that CADRs are possible in persons of various age. Nevertheless, the largest percentage of cases was detected in young and middle-aged adults, which implies that this cohort could be exposed to medications related to dermatological adverse reactions more often.

Table 1. Demographic Profile (n = 80)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	39	48.75
	Female	41	51.25
Age Group	<20 years	10	12.5
	21–40 years	30	37.5
	41–60 years	25	31.25
	>60 years	15	18.75

Figure 1 shows the demographic distribution of patients with cutaneous adverse drug reactions by age category and gender.

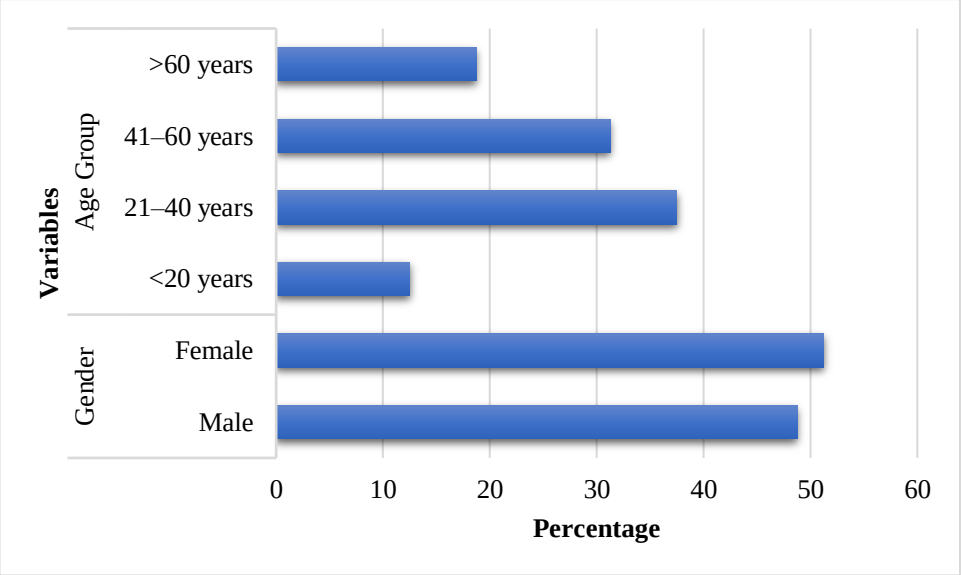

Figure 1. Demographic distribution of patients with CADRs

The figure shows that CADRs were found in various age groups with the highest percentage of the elderly aged between 21 and 40 years. The ratio of men and women is fairly equal indicating that the two genders were equally hit.

3.2 Clinical Characteristics of the Study Population

Critical clinical features of the research participants such as age, reaction onset period, and severity level are depicted in Table 2. The results show that the population of the study reflected a great age spectrum, which proves that CADRs can influence a person at various life periods. The mean latent period indicates that responses in the skin occur within a relatively short period after exposure to the drug. Moreover, the variation in the severity scores indicates variation in the degree of reactions and experience of the patients.

Table 2. Mean and Standard Deviation of Study Variables

Variable	Mean	Standard Deviation (SD)
Age of patients (years)	42.6	15.8
Time of onset of CADR (days)	5.3	2.4
Severity score	2.1	0.8

3.3 Drug Classes Implicated in Cutaneous Adverse Drug Reactions

The distribution of the therapeutic agents that are related to CADRs can be seen at Table 3. The analysis showed that there were a number of drug classes that are frequently prescribed and led to the occurrence of cutaneous reactions. The antibiotics were the most prevalent type of implicated medication, followed by non-steroidal anti-inflammatory drugs and antiepileptic medications in the second and third positions respectively. There were also other cases involving antitubercular and antifungal drugs and this implies that a wide range of pharmacological agents could be attributed to dermatological adverse events.

Table 3. Drug Classes Associated with CADRs

Drug Class	Number of Cases	Percentage (%)
Antibiotics	24	30
NSAIDs	18	22.5
Antiepileptics	14	17.5
Antitubercular drugs	10	12.5
Antifungals	7	8.75
Others	7	8.75
Total	80	100

Figure 2 shows the distribution of the drug classes involved in cutaneous adverse drug reactions in the study sample.

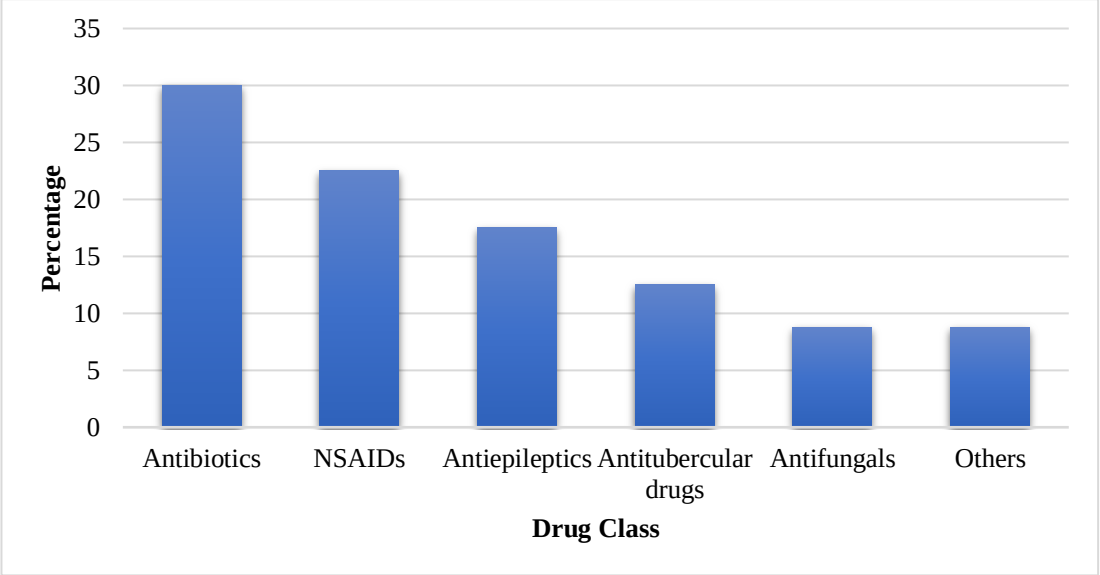

Figure 2. Distribution of drug classes associated with cutaneous adverse drug reactions

The most frequently involved group of drugs were antibiotics, then NSAIDs, and antiepileptic drugs, and the proportion of antitubercular drugs, antifungals, and others was much smaller.

3.4 Clinical Spectrum of Cutaneous Adverse Drug Reactions

Table 4 shows different patterns of skin reactions to drugs found among the study population. The findings show that CADRs had different faces in dermatology, with mild eruptions and severe skin diseases. The most common reaction was maculopapular rash, urticaria, and fixed drug eruption were also common responses. Serious conditions like Stevens-Johnson syndrome and toxic epidermal necrolysis were again found in very few patients although they were less common.

Table 4. Clinical Patterns of Cutaneous Adverse Drug Reactions

Type of Reaction	Number of Cases	Percentage (%)
Maculopapular rash	28	35
Urticaria	16	20
Fixed drug eruption	14	17.5
Stevens–Johnson syndrome	8	10
Toxic epidermal necrolysis	4	5
Others	10	12.5
Total	80	100

Figure 3 shows the distribution of various kinds of cutaneous adverse drug reactions that were witnessed among the patients.

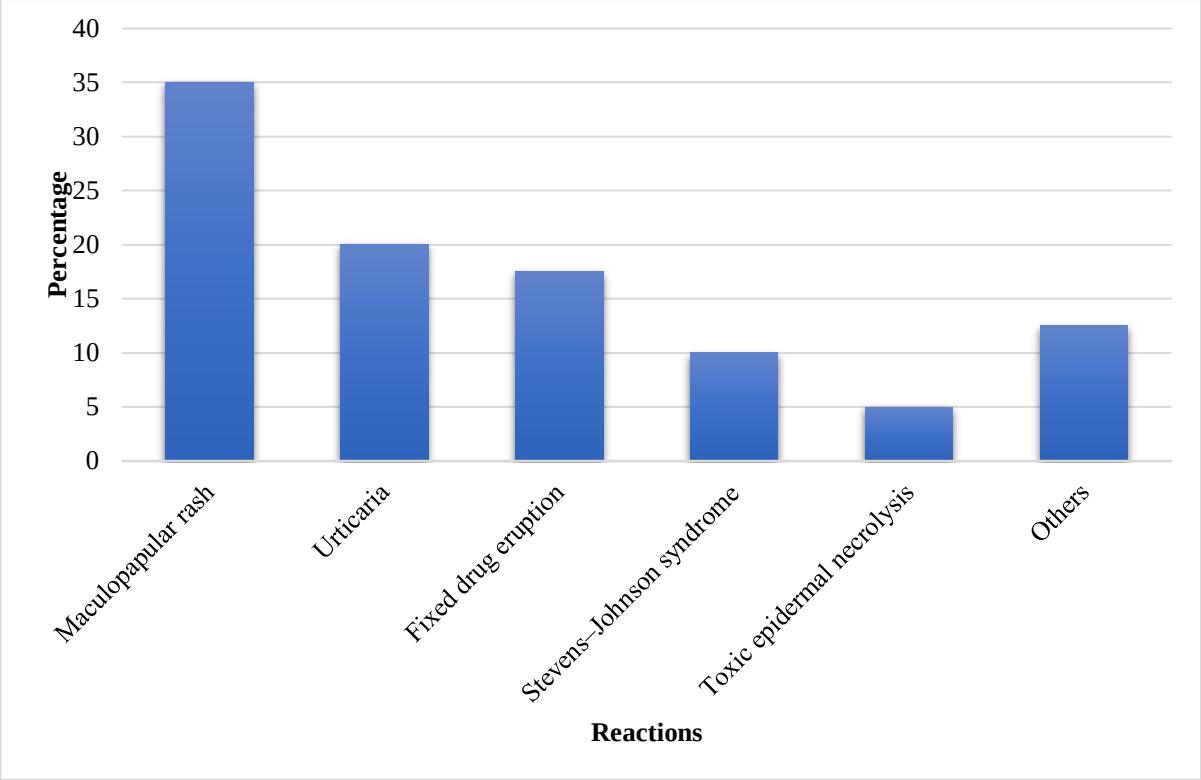

Figure 3. Distribution of clinical patterns of cutaneous adverse drug reactions

As indicated by the figure, the most common reaction was the maculopapular rash, urticaria, and fixed drug eruption, whereas severe reactions, in particular, Stevens-Johnson syndrome and toxic epidermal necrolysis were less prevalent.

3.5 Relationship Between Clinical Variables

The correlation table of the relationships between age, time of onset of reaction and severity of CADRs is in Table 6. The results of the analysis show that some variables have positive relationships, which prove that patient characteristics and clinical factors could determine the severity and development of drug-induced dermatological reactions.

Table 5. Correlation Matrix of Study Variables

Variable	Age	Time of Onset	Severity
Age	1	-	-
Time of Onset	0.28*	1	-
Severity	0.34*	0.41*	1

$p < 0.05$

4. Discussion

The study assessed the prevalence and the trends of the cutaneous adverse drug reactions (CADRs) in patients who were being given regularly used therapeutic agents within a tertiary care hospital. The results give valuable information about the demographic distribution, drug classes related to CADRs, clinical manifestations of reactions, and correlations between the chosen clinical variables. The findings obtained indicate that CADRs are common in a large group of patients and can be manifested by a significant variety of dermatological symptoms, which underlines the significance of observing drug safety in medical practice. The demographic data revealed that the CADRs were found in both genders with the ratio being fairly equal. This indicates that there is no close restriction of vulnerability to drug-related dermatological reactions to specific gender groups. The age distribution showed that young and middle-aged adults constituted a higher percentage of the reported cases and this could possibly be attributed to the fact that the population is more likely to be exposed to medications since they are treated to various acute and chronic illnesses. The descriptive statistics also revealed that the cutaneous reactions usually appeared within a very limited time following the drug administration, which means that early monitoring in the pharmacotherapy is essential to the detection and management of adverse reactions in a timely manner. It was also established that there were various categories of drugs which were associated with CADRs. Antibiotics were found to be the most frequently involved group of them, and it was preceded by non-steroidal anti-inflammatory drugs (NSAIDs) and antiepileptic drugs. These findings highlight the reality that therapeutic agents that are commonly used can be significant causative agents of dermatological adverse events. Clinically, such observations reflect the need to take caution in choosing the drugs administered and advise the patient of potential adverse effects and be on the alert to watch the patient undergoing therapy, particularly when using drugs that are known to have a higher risk profile. Apparently on as far as clinical manifestations go, the study depicted that the

CADRs can possess a variety of skin eruptions, mild to severe. The commonest reaction in the study participants was maculopapular rash, urticaria and fixed drug eruption. Despite the fact that the severe reactions like Stevens-Johnson syndrome and toxic epidermal necrolysis were not that widespread, their occurrence in the study group lays emphasis on the seriousness of drug-related dermatological disorders. The correlation analysis also indicated that some of the clinical variables such as age, period at which the reaction was in effect, and severity could give positive associations. What this means is that the patient and treatment related factors might have a bearing on the development and severity of CADRs.

The results of the current study are in line with various past studies that have been conducted to study patterns of cutaneous adverse drug reactions. Indicatively, a retrospective study that was carried out by Shalayel et al. (2018) purported that antibiotics were some of the most implicated drugs that caused CADRs, and this is in line with the current study findings. On the same note, a study conducted by Sudha et al. (2021) on adverse drug reactions in a tertiary care hospital also found antibiotics and analgesic drugs to be the most common triggers of dermatological reactions. The clinical spectrum of CADRs has also been reported to have a wide range in previous literature. Shiohara and Mizukawa (2019) talked about severe drug-induced hypersensitivity reactions, including the DRESS syndrome, and noted that dermatological reactions to drugs can manifest in mild manifestations and life-threatening systemic, as well. Moreover, research on pharmacological toxicity has emphasized on the need to identify drug-related adverse events in clinical practice. Indicatively, Tsegaye et al. (2018) found that the incidence of adverse reactions due to the use of drugs can occur due to the use of common drugs in community and healthcare institutions, which supports the necessity of pharmacovigilance. Other studies also have investigated more serious forms of cutaneous adverse reaction. Wang et al. (2018) reviewed the issue of severe immune-mediated cutaneous reactions and highlighted the importance of timely clinical intervention to eliminate complications. On the same note, a systematic review conducted by Wang et al. (2018) emphasized that some of the newer therapeutic agents, especially immunotherapies, are potentially linked to serious or even fatal toxic reactions. These results justify the need to keep it under observation and identify the adverse reaction that may be caused by a drug at its initial stages of emergence in clinical practices.

There are quite a few implications of the results of the current research regarding clinical practice and pharmacovigilance. Firstly, the fact that the classes of drugs, which are regularly engaged, are identified emphasizes the need to be highly attentive to the prescription of drugs the relationship of which with the adverse effects on the dermatological effect has been identified. Second, prompt identification of CADRs may have a positive impact on patient outcomes, allowing patients to end offending drug intake in time and follow a proper course of clinical treatment. Also, a better understanding of medical participants and healthcare professionals about possible skin reactions to drugs can be employed to minimize the risk of adverse complications.

The current research can be characterized with some limitations though it presents important information about CADRs, and they should be taken into account when interpreting the findings. The retrospective design makes use of already documented clinical information which is not always complete or consistent. Moreover, the research was carried out in one tertiary care hospital and a fairly small sample which could impact the application of the findings to other groups or healthcare institutions. In addition, not all of the clinical factors such as genetic predisposition or extensive pharmacological history were properly studied due to the limitations of the medical history.

Future research should be done in regards to bigger multicenter researches so as to have more detailed outlook of CADR trends in different populations and healthcare environment. The future studies would provide more data about the time-related relationship between the exposure to drugs and the response time as well. In addition, the introduction of pharmacogenetic research and advanced pharmacovigilance instruments can also help to determine the patients, who are more likely to experience adverse drug reactions. The practices can aid in ensuring that prescription is safer and that patient safety in clinical medicine is improved.

5. Conclusion

The study assessed the rate and clinical patterns of cutaneous adverse drug reactions (CADRs) in the event of the common therapeutic drugs in a tertiary hospital. The findings suggest that CADRs represent an important form of adverse drug reactions that may affect different patients of diverse genders and ages. The demographic analysis implied that certain reactions would be observed having an incredible diversity of patients and the ratio between males and female participants was quite even. The percentage of cases was high among young and middle-aged adult population, and this fact suggests that exposure of young and middle-aged adults to drugs might be one of the factors that promote the number of cases of drug-related skin reactions. The study also identified some of the classes of therapeutic drugs that were related to CADRs. Drugs that were most commonly involved were antibiotics and followed by the non-steroidal anti-inflammatory drugs and antiepileptic drugs. The outcomes show that drugs of the first-line interest may be a considerable source of dermatological adverse events, and the patients must be followed up closely during pharmacotherapy. The most frequent presentation was clinically the maculopapular rash, Urticaria, and fixed drug eruption were also frequent. Serious reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis were also found albeit in few cases but this could indicate that drug-induced skin diseases can be extremely dangerous. Generally, the article has shown the importance of early detection and surveillance of CADRs in clinical practice. The improved pharmacovigilance systems, the improvement of adverse reaction reporting, and the establishment of an awareness among the healthcare personnel can help to make the drugs use safer and contribute to the improved patient outcomes.

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