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COMPREHENSIVE ANALYSIS OF CUTANEOUS ADVERSE DRUG REACTIONS DURING HOSPITALIZATION: UNVEILING NUANCED COMPLEXITIES AND ENSURING PATIENT SAFETY

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ABSTRACT

Background: The spectrum of cutaneous drug reactions encompasses a broad range from benign rashes to potentially life-threatening conditions. The present study aims to comprehensively investigate the frequency, type, causality, preventability, and severity of adverse drug reactions (CADRs) occurring during hospitalization. **Methods:** Conducted at SKIMS Medical College Hospital over a comprehensive six-month duration, this study systematically monitored the occurrence of cutaneous drug reactions. These reactions' causality, severity, and preventability assessments were meticulously conducted using established classifications such as the Wills and Brown classification, WHO criteria, Hartwig scale, and modified Schumock and Thornton scales. **Result and discussion:** Involving a cohort of 300 admissions, the study identified an incidence of adverse drug reactions (CADRs) at 8%. Detailed analysis revealed no significant associations between CADRs and gender, drug allergy history, or the number of drugs administered. Notably, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), particularly Dapsone, emerged as the most common drug class associated with cutaneous adverse drug reactions (CADRs), accounting for 41.67% of cases. Antibiotics, including linezolid (12.5%) and amikacin (12.5%), followed closely. Itching (37.5%), followed by red raised lesions (33.33%), emerged as the predominant reported reactions, showcasing associations with various drugs. Notably, a significant proportion of CADRs were categorized as mild (50%), with 95.83% deemed not preventable. **Conclusion:** The prevalence of mild reactions, particularly linked to NSAIDs and antibiotics, underscores the nuanced complexities in drug responses. The research enriches the broader comprehension of adverse drug reactions, underscoring the imperative for meticulous surveillance and scholarly inquiry to elevate patient safety.

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INTRODUCTION

In the intricate realm of hospital settings, cutaneous drug reactions hold considerable significance for healthcare providers. These reactions, characterized by diverse skin manifestations, pose a complex challenge in patient care. As hospitals serve as hubs of comprehensive medical treatment, understanding and effectively managing cutaneous drug reactions become integral to healthcare delivery. The spectrum of cutaneous drug reactions spans from benign rashes to more severe and potentially life-threatening conditions. Cutaneous adverse drug reactions (CADRs) stand out as the most frequently recorded adverse drug reactions (ADRs) in the medical literature.[1] Recent epidemiological studies have highlighted adverse drug reactions (ADRs) as significant contributors to mortality, ranking among the fourth to sixth leading causes of death. This underscores the growing importance of detecting ADRs, particularly in light of the introduction of numerous potent and potentially toxic chemicals as pharmaceutical agents over the past few decades [1,2]. Consequently, it has become imperative to diligently monitor both known and unknown adverse effects of medicines. Commonly implicated drugs in adverse reactions include antimicrobials, nonsteroidal anti-inflammatory drugs (NSAIDs), anti-epileptic drugs, and anti-gout agents. The patterns of cutaneous reactions and the drugs responsible may vary depending on prescribing practices and the level of healthcare. Cutaneous adverse drug reactions (CADRs) are prevalent, constituting 10-30% of all reported adverse drug reactions, with an estimated incidence of 2-3% among hospitalized patients [1-3]. Interestingly, the prevalence and patterns of CADRs and the causative drugs implicated exhibit significant variation across diverse populations studied in regions such as Europe, Israel, and Asia [2-4].

Prompt and accurate identification of these reactions is paramount for alleviating patient discomfort and preventing the escalation of adverse effects. In a hospital setting where patients may be concurrently receiving multiple medications, the potential for drug-induced skin reactions adds layers of complexity to clinical practice. Despite the prominence of CADRs in clinical settings, underreporting persists in this region, highlighting the need for comprehensive, evidence-based studies to enhance our understanding of their incidence, patterns, and associated risk factors. This study aims to thoroughly examine CADRs, seeking to elucidate their prevalence, characteristics, and clinical significance across diverse patient populations. Our hypothesis posits that there are no significant associations between CADRs and gender, drug allergy history, or the number of drugs administered. Additionally, we anticipate that NSAIDs will emerge as the predominant class of drugs associated with CADRs.

METHODS

This prospective observational study, which obtained approval from the Institutional Ethical Committee, was conducted collaboratively by the Department of Pharmacology in conjunction with various departments at SKIMS Medical College and Hospital (SKIMS MCH) over six months. Informed consent from each patient was imperative, with an unwavering commitment to maintaining confidentiality throughout the study. The primary focus was on monitoring patients for the occurrence of adverse reactions to prescribed drugs administered in the outpatient department (OPD) or during their inpatient stay. Identification of cutaneous adverse drug reactions (CADRs) and suspected drugs adhered to the WHO definition of ADR, which characterizes it as a response to a drug that 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 [5]. Moreover, CADRs were identified through patient interviews, assessment of drug history preceding the development of CADRs, clinical examinations, review of case records, and dechallenge (withdrawal of the suspected drug to observe the effect on the reaction). Rechallenge (re-introduction of the suspected drug) was avoided for ethical reasons; however, information regarding accidental rechallenge was considered whenever available to identify suspected drugs. Only CADRs attributed to systematically administered drugs were included in the study; CADRs resulting from locally applied drugs were excluded. Active surveillance methods were employed to detect CADR. Various strategies for active reporting were implemented, including regular ward visits to identify "suspected CADRs" and eliciting feedback from the involved staff. Once a suspected CADR was reported, it was documented in a specially designed proforma, including relevant patient information, the resultant CADR reaction, and the suspected drug. Simultaneously, CADR reporting forms, designated by the Indian Pharmacopoeia Commission (IPC) within the Pharmacovigilance Programme of India, were duly filled and submitted to the Adverse Drug Reactions Monitoring Centre (AMC) at SKIMS Soura. After confirmation by the attending physician, the reported CADRs

underwent a comprehensive evaluation, including causality assessment using the WHO-UMC scale, classification based on the Wills and Brown criteria, preventability analysis utilizing the Modified Schumock and Thornton scale, and severity determination employing the Modified Hartwig and Siegel scale [5-7]. The study emphasized a commitment to ethical standards and patient confidentiality throughout all phases of research. Rigorous methodologies, including active surveillance strategies and standardized evaluation protocols, were meticulously employed to ensure accurate detection, documentation, and analysis of CADRs. By adhering to established classification systems and coding methods, the study aimed to minimize biases and enhance the reliability and validity of its findings.

Data Collection:

Data collection involved using a pro forma to gather information on demographics, diagnosis, investigations, adverse reactions, their clinical morphology, causative drugs with dosage, route, frequency, and duration of administration, lag period to develop reaction (period between administration of drugs and appearance of lesions), treatment, outcome, severity, and concomitant medications. The Anatomical Therapeutic Chemical classification system was utilized to code the causative drugs. This approach ensured comprehensive data collection for accurate analysis and interpretation of results.

Statistical Analysis

The acquired data underwent consolidation and entry into a spreadsheet using Microsoft Excel, which was then transferred to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA) for further analysis. Categorical variables were succinctly summarized as frequency and percentages. Chi-square test was employed to analyze the association between categorical variables.

RESULTS AND DISCUSSION

Among the total 300 admissions during the study period, 24 cases were identified with CADRs, thus placing the CADRs incidence rate at 8%. An investigation into the correlation between adverse drug reactions and gender revealed the following findings: Among males, 35.71% experienced one adverse drug reaction, 33.34% encountered two, and 50% had three adverse drug reactions. For females, these figures were 64.28%, 66.66%, and 50%, respectively. There was a female predominance over males (15(62.5%) vs 9(37.5%)). The Chi-square test yielded a value of 0.33 with 2 degrees of freedom, resulting in a non-significant P-value of 0.847. The analysis suggested no significant association between the number of adverse drug reactions and gender (table 1). In examining the association between the number of adverse drug reactions and a history of drug allergy (table 2), it was observed that among individuals with a history of drug allergy, 5 cases (31.25%) reported one adverse drug reaction, 2 cases (40%) experienced two adverse drug reactions, and 1 case (33.34%) encountered three adverse drug reactions. The Chi-square test yielded a value of 0.1313 with 2 degrees of freedom, resulting in a non-significant P-value of 0.9365. In individuals without a history of drug allergy, varying numbers of adverse drug reactions were observed: 11 cases (68.75%) reported one reaction, 3 cases (60%) experienced two reactions, and 2 cases (66.66%) encountered three reactions. However, no significant association was found between the number of adverse drug reactions and a history of drug allergy. Similarly, the analysis of the association between the number of drugs taken and adverse reactions revealed no significant correlation. Among those taking one drug, 10 cases (66.66%) reported one adverse reaction, 3 cases (42.85%) experienced two reactions, and 1 case (50%) encountered three reactions. For individuals taking two drugs, 3 cases (20%) had one reaction, 2 cases (28.57%) reported two reactions, and 1 case (50%) experienced three reactions. Among those on three drugs, 2 cases (13.33%) reported one reaction, 1 case (14.28%) experienced two reactions, and none reported three reactions. For individuals on four drugs, 1 case (14.28%) reported two reactions, with none reporting one or three reactions. The Chi-square test yielded a non-significant P-value of 0.6929, indicating no significant association between the number of drugs and adverse drug reactions.

In this study, the administration of drugs was categorized into various classes, encompassing Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as Dapsone (100 mg, Oral, OD) representing 41.67% of cases, Antiepileptic medications like Valproate (500 mg, Oral, OD) constituting 8.33%, Sedative/Hypnotic drugs exemplified by Phenobarbital (60 mg, Oral, BD) at 4.17%, and Antimalarial treatment with Hydroxychloroquine (5 mg, Oral, BD) accounting for 4.17% (see table 4). Additionally, Antibiotics, including Linezolid (600 mg, Oral, BD) and Amikacin (500 mg, IV, OD), comprised 12.5% each. Antiepileptic drug Phenytoin (10 mg, Oral, BD) constituted 4.17%, while the intravenous administration of

antibiotics through Inj Elcin (500 mg, IV, Once) and Inj Piptaz (4.5 gm, IV, Once) represented 4.17% and 8.33%, respectively. Table 5 illustrates the distribution of cutaneous reactions among patients, providing details on the number and percentage of each reaction and the specific drugs implicated in causing these reactions. Itching was the most frequently reported reaction, accounting for 37.5% of cases, with Dapsone [4], Valproate [1], Phenobarbital (3), and Piptaz (1) identified as the associated drugs. Erythematous rash and red raised lesions were observed in 25% and 33.33% of cases, respectively, with HCQ (4), Valproate (2), and Dapsone (4) among the implicated drugs. Urticaria/hives were observed in 1 case, accounting for 4.17% of the total reactions. This reaction was specifically associated with Levotab. Red patches were reported in 3 cases, constituting 12.5% of the reactions. Levotab, Piptaz, and Phenytoin were the implicated drugs in these cases. The burning sensation occurred in 1 case, representing 4.17% of the reactions, and was linked to Dapsone. Allergic dermatitis was reported in 1 case, contributing to 4.17% of the reactions, with Piptaz identified as the causative drug. The adverse drug reaction assessment revealed that, according to the Wills and Brown causality assessment, 62.50% of cases were deemed probable and 37.50% possible. In the WHO probability assessment, 58.33% were classified as probable, with 41.67% as possible. Hartwig's severity assessment indicated an even distribution between mild (50.00%) and moderate (50.00%) reactions. Assessing predictability, 75.00% of cases were considered predictable, while 25.00% were labeled as not predictable. The preventability assessment showed that 95.83% of cases were deemed not preventable, while 4.17% were considered probably preventable.

Table 1: Association of no. of adverse drug reactions with gender

Gender	Male	Female
One	5 (35.71%)	9 (64.28%)
Two	2 (33.34%)	4 (66.66%)
Three	2 (50%)	2 (50%)
Chi-square	0.33, df=2	
P-value	0.847	

In the present study, our study revealed an observed incidence of Clinically Adverse Drug Reactions (CADR) at 8%. This finding is similar to the results of Noel M. V et al. and Atzori L et al., whose respective studies reported a comparable % incidence rate of 10% [8,9]. Sushma M et al. reported the incidence of cutaneous CADRs as 11.4%, which is compatible with our study. 10 The alignment in CADR incidence rates among these studies signifies a noteworthy consistency in the prevalence of adverse drug reactions, reinforcing the reliability of these independent research endeavors. It is noteworthy, however, that some studies in the literature have reported lower incidence rates ranging between 2% and 4% [10-12]. This variance could be attributed to differences in study populations, methodologies, or healthcare practices across diverse settings. Variations in patient demographics, drug regimens, and criteria for identifying adverse drug reactions may lead to differences in incidence rates.

Understanding these variations is crucial for contextualizing CADR prevalence across studies and informing clinical practice. In our analysis, we found no significant association between the number of adverse drug reactions and gender. Among males, 35.71% experienced one CADR, 33.34% had two, and 50% encountered three. For females, 64.28% reported one, 66.66% had two, and 50% experienced three CADRs. The Chi-square test yielded a non-significant P-value of 0.847 ($\chi 2 = 0.33$, df = 2), aligning with Mulla FA et al.'s findings [13]. Remarkably, a discernible female predominance existed over males, with proportions of 62.5% and 37.5%, respectively. This observation aligns with findings from various studies, as documented in Chatterjee S et al., Mulla FA et al., and Nandha R et al. [12-14]. The underlying reasons for female predominance may be multifaceted, potentially stemming from variations in biological responses. To medications, hormonal influences, or differences in healthcare-seeking behavior between genders. Exploring the underlying reasons for this gender predominance, such as biological responses to medications or healthcare-seeking behavior, could provide valuable insights into optimizing patient care. Our study observed that 33.33% of patients had a history of drug allergy, while 66.67% did not. Surprisingly, despite this disparity, our analysis did not reveal a significant association between adverse drug reactions and drug allergy history (p=0.9365). This finding is consistent with prior research conducted by Mulla et al. and Dubey AK et al., who also reported a similar proportion of patients with prior drug allergy (30%) and found no significant association with adverse drug reactions [13,15]. This lack of association suggests that while drug allergy history is an important consideration in patient care,

it may not be a reliable predictor of adverse drug reactions in all cases. The non-significant association between drug allergy history and adverse drug reactions implies that other factors, such as individual drug sensitivities or immune responses, may play a more significant role in determining the likelihood of experiencing adverse reactions. This insight underscores the complexity of adverse drug reactions and emphasizes the need for comprehensive patient assessment beyond just a history of drug allergy. Additionally, our analysis of drug numbers and adverse reactions revealed diverse patterns. Still, similarly, no significant association was found (p=0.6929), aligning with the findings of Mulla et al. [13]. This lack of association suggests that the number of drugs administered may not be a reliable indicator of the risk of experiencing adverse reactions. Drug interactions, dosage, and individual patient characteristics may contribute to the variability in adverse reaction patterns observed across patients. Overall, our findings highlighted the need for further investigation into the relationship between drug allergy history, drug administration patterns, and adverse drug reactions to understand the underlying mechanisms better and identify strategies for mitigating the risk of adverse events in clinical practice.

Table 2: Association of Number of Adverse Drug Reactions with Patient History

History of drug allergy	Yes	No
One	5 (31.25%)	11(68.75%)
Two	2 (40%)	3 (60%)
Three	1(33.34)	2(66.66%)
Chi-square, df	0.1313, 2	
P-value	0.9365	

Table 3: Association between the Number of Drugs and the Number of Adverse Drug Reactions

No. of drugs	One	Two	Three	Four
One	10 (66.66%)	3 (20%)	2 (13.33%)	0
Two	3 (42.85%)	2 (28.57%)	1 (14.28)	1 (14.28%)
Three	1(50%)	1(50%)	0	0
Chi-square	3.88, 6			
P-value	0.6929			

Table 4: Distribution of Drugs and Corresponding Categories involved in CADR

No.	Drug class	Dose	Route	Frequency	Type of Drug	N	%age
1	Dapsone	100 mg	Oral	OD	NSAID	10	41.66667
2	Valproate	500 mg	Oral	OD	Antiepileptic	2	8.333333
3	Phenobarbital	60 mg	Oral	BD	Sedative/Hypnotic	1	4.166667
4	HCQ	5 mg	Oral	BD	Antimalarial	1	4.166667
6	Linezolid	600 mg	Oral	BD	Antibiotic	3	12.5
	Amikacin	500 mg	IV	OD	Antibiotic	3	12.5
7	Phenytoin	10 mg	Oral	BD	Antiepileptic	1	4.166667
8	Inj Elcin	500 mg	IV	Once	Antibiotic	1	4.166667
9	inj Piptaz	4.5 gm	IV	Once	Antibiotic	2	8.333333

Table 5: Distribution of Cutaneous Reactions and Implicated Drugs

Type of reaction	No.	%age	Drugs implicated
Itching	9	37.5	Dapsone=4, Valproate=1, Phenobarbital=3, Piptaz=1
Erythematous rash	6	25	HCQ=4, Valproate=2
Red raised Lessions	8	33.33333	D Dapsone=4, Valproate=2, Phenobarbital=1, Phenytoin=1
Urticaria/Hives	1	4.166667	Levotab=1
Red patches	3	12.5	Levotab=1, piptaz=1, Phenytoin=1
Burning sensation	1	4.166667	Dapsone=1
Allergic dermatitis	1	4.166667	Piptaz=1

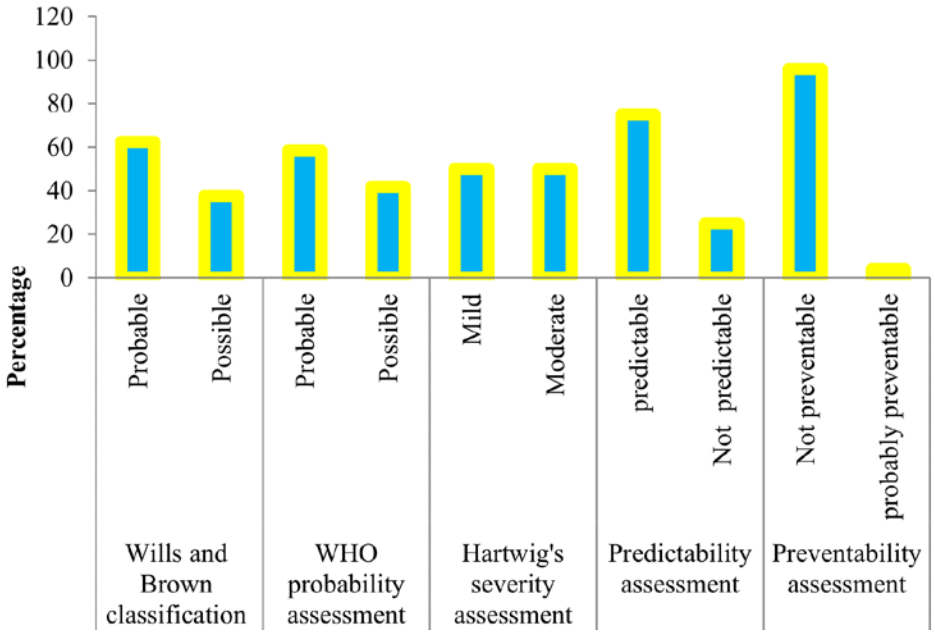

Figure 1: Adverse Drug Reaction Assessment Summary

In our study, the prevalent utilization of NSAIDs, specifically Dapsone, mirrors the findings observed in a study conducted in Oman, where NSAIDs were identified as one of the predominant drug classes associated with Clinically Adverse Drug Reactions (CADRs).[16] Nevertheless, the specific NSAIDs implicated in adverse reactions exhibit variability between the studies. While Dapsone emerged as the primary NSAID in our study, the Omani study underscored ibuprofen as the most frequently associated NSAID-causing CADRs [16]. The literature further accentuates the role of NSAIDs, with Mulla MF pinpointing ibuprofen as the NSAID with the highest CADR incidence, closely followed by diclofenac [13]. Disparate outcomes regarding the most common NSAID-causing CADRs are evident in studies by Kasemsarn et al. and Neupane et al., emphasizing ibuprofen. At the same time, Verma et al. identified diclofenac and aceclofenac [17-19]. Paracetamol consistently featured as the foremost drug causing CADRs, as reported by Bharani et al., with diclofenac and ibuprofen following suit [20]. While our study aligned with previous research recognizing NSAIDs as a prominent class associated with CADRs, the specific NSAIDs implicated vary across studies. This variability highlights the nuanced prevalence of individual drugs within the NSAID class causing adverse reactions, suggesting that factors such as regional prescribing patterns and patient demographics may influence drug-specific adverse reaction profiles. Future research could focus on elucidating the mechanisms underlying the differential risk profiles of individual NSAIDs and exploring strategies for personalized risk assessment and management in clinical practice. Additionally, antibiotics, particularly Linezolid and Amikacin, constituted a substantial proportion of our study, aligning with multiple studies, including the Omani study's recognition of antimicrobials as prevalent contributors to CADRs [14,16,19,21]. Amoxicillin was specifically identified in a few studies among penicillins [21]. However, the variability in the specific antibiotics implicated in adverse reactions across studies underscores the need for tailored approaches to antibiotic stewardship and adverse reaction monitoring. Future research directions may involve investigating the factors contributing to antibiotic-related adverse reactions, such as microbial resistance patterns, patient comorbidities, and antibiotic prescribing practices, to inform the development of targeted interventions to minimize the risk of adverse reactions while optimizing antimicrobial therapy outcomes [21].

The prevalence of Antiepileptic medications in our study, as exemplified by Valproate and Phenytoin, aligns with the Omani study, which identified Antiepileptic drugs as one of the common classes causing CADRs [16,22]. The literature, particularly a study by Tennis et al., warns about the potential for cutaneous eruptions evolving into more serious reactions during the initial weeks of initiating therapy with phenytoin or carbamazepine [22]. However, the specific drugs within this class associated with adverse reactions differ between the studies, suggesting a possible influence of regional variations in drug prescribing practices, heterogenic demographics, and healthcare protocols. Interestingly, our study revealed a

substantial utilization of sedative/hypnotic drugs (phenobarbital) and Antimalarial treatment (Hydroxychloroquine), which were not explicitly addressed by Neupane et al. and the Omani study [16,18]. These findings highlight the importance of considering a broad spectrum of drug classes and their specific members in understanding the landscape of adverse drug reactions in diverse clinical contexts.

Our observations in this study revealed that itching was the most frequently reported adverse reaction, accounting for 37.5% of cases. This aligns with findings from the study conducted by Muffa et al., where itching (pruritus) was reported as the most frequent Clinically Adverse Drug Reaction (CADR), affecting approximately 56.5% of patients [13]. Notably, a Korean study also identified itching as a major presenting complaint. However, the exanthematous eruption was the predominant manifestation of CADRs [21]. Our study observed erythematous rash and red raised lesions in 25% and 33.33% of cases. Erythematous drug eruptions have been consistently identified as the most common drug reactions in several studies, supporting our findings [23,24]. Specifically, red patches were reported in 3 cases, representing 12.5% of the reactions, and urticaria/hives were noted in 1 case, constituting 4.17% of the total reactions. Additionally, a burning sensation occurred in 1 case (4.17% of reactions), and allergic dermatitis was reported in 1 case (4.17%). Comparing our findings to existing literature, a study by Mbuagbaw et al. highlighted fixed drug eruptions as the most common CADRs [25]. However, Verma et al. and Nandha et al. reported maculopapular rashes as the most frequent CADRs, with varying incidence rates (29.4% and 42.85%, respectively) [14,19]. In a study by Chatterjee et al., macular rashes were identified as the third most common type (25.4%) of CADR [12]. The diversity in reported types of CADRs underscores the variability in patient responses to drugs across different studies. It is noteworthy that many studies have reported life-threatening CADRs, including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) [14,19,26]. However, in our present study, none of the patients developed severe CADRs, indicating a favorable outcome without these potentially life-threatening reactions. This discrepancy may be attributed to differences in patient populations, drug regimens, or healthcare practices across various study settings. Our adverse drug reaction assessment, employing both the Wills-Brown causality and WHO probability assessment scales, yielded insightful findings. According to the Wills-Brown causality assessment, 62.50% of cases were categorized as probable, aligning with a study by Nandha R et al., which reported 76.9% of Clinically Adverse Drug Reactions (CADRs) as probable [14]. This consistency is further supported by several studies that predominantly classified CADRs as probable [27,28]. Our study stands out for its unique utilization of the Wills-Brown algorithm and the WHO causality assessment scale, revealing no significant difference concerning the causality of reported Adverse Drug Reactions (ADRs). In terms of severity, our study, similar to observations in a retrospective study by Mbuagbaw et al., witnessed an even distribution between mild (50.00%) and moderate (50.00%) reactions [25]. Furthermore, findings from Acharya et al., another study, and Sharma et al. revealed that most CADRs were moderate, with some cases classified as severe, reinforcing the prevalence of moderate reactions in diverse clinical contexts [27,29]. A cross-sectional analytical study by Jamunarani et al. reported varying severity levels, with 66.7% of CADRs being moderate and 27.3% severe and life-threatening [28]. Consistent with these observations, Vijendra et al. reported that the majority of CADRs in their study were mild to moderate, aligning with our findings [30]. Notably, our study did not report any preventable CADRs, aligning with the majority of cases (95.83%) being deemed not preventable. This contrasts with studies reporting severe CADRs leading to mortality, highlighting the importance of comprehensive adverse drug reaction assessments for effective patient management and safety. Overall, aligning our findings with a diverse range of studies underscores the robustness and generalizability of our results in the broader context of adverse drug reaction assessments.

CONCLUSION

This study's recorded incidence rate of Clinically Adverse Drug Reactions (CADRs) was 8%. Remarkably, no statistically significant associations were discerned between CADRs and gender, drug allergy history, or the number of drugs administered. The study systematically categorized drug classes, with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) emerging as the most prevalent, followed by antibiotics such as Linezolid and Amikacin. Itching constituted the predominant reported reaction at 37.5%, associated with various drugs, while additional observations included erythematous rash and red raised lesions. The comprehensive assessment, employing both Wills-Brown and WHO scales, revealed a probable causality in most cases. Severity analysis indicated an even distribution

between mild and moderate reactions. The predictability assessment underscored that most cases were foreseeable, with the majority considered not preventable. These findings contribute to a nuanced comprehension of CADRs within the studied population, highlighting the intricate nature of drug reactions. The study underscores the need for continuous monitoring and ongoing research to bolster patient safety protocols.

Limitations of the study

Despite active surveillance strategies, underreporting of CADRs may still occur. Patients and healthcare providers may fail to recognize or report milder reactions, leading to underestimating the true incidence and severity of CADRs. Moreover, the study was conducted in a single medical college hospital; the findings may not fully represent the broader population, as prescribing practices and patient demographics could vary, introducing biases in observed CADR patterns. Despite efforts to control confounding variables like gender and drug allergy history, unaccounted factors such as underlying medical conditions and concomitant medications might have influenced the results, complicating the interpretation of associations with CADRs.

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTION

Junaid Ahmed Ahangar was pivotal in the study's conceptualization and design. His contributions also included drafting and revising the initial manuscript for critical intellectual content. Semira provided essential guidance and oversight throughout the study. She significantly contributed to the methodology design and data validation and ensured the study adhered to ethical standards. She also played a crucial role in the final review and editing of the manuscript. Seema Qayoom was instrumental in the clinical evaluation of adverse drug reactions and contributed to the interpretation of dermatological data. Her input was vital in framing the discussion section and ensuring the clinical relevance of the findings. Mudasir Ahmad Bhat assisted in the critical revision of the manuscript, particularly in sections related to physiological mechanisms and patient safety implications. Adil Rashid contributed significantly to the statistical analysis and data interpretation.

REFERENCES

[1] Lee A, Thomson J. Drug-induced skin reactions. In: Lee A, editor. Adverse Drug Reactions. 2nd ed. London, UK: Pharmaceutical Press; 2006: 126-155. *Current Therap Res.* **69**, 118-29 (2008)

[2] Chan A, Lee H, Ho C, Cham T, Lin S. Cost evaluation of adverse drug reactions in hospitalized patients in Taiwan: A prospective, descriptive, observational study. *Arch Dermatol*. **137**, 765-70 (2001)

[3] Bigby M. Rates of cutaneous reactions to drugs. *Contact Dermatitis*. **19**(3), 195-201 (1988)

[4] De Groot A, Beverdam E, Ayong C, Coenraads P, Nater J. The role of contact allergy in the spectrum of adverse effects caused by cosmetics and toiletries. *Pharmacol Res.* **54**, 226–233 (2006)

[5] Jose J., Rao P.G. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Am J Hosp Pharm*. **49**(9), 2229-32 (1992)

[6] Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Hosp Pharm*. **27**(6), 538 (1992)

[7] Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Indian J Pharmacol*. **36**, 292-5 (2004)

[8] Noel M V, Sushma M, Guido S. Cutaneous adverse drug reactions in hospitalized patients in a tertiary care center. *J Eur Acad Dermatol Venereol*. **26**(11), 1424-30 (2011)

[9] Atzori L, Pinna A, Mantovani L, Ferreli C, Pau M, Mulargia M, et al. Cutaneous adverse drug reactions to allopurinol: 10-year observational survey of the dermatology department - Cagliari University (Italy). *Pharmacoepidemiol Drug Saf.* **14**(8), 567–70 (2005)

[10] Sushma M, Noel MV, Ritika MC, James J, Guido S. Cutaneous adverse cutaneous drug: a 9 year study from a South Indian Hospital. *Int J Dermat.* **6**(2), 1-6 (2007)

[11] Mbuagbaw J, Mbuagbaw LE, Chiabi A, Bisseck C, Nkam M. Mucocutaneous adverse drug reactions. In:A Hospital Setting in Cameroon. *Indian J Pharmacol*. **38**(6), 429 (2006)

[12] Chatterjee S, Ghosh A, Barbhuiya J, Dey S. Adverse cutaneous drug reactions:A one-year survey at a dermatology outpatient clinic of a tertiary care hospital. *Int J Res Dermatol.* **5**, 231-8 (2019)

[13] Mulla FA, Sridhar SB, Hassan GAA, Shariff A. Prospective monitoring of cutaneous adverse drug reactions in a

secondary care hospital, UAE. *Int J App Basic Med Res*. **1**(1), 50 (2011)

[14] Nandha R, Gupta A, Hashmi A. Cutaneous adverse drug reactions in a tertiary care teaching hospital: A North Indian perspective. *J Pak Assoc Dermatol*. **16**, 28-38 (2008)

[15] Dubey AK, Prabhu S, Shankar PR, Subish P, Prabhu MM, Mishra, et al. Dermatological adverse drug reactions due to systemic medications. A review of literature. *Oman Med J*. **23**(1), 21-7 (2011)

[16] Al Raai F, Banodakar D, Epidemiological study of cutaneous adverse drug reactions in Oman. *J Drugs Dermatol*. **10**(10), 1160-7 (2011)

[17] Kasemsarn P, Kulthanan K, Tuchinda P, Dhana N, Jongjarearnprasert K. Cutaneous reactions to nonsteroidal anti-inflammatory drugs. *J Clin Diagn Res*. **6(**3), 445-8 (2012)

[18] Neupane S, Sharma SR. Adverse Drug Reactions: A 6-Month Teaching Hospital Based Study from MidWestern Nepal. *IOSRJDMS.* **13**(7), 102-9 (2014)

[19] Verma R, Tiwari S, Gupta CM, Verma N. Cutaneous Adverse Drug Reactions-A Study of Clinical Patterns, Causality, Severity and Preventability. *IOSRJDMS*.**13**(7):102-9 (2014)

[20] Bharani KR, Chandel NR, Goyal CA. Dermatological Manifestations of Adverse Drug Reactions: An Observational Study from Tertiary Care Center of Central India. *J Pharm Biomed Sci*. **4**(3), 208-14 (2014)

[21] Son Y, Lee J, Roh J. Causality assessment of cutaneous adverse drug reactions. *Ann Dermatol.* **23(**4), 432 (2011)

[22] Tennis P, Stern RS. Risk of serious cutaneous disorders after initiation of use of phenytoin, carbamazepine, or sodium valproate: a record linkage study. Neurology. 49(2), 542-6 (1997)

[23] Mani MZ, Mathew M. A study of 218 drug eruptions. *Indian J Dermatol Venereol Lepr*. **49**, 109-17 (1983)

[24] Puavilai S, Timpatanapong P. A prospective study of cutaneous drug reactions*. J Med Assoc Thai.* **72**, 167-71 (1989)

[25] Mbuagbaw J, Mbuagbaw LE, Chiabi A, Bisseck C, Nkam M. Mucocutaneous adverse drug reactions. In:A Hospital Setting in Cameroon. *Int J Dermat*. **6**(2), 1-6 (2007)

[26] Sudershan V, Siddiqua S, Aruna D, Manmohan, Ramesh S, Nazia Y. Cutaneous adverse drug reactions in a tertiary care hospital. *Der Pharmacia Lettre*. **3**(6), 210-7 (2011)

[27] Acharya L, Rao P, Ghosh S. Study and evaluation of the various cutaneous adverse drug reactions in Kasturba hospital, Manipal. *Ind J Pharm Sci.* **68**(2), 212 (2006)

[28] Jamunarani R, Priya M. analysis of adverse drug reaction related hospital admissions and common challenges encountered in ADR reporting in a tertiary care teaching hospital. *Asian J Pharm Clin Res.* **7**(1), 141-3 (2014)

[29] Sharma VK, Sethuraman G. and Kumar B. Cutaneous adverse drug reactions: clinical pattern and causative agents--a 6 year series from Chandigarh, India. *J Postgrad Med*. **47**, 95 (2001)

[30] Vijendra R, Pundarikaksha HP, Gopal MG, Girish K, Vasundara K, Jyothi R. A prospective study of cutaneous adverse drug reactions in a tertiary care hospital. *Nat J Basic Med Sci.* **3**(1), 44- 51 (2012)