Assess Incidence and Presentation of Cutaneous Adverse Drug Reactions in Patients Presenting at Jeddah's Tertiary Care Facilities

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Abstracts

Background: It is often necessary to differentiate cutaneous signs of adverse medication reactions from other similar appearances. Because patients frequently fail to recognize the connection between drug consumption and ensuing cutaneous manifestations, early detection of these responses is imperative. Purpose: Investigating the prevalence of Cutaneous Adverse Drug Reactions (CADRs) at a teaching hospital for tertiary care is the goal of this study. Methods: A self-reporting technique was used to select cases in a prospective, observational trial that lasted six months in Saudi German hospital in Jeddah . The following categories applied to Cutaneous Adverse Drug Reactions: definite, potential, and probable. Results: The most common cutaneous manifestation of ADRs (42.85%) was maculopapular rash, which was linked to antimicrobials (48.30%) and nonsteroidal anti-inflammatory drugs (21.90%) during the study period, which resulted in 91 cases of Cutaneous Adverse Drug Reactions. Conclusion: Since cutaneous adverse drug reactions are common, raising awareness of them is crucial to diagnosing and preventing them.

Keywords: Pharmacovigilance, Drug rash, Drug reaction, and Cutaneous adverse drug responses.

1. Introduction

ADRs, or adverse drug reactions, are a major contributor to morbidity, hospitalization, higher medical expenses, and sometimes even death. Serious ADRs are responsible for 6.7% of hospital admissions in the United States, according to a meta-analysis. ADRs accounted for 1.8% of all hospital fatalities and 0.7% of all admissions. One of the most prevalent kinds of ADRs is a cutaneous adverse drug reaction (CADR). Research has indicated that the prevalence of CADRs

is between 1-3 percent in wealthy nations, and between 2-5 percent in underdeveloped nations. Reporting ADRs improves general awareness and may affect regulatory agencies' suggestions on drug use. (Martin et al., 2008)

Cutaneous adverse drug reactions (CADRs) can manifest in various forms, ranging from mild rashes and urticaria to severe conditions such as Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). These reactions not only cause significant discomfort and distress to patients but can also lead to prolonged hospital stays and increased medical interventions. The early identification and management of CADRs are crucial to minimizing their impact and preventing severe outcomes. Despite the frequency and potential severity of CADRs, they are often underreported, especially in developing countries, where healthcare resources and ADR monitoring systems may be limited. (Sushma et al., 2005)

The etiology of CADRs is multifactorial, involving drug-specific factors such as chemical structure and dose, as well as patient-specific factors including genetics, age, gender, and concurrent medical conditions. An increased chance of having severe CADRs, for example, has been linked to specific genetic predispositions. Pharmacogenetic testing can help identify at-risk individuals, thereby improving drug safety and efficacy. However, the implementation of such testing is often hindered by high costs and limited accessibility, particularly in resource-constrained settings. Therefore, there is a pressing need for comprehensive surveillance and reporting systems to better understand the patterns and predictors of CADRs. (Ramesh et al., 2003)

At tertiary care hospitals, where patients are often treated with complex drug regimens, the risk of CADRs may be amplified. These settings provide a unique opportunity to study the incidence, presentation, and management of CADRs due to the diverse patient population and variety of medications used. Investigating CADRs in a tertiary care context can yield valuable insights into their prevalence, risk factors, and clinical outcomes, ultimately guiding better clinical practices and informing healthcare policies. As part of a larger effort to improve pharmacovigilance procedures and patient safety, this study attempts to evaluate the frequency and manifestation of CADRs in patients who arrive at a tertiary care facility. (Noel et al., 2004)

2. Methodology

An Institutional Ethics Committee at a tertiary care teaching hospital approved the study, which was conducted over a period of six months in Saudi German hospital in Jeddah and was prospective in nature. Using spontaneous ADR reporting as a means of data collection, the Department of Pharmacology and the Department of Dermatology conducted the study. This covered all patients who were referred from other departments to the dermatology outpatient department (OPD) and who presented with cutaneous symptoms following medication usage. Hospitalization was required for additional care for referral and OPD patients when needed.

The senior dermatologist on call made the diagnosis of CADRs. Examining a patient's medical history, determining a time correlation with the ADR, and tracking the patient's reaction after stopping the medication and resuming it were all necessary for determining the causality of the

reported ADRs. With the patient's permission and following a suitable drug-free period determined by the patient's clinical condition and the risk-benefit ratio, the patient underwent a rechallenge. ADRs were categorized using the WHO causality assessment scale as definite, plausible, or probable.

The final analysis did not include cutaneous reactions stemming from drug addiction, medication delivery problems, or inadequate patient histories. Due to the increased risk of CADRs associated with alternative medicine usage, patients were asked explicitly about their use, and those instances were also removed from the study. The senior dermatologist classified all reactions into unique dermatological patterns, and a pharmacologist used a standard proforma to record each reaction. Depending on the severity of their CADR, each patient received the proper care, which may have included steroids, oral or local antibiotics, or calming lotions. Data analysis was done using descriptive statistics, and the outcomes were given as percentages.

3. Results

The investigation yielded 91 instances, of which 47 (51.7%) were reported as female and 44 (48.3%) as male. This means that the male-to-female ratio was 0.93:1. The age group of 21–30 years old had the highest incidence of cases (25.27%), followed by the age group of 31–40 years old (23.07%).

Antimicrobials accounted for 48.30% of CADRs, with nonsteroidal anti-inflammatory drugs (NSAIDs) coming in second at 21.90% and anti-epileptic medications in third place at 13.20 percent. Benzoyl peroxide (n = 1, 1.09%), amlodipine (n = 1, 1.09%), ramipril (n = 1, 1.09%), enalapril (n = 1, 1.09%), oral contraceptives (n = 1, 1.09%), folic acid (n = 1, 1.09%), benzoyl peroxide (n = 1, 1.09%), and chlorpromazine (n = 1, 1.09%) were among the other medications linked to CADRs. Tetracycline and ibuprofen (n = 1, 1.09%), diclofenac and allopurinol (n = 1, 1.09%), rifampicin and isoniazid (n = 1, 1.09%), and dapsone and clofazimine (n = 1, 1.09%) were among the fixed medication combinations that resulted in cutaneous responses. Ciprofloxacin was administered for a suspected case of enteric fever; nonetheless, it was associated with one fatal CADR, toxic epidermal necrolysis (TEN).

Maculopapular rash (n = 39, 42.85%) was the most frequent CADR. It was followed by photosensitivity (n = 4, 4.39%), urticaria (n = 11, 12.08%), and fixed drug eruption (FDE, n = 19, 20.87%). One patient (1.09%) had lichenoid eruption, TEN, bullous eruption, and erythema multiforme. Fourteen cases (15.38%) were related to other CADRs.

There were differences in the amount of time that passed between beginning the medication and the onset of cutaneous reactions; most instances (n = 73, 80.2%) happened between 2 and 14 days, 2 cases (2.19%) within 2 days, and 16 cases (17.58%) between 15 and 30 days. Of the ninety-one cases, three (3.29%) were categorized as certain, seventy-six (84.98%) as probable, and eighteen (18) as potential. Results revealed that 1 (1.11%) patient passed away, 25 (27.47%) improved, and 65 (71.42%) patients were cured.

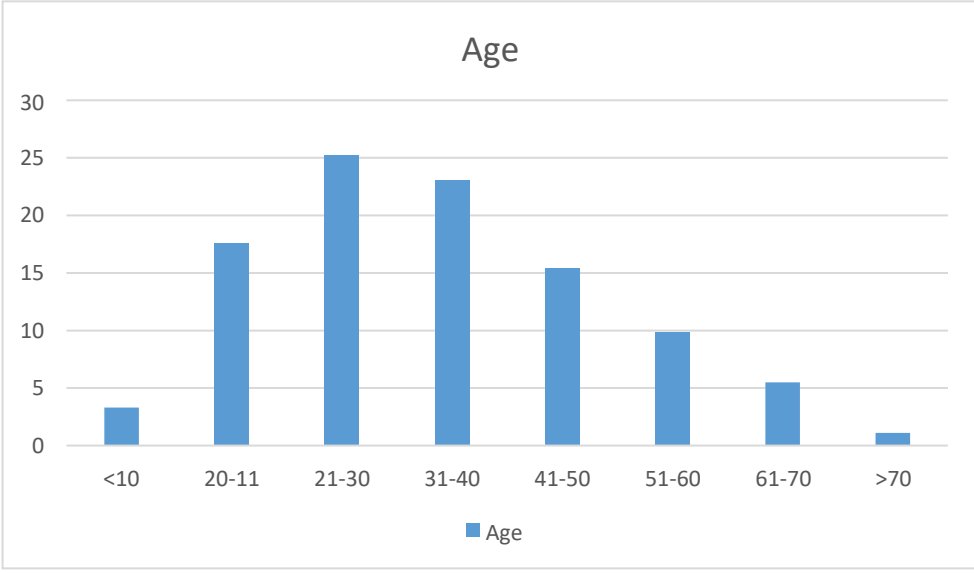

Fig 1: Age

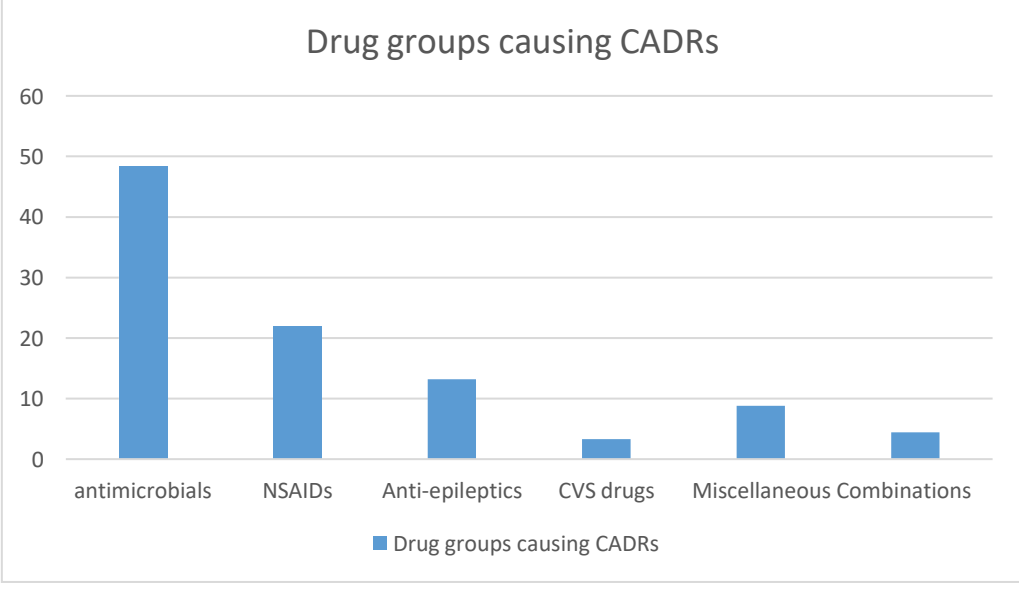

Fig 2: Drug groups causing CADRs

4. Discussion

The most common way that ADRs express themselves are cutaneous responses. They can be brought on by a variety of medication classes and include a broad range of symptoms, such as maculopapular rashes and TEN. Among these responses are exfoliative dermatitis, erythema multiforme, maculopapular and morbilliform rashes, and pruritus. Serious morbidity and even death are possible outcomes of severe CADRs. Erythematous, morbilliform, or maculopapular skin eruptions are the most common types caused by drugs.

There were 91 CADRs reported in this study. Due to the exclusion of patients with ambiguous diagnoses and inadequate medical histories, this figure may not accurately represent the true prevalence of CADRs during this time period. Furthermore, the reduced prevalence of CADRs found may have been attributed to patient underreporting and the elimination of several mild cutaneous reactions that did not necessitate hospitalization. Consistent with previous research, there was a little female predominance of CADRs over men. This disparity might arise from the fact that, although men may overlook or fail to notice small reactions, females are more likely to recognize and report cutaneous reactions. However, other research has indicated a majority of men.

The primary cause of CADRs in this study was antimicrobials; comparable results have been reported in other studies, where antimicrobials accounted for 38.6% of CADRs; other studies reported incidences of 56.9% and 55.88%; in a study involving hospitalized patients, antimicrobials accounted for 32% of CADRs; the most frequently implicated drug was cotrimoxazole, which accounted for 23.07% of cases; and sulfonamides have been identified as the primary causative agents in multicentric analyses from Italy and in a six-year study. One CADR, TEN, was deadly in this study and was caused by ciprofloxacin. The study by Sharma et al. discovered a greater prevalence of fatal CADRs, such as TEN and Steven Johnson Syndrome (SJS) (11.4%). According to the Italian study, the incidence of SJS was 1.82% and TEN was 0.2%. Variations in prescription patterns may be the cause of incidence differences. In line with findings by Sharma et al., who found that NSAIDs produced CADRs in 18% of patients, NSAIDs were the second most common cause of CADRs in this study (21.90%).

Maculopapular rash, observed in 42.8% of patients, was the most frequent of the different cutaneous symptoms of medication responses, followed by FDE in 20.8% and urticaria in 12.08%. Consistent with earlier research, the use of NSAIDs was found to be associated with a lower incidence of maculopapular rash than that of antimicrobial medicine. Anticonvulsants were also listed by Sharma et al. as the most typical cause of maculopapular rash. Similarly, after using antiepileptics, the most frequent CADR discovered in this study was maculopapular rash. Cotrimoxazole was the most common cause of FDE, a finding that was also observed in other research. A definitive correlation with tetracycline usage was difficult to establish since just one FDE case was connected to tetracycline use in a patient who had taken tetracycline and ibuprofen together. Other research have reported similar findings. ADR cutaneous symptoms have been surprisingly uniform between medications.

Conclusively, adverse drug reactions (ADRs) represent preventable sources of medical attention, elevating the burden of treatment and occasionally leading to lethal consequences, thereby

exacerbating unfavorable opinions about allopathy. Given the yearly rise of pharmaceuticals coming onto the market, it is essential to fully comprehend any potential negative effects. Only with sufficient training and alertness among doctors can this be possible. Clinicians should always be on the lookout for ADRs, and a strong system for reporting ADRs is imperative. Clinicians' main goals should be to anticipate, prevent, identify, and respond to adverse drug reactions (ADRs) in order to reduce their frequency.

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