Journal of Pakistan Association of Dermatologists. 2023;**33(3)**:912-919.

Original Article

Severe cutaneous adverse reactions in a local hospital setting in Bangladesh: A 5-year retrospective study

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Abstract

Bangladesh Cutaneous Adverse Drug Responses (CADR) are common adverse drug reactions that can manifest in many ways and range in severity. The most typical drug allergy symptom is skin manifestation, underscoring how crucial it is to identify the offending medication and stop using it doing so could even save your life in some cases.

Objective This study aims to investigate the incidence of severe and fatal cutaneous adverse medication reactions (SCAR) in hospitalized Bangladeshi patients and the prevalence of severe and fatal cutaneous adverse drug reactions (SCAR) in hospitalized patients.

Methods Inpatient records from the Department of Dermatology and Venereology, Combined Military Hospital (CMH), Dhaka, were used to gather data retroactively throughout the time frame of January 2012 to December 2016. Age, gender of the patients, implicated drugs, observed drug reactions, course of treatment, and results were some variables we examined (mortality and morbidity).

Results Clinical evaluation of the study participants revealed that 46% of cases were SJS, 29% were TEN, 16% were DRESS, and 10% were AGEP. The age range of 31 to 50 years saw the highest incidence (46%) of cases. Drug classes that contain anticonvulsants may have the highest incidence of SCADRs. Phenytoin caused 16% of patients' SCADRs, followed by carbamazepine in 22% of instances and phenobarbital in 14% of cases.

Conclusion SCADRs have been a serious issue in healthcare for decades. The majority of SCADR is caused by medications that doctors give. SCADRs were more frequently observed with anticonvulsants from the carbamazepine and phenytoin categories. Continuous monitoring of SCADRs is necessary to develop preventive measures.

Key words
SCADRs; SJS; TEN; Anticonvulsant drugs; Drug eruption.

Introduction

A severe cutaneous adverse reaction (SCAR) poses a threat to one's life. It consists of Stevens-Johnson syndrome/ toxic epidermal necrolysis (SJS/ TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP) and generalized bullous fixed drug eruptions (GBFDE).[1] Although infrequent, severe cutaneous adverse reactions (SCAR) are important causes of patient morbidity and mortality.[2] Adverse Drug Reactions (ADRs) are the most common cause of hospital-related injuries in undeveloped countries.[3] Thalidomide has a significant positive effect when used alone

or as an adjuvant therapy drug in a number of dermatoses, but its use is restricted due to its numerous, frequently dangerous side effects.[4] The "Thalidomide controversy" refers to what happened to the Thalidomide babies and the accompanying legal processes in Germany.

Adult inpatients account for just 6.5% of all ADRs, compared to outpatients, who account for 27.4%.[5] A meta-analysis of 39 prospective studies conducted in the United States over 32 years revealed that the probability of severe and fatal adverse drug reactions (ADRs) was 6.7%.[6]

Acute global exanthematous pustulosis (AGEP) is a severe adverse cutaneous reaction characterized by the rapid development of nonfollicular, sterile pustules on an erythematous base. The most frequent cause of acute widespread exanthematous pustulosis is antibiotic usage. Generally, fever and pustulosis with leukocytosis appear acutely within 48 hours of taking the drug that causes them. Therapy focuses on getting rid of the offending substance, providing supportive care, preventing infections, and occasionally helping patients by using a strong topical steroid.[7]

The most frequent and complex forms of various adverse responses are cutaneous adverse drug reactions (CADRs). Any unwanted or harmful changes to the skin, its appendages, or its mucous membranes are referred to as CADR, which also covers all adverse events connected to a medication eruption.[6]

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Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are two life threatening severe adverse cutaneous reactions (SCARs). They are caused by drugs and mediated by cytotoxic T cells.[9]

According to the advancement of SJS/TEN research, T cell receptors are crucial for the immune system of SJS/TEN, and cytotoxic T cells that are triggered mainly by drugs interact with the human leukocyte antigen (HLA). The prognosis of SJS/TEN has been improved by using novel therapeutic strategies and biologics such as TNF-alpha antagonists.[9]

Drug-induced hypersensitivity syndrome, or DRESS, is a severe, systemic pharmaceutical response connected most commonly to sulfanamides, allopurinol, and aromatic anticonvulsants.[8]

Fever, facial oedema, lymphadenopathy, and a morbilliform eruption are among the symptoms. In some cases, these symptoms may develop to an erythematous rash and exfoliative dermatitis.[11]

Patients with TEN may experience a mortality rate as high as 50%.[12] When less than 10% of the body's surface is affected, SJS develops, whereas TEN impacts more than 30%.[12] They have a significant influence on costs and the availability of medical services.[3] Since it is inevitable that some of the patients they treat may have ADRs, all doctors should have some understanding of them, even though patient outcomes can be enhanced by early CADR detection.

Few studies have looked at the clinical presentation and consequences of CADR in hospitalized patients, which results in inadequate reporting of CADR in the literature. Patterns of CADR may change over time due to the

development of new drugs and modifications in prescribing practices.[6,13] This study aims to investigate the incidence of severe cutaneous adverse drug reactions (SCAR) in patients at the Joint Military Hospital in Dhaka from January 2012 to December 2016 throughout a five-year period.

Methods

Data were gathered retrospectively from inpatient records of patients who were treated for the disease at the inpatient department of the Combined Military Hospital (CMH), Dhaka, between January 2012 and December 2016. These patients had severe cutaneous adverse effects. A tertiary care hospital in Dhaka is called CMH. The study comprised 50 patients with CADR diagnoses in total.

The intended sample size of 50 samples was reached using information gathered from patient data collected throughout the research period.

Age, sex, clinical presentation, drug consumption history, allergic responses, past drug interactions, investigations, and patient therapy were all documented for each patient. The patients were kept under observation until they were allowed to leave the hospital.

Results

There were 50 (37 men and 13 women) patients with SCAR who visited the dermatology inpatient department overall throughout the six-month period. The diagnosis was made between January 2012 and December 2016 **(Figure 1)**.

Table 1 Demographic characteristics of the patients (n=50).

Age	*Frequency*		*Total*
	Male (37)	*Female (13)*	
16-30	12 (32.43%)	4 (30.76%)	16
31-50	15 (40.54%)	8 (61.53%)	23
51-70	7 (18.91%)	1 (7.69%)	8
>70	3(8.10%)	0	3
Mean±SD	37.42 ± 5.3		

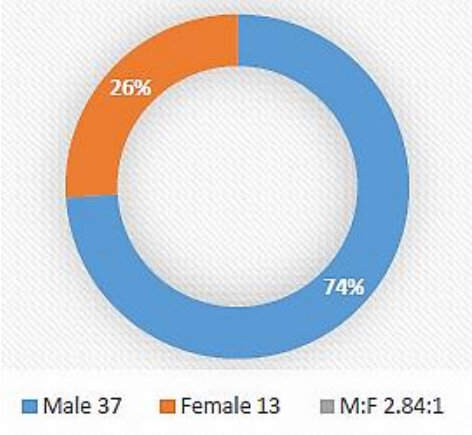

Figure 1 Gender distribution of patients (n=50).

The patients were 37.42 5.3 years old on average. Males comprised 74% of cases, while females comprised 26%. The prevalence of severe adverse drug reactions was highest in the middle age group in both sexes but predominantly in females **(Table 1)**.

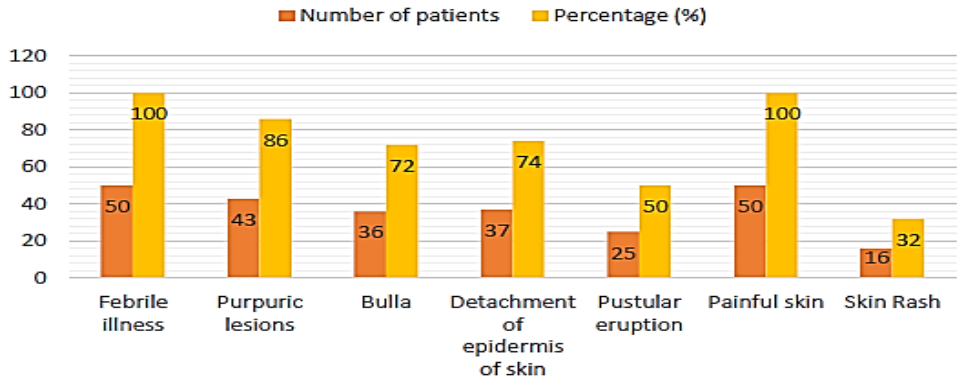

Figure 2 Clinical symptoms of the study subject.

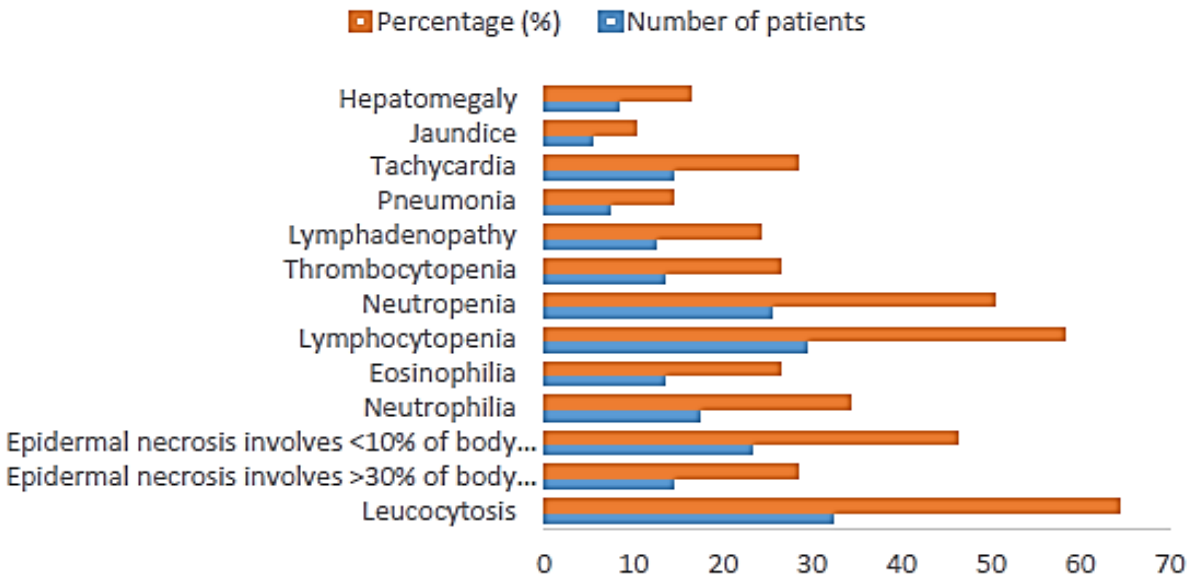

Figure 3 Clinical sign and laboratory profile of severe cutaneous adverse drug reactions.

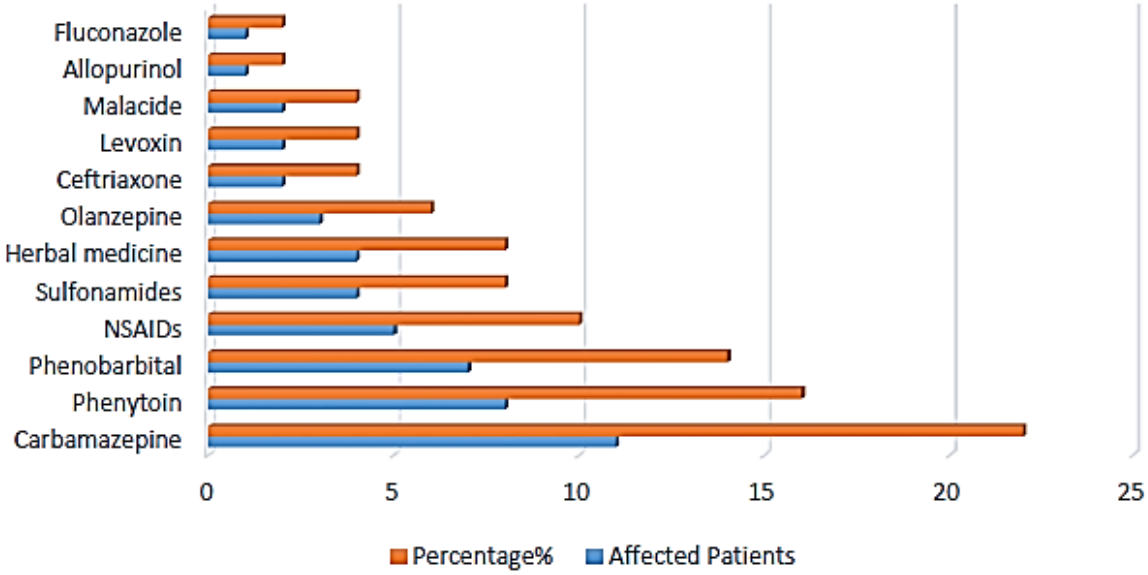

Figure 4 Name the culprit drugs causing severe cutaneous adverse drug reactions (SCAR).

The most frequent symptoms in all patients-present in 100% of cases-were febrile sickness and a fast, painful skin progression. The data also suggests that pustular eruption, bulla, and purpuric lesions were the most frequent clinical manifestations (86.0%, 72.0%, and 50.0%, respectively) **(Figure 2)**.

Leukocytosis was found in 64.0% of patients, followed by lymphocytopenia in 58.0% of patients, neutropenia in 50% of patients, epidermal necrosis on less than 10% of body surface area in 46.0% of patients, and neutrophilia in 34.0% of patients. 23 (46%) of the patients had an affected part of the body that covered 10% of its surface, 13 (26%) had an affected part that covered 10% to 30%, and 14 (28%) had an affected part that covered more than 30% **(Figure 3)**.

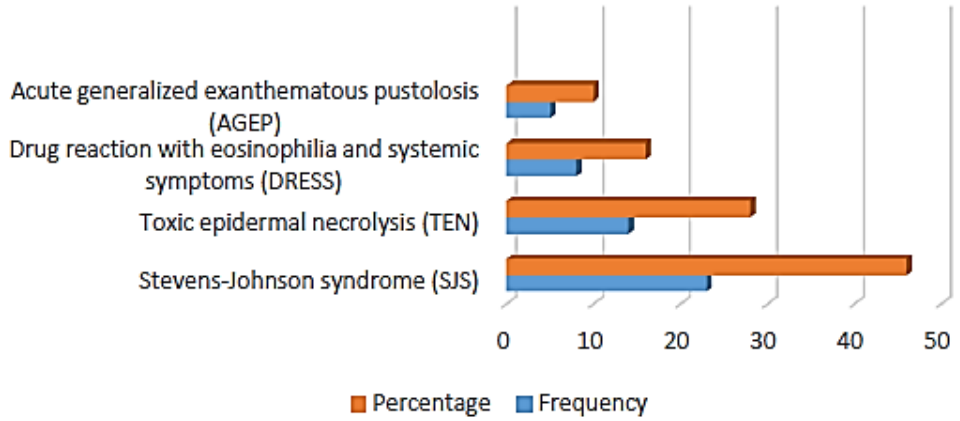

Figure 5 Clinical diagnosis of severe cutaneous adverse drug reactions (SCAR).

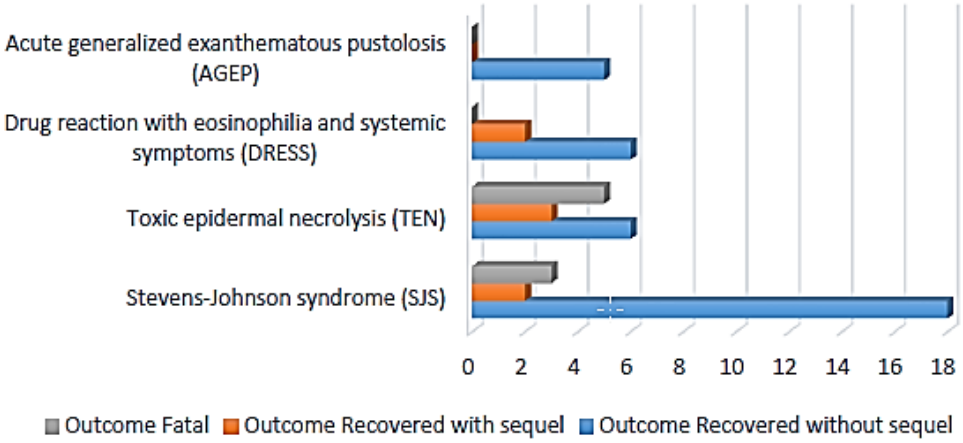

Figure 6 Outcome and fate of severe cutaneous adverse drug reactions patients.

It is worth remembering that the anticonvulsant medication class has the potential to cause ADRs with the highest incidence and a variety of morphological forms. In 22.0% of cases of severe cutaneous adverse medication reactions, carbamazepine was blamed, followed by phenytoin in 16.0% of patients' cases and phenobarbital medicines in 14.0% of cases **(Figure 4)**. Antimicrobials, NSAIDs, and herbal medicines were also problematic substances, however.

Clinical features and pertinent research findings were carefully assessed. Stevens-Johnson syndrome (SJS) was diagnosed in 46.0% of patients with severe cutaneous adverse drug reactions (SCAR), toxic epidermal necrolysis (TEN) was found in 28.0% of patients, drug reaction with eosinophilia and systemic symptoms (DRESS) was found in 16.0% of patients, and acute generalized exanthematous pustulosis (AGEP) was found in 10.0% of patients **(Figure 5)**.

Stevens-Johnson syndrome (SJS) patients had a recovery rate of 78.2% (18/23), toxic epidermal necrolysis (TEN) patients had a recovery rate of 42.8% (6/14), drug reaction with eosinophilia and systemic symptoms (DRESS) patients had a recovery rate of 75.0% (6/8), and acute generalized exanthematous pustulosis (AGEP) patients had a recovery rate of 100%. In patients with toxic epidermal necrolysis (TEN), the complication rate was higher, at 57.1% (8/14),

compared to 21.7% (5/23), for Stevens-Johnson syndrome (SJS) and 25.0% (2/8), for drug reaction with eosinophilia and systemic symptoms (DRESS). Overall results, therefore, suggest that the prognosis for toxic epidermal necrolysis is dismal **(Figure 6)**. Patients had complications from the septic shock that turned into multiple organ disorder syndromes (MODS), which eventually caused death.

Discussion

The most frequent ADR symptoms are cutaneous responses. Diverse medication classes have the potential to cause a wide variety of cutaneous symptoms, from exanthematous rashes to TEN. Certain severe cutaneous adverse drug reactions (CADRs) can lead to substantial morbidity or even death.[3]

A total of 50 patients were included in the current study. Due to the exclusion of patients with drug responses caused by herbal or homoeopathic medications as well as individuals in whom the drug could not be identified, this statistic may need to accurately reflect the real prevalence of CADRs during this time.

The design of this study highlights several significant methodological concerns, such as patient selection, follow-up, sample size, and the detection of the incidence of severe and fatal cutaneous adverse drug reactions (CADRs) in hospitalized patients. The majority of the 50 cases in the research (74.0%) were men, while only 26.0% involved women. According to a survey, there were 88 women and 112 men. Similar findings were also observed in the group of 298 (59.6%) males and 202 (40.4%) females.[14] According to another research conducted in Bangladesh, the male- to-female ratio was 1:1.14, with 56% of the 50 patients evaluated being female and 44% male. Age ranged from 5 to 75 years old.[15]

This study reveals that fever and a rapidly increasing painful skin manifestation were the most prevalent symptoms among all patients, present in every single instance. The other frequent clinical manifestation (86.0%, 72.0%, and 50.0%, respectively) was pustular eruption, bulla, and purpuric lesions. Leukocytosis was seen in 64.0% of the patients, followed by lymphocytopenia in 58.0% of the patients, neutropenia in 50% of the patients, epidermal necrosis affecting less than 10% of the body surface area in 46.0% of the patients, and neutrophilia in 34.0% of the patients.

It is important to keep in mind that the anticonvulsant medicine class is associated with the highest prevalence and variety of ADR morphological aspects. Carbamazepine was the drug that produced the most (22.0%) severe cutaneous adverse drug reactions, followed by phenytoin (16.0%) and phenobarbital (14.0%). According to the study, SJS, erythema multiforme, and urticaria accounted for the majority of adverse drug reactions among the 53 individuals who had them.[16]

The main classes of medications covered in this study, like in other research, were anticonvulsants, antibiotics, and NSAIDs. Different drugs and mortality did not differ in a statistically meaningful way.[8,17,18]

Clinical manifestations and pertinent research findings were carefully assessed. Stevens-Johnson syndrome (SJS) was identified in 46.0% of patients with severe cutaneous adverse drug reactions (SCAR), toxic epidermal necrolysis (TEN) was identified in 28.0% of patients, drug reaction with eosinophilia and systemic symptoms (DRESS) was identified in 16.0% of patients, and acute generalized exanthematous pustulosis (AGEP) was identified in 10.0% of patients. CADR incidence was found to be 36.1%. The three most often

reported medications were phenytoin (19.7%), allopurinol (15.5%), and unknown medications (9.09%).[19]

In their research, the incidence of SJS and TEN was 5.61%, whereas previous studies reported incidences of 4% and 22.2%.[20]

Patients with Stevens-Johnson syndrome recovered at a rate of 78.2% (18/23) while those with toxic epidermal necrolysis recovered at a rate of 42.8% (6/14), those with drug reaction with eosinophilia and systemic symptoms (DRESS) recovered at a rate of 75.0% (6/8), and those with acute generalized exanthematous pustulosis (AGEP) recovered at a rate of 100%. Analysis of the recovered with sequel research shows that patients with toxic epidermal necrolysis (TEN) had a higher complication and mortality rate than those with Stevens-Johnson syndrome (SJS) or drug reaction with eosinophilia and systemic symptoms (DRESS), with a complication rate of 57.1% (8/14) vs. 21.7% (5/23) or 25.0% (2/8), respectively (DRESS). In conclusion, studies have shown that toxic epidermal necrolysis has a dismal prognosis.

The higher mortality rate resulting from TEN has previously been extensively discussed. According to studies, the degree of skin detachment is directly correlated with a death risk of up to 50%.[21]

Conclusion

Even though some cutaneous medication responses are self-limiting, others might be fatal if not identified and treated well and soon. The most prevalent morphological kinds were those with Stevens Johnson Syndrome (SJS). Overall results, therefore, suggest the prognosis for toxic epidermal necrolysis is poor. Despite being uncommon, SCAR warrants ongoing attention because a better understanding of the mechanisms of lesions in SCAR will have implications for other areas of medicine in addition to enhancing the safety of drugs. A multispecialty approach is required in SCARs since many organ systems are involved.

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