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Clinical Profile and Treatment Outcome of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis at a Tertiary Hospital of Nepal

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Abstract

Introduction: Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe forms of severe cutaneous adverse reactions (SCAR) with high morbidity and mortality. Due to its rarity and severe acute nature, there is limited data from controlled trials. This study seeks to contribute to the existing knowledge on the etiology and treatment outcomes of SJS/TEN.

Objectives: To assess the clinical profile and treatment outcomes of SJS and TEN patients.

Materials and Methods: A retrospective analysis of patients' admissions and discharge records was done from April 2020 to November 2024. The variables analyzed included the clinical types (SJS, TEN, SJS/TEN overlap), causative drugs, treatment undertaken, mean duration of hospital stay, and treatment outcome.

Results: Among 27 patients, SJS accounted for 81.48% (n=22), TEN 14.8% (n=4), and SJS/TEN overlapped 3.70% (n=1) of the cases. Non-steroidal anti-inflammatory drugs (NSAIDs) were the most commonly implicated culprit drugs, followed by amoxicillin. The mean time of appearance of the lesion after the medication was 29.14±22.93 days. All the patients received steroids-hydrocortisone 81.48% (n=22); hydrocortisone and dexamethasone 7.40% (n=2) and methylprednisolone 7.40% (n=2) with supportive management. The mean duration of hospital stay was 12.03±10.52 days, and the recovery rate without complication was 88.89% (n=24).

Conclusion: SJS is the most common clinical type in the SJS-TEN spectrum. NSAIDs and antibiotics were the common causes of SJS/TEN. Corticosteroids proved beneficial in managing SJS/TEN in our patients.

Keywords: Corticosteroid; Stevens-Johnson Syndrome; Toxic Epidermal Necrolysis

Introduction

SJS and TEN are severe cutaneous adverse reactions characterized by mucosal erosion, epidermal detachment, and necrosis. SJS is defined as epidermal detachment of <10% Body Surface Area (BSA); TEN is defined as epidermal detachment of >30% BSA, and SJS/TEN overlap is 10-30% BSA epidermal detachment.[1] It affects 1 to 5 individuals per million populations per year.[2] Drugs are the leading cause of the offense, with infections as a secondary factor. Allopurinol, aromatic anti-seizure medications, lamotrigine, nevirapine, NSAIDs, and antibiotics are some common culprits.[1,3] Along with the withdrawal of the culprit drug and supportive care, usual therapeutic management includes systemic corticosteroids, cyclosporin, and intravenous immunoglobulins.[4,5] SJS/TEN is a disease spectrum with high mortality, accounting for up to 5.4%, 14.4%, and 15.3% mortality in the SJS, SJS-TEN overlap, and TEN groups, respectively.[6] Owing to the rarity and life-threatening nature, prospective

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studies and randomized control trials regarding its management are lacking. This study aims to report the common offending drugs, clinical presentation, and treatment outcomes of SJS/TEN patients managed in a tertiary hospital in Nepal.

Materials and Methods

After ethical approval from the Institutional Review Committee, a hospital-based, retrospective, descriptive study was conducted at the Department of Dermatology in a tertiary hospital, Tribhuvan University Teaching Hospital in Nepal. [Ref. 367(6-11) E2 081/082] Information on the patients admitted with the diagnoses of SJS, TEN, and SJS/TEN from April 2020 to November 2024 was extracted from the department's database and the hospital's record section. A predetermined proforma was used to record demographic and clinical data. The outcome was assessed by considering the length of hospital stay, ICU stay, and mortality. Final data were analyzed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA).

Results

There were 234 new admissions under the dermatology department over four years, out of which 27 (11.53%) of inpatient admissions accounted for SJS/TEN. Among them, 59.25% (n=16) were males, and 40.74% (n=11) were females. The mean age of the patients was 33.78 ±17.59 years (range 7-75 years). The commonest age group to be affected was 16-45 years. SJS accounted for 81.48% (n=22), TEN 14.81% (n=4), and SJS/TEN overlap 3.70% (n=1) of the cases.

Diagnosis	Drugs taken before presentation n(%)			
	Single	Multiple	None	Total
SJS	8(29.63%)	9(33.33%)	5(18.52%)	22(81.48%)
SJS/TEN overlap		1(3.70%)		1(3.70%)
TEN	1(3.70%)	1(3.70%)		2(7.41%)
TEN overlap DRESS	1(3.70%)	1(3.70%)		2(7.41%)
Total	**10(37.04%)**	**12(44.44%)**	**5(18.52%)**	**27(100%)**

Table 1: Distribution of drug intake across the clinical spectrum of SJS/TEN

		Clinical spectrum n(%)				
	Drugs Implicated	SJS	SJS/TEN overlap	TEN	TEN overlap DRESS	Total
	Allopurinol	1(3.70%)				1(3.70%)
	Carbamazepine	3(11.11%)				3(11.11%)
	Sulphasalazine	1(3.70%)				1(3.70%)
Antibiotics	Amoxicillin	3(11.11%)	1(3.70%)			4(14.81%)
	ATT	2(7.40%)		1(3.70%)		3(11.11%)
	Tazobactam Piperacillin				1(3.70%)	1(3.70%)
	Azithromycin	1(3.70%)				1(3.70%)
	Ciprofloxacin	1(3.70%)				1(3.70%)
	Ceftriaxone		1(3.70%)			1(3.70%)
	Cotrimoxazole	1(3.70%)				1(3.70%)
	Dapsone				1(3.70%)	1(3.70%)
NSAIDs	Ibuprofen	3(11.11%)				3(11.11%)
	Nimesulide	1(3.70%)				
	Naproxen	1(3.70%)				
	Etoricoxib	1(3.70%)				
	Paracetamol	2(7.40%)				2(7.40%)
	Febuxostat	1(3.70%)				1(3.70%)
	Clobazam			1(3.70%)		1(3.70%)
	Leflunomide				1(3.70%)	1(3.70%)
	Fluconazole	1(3.70%)				1(3.70%)

Table 2: Drugs implicated across the SJS/TEN spectrum

While 44.45% (n=12) patients had a history of polypharmacy, only 37.03% (n=10) gave a history of single medication use, and 18.51% (n=5) of the patients could not recall using any medications, among whom 11.12% (n=3) had symptoms suggestive of viral infection and 3.70% (n=1) patient had a history of vaccination with SARS-CoV-2 Vaccine (VeroCell) 23 days before lesion onset (Table 1). Among the patients, 14.81% (n=4) had pre-existing neurological disorders, 11.12% (n=3) had systemic lupus erythematosus, 11.12% (n=3) had tuberculosis, 7.40% (n=2) had chronic kidney disease, and 3.70% (n=1) was HIV positive.

NSAIDs were the most commonly implicated culprit drugs, affecting 22.23% (n=6) of the patients, followed by amoxicillin in 14.81% (n=4). Carbamazepine was implicated in 11.12% (n=3) and Anti Tubercular Therapy (ATT) in 11.12% (n=3). Among other antibiotics, azithromycin, ceftriaxone, ciprofloxacin, cotrimoxazole, and dapsone each implicated as the cause in 3.70% (n=1) patients (Table 2).

The mean time of appearance of the lesions after first taking medication was 29.14±22.93 days (range 7 to 120 days), with a single patient reporting having started ATT 3 months prior.

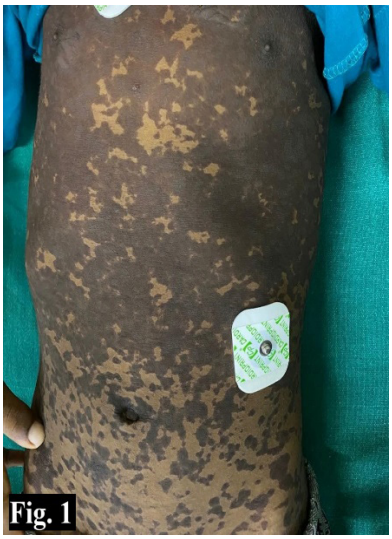
At admission, 74.07% (n=20) patients presented with dusky purpuric macules, 18.51% (n=5) had cutaneous erythema and erosions, and 7.40% (n=2) had re-epithelialization of lesions (Table 3). Mucosal involvement comprised oral and conjunctival involvement in 33.34% (n=9), oral and genital involvement in 14.81% (n=4), while oral, conjunctival, and genital mucosa were all involved in 48.15% (n=14). At presentation, 40.74% (n=11) of patients had a positive Nikolsky's sign (Figure 1-3).

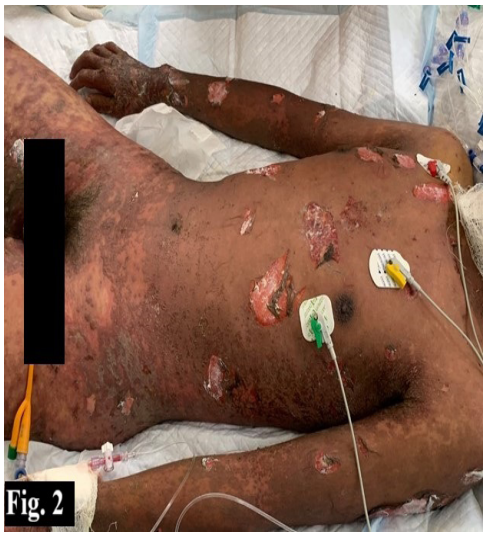
At the time of admission, 18.51% (n=5) had leukocytosis, 14.81% (n=4) had leukopenia, 14.81% (n=4) had anemia, and thrombocytopenia was observed in 25.92% (n=7). Liver function tests were deranged in 66.67% (n=18), and renal function tests were deranged in 11.12% (n=3). Raised random blood sugar was observed in 7.40% (n=2), hypoalbuminemia was observed in 40.74% (n=11), and a positive antinuclear antibody (ELISA) in 14.81% (n=4). A record of Arterial Blood Gas (ABG) analysis could be retrieved for 9 patients only, showing a decrease in HCO3- in 25.92% (n=7) patients and an increase in lactate in 11.12% (n=3).

All the patients received steroids with supportive management. Supportive management included care at ambient room temperature, appropriate fluid, electrolyte, and nutrition supplementation, wound care, and pain management. Among them, 81.48% (n=22) patients received hydrocortisone in tapering dose for 5 days per department practice of IV hydrocortisone 200mg QID on Day 1, 200mg TDS on Day 2, 200mg BD on Day 3, 100mg BD on Day 4, followed by100mg OD on Day 5 then stopped. While 7.40% (n=2) received the same dose of hydrocortisone with dexamethasone 100mg for 3 days, the other 7.40% (n=2) received only methylprednisolone 500mg for 3 days, and 3.70% (n=1) received prednisolone alone. Oral prednisolone was continued in tapering dose in 25.92 % (n=7) patients. On average, hydrocortisone was administered 4.63±2.76 days after the first appearance of the lesions (range 1-12 days). One patient of Drug Reaction with Eosinophilia and Systemic Symptoms

		Clinical Presentation n(%)					
Diagnosis	**Mucosal involvement**	**Cutaneous erythema and erosions**	**Dusky purpuric macules**	**Dusky purpuric macules and Bulla**	**Erythema and sheet-like erosions**	**Re-epi-theliali-zation**	**Total**
SJS		3(11.11%)	16(59.25%)	1(3.70%)		**2(7.40%)**	**22(81.48%)**
	Oral + Conjunctival		8(29.62%)			1(3.70%)	**9(33.33%)**
	Oral + Genital	2(7.40%)	2(7.40%)				**4(14.81%)**
	Oral + Conjunctival + Genital	1(3.70%)	6(22.22%)	1(3.70%)		1(3.70%)	**9(33.33%)**
SJS/TEN overlap	Oral + Conjunctival + Genital		1(3.70%)				**1(3.70%)**
TEN	Oral + Conjunctival + Genital				2(7.40%)		**2(7.40%)**
TEN overlap DRESS	Oral + Conjunctival + Genital		2(7.40%)				2(7.40%)
Total		3(11.11%)	19(70.37%)	1(3.70%)	2(7.40%)	2(7.40%)	27(100%)

Table 3: Clinical presentation across the SJS/TEN spectrum





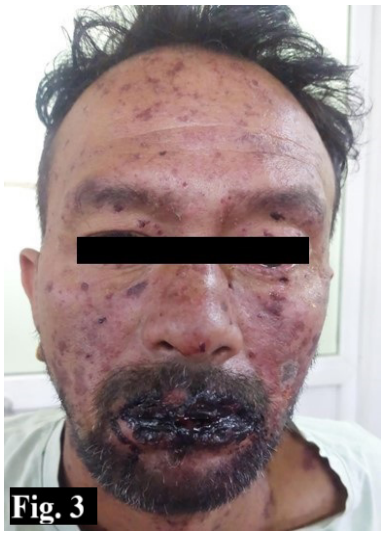


Figure 1: Discrete to confluent dusky purpuric macules over trunk; **Figure 2**: Widespread erythema and epidermal detachment in a case of TEN; **Figure 3**: Hemorrhagic crusting of vermillion lips and cutaneous purpuric macules in a case of SJS

(DRESS) overlapping with TEN received ciclosporin for 3 days but was stopped due to sepsis. Of these, 25.92% (n=7) patients received appropriate antibiotics following a positive result in skin swab, urine, and/or blood cultures.

The mean duration of hospital stay was 12.03±10.52 days (range 1-51 days). Out of 27, 10 patients were cared for in Intensive Care Unit (ICU). The mean duration of ICU stay was 2.92±4.91days (range 3-19 days). Despite optimal management, 3.70% (n=1) of patients succumbed to septic shock; 88.89% (n=24) improved and were discharged without complications, while 7.40% (n=2) recovered but developed corneal ulcers.

Discussion

SJS/TEN are severe, life-threatening mucocutaneous reactions characterized by purpuric macules, mucositis, extensive blistering, and skin sloughing. They accounted for 11.53% of all inpatient admissions in our department.

NSAIDs were the most frequently implicated culprit drug in the causation of SJS/TEN in our study, which was followed by amoxicillin, carbamazepine, and ATT, respectively. A study in the Chinese population by Yang et al., and a review of multi-national studies from the Southeast Asian region by Lee et al., reported carbamazepine, allopurinol, and penicillins to be the most frequently implicated culprit drugs in the causation of SJS/TEN.[7,8] A study by Shrestha et al., conducted two decades ago at the same center as ours, examined 27 SJS/TEN, and 3 cases of Erythema Multiforme. The most common drugs implicated were antibiotics (sulfonamides, penicillins, quinolones), found in half of the patients, followed by anticonvulsants, particularly carbamazepine, in the majority of the other half.[9] This may be attributed to a change in the prescription patterns of these drugs in recent years.

In our study, the latency period of drugs ranged from 7 to 120 days, with a median of 23 days. The latency period ranges widely across studies and different drugs. Abe et al., reported the median durations for SJS/TEN caused by allopurinol, carbamazepine, lamotrigine, phenytoin, and ACE inhibitors to lie between 19 and 27 days, which is similar to our study findings. But interestingly, the latency period for antipyretic analgesics was reported as low as within 4 days.[10] A study by Ordoñez et al., reported that the mean latency period of antiepileptic drugs for SJS/TEN did not exceed a month, which is consistent with our study.[11]

All the patients in our study were given systemic steroids in combination with supportive care after discontinuing the offending drug. The majority i.e. 88.89%(n=24) of the patients, received a short course of high-dose hydrocortisone in tapering dose. Similar to our study, Tan et al., reported the use of high-dose hydrocortisone (300-400 mg/day for 7-10 days) in eleven patients of SJS with a favorable outcome.[12] While earlier studies argue against the overall benefit of the use of steroids, a study conducted in Bangkok comparing two groups of patients, those who did not receive steroids and those who did, showed a reduction in mortality from 25% in the non-steroid group to 13.7% in the steroid-treated group.[13,14] A retrospective study by Liu et al., in 70 patients found notable differences between expected and actual mortality rates for SJS/TEN, supporting the use of steroids.[15]

While our study provides limited data on high-dose methylprednisolone, dexamethasone, and other systemic immunomodulatory treatments for SJS/TEN, recent reviews and guidelines offer strong evidence and high recommendations for their use either solely or in combination. An expert consensus recommendation from Indian dermatologists has concluded a grade of recommendation B for the use of steroids, cyclosporin, and intravenous immunoglobulin

(IVIg), whereas in other studies, a combination of corticosteroids and IVIg has been found to significantly reduce mortality in patients with SJS/TEN compared to other treatments.[5,16,17]

Our study, prescribed antibiotics to 25.92% (n=7) of patients based on culture results. In contrast, antibiotics were prescribed prophylactically in all patients in the study by Shrestha et al.[9]

This partly reflects a shift in practices towards focusing on supportive care and minimizing the use of pharmaceuticals whenever possible.

The mean duration of hospital stay in our study was 12.03±10.52 days. Krajewski et al.,'s meta-analysis and meta-regression of 42 observational studies reported an average hospital stay of 19.99 days (95% CI, 16.53-23.44).[18] The favorable outcome in our study may be attributable to the majority of cases being SJS and a prompt introduction of immunomodulatory therapy.

Conclusion

Our study's findings align with the existing literature. In resource-limited settings like ours, steroids remain an effective immunomodulatory treatment. Hydrocortisone shows favorable outcomes in the management of SJS patients. Further research is needed to explore the use of different steroids and alternative immunomodulators in the context of Nepal.

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