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**Original Research Article**

# Clinical Spectrum and Implicated Drugs in Severe Cutaneous Adverse Drug Reactions: A Hospital-Based Observational Study from South India

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**ABSTRACT**
**Background:** Severe cutaneous adverse reactions (SCARs) are uncommon but potentially life-threatening drug reactions that may involve the skin, mucosae and internal organs. Local data on their clinical spectrum and suspected culprit drugs can support recognition and pharmacovigilance.
**Objectives:** To describe the clinical and epidemiological profile of SCARs and the drugs implicated among patients attending a tertiary-care centre in South India.
**Methods:** This hospital-based observational study was conducted in the Department of Dermatology, Venereology and Leprosy, Government Rajaji Hospital and Madurai Medical College, Madurai, Tamil Nadu, from 1 January to 31 December 2024. Forty-eight patients with SCARs were included. Demographic details, suspected drugs, latency, clinical features, investigations, histopathology, treatment and hospital stay were recorded. Drug causality was assessed using the Naranjo adverse drug reaction probability scale. Data are presented descriptively.
**Results:** The patients were aged 2–70 years (mean 39.4 ± 17.6 years); 26 (54.2%) were male. Drug reaction with eosinophilia and systemic symptoms (DRESS) was the most frequent diagnosis (18/48, 37.5%), followed by toxic epidermal necrolysis (12/48, 25.0%), Stevens–Johnson syndrome (11/48, 22.9%), exfoliative dermatitis (5/48, 10.4%) and acute generalised exanthematous pustulosis (2/48, 4.2%). Anticonvulsants were the most frequently implicated drug group (21/48, 43.8%), chiefly phenytoin (12 cases) and carbamazepine (9 cases). Mean hospital stay was longest for toxic epidermal necrolysis (40.7 days). All patients received systemic corticosteroids and supportive care; two patients with severe SJS/TEN received intravenous immunoglobulin, and two patients with DRESS received methylprednisolone pulse therapy. Full recovery was recorded for all patients.
**Conclusion:** DRESS was the commonest SCAR in this series, and anticonvulsants, particularly phenytoin and carbamazepine, were the most frequently implicated drugs. Early recognition, withdrawal of the suspected drug, supportive care and pharmacovigilance remain important.

**Keywords:** Severe Cutaneous Adverse Drug Reaction, DRESS, Stevens–Johnson Syndrome, Toxic Epidermal Necrolysis, Anticonvulsants

## INTRODUCTION

Severe cutaneous adverse reactions (SCARs) comprise a heterogeneous group of potentially life-threatening drug reactions, including Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP) and drug-induced exfoliative dermatitis. Their clinical course ranges from an acute pustular eruption to extensive epidermal necrosis or delayed multisystem inflammation. Early recognition is essential because prompt withdrawal of the suspected culprit drug and appropriate supportive care are central to management.[1-3]

The clinical phenotype and latency vary by reaction and drug. Anticonvulsants, antimicrobials, non-steroidal anti-inflammatory drugs and other medications have been implicated, while host genetic susceptibility contributes to selected drug–reaction associations.[3,4] As prescribing patterns and referral populations differ across settings, local descriptions can help clinicians identify common

presentations and suspected drugs. This study describes the clinico-epidemiological profile, implicated medications, clinical manifestations and inpatient outcomes of SCARs managed at a tertiary-care centre in Madurai, Tamil Nadu.

## MATERIALS AND METHODS

This hospital-based observational study was conducted in the Department of Dermatology, Venereology and Leprosy, Madurai Medical College and Government Rajaji Hospital, Madurai, Tamil Nadu, from 1 January to 31 December 2024. The study included patients of any age or sex who presented with clinical features fulfilling the study's diagnostic criteria for SCAR. Patients whose reactions did not qualify as SCAR and those with reactions attributed to non-drug exposures, including alternative or herbal medications, were excluded. The final analytic sample comprised 48 eligible patients; two cases attributed to alternative medications were excluded.

A pre-designed proforma was used to record age, sex, indication for drug use, medication history, time from drug exposure to onset of lesions, clinical and mucosal features, systemic manifestations, laboratory findings, histopathology, treatment and duration of hospitalisation. The most likely culprit drug was assessed from the medication history, temporal association, clinical phenotype and course after drug withdrawal. Causality was also assessed using the Naranjo adverse drug reaction probability scale.[5] Skin biopsy and laboratory investigations were used when clinically indicated to support the diagnosis and assess systemic involvement.

Institutional Ethics Committee approval was obtained before the study began. Written informed consent was obtained from eligible participants for study inclusion and clinical photography; consent/assent procedures were used for minors. The IEC approval number should be added once confirmed.

Data were summarised descriptively. Categorical variables are presented as counts and percentages; age, latency and hospital stay are summarised using means where calculable. Subtype-specific latency and hospital-stay means were calculated from the recorded patient-level data. No inferential statistical testing was performed.

## RESULTS

### Participant Characteristics and Reaction Patterns

Forty-eight patients were included. Age ranged from 2 to 70 years (mean 39.4 ± 17.6 years). The largest age group was 31–40 years (12/48, 25.0%), followed by 41–50 years (9/48, 18.8%). There were 26 males (54.2%) and 22 females (45.8%). DRESS was the most frequent phenotype (18/48, 37.5%), followed by TEN (12/48, 25.0%), SJS (11/48, 22.9%), exfoliative dermatitis (5/48, 10.4%) and AGEP (2/48, 4.2%) (Table 1).

| Characteristic | n (%) or Value |
|---|---|
| Total participants | 48 |
| Age, years, mean ± SD | 39.4 ± 17.6 |
| Age range, years | 2–70 |
| First decade | 4 (8.3) |
| Second decade | 4 (8.3) |
| Third decade | 6 (12.5) |
| Fourth decade | 12 (25.0) |
| Fifth decade | 9 (18.8) |
| Sixth decade | 5 (10.4) |
| Seventh decade | 8 (16.7) |
| Male | 26 (54.2) |
| Female | 22 (45.8) |
| DRESS | 18 (37.5) |
| TEN | 12 (25.0) |
| SJS | 11 (22.9) |
| Exfoliative dermatitis | 5 (10.4) |
| AGEP | 2 (4.2) |

***Table 1. Demographic characteristics and distribution of SCAR phenotypes***

*Note: Percentages are calculated using n = 48. Abbreviations: AGEP, acute generalised exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis*

**Indication for drug use and suspected culprit drugs**

The most common indication for the medication preceding SCAR was infection (14/48, 29.2%), followed by seizure disorders (8/48, 16.7%), road traffic accidents (7/48, 14.6%) and space-occupying lesions (5/48, 10.4%). Anticonvulsants were implicated in 21 cases (43.8%), antibiotics in 9 (18.8%), non-steroidal anti-inflammatory drugs in 5 (10.4%) and other drugs in 13 (27.1%). Phenytoin was the most frequently implicated individual drug (12/48, 25.0%), followed by carbamazepine (9/48, 18.8%) (Table 2

| Drug Group / Agent | n (%) |
|---|---|
| Anticonvulsants | 21 (43.8) |
| Phenytoin | 12 (25.0) |
| Carbamazepine | 9 (18.8) |
| Antibiotics | 9 (18.8) |
| Non-steroidal anti-inflammatory drugs | 5 (10.4) |
| Other drugs | 13 (27.1) |

***Table 2. Suspected culprit drug groups and most frequent individual drugs***

*Note: "Other drugs" included anti-tuberculosis treatment, dapsone, terbinafine, metoprolol, methotrexate, leflunomide, griseofulvin and omeprazole*

**Clinical and Extracutaneous Findings**

All patients had cutaneous lesions. Oral lesions were recorded in 21 patients (43.8%), genital lesions in 19 (39.6%), fever in 13 (27.1%), ocular lesions in 12 (25.0%) and itching in 12 (25.0%). Facial oedema and hepatomegaly were each recorded in six patients (12.5%). Eosinophilia was recorded in 14 patients (29.2%). Raised total bilirubin was documented in 31 patients (64.6%). (Table 3)

Clinically, DRESS was characterised predominantly by a maculopapular eruption, sometimes with facial oedema, pedal oedema, fever, eosinophilia and hepatic abnormalities. SJS and TEN presented with cutaneous lesions and mucosal involvement; TEN was associated with the longest inpatient stay. AGEP cases showed pustules on an erythematous base. Histopathological findings included subcorneal pustules and papillary dermal oedema in AGEP; spongiosis, basal vacuolar alteration, a lymphocytic infiltrate and eosinophils in DRESS; and keratinocyte/epidermal necrosis with subepidermal blistering in SJS/TEN. These findings were used as supportive diagnostic information, not as evidence of drug causality on their own.[13-15]

| Feature | n (%) |
|---|---|
| Cutaneous lesions | 48 (100.0) |
| Oral lesions | 21 (43.8) |
| Genital lesions | 19 (39.6) |
| Fever | 13 (27.1) |
| Ocular lesions | 12 (25.0) |
| Itching | 12 (25.0) |
| Facial oedema | 6 (12.5) |
| Hepatomegaly | 6 (12.5) |
| Eosinophilia | 14 (29.2) |
| Raised total bilirubin documented | 31 (64.6) |

***Table 3. Clinical and extracutaneous features among participants***

*Note: Percentages are calculated using the total sample size of 48*

**Latency, Treatment and Outcome**

The interval between drug exposure and onset ranged from 5 to 42 days. The mean latency was shortest for AGEP (7.0 days) and longest for DRESS (25.1 days), although some individual DRESS cases had a latency of 42 days. Mean hospital stay was longest for TEN (40.7 days), followed by DRESS (33.8 days), SJS (24.8 days), exfoliative dermatitis (23.2 days) and AGEP (13.0 days) (Table 4). All 48 patients were classified as having a probable adverse drug reaction by the Naranjo scale.

| Phenotype | n | Mean Latency (days) | Mean Hospital Stay (days) |
|---|---|---|---|
| AGEP | 2 | 7.0 | 13.0 |
| SJS | 11 | 13.4 | 24.8 |
| TEN | 12 | 14.3 | 40.7 |
| Exfoliative dermatitis | 5 | 19.6 | 23.2 |
| DRESS | 18 | 25.1 | 33.8 |

***Table 4. Mean latency and duration of hospital stay by SCAR phenotype***

*Note: Means were calculated from recorded individual latency and hospital-stay values*

All patients received withdrawal of the suspected culprit drug, systemic corticosteroid therapy and supportive care. Two patients with severe SJS/TEN received intravenous immunoglobulin, and two patients with DRESS received methylprednisolone pulse therapy. Full recovery was recorded for all patients. Two patients with DRESS experienced a flare during steroid tapering and improved after the corticosteroid dose was increased and tapered more slowly. Drug-alert cards listing the suspected drug and potential cross-reacting drugs were provided.

## DISCUSSION

This hospital-based series describes 48 patients with SCARs managed over one year at a tertiary-care centre in South India. DRESS was the commonest phenotype, and anticonvulsants were the most frequently implicated drug group. Phenytoin and carbamazepine together accounted for 21 cases, highlighting the importance of careful drug history-taking in patients presenting with delayed eruptions and systemic findings. The high proportion of anticonvulsant-associated cases may reflect local prescribing and referral patterns, particularly among patients receiving treatment for seizure disorders or following neurological events.

The sex distribution showed a modest male predominance, and most patients were in the fourth and fifth decades. This pattern is broadly similar to several Indian hospital-based studies that have reported male predominance, although the age distribution varies by study and population.[6-10] Comparisons should be interpreted cautiously because many published studies include all cutaneous adverse drug reactions rather than SCARs alone, making the case mix and culprit-drug proportions non-equivalent.

Anticonvulsants accounted for 43.8% of suspected reactions in the present series, followed by antibiotics and NSAIDs. In contrast, general CADR studies from other settings have often reported antimicrobials as the leading implicated group.[7-12] Differences may be related to the restriction of the present study to severe phenotypes, regional prescribing practices, referral patterns, and the mix of underlying indications. The results reinforce the need to document the start date, dose and chronology of every medication, including recently discontinued drugs, rather than attributing a reaction solely on the basis of a drug's known association.

The subtype-specific latency pattern showed the longest mean latency in DRESS, consistent with its often delayed presentation and potential for systemic involvement.[12] The longest hospital stay occurred in TEN, reflecting the clinical burden of extensive epidermal loss and mucosal disease. SCAR management requires prompt culprit-drug withdrawal, careful assessment of organ involvement and supportive measures; treatment should be individualised according to the phenotype and severity. In this series, all patients received systemic corticosteroids, while a small number received IVIG or pulse methylprednisolone. Because treatments were not compared and there was no untreated or alternative-treatment group, these outcomes do not establish the comparative efficacy of any immunomodulatory regimen.

Histopathology can support differentiation among SCAR phenotypes, particularly when interpreted with the clinical timeline and systemic findings. However, overlapping inflammatory and epidermal injury patterns may occur, and biopsy alone cannot establish which drug caused the reaction.[13-15] The documentation of drug-alert cards at discharge was a practical pharmacovigilance measure intended to reduce inadvertent re-exposure.

The study has limitations. It was conducted at a single tertiary centre and included a relatively small sample, which limits generalisability and does not permit reliable comparisons between rare phenotypes. The available dataset is descriptive, with no inferential analysis. Follow-up outcomes after discharge were not detailed,

and the single-centre sample limits generalisability.

## LIMITATIONS

This study has certain limitations. Being a single-centre observational study with a relatively small sample size, the findings may not be generalisable to the wider population. The descriptive study design and absence of a control group or inferential statistical analysis limit the assessment of associations between culprit drugs and specific SCAR phenotypes. Drug causality was assessed using clinical history and the Naranjo adverse drug reaction probability scale, without definitive confirmatory testing. Referral bias may also have influenced the clinical spectrum observed. Furthermore, long-term post-discharge follow-up was not available to assess delayed complications and long-term outcomes. As treatment was not standardised or compared between groups, the therapeutic outcomes cannot be used to establish the comparative efficacy of individual treatment modalities.

## CONCLUSION

DRESS was the most frequent SCAR phenotype in this series, and anticonvulsants-particularly phenytoin and carbamazepine-were the most commonly implicated drugs. TEN was associated with the longest hospital stay. Timely recognition, discontinuation of the suspected drug, supportive management and clear documentation of drug hypersensitivity are essential. Improved drug history documentation, patient education regarding drug hypersensitivity and strengthened pharmacovigilance practices are essential to prevent inadvertent re-exposure and improve patient safety.

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