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**Case Series**

# Clinical spectrum of cutaneous adverse drug reactions in the peri-procedural period: a case series

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## ABSTRACT

Cutaneous adverse drug reactions (CADRs) are among the frequent adverse effects of medications prescribed during the postoperative period. Their diverse clinical presentations often pose diagnostic challenges, particularly when eruptions develop after completion of short-course of therapy following surgical and medical interventions. A prospective observational case series of patients presenting with suspected CADR over a 6-month period was conducted. Clinical characteristics, suspected medications, morphology, latency, treatment, and outcomes were assessed. Seventeen patients were identified, with the onset of skin lesions ranging from post intervention day 2 to day 12. The majority of patients (11/17, 64.7%) developed cutaneous eruptions between 5 and 10 days after drug exposure**.** Maculopapular exanthem was the predominant presentation, observed in 13 patients (76.5%), including one case with accompanying pustules. An acneiform eruption and erythematous macules were observed in one patient each (5.9%), while erythematous papules were observed in 2 (11.8%) patients. Photoexposed areas were involved in 8 patients (47.1%). Most patients had received short course of postoperative antibiotics and/or NSAIDs before the onset of the eruption. Appropriate dermatological management resulted in complete recovery in most of the patients. Delayed perioperative CADRs were most commonly manifested as maculopapular exanthems in our series, although a spectrum of atypical morphologies were also observed. Recognition of these varied clinicomorphological presentations especially after completion of postoperative antimicrobial therapy may facilitate timely diagnosis and appropriate management.

**Keywords:** Cutaneous adverse drug reactions, Drug eruptions, Perioperative care, Exanthema, Photosensitivity disorders

## INTRODUCTION

Cutaneous adverse drug reactions (CADRs) represent a frequent cause of dermatological consultations and are associated with significant morbidity. They encompass a wide spectrum of clinical manifestations ranging from mild self-limiting eruptions to severe life-threatening reactions such as Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS). Early recognition and prompt withdrawal of the offending drug are crucial to reduce morbidity and prevent disease progression.[1,2]

Patients undergoing surgical procedures, obstetric interventions, and other invasive procedures are commonly exposed to multiple medications, including antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, proton pump inhibitors, and other supportive drugs. Simultaneous exposure to several medications poses a diagnostic challenge in identifying the offending agent, particularly when cutaneous

eruptions develop several days after the procedure. Several causality assessment methods have been used in CADR studies, including structured algorithms such as the Naranjo algorithm and the WHO-UMC system, with considerable variation in the criteria and categorization used across studies.[3]

Although perioperative drug hypersensitivity has been widely described in relation to immediate allergic reactions and anaphylaxis, published data on delayed CADRs in the perioperative period, particularly their clinic-morphological spectrum and latency patterns, remain limited. Most available reports are isolated case reports or focus on severe reactions, with relatively few studies describing the spectrum of delayed CADRs encountered in routine dermatology practice.

The present study was undertaken to describe the demographic profile, latency, clinico-morphological spectrum, suspected offending drugs, and causality assessment of delayed perioperative CADRs encountered at a tertiary care hospital.

## CASE SERIES

This was a prospective observational case series conducted over a six-month period from February 2026 to July 2026 in the Department of Dermatology of a tertiary care teaching hospital. After obtaining informed consent, all consecutive patients attending to the Dermatology OPD with suspected CADRs and those referred from other departments following administration of peri-procedural medications were clinically evaluated and included in the study. Causality assessment of the reported ADR was done by establishing the drug use with elaborate elicitation of the history, temporal association with ADR, ADRs were graded as definite, possible and probable according to WHO causality assessment scale. Clinical differentials, including allergic or irritant contact dermatitis related to peri-procedural exposures, were considered where appropriate based on lesion morphology and distribution.

In this case series of 17 patients with CADRs, the maximum number of patients were in the age group of 21 to 60 years. The youngest CADR patient was 4 years old and the eldest was 80 years old. The mean age was 34.9±23.6 years (range, 4-80 years). Females predominated, accounting for 13 (76.5%) patients, with a female-to-male ratio of 3.25:1.

Perioperative exposure to multiple medications were common in our series. Antibiotics were implicated in all 17 patients, with Cephalosporins being most frequently represented antibiotic class, with exposure in 13 (76.5%) patients, followed by ciprofloxacin in 3 (17.6%) patients and metronidazole, amoxicillin-clavulanate, clindamycin, and cotrimoxazole in 1 patient each (5.9% each). Some patients had been exposed to more than one antibiotic sequentially, including change from parenteral to oral therapy. Among analgesics, paracetamol was co-administered in 8 (47.1%) patients, while diclofenac-containing regimens were used in 2 (11.8%) patients.

The latency period after drug exposure ranged from 2 to 12 days, with 5 patients (29.4%) developing eruptions within 4 days, 11 patients (64.7%) between 5 and 10 days and 1 patient (5.9%) after more than 10 days. The clinico-demographic characteristics, morphological patterns, rash distribution are summarized (Table 1).

**Table 1: Demographic and clinical characteristics of patients with cutaneous adverse drug reactions (n=17).**

| Variables | Category | N (%) |
|---|---|---|
| **Age group (in years)** | ≤20 | 7 (41.2) |
| | 21-60 | 8 (47.1) |
| | >60 | 2 (11.8) |
| **Sex** | Male | 4 (23.5) |
| | Female | 13 (76.5) |
| **Morphology** | Maculopapular eruption | 13 (76.5) |
| | Papular eruption | 1 (5.9) |
| | Acneiform eruption | 1 (5.9) |
| | Pustular + maculopapular eruption | 1 (5.9) |
| | Erythematous macules | 1 (5.9) |
| **Photoexposed distribution** | Present | 8 (47.1) |
| | Absent | 9 (52.9) |
| **Clinical setting/procedure** | Obstetric procedures (Caesarean section + vaginal delivery) | 6 (35.3) |
| | Orthopaedic procedures | 6 (35.3) |
| | Ophthalmic procedures | 2 (11.8) |
| | ENT procedure | 1 (5.9) |
| | Hysterectomy | 1 (5.9) |
| | Neurosurgical procedure | 1 (5.9) |
| | Pleural tapping | 1 (5.9) |

Continued.

| Variables | Category | N (%) |
|---|---|---|
| **Rash distribution** | Trunk | 11 (64.7) |
| | Upper limbs | 10 (58.8) |
| | Face | 8 (47.1) |
| | Lower limbs | 2 (11.8) |
| | Palms | 2 (11.8) |

Maculopapular eruption was the predominant morphological presentation, observed in 13 patients (76.5%), including one case with accompanying pustules (Figure 1 A-E). An acneiform eruption and erythematous macules were observed in one patient each (5.9%), while papular eruption on a mildly erythematous background was observed in 2 (11.8%) patients (Figure 2 A-C).

Patient with acneiform papules over the upper back had pre-existing truncal acne, and these papules subsequently progressed over four days to involve the limbs, consistent with a suspected drug-induced acneiform eruption.

Photo-distributed involvement was observed in 8 (47.1%) patients. Among these, cefixime, cefuroxime/cefuroxime axetil, ciprofloxacin, cotrimoxazole and amoxicillin-clavulanate were the recorded antibiotic exposures, while paracetamol was concomitantly used in 6 (75%) patients (Figure 3 A-H).

Previous history of drug allergy was noticed in one Patient who had reactions to penicillin, NSAID(Aceclofenac) and cephalosporins two years back. During the present episode, he had received clindamycin and Tramadol.

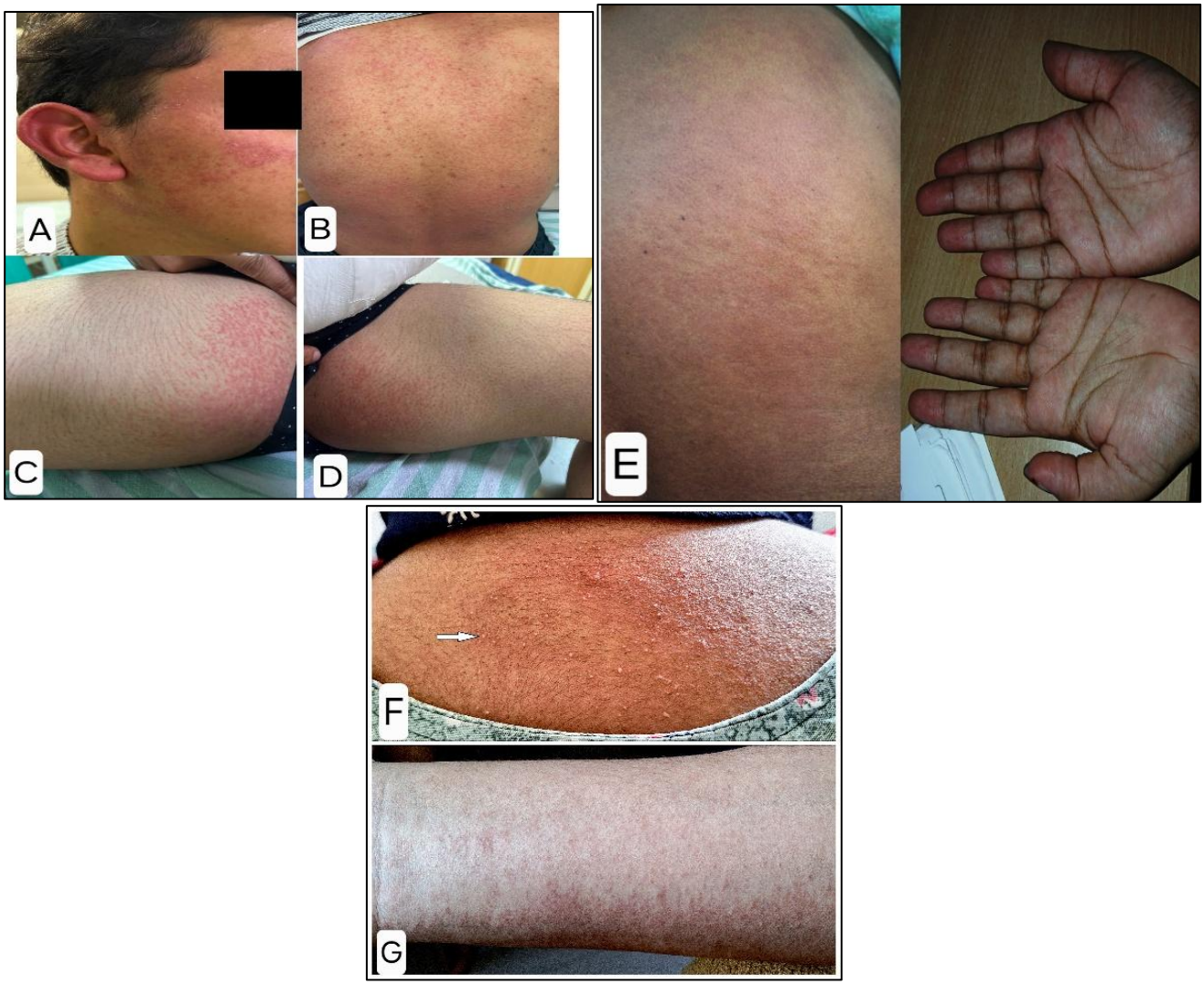


**Figure 1 (A-G): (A-D) Maculopapular eruption in one patient involving the face, ear, back of the trunk and inner thigh (E) Exanthematous papules involving trunk, palms (F-G) Pustular eruption (arrow) predominantly involving the upper back with maculopapular lesions over the forearms in another patient.**

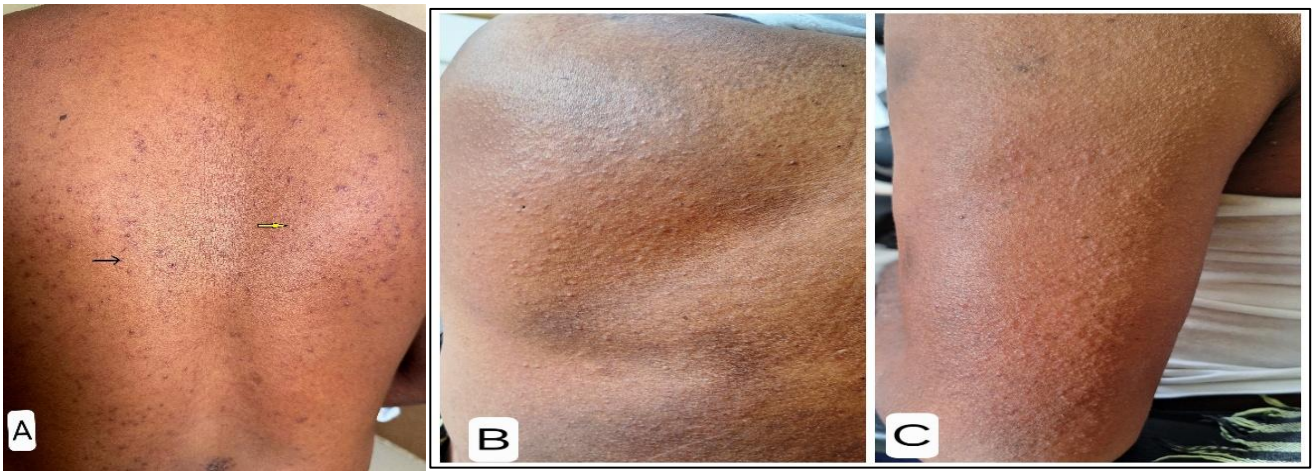


**Figure 2 (A-C): (A) Monomorphic erythematous acneiform papules (yellow arrows) over the upper back, superimposed on pre-existing truncal acne (black arrow) in one patient. (B-C) Papular eruption involving the trunk and upper limbs in another patient.**

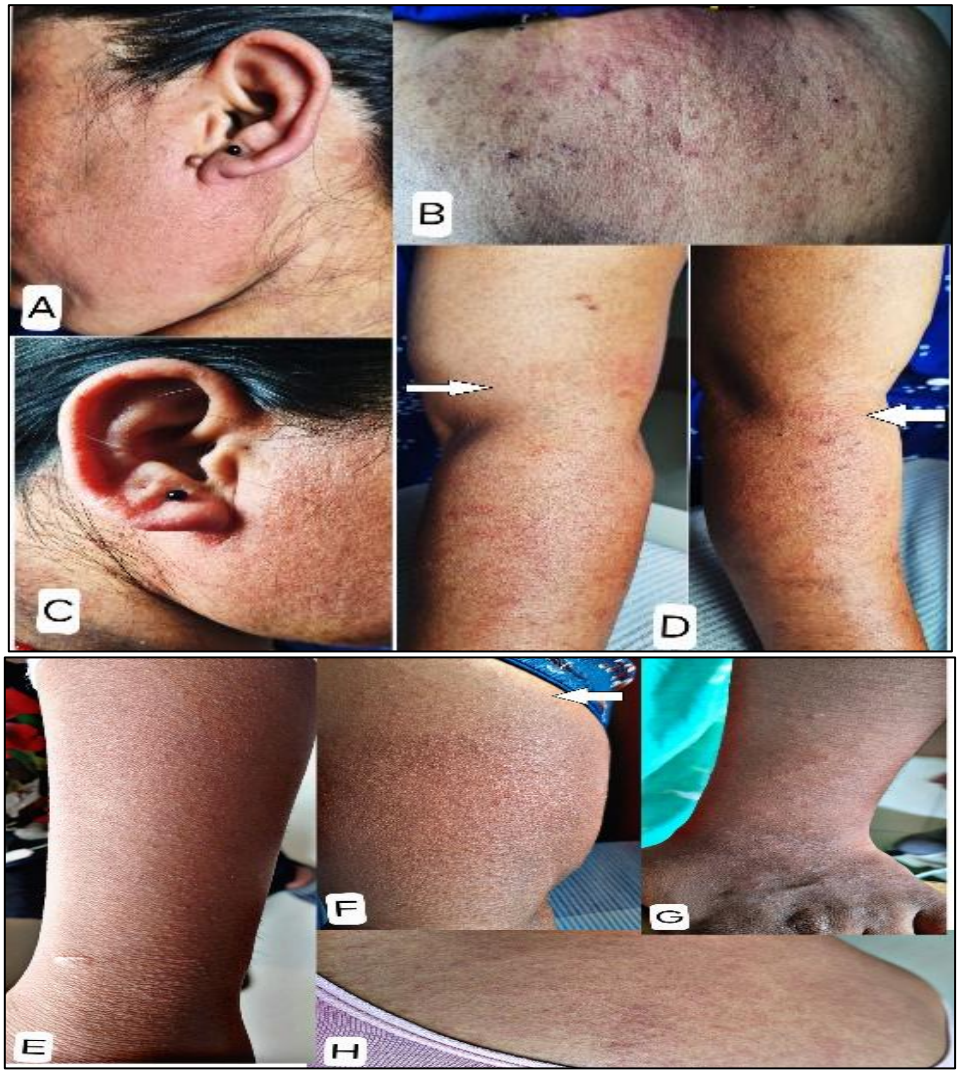


**Figure 3 (A-F): Photo-distributed cutaneous adverse drug reactions in representative patients. (A–D) Maculopapular eruption in one patient involving the face, ear, upper back and exposed areas of forearms. (E-H) Erythematous/maculopapular lesions involving photoexposed areas of the upper extremities and upper back. In (D and F), the arrow indicates the sharp demarcation of lesions between photoexposed and covered skin.**

## DISCUSSION

Cutaneous adverse drug reactions (CADRs) are the most common medication-related adverse events encountered in clinical practice and frequently require dermatological evaluation. Although the clinical spectrum ranges from mild exanthematous eruptions to severe cutaneous adverse reactions such as Stevens-Johnson syndrome or TEN (SJS/TEN) and uncomplicated maculopapular exanthem continues to be the predominant presentation in most hospital-based studies. Antimicrobial agents, anticonvulsants and NSAIDs consistently remain the leading implicated drug groups.[1-3]

In the present case series, maculopapular eruption was the predominant type of CADR observed in 13 (76.5%) patients after initiation of inpatient medications, consistent with previous Indian studies, which also reported maculopapular exanthem as the predominant type of CADR, whereas fixed drug eruption (FDE) was the most common eruption reported in a study conducted in South India by Pudukadan et al.[1-4] However, the occurrence of papular, acneiform, and pustular morphologies in our series highlights the broader clinicomorphological spectrum that may be encountered in the perioperative setting.

The temporal profile in our study is compatible with delayed exanthematous drug eruptions, which showed eruptions between the fifth and tenth day of Latency period after drug exposure in 66.7% of patients. This delayed presentation may obscure the causal relationship because the suspected medications, which have already been discontinued as the short course treatment been completed by the time patients seek dermatological evaluation. Usually, the lesions subsides after 1-2 weeks without any sequelae, sometimes it may present with post inflammatory desquamation.[5]

The principal differential diagnoses for morbilliform eruptions are viral exanthem, allergic contact dermatitis to surgical dressings or antiseptics, and postoperative wound-related dermatoses. Viral exanthem was considered less likely because systemic prodromal symptoms were absent and the lesions commonly have brighter erythema and less pruritus with mucosal involvement. However, differentiation from drug-induced morbilliform eruptions can be challenging because of considerable overlap in distribution of the lesions. Irritant or allergic contact dermatitis were also considered; however, most eruptions were generalized or multifocal, rather than confined to the operative site or areas corresponding to adhesives or antiseptic application. Hence based on the morphology of lesions and onset of the rashes, diagnosis in our patients favoured exanthematous drug eruption, together with the temporal relationship to drug exposure.[5,6]

Histopathology has limited value in differentiating these conditions because both viral and drug reactions are characterized by vacuolar interface change, dyskeratosis, and dermal infiltrate that may include eosinophils. Although some studies showed dermal infiltrate which are more highly associated with drug eruptions than viral but there are no statistically significant association with histopathology.[6]

In our prospective observational series, most of our patients had received cefixime, either alone or in combination with NSAIDs, before the onset of delayed maculopapular eruptions. While trimethoprim-sulfamethoxazole, penicillins, and fluoroquinolones are among the antimicrobials most frequently implicated in CADRs.[7] Although reports of cefixime-associated maculopapular exanthems are limited, it has been associated with a spectrum of CADRs, including acute generalized exanthematous pustulosis, FDE, erythema multiforme, and SJS/TEN.[8-10] Hence cefixime may be considered a potential culprit, particularly when cutaneous eruptions develop after completion of a short course of therapy. Nevertheless, the concurrent use of multiple medications in our patients precluded definitive attribution of the eruptions to cefixime.

Immunologically, many CADRs are mediated by type IV hypersensitivity reactions, and the risk of CADRs may be increased in multimorbid patients because of polypharmacy, when exposed to multiple medications.[11] As these drugs were administered concurrently in our case series, identification of a single culprit drug was not possible and causality assessment in CADRs can be challenging. However, both classes of drugs (Cephalosporins and NSAIDs) are well-recognised triggers of delayed exanthematous drug eruptions and structured causality tools may aid assessment of drug–reaction relatedness.[5]

Another notable finding in our study was the predominance of female patients. Similar female predominance has been documented in several Indian pharmacovigilance studies, although others have reported an equal sex distribution or slight male predominance. The variation may reflect the differences in prescribing practices, healthcare utilisation, and study populations rather than an inherent biological susceptibility.[2,3,12] In our case series, the female predominance may partly be attributable to the clinical setting, as several female patients developed CADRs following Caesarean section or vaginal delivery, with exposure to multiple peri-procedural medications.

An interesting observation was the occurrence of eruptions predominantly involving photo-exposed areas of the face and forearms in several patients. Classical exanthematous drug eruptions usually begin on the trunk and spread symmetrically to the extremities.[11] Predominant involvement of photo-exposed sites is less frequently described and may represent photo-accentuation of a drug eruption or drug-induced photosensitivity. Certain antimicrobial agents and

NSAIDs have been implicated in phototoxic and photoallergic reactions, and this possibility should be considered when evaluating postoperative or inpatient rashes with a predominantly sun-exposed distribution. Recognition of this pattern may help avoid misdiagnosis as primary photodermatoses or connective tissue diseases.[5,13]

One patient developed a localized eruption consisting predominantly of sterile non-follicular pustules over the upper back with limited maculopapular lesions over the forearms following Ceftriaxone administration. Although the clinical features were suggestive of acute localized exanthematous pustulosis (ALEP), histopathological confirmation was unavailable, and the diagnosis remained presumptive. ALEP is most frequently drug-induced and has been associated with antibiotics and NSAIDs.[14]

Most patients responded to symptomatic treatment with oral antihistamines with or without topical corticosteroids. Because many patients did not return after clinical improvement, long-term follow-up could not be assessed. This reflects routine clinical practice but limits evaluation of recurrence or delayed sequelae.

The present study has certain limitations. Its relatively small sample size, concurrent administration of multiple perioperative medications, and absence of standardized causality assessment, limited precise identification of the offending drug. Despite these limitations, the study highlights an important and frequently overlooked clinical scenario in which delayed exanthematous drug eruptions become apparent only after completion of a short inpatient medication course.

## CONCLUSION

In conclusion, clinicians should maintain a high index of suspicion for delayed CADRs in patients presenting with new-onset maculopapular eruptions approximately one week after hospitalization or surgery, even when antibiotics or NSAIDs have already been discontinued. Early recognition and prompt dermatological evaluation may prevent unnecessary investigations, inappropriate antimicrobial escalation, and delayed diagnosis.

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