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Original Article

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Correlation of Serum IgE Levels and Clinical Manifestations in Patients Presenting with Cutaneous Adverse Drug Reactions in a Tertiary Care Centre, Eastern Zone of India

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Abstract

Objective: To examine the correlation between serum Immunoglobulin E (IgE) levels and the clinical spectrum and severity of Cutaneous Adverse Drug Reactions (CADRs) in patients attending a tertiary care center in Eastern India, evaluating IgE as a surrogate marker of immunopathological severity. ***Design:*** Cross-sectional, institution-based observational study conducted over twelve months, integrating clinical, pharmacovigilance, and immunoserological assessments. ***Subjects/Patients:*** Seventy-three patients with clinically diagnosed CADRs, aged 10-70 years (mean 38.25 ± 14.58 years), with slight female predominance (52.1%). ***Methods:*** Patients underwent detailed history, lesion morphology classification, and WHO-UMC (World Health Organization - Uppsala Monitoring Centre) causality assessment. Serum total IgE levels and absolute eosinophil counts were quantified. Statistical associations between IgE elevation and severity were analyzed using chi-square and t-tests. Patients were stratified into Severe Cutaneous Adverse Reactions (SCARs) and non-SCARs, with drug classes systematically mapped. ***Results:*** Fixed drug eruption (51.6%) was most frequent; SCARs comprised 12.3% (Stevens-Johnson Syndrome, TEN, DRESS). Antibiotics (40%) and NSAIDs (26.3%) were leading culprits. Mean IgE was 373.4 ± 341.7 IU/mL. Elevated IgE (>100 IU/mL) occurred in 81% of SCARs versus 36.5% of non-SCARs ($p < 0.001$). Eosinophilia was noted in 26%, especially in DRESS. ***Conclusion:*** Elevated IgE strongly correlates with CADR severity, positioning it as a pragmatic biomarker for SCAR triage and immunodermatologic risk stratification.

Keywords: ***Cutaneous Adverse Drug Reactions (CADRs), Severe Cutaneous Adverse Reactions (SCARs), Serum Immunoglobulin E (IgE), Drug Hypersensitivity, Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Immunopathogenesis, Biomarker Stratification.***

Introduction

Cutaneous adverse drug reactions (CADRs) represent a formidable challenge in contemporary clinical dermatology, not merely for their protean morphologies but for their inherent potential to engender catastrophic systemic sequelae. These dermatopharmacologic phenomena encapsulate a broad nosological continuum, encompassing benign exanthematous eruptions on one end of the spectrum and life-threatening entities such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) at the other extreme [1,2]. The increasing ubiquity of polypharmacy, coupled with escalating pharmacotherapeutic complexity, has led to a surge in iatrogenic immunotoxicity, rendering CADRs an epidemiological and immunopathological exigency [3].

The pathomechanisms underpinning CADRs are an intricate interplay of pharmacogenomics, immune dysregulation, and biochemical idiosyncrasies. Immunologically, these reactions traverse the Gell and Coombs classification of hypersensitivity, with Type I (immediate IgE-mediated) and Type IV (delayed, T-cell-mediated) responses predominating [3,12]. Notably, the classical dichotomy between these hypersensitivity archetypes has been increasingly blurred by emerging evidence delineating overlapping immune effector pathways. In particular, the subset of Type IVb hypersensitivity-characterized by a T-helper 2 cell-mediated response with eosinophilic infiltration and elevated serum IgE-exemplifies this immunological convergence, suggesting that even delayed reactions may have an IgE-dependent underpinning [3,14].

Serum IgE, historically perceived as the immunoglobulin isotype mediating atopic disorders and anaphylaxis, has now emerged as a potential surrogate of systemic immune activation in specific subsets of CADRs, including DRESS and generalized exanthematous pustulosis (AGEP) [4,5,15]. The quantification of total serum IgE levels, while non-specific in isolation, may provide

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valuable corollary information when contextualized with clinical severity, cutaneous morphology, and systemic involvement. Its elevation in SCARs implies a milieu of hyper-reactive Th2 skewing, perhaps catalyzed by drug-hapten complexes, latent viral reactivation, or host genetic predisposition, such as HLA polymorphisms [13,15,19].

Despite these advances, the integration of immunoserologic parameters like serum IgE into the routine diagnostic algorithm for CADRs remains nascent, particularly in resource-constrained regions such as the Eastern Indian subcontinent. Here, the pharmacovigilance infrastructure–though expanding under the aegis of the Pharmacovigilance Programme of India (PvPI)–continues to be beleaguered by underreporting, fragmented data acquisition, and limited biomarker surveillance [6,11]. Despite global attention to immunobiomarkers in CADRs, resource-limited settings such as Eastern India remain under-represented in such investigations. Here, the epidemiological burden of CADRs is compounded by the indiscriminate use of antimicrobials, NSAIDs, and non-regulated indigenous formulations, many of which are inadequately labelled and pharmacovigilantly underreported [6,11,17]. Moreover, serum IgE estimation remains underutilized in clinical pharmacovigilance, despite its potential utility as a biomarker for disease severity and systemic involvement.

Given these lacunae, the present study seeks to interrogate the correlation between serum IgE levels and the spectrum of clinical manifestations in CADRs, thereby establishing whether IgE could serve as a stratification tool for assessing reaction severity and informing clinical decision-making in dermatologic pharmacovigilance.

As this tertiary care centre in Eastern India transitions into a regional pharmacovigilance nucleus, there exists an opportune moment to interrogate the clinical relevance of serum IgE in CADR stratification.

Accordingly, this study undertakes an ambitious and methodologically rigorous exploration of the correlation between serum IgE levels and the clinical severity of CADRs, aiming not only to elucidate immuno-pathogenetic undercurrents but to potentiate serum IgE as a risk stratifier in dermatopharmacologic vigilance.

Methods

1. Aims and Objectives

Aim

To critically evaluate the correlation between serum Immunoglobulin E (IgE) levels and the clinical spectrum and severity of Cutaneous Adverse Drug Reactions (CADRs) in patients attending a tertiary care hospital in Eastern India, thereby elucidating the immunological underpinning and potential prognostic value of IgE in drug-induced dermatologic morbidity.

Primary Objectives

1. To measure serum total IgE levels in patients presenting with clinically confirmed CADRs across various morphological and immunopathological subtypes.
2. To characterize the clinical phenotypes of CADRs (e.g., Fixed Drug Eruption, SJS/TEN, DRESS, urticaria, etc.) and classify them based on severity (SCAR vs non-SCAR).
3. To evaluate the correlation between elevated serum IgE levels and severity of CADRs, using statistical tools to determine significance (e.g., Fisher's exact test, Chi-square).
4. To identify the spectrum of drugs implicated in inducing CADRs and analyze their associations with serum IgE levels and reaction severity.

Secondary Objectives

1. To assess the prevalence of eosinophilia and explore its association with serum IgE levels and clinical phenotypes.
2. To stratify the study population based on demographic parameters (age, sex, rural/urban background, comorbidities) and correlate them with CADR severity and IgE levels.
3. To evaluate causality of the suspected drug using the WHO-UMC causality assessment scale, thereby integrating pharmacovigilance criteria into clinical correlation.
4. To promote biomarker-based vigilance, advocating for the integration of serum IgE estimation into routine diagnostic algorithms for moderate-to-severe CADRs in tertiary care setups.

2. Study Design

The proposed investigation shall adopt an institution-centric, descriptive, cross-sectional framework, designed to elucidate clinical patterns and associations in patients diagnosed with cutaneous adverse drug reactions (CADRs). Individuals presenting with pigmentary or inflammatory dermatoses suspected to be drug-induced-who satisfy the stipulated inclusion criteria and voluntarily provide informed written consent-shall constitute the analytic cohort.

3. Study Setting and Temporal Framework

The study shall be conducted within the Department of Dermatology, Medical College and Hospital, Kolkata, which serves as a tertiary referral hub catering to a diverse and densely populated catchment area.

Patient recruitment and prospective data accrual shall span from June 2023 to June 2024.

Literature review and data processing shall be undertaken concomitantly during June 2023 to May 2024.

Thesis documentation, manuscript preparation, and final submission shall occur from June 2024 through August 2025.

4. Study Locale

The operational locus of the study shall encompass both outpatient (OPD) and inpatient (ward-based) services of the Dermatology Department, Medical College & Hospital, Kolkata, ensuring access to a comprehensive spectrum of CADR manifestations.

5. Study Duration

The investigative period for active recruitment and data acquisition is delineated as June 2023 to May 2024, encapsulating one complete dermatologic calendar cycle to accommodate seasonal variability.

6. Study Population

The target population shall comprise all patients presenting to the dermatology OPD or admitted to the dermatology ward of the aforementioned institution, who are diagnosed with cutaneous manifestations attributable to adverse pharmacologic exposure, contingent upon meeting eligibility criteria.

7. Sample Size Determination

The sample size was empirically determined to be 73 subjects, computed using the classical formula:

$$n = 4pq/l^2,$$

Where:

n denotes the requisite sample size,
p represents the estimated prevalence rate of CADRs derived from antecedent literature (p = 0.24),

$$q = 1 - p \ (q = 0.76),$$

l represents the permissible relative error (10% in this context).

Thus:

n = 4pq/l^2, where p = 0.24 q = 1-p= 0.76, l = loss% (10%)
n = 4·0.24·0.76/0.01 = 72.9 ~ 73

This statistically justified cohort size is deemed adequate for primary inferential objectives under a descriptive paradigm.

8. Sampling Strategy

A consecutive, non-randomized sampling technique shall be employed. Every eligible subject presenting with clinically suspected CADRs during the defined study window shall be systematically recruited, contingent upon informed consent. Recruitment will be governed by the following eligibility schema:

Inclusion Criteria

1. All patients, irrespective of age or sex, manifesting cutaneous adverse drug reactions, as evaluated by clinical acumen and patient history, and presenting to the Dermatology OPD/IPD of Medical College & Hospital, Kolkata.

Exclusion Criteria

1. Subjects unwilling or unable to provide informed consent.
2. Patients with non-drug-related dermatoses mimicking CADRs, including but not limited to autoimmune bullous disorders, viral exanthems, and phototoxic reactions.

9. Variables and Parameters of Interest

The following parameters will be meticulously documented and analyzed:

A. Sociodemographic Data

1. Age, sex, body weight, and occupational exposure

B. Symptomatology

1. Pruritus, burning sensation, pain, discharge, and constitutional symptoms

C. Drug-Related History

1. Probable offending agent and its indication
2. Route, dosage, and frequency of administration
3. Temporal interval between drug initiation and onset of reaction
4. Duration of drug intake prior to eruption

D. Morphological Documentation

1. Type, distribution, configuration, and evolution of cutaneous lesions

10. Study Instruments and Tools

The research will employ a structured and validated data acquisition matrix comprising:

1. Outpatient Department admission registers and clinical tickets
2. Patient Informed Consent Forms
3. Suspected Adverse Drug Reaction Reporting Templates (PvPI format)
4. Peer-reviewed journals and dermatologic compendia
5. Digital dermatologic imaging systems for lesion documentation

11. Study Technique and Clinical Workflow

Each enrolled participant will undergo a comprehensive clinical evaluation by dermatology consultants. After informed consent is duly obtained, a detailed history encompassing pharmacologic exposure, temporal drug-eruption relationship, and prior allergic tendencies will be elicited. A thorough dermatologic examination will be performed and recorded. No invasive interventions (e.g., biopsy, patch testing) shall be pursued. Likewise, drug rechallenge is explicitly precluded on ethical grounds due to risk of precipitating recurrence or systemic complications.

Clinical data will be recorded using standardized case report forms and transcribed into electronic spreadsheets (Microsoft Excel). Lesions will be documented photographically using high-resolution digital imaging under consistent lighting conditions to facilitate objective phenotypic categorization.

12. Statistical Analysis

Descriptive and inferential statistical techniques will be deployed:

1. Continuous variables (e.g., age, serum IgE levels) will be expressed as mean ± standard deviation and analyzed using independent samples t-tests, provided normality assumptions are satisfied.
2. For non-normally distributed continuous data, the Mann-Whitney U test will be utilized.
3. Categorical variables (e.g., gender, type of CADR) will be analyzed using Chi-squared tests or Fisher's exact test as appropriate.
4. All statistical computations will be executed using Microsoft Excel and MedCalc statistical software (latest version).
5. A p-value ≤ 0.05 will be considered indicative of statistical significance.

13. Ethical Considerations

1. All patients will be recruited only upon provision of written informed consent.
2. No therapeutic modifications or rechallenge procedures will be undertaken.
3. The protocol complies with institutional ethical guidelines and conforms to the Declaration of Helsinki.

14. Conflict of Interest

The principal investigator declares no conflict of interest, financial or otherwise, in the conduct of this study.

15. Source of Funding

All logistical and financial obligations, including laboratory assessments, documentation, and data acquisition tools, shall be borne exclusively by the investigator, with no external funding.

Results

The present investigation was conducted on a total of 73 patients who presented with clinically and pharmacovigilantly corroborated

Cutaneous Adverse Drug Reactions (CADRs) over a period of twelve months at a tertiary care center in Eastern India. Each subject underwent comprehensive dermatological evaluation, detailed drug history documentation, hematological profiling, and serum IgE quantification, in an effort to correlate immune-serological parameters with phenotypic severity of CADRs.

1. Demographic and Epidemiological Distribution

The mean chronological age of the cohort was 38.25 ± 14.58 years, spanning an age range of 10 to 70 years, reflecting susceptibility across a broad demographic bandwidth. Of the 73 participants, 38 were female (52.1%) and 35 were male (47.9%), indicating a slight female preponderance, although this did not translate into statistically significant variation in either serum IgE levels or severity distribution ($p > 0.05$).

Geospatial stratification revealed a near-equal urban-rural distribution, with 36 (49.3%) hailing from rural sectors and 37 (50.7%) from urban/semiurban localities. Comorbid illnesses were documented in 28.7% of patients, the most prevalent being diabetes mellitus (64%) and hypertension (57%), which were not independently correlated with elevated IgE levels.

Table 1: Demographic Characteristics of Study Population (n = 73)

Variable	Value
Mean Age (years)	38.25 ± 14.58
Age Range (years)	10–70
Sex Distribution	Male: 35 (47.9%), Female: 38 (52.1%)
Residence	Urban: 37 (50.7%), Rural: 36 (49.3%)
Comorbidities Present	21 (28.7%)
Common Comorbidities	Diabetes (64% of comorbid), Hypertension (57%)

2. Morphological Phenotypes of CADRs

Among the total presentations, the most frequently encountered clinical entity was Fixed Drug Eruption (FDE), comprising 51.6% (n = 38) of the total sample. The classical morphological features included solitary or multifocal violaceous macules and plaques, with or without bullous transformation or post-inflammatory hyperpigmentation.

Severe Cutaneous Adverse Reactions (SCARs)–including Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)–were observed in 12.3% (n = 9) of the cohort.

Other non-severe phenotypes included:

Urticaria/angioedema - 8.2% (n = 6)
Morbilliform eruptions - 9.6% (n = 7)
Lichenoid drug eruptions - 5.4% (n = 4)
Erythroderma/exfoliative dermatitis - 4.1% (n = 3)
Erythema multiforme & others - 8.2% (n = 6)

Table 2: Morphological Spectrum of Cutaneous Adverse Drug Reactions

CADR Type	Frequency (n)	Percentage (%)
Fixed Drug Eruption (FDE)	38	51.6%
Stevens-Johnson Syndrome (SJS)	4	5.5%
Toxic Epidermal Necrolysis (TEN)	2	2.7%
DRESS Syndrome	3	4.1%
Urticaria/Angioedema	6	8.2%
Morbilliform Eruption	7	9.6%
Lichenoid Drug Eruption	4	5.4%
Erythroderma/Exfoliative Dermatitis	3	4.1%
Erythema Multiforme	2	2.7%
Others	4	5.5%
Total	73	100%

3. Offending Drug Categories and Causative Pharmacologic Agents

Assessment of drug causality based on patient history and WHO-UMC classification yielded the following distribution of incriminated pharmacologic classes:

Antibiotics - 40.0% (n = 29), with beta-lactams (amoxicillin, cefixime) leading the cohort
NSAIDs - 26.3% (n = 19), notably diclofenac, ibuprofen, and nimesulide
Antiepileptics - 5.4% (n = 4), primarily phenytoin and carbamazepine
Proton Pump Inhibitors (PPIs) - 2.7% (n = 2)
Anti-tubercular therapy (ATT) - 4.1% (n = 3)
Alternative systems of medicine (Ayurvedic/homeopathic) - 7.4% (n = 5)
Miscellaneous agents (H2 blockers, antihypertensives, etc.) - 13.6% (n = 10)

Notably, the proportion of SCAR cases attributable to alternative therapies and antiepileptics was disproportionately higher compared to their usage frequency in the overall cohort, suggesting a predilection for severe reactions among these classes ($p = 0.006$).

Table 3: Drug Classes Implicated in CADRs

Drug Class	Number of Cases (n)	Percentage (%)
Antibiotics	29	40.0%
NSAIDs	19	26.3%
Antiepileptics	4	5.4%
Proton Pump Inhibitors (PPI)	2	2.7%
Anti-Tubercular Therapy (ATT)	3	4.1%
Alternative Medicines	5	7.4%
Miscellaneous (e.g., H2 blockers, antihypertensives)	11	13.6%
Total	73	100%

4. Serum Immunoglobulin E (IgE) and Eosinophil Parameters

Total Serum IgE

The mean total serum IgE level across the cohort was 373.4 ± 341.7 IU/mL, with values ranging from 30 IU/mL to 2416 IU/mL. When stratified:

Among SCAR patients (n = 9), 81% (n = 7) had serum IgE > 100 IU/mL
In contrast, among non-SCAR patients (n = 64), only 36.5% (n = 23) exhibited IgE elevation

This disparity was statistically robust with $p < 0.001$, confirming a significant positive correlation between serum IgE elevation and reaction severity.

Absolute Eosinophil Count (AEC)

The mean peripheral eosinophil count was 280.9 ± 189.1 cells/cumm. Elevated eosinophilia (AEC > 450 cells/cumm) was noted in 26% (n = 19) of patients, with the highest mean counts recorded in those with DRESS and exfoliative presentations. A moderate correlation between eosinophilia and elevated IgE was observed ($p = 0.06$), suggesting co-activation of Th2 pathways.

Table 4: Serum IgE and Eosinophil Profile

Parameter	Value
Mean Serum IgE (IU/mL)	373.4 ± 341.7
Range of Serum IgE (IU/mL)	30 – 2416
Patients with Elevated IgE (>100)	41 (56.2%)
Mean Eosinophil Count (cells/cumm)	280.9 ± 189.1
Patients with Eosinophilia (>450)	19 (26.0%)

5. Statistical Stratification and Correlation

Upon severity stratification:

Table 5: Correlation Between SCAR and Serum IgE Levels, p - value: < 0.001 (Fisher's Exact)

Parameter	SCAR (n = 9)	Non-SCAR (n = 64)	p-value
Elevated IgE (>100 IU/mL)	81.0% (7/9)	36.5% (23/64)	<0.001
Mean IgE (IU/mL)	712.8 ± 415.4	310.5 ± 201.1	<0.001
Mean Eosinophil Count	426.3 ± 255.2	246.8 ± 160.7	0.063
Antibiotics as Cause	22.2%	43.7%	0.048
Alternative/Unregulated Drugs	33.3%	3.1%	0.002

These findings strongly affirm the hypothesis that serum IgE acts as a significant immunological correlate of CADR severity, particularly in Type IVb-mediated SCAR phenotypes, wherein eosinophilia may also serve as a secondary biomarker.

6. Ancillary Observations

A prior history of atopy or allergy was found in 21.9% (n = 16), with a strong trend toward higher IgE levels in this subset.

No re-challenges were ethically permitted in SCAR patients; however, inadvertent rechallenge in 2 non-SCAR cases led to reproducible reactions, strengthening causality categorization.

Time to onset ranged from 30 minutes (urticaria) to 21 days (DRESS), with SCARs having a significantly longer mean latency period of 9.4 ± 4.1 days, reflecting the delayed hypersensitivity immunoarchitecture.

Table 6: Ancillary Observations in the Study Population

Observation	Frequency (n)	Percentage (%)
Prior History of Atopy/Allergy	16	21.9%
Inadvertent Rechallenge with Suspected Drug	2	2.7%
Mean Latency (Drug Start to Reaction Onset)	SCAR: 9.4 ± 4.1 days	
Cases with Digital Photography Recorded	73	100%
Rechallenge Attempted (Intentional)	0	0%

Discussion

This study affirms that elevated serum IgE is significantly associated with severe cutaneous drug reactions, especially SCARs. While IgE is traditionally implicated in Type I hypersensitivity (e.g., urticaria, anaphylaxis), its elevation in delayed-type presentations like SJS/TEN and DRESS hints at Type IVb immunopathogenesis involving eosinophils and IL-5-mediated recruitment [3,4].

Earlier literature (e.g., Cuevas-Gonzalez et al., 2016) showed similar IgE elevation in chronic dermatoses like actinic prurigo, suggesting IgE's broader role in dermatologic immune modulation [7]. Our findings corroborate this within a pharmacovigilant cohort, leveraging WHO-UMC causality scales.

Moreover, antibiotic-related CADRs showed statistically lower severity than those due to NSAIDs or alternative medications, a trend also observed by Deepthi et al., and Montastruc et al. in drug-drug interaction assessments [8,9].

Significantly, this study also underscores systemic underreporting and the need for serology-integrated pharmacovigilance strategies, particularly in resource-limited or underrepresented geographies [10,11].

The interplay between pharmacologic exposure and immunologic idiosyncrasy forms the central paradigm in the pathogenesis of cutaneous adverse drug reactions (CADRs). These manifestations–ranging from morbilliform exanthems to potentially fulminant toxic epidermal necrolysis–represent an immunologically charged terrain where the innate and adaptive arms of immunity intersect. Within this spectrum, the role of serum immunoglobulin E (IgE) as a potential surrogate biomarker of immunological perturbation, especially in SCARs, warrants exhaustive dissection.

In the present investigation, a statistically robust correlation was unveiled between elevated serum IgE levels and the severity of CADRs, particularly in phenotypes falling within the SCAR category. The prevalence of elevated IgE in 81% of SCAR patients (as opposed to 36.5% in non-severe CADRs) suggests a distinct immunoallergic milieu, wherein Type I and Type IVb hypersensitivity axes may converge–a notion corroborated by modern immunopathological paradigms that acknowledge the non-mutual exclusivity of hypersensitivity archetypes [12].

Recent investigations have delineated a complex immunogenetic tapestry involving HLA-B1502, HLA-A3101, and polymorphic alleles modulating cytokine profiles such as IL-5, IL-13, and IL-33, which may indirectly potentiate IgE synthesis and eosinophil activation in SCARs [13]. These interleukins, through upregulation of STAT6 and GATA3, facilitate IgE isotype switching in B cells, promoting a milieu conducive to eosinophilic infiltration and mast cell degranulation–two immunophenotypic hallmarks of SCAR pathology [14].

Furthermore, the elevated eosinophil counts in tandem with raised IgE levels reinforce the hypothesis that Th2-skewed responses are operative in at least a subset of SCAR presentations, particularly DRESS, where eosinophilia is not only a diagnostic criterion but also a pathogenetic protagonist. This is consistent with findings from Japanese and European registries where transient hypereosinophilia and hyper-IgE states have been noted during the acute phase of DRESS [15].

Another critical interpretative axis of this study lies in the drug class-specific analysis. The observation that non-antibiotic agents, particularly NSAIDs and alternative medications, are significantly associated with severe reactions contrasts with traditional pharmacovigilance data which implicate β-lactam antibiotics as predominant offenders [16]. This epidemiological shift may be reflective of increased over-the-counter NSAID usage and non-regulated indigenous medicines in the Indian subcontinent–a hypothesis supported by WHO-Uppsala Monitoring Centre reports on emerging non-traditional pharmacotoxicology signals in Asia-Pacific zones [17].

Moreover, alternative medicinal formulations, often containing heavy metals, corticosteroids, or immunogenic plant alkaloids, are increasingly being reported as sources of unlabelled

allergens capable of inducing Type I hypersensitivity through IgE priming and subsequent effector cell activation [18]. This phenomenon raises urgent questions about regulatory oversight, patient counselling, and post-marketing surveillance mechanisms in ethnopharmacologically diverse regions such as Eastern India.

Another point of analytical relevance pertains to the temporal dynamics of IgE elevation. While acute elevation may signify immediate-type reactions, sustained IgE levels–as observed in this cohort–may be indicative of a chronic immunostimulatory environment, potentially fuelled by genetic predisposition, polypharmacy, or environmental adjuvants such as viral co-infections (e.g., HHV-6 or EBV) known to reactivate during SCAR evolution [19]. Such viral reactivation may not only exacerbate hypersensitivity but also amplify IgE production via IL-4/IL-13-mediated pathways, thus creating a cyclical pathogenic loop [20].

In the broader pharmacovigilant framework, these findings carry substantial implications. First, serum IgE estimation, being a relatively inexpensive and accessible assay, could be adopted as a triage biomarker in suspected SCAR cases to prioritize dermatologic referral and systemic workup. Second, integration of immunoserologic data into national PvPI databases and VigiBase® would enhance the granularity of ADR signal detection, particularly for immunologically driven reactions which are often misclassified or underreported [21].

Lastly, our findings reiterate the exigency of incorporating immune monitoring protocols into routine dermatovigilance. While current WHO-UMC causality tools emphasize chronological plausibility, clinical dechallenge, and re-exposure dynamics, they remain agnostic to immunologic endophenotypes. A shift toward biomarker-driven causality models, incorporating parameters like serum IgE, TARC/CCL17, and IL-5, may revolutionize the precision of ADR attribution and improve patient outcomes [22].

An often underutilized yet diagnostically pivotal modality in the elucidation of cutaneous adverse drug reactions is the histopathological examination of lesional skin via biopsy, which serves as a morphological bridge between clinical suspicion and immunopathological affirmation. In the kaleidoscopic realm of CADRs, where phenotypic mimicry and morphologic overlap with other dermatoses are the rule rather than the exception, skin biopsy assumes an indispensable role in demarcating interface dermatitis from vasculitic pathology, resolving the subtleties between fixed drug eruption and lichenoid reactions, and distinguishing early SCAR entities from benign exanthems. The architectural disposition of the epidermis and dermoepidermal junction, the nature and distribution of inflammatory infiltrates, and the presence of necrotic keratinocytes, eosinophils, or atypical lymphocytes not only lend credence to the clinical diagnosis but also hint at the underlying immune mechanism–whether cytotoxic, eosinophilic, or immune-complex mediated. Although the absence of pathognomonic features in drug reactions tempers the specificity of histology, its utility lies in refining differential diagnosis, excluding mimickers, and, in select scenarios, guiding therapeutic de-escalation or escalation, particularly in cases veering toward systemic involvement. Thus, in the pursuit of immunodermatologic precision, skin biopsy emerges not as a confirmatory relic but as a dynamic adjunct in the diagnostic algorithm of CADRs.

While conventional histopathology offers a foundational morphological landscape, the deployment of immunohistochemical (IHC) and direct immunofluorescence (DIF) modalities serves as a highly sophisticated extension, enabling molecular and immunoregulatory delineation of cutaneous adverse drug reactions, especially in diagnostically ambiguous or high-stakes clinical scenarios. In SCAR phenotypes such as DRESS and TEN, where the histological milieu may be histiocytic or interface-dominant but insufficiently discriminatory, the application of IHC markers–such as granzyme B, perforin, CD8+, and CD30+ cytotoxic lymphocyte profiling–unveils the effector cell architecture, implicating precise cytolytic cascades and assisting in stratifying immunophenotypic severity. Moreover, in clinical contexts where autoimmune vesiculobullous disorders are potential mimickers–namely, pemphigus vulgaris or bullous pemphigoid–DIF studies revealing linear or intercellular IgG, IgA, C3, or fibrinogen deposition patterns serve as definitive exclusionary tools, distinguishing immune-complex deposition from drug-induced basal vacuolization or keratinocyte apoptosis. Furthermore, the nuanced detection of perivascular immune deposits or granular immunoglobulin localization in drug-induced vasculitis augments the diagnostic fidelity far beyond routine microscopy. Thus, IHC and DIF do not merely supplement histological interpretation; they crystallize the immunopathogenic narrative, offering a molecular window into the host-drug interface, and guiding both nosological classification and therapeutic direction with unprecedented granularity.

Conclusion

The present investigation, anchored within the dermatologic precincts of a tertiary care academic institution in Eastern India, offers a novel immunoserological lens into the pathophysiological undercurrents and prognostic connotations of serum Immunoglobulin E (IgE) in patients afflicted with cutaneous adverse drug reactions (CADRs). By systematically interrogating the interface between quantitative IgE derangement and phenotypic severity, the study elucidates a compelling immunological substratum that transcends the traditional dichotomy of Type I versus Type IV hypersensitivity.

The demonstrable elevation of serum IgE levels in a preponderant proportion of patients manifesting with severe cutaneous adverse reactions (SCARs)–including Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, and DRESS–attests to the recruitment of Th2-biased effector pathways and suggests that IgE may not merely serve as an epiphenomenon but rather as an active sentinel of immunological dysregulation. This supports the evolving paradigm that Type IVb hypersensitivity reactions may harbor latent IgE-driven amplification loops, perhaps potentiated by eosinophilic chemotaxis and cytokine milieu dysbalance.

From a clinical standpoint, this study advances the proposition that serum IgE estimation could serve as a pragmatic surrogate biomarker, augmenting the clinical stratification of CADRs, particularly in resource-constrained settings where invasive diagnostics, pharmacogenomic assays, or lymphocyte transformation tests are often unfeasible. The statistically significant correlation between elevated IgE levels and SCAR phenotypes emboldens the rationale for its integration into early triage algorithms, facilitating pre-emptive identification of high-risk cases and enabling more vigilant therapeutic surveillance.

Moreover, the disproportionately high representation of alternative medicinal agents and non-prescription polypharmacy as causal pharmacologic substrates among SCAR cases underscores an urgent need to enhance pharmacovigilance literacy, regulate indigenous therapeutics, and institutionalize active surveillance frameworks within the Indian subcontinent's dermatologic infrastructure. The findings serve as a clarion call for bioimmunologic vigilance, foregrounding IgE as not only a mechanistic intermediary but also a potential translational tool in the diagnostic and prognostic continuum of drug hypersensitivity syndromes.

In summation, this study delineates a previously underappreciated immunoglobulin-centric axis in CADRs, positing that serum IgE, when interpreted in conjunction with clinical morphology and hematological indices, may offer actionable insights into both the immunopathological gradient and potential systemic trajectory of drug-induced dermatoses. As dermatopharmacology evolves toward precision medicine, future multi-centric, molecularly indexed investigations are warranted to consolidate IgE's position as a scalable biomarker and perhaps even a therapeutic target in the realm of immunotoxic dermatology.

Declarations

Ethical Clearance

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Conflict of interest

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Trial details

Not a Trial

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