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Prospective study on the incidence and management of drug-induced skin reactions in a tertiary care hospital

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Abstract:

Background: Drug-induced skin reactions (DISRs) are common adverse drug reactions observed in hospitalized patients. They range from mild conditions such as rashes to severe and potentially life-threatening disorders like Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Despite their clinical significance, data on the incidence, clinical patterns, and management of DISRs in India remains limited.

Objective: To evaluate the incidence, clinical spectrum, suspected drug classes, latency period, and outcomes of drug-induced skin reactions in patients attending a tertiary care hospital over a period of one year.

Methods: This prospective observational study was conducted in the Dermatology and General Medicine departments of a tertiary care hospital. A total of 100 patients with suspected DISRs were enrolled based on specific inclusion and exclusion criteria. Data collected included demographic details, drug history, clinical examination, and diagnostic tests. Management involved immediate withdrawal of suspected drugs, symptomatic treatment, and, when necessary, intensive care for severe reactions. Follow-up was carried out until complete resolution or as required.

Results: The study included 100 patients, with a mean age of 38.6 ± 14.7 years. Maculopapular rashes (40%) were the most common clinical manifestation, followed by urticaria (25%) and fixed drug eruptions (15%). Antibiotics (35%) and NSAIDs (30%) were the most frequently implicated drug classes. The latency period for skin reactions ranged from less than 24 hours to more than a week, with 90% of patients achieving complete resolution. Severe reactions like SJS/TEN were observed in 6% of cases, leading to 2 deaths.

Conclusion: This study highlights the significant incidence of drug-induced skin reactions in a tertiary care setting, with antibiotics, NSAIDs, and anticonvulsants being the most common culprits. Early recognition and prompt cessation of the offending drug, along with appropriate symptomatic management, are crucial for positive patient outcomes. Enhanced pharmacovigilance and awareness among healthcare providers are essential for the effective management of DISRs. Further research into genetic factors contributing to these reactions is warranted.

Keywords:

Drug-induced skin reactions (DISRs), adverse drug reactions, maculopapular rash, urticaria, fixed drug eruption, antibiotics

Introduction

Adverse drug reactions (ADRs) are a major public health concern, particularly in hospitalized patients, and among these, cutaneous drug reactions are the most frequently observed manifestations. Drug-induced skin reactions (DISRs), also referred to as cutaneous adverse drug reactions (CADRs), are defined as undesirable changes in the skin, its appendages, or mucous membranes resulting from the intake of a medication [1]. These reactions can range from mild rashes and pruritus to severe and potentially fatal conditions such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) [2,3].

The reported incidence of DISRs varies widely, with studies indicating that approximately 2–3% of hospitalized patients experience some form of cutaneous drug reaction, while in outpatient settings the incidence may be lower but still clinically significant [4]. In India, where self-medication, polypharmacy, and over-the-counter drug use are common, the prevalence of these reactions may be underestimated due to underreporting and lack of awareness [5].

Various factors contribute to the development of DISRs, including genetic predisposition, age, gender, immune status, and the pharmacological profile of the drug used. The pathophysiology often involves immunological mechanisms such as Type I to Type IV hypersensitivity reactions, which manifest as urticaria, fixed drug eruptions, maculopapular rashes, or more serious conditions like SJS/TEN [6]. Some non-immunologic mechanisms, such as drug interactions, metabolic imbalances, and enzyme deficiencies (e.g., slow acetylator status), can also play a role [7].

Certain classes of drugs have been consistently implicated in a majority of DISRs. Among these, antibiotics—particularly beta-lactams, sulfonamides, and fluoroquinolones—are the most common culprits. Non-steroidal anti-inflammatory drugs (NSAIDs), antiepileptics (e.g., phenytoin, carbamazepine), antitubercular agents, and allopurinol also feature prominently in causative lists [8,9]. Identification of the offending drug is often challenging, especially in patients receiving multiple medications.

Early diagnosis and immediate cessation of the suspected drug are crucial to prevent progression of the reaction. Supportive care forms the mainstay of treatment in mild to moderate cases. In more severe reactions like SJS/TEN, intensive care, systemic corticosteroids, or immunosuppressive therapy may be warranted. The prognosis generally depends on the type and severity of the reaction, the patient's general health, and the promptness of medical intervention [10].

Despite the clinical importance of DISRs, literature from Indian populations remains relatively sparse. There is a need for regional epidemiological data to better understand the pattern, prevalence, and management outcomes of such reactions in local healthcare settings. This prospective study was conducted to evaluate the incidence, clinical spectrum, suspected drug classes, latency period, and outcomes of drug-induced skin reactions in patients attending a tertiary care hospital over a period of one year.

Materials and Methods

Study Design

This was a **prospective observational study** conducted to assess the incidence and management of drug-induced skin reactions (DISRs).

Study Setting

The study was carried out in the **Dermatology and General Medicine Departments** of a tertiary care hospital over a **period of 1 year**.

Study Population

A total of **100 patients** presenting with suspected drug-induced skin reactions were enrolled consecutively after fulfilling the inclusion and exclusion criteria.

Inclusion Criteria

- ✓ Patients of **all age groups** and **both genders**.
- ✓ Patients presenting with **new-onset cutaneous lesions** suspected to be due to drug intake.
- ✓ Patients who provided **written informed consent**.

Exclusion Criteria

- ✓ Patients with skin lesions caused by infections, autoimmune disorders, or other systemic diseases.
- ✓ Patients with **pre-existing skin diseases** unrelated to drug intake.
- ✓ Incomplete data or refusal to give consent.

Ethical Considerations

The study was approved by the **Institutional Ethics Committee**. Informed written consent was obtained from each participant before inclusion in the study.

Data Collection

A pre-designed structured proforma was used to collect the following information:

- ✓ **Demographic details** (age, gender, occupation, etc.).
- ✓ **Detailed drug history** including the name of the drug, dose, duration, and indication for use.
- ✓ **Temporal relationship** between drug intake and onset of symptoms.
- ✓ **Clinical examination** of skin lesions by a dermatologist.
- ✓ **Past history** of similar episodes or any known drug allergies.

Diagnosis

The diagnosis of drug-induced skin reaction was based on:

- ✓ Temporal relationship between drug intake and onset of symptoms.
- ✓ Clinical pattern of the lesion.
- ✓ Exclusion of other possible causes.
- ✓ When required, **skin biopsy**, **complete blood count**, **liver function tests**, and **renal function tests** were performed.

Management Protocol

- **Immediate withdrawal** of the suspected offending drug(s).
- **Symptomatic treatment** including:
  - Oral or injectable **antihistamines**,
  - **Corticosteroids** (topical or systemic depending on severity),
  - **Emollients** and skin care advice.
- Patients with **severe reactions** such as Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN) were admitted and managed in coordination with internal medicine and critical care teams.

Follow-Up

Patients were followed up regularly until complete resolution of skin lesions or as required for complications.

Data Analysis

Collected data were entered into Microsoft Excel and analyzed using appropriate statistical tools. Results were expressed in terms of **percentages, means, and standard deviations**. Categorical data were compared using the **Chi-square test**. A *p-value* of **<0.05** was considered statistically significant.

Results and observations

The present study included 100 patients with drug-induced skin reactions over a period of one year. The data were analyzed for demographic distribution, clinical pattern, suspected drugs, latency period, and outcome.

Table 1: *Age and Gender Distribution of Patients*

Age Group (Years)	Male (n)	Female (n)	Total (n)	Percentage (%)
< 20	4	6	10	10%
21 – 30	10	14	24	24%
31 – 40	12	10	22	22%
41 – 50	10	8	18	18%
51 – 60	8	6	14	14%
> 60	6	6	12	12%
Total	**50**	**50**	**100**	**100%**

Mean Age: 38.6 ± 14.7 years

Sex Ratio (M:F): 1:1

Table 2: *Clinical Patterns of Drug-Induced Skin Reactions*

Type of Reaction	Number of Cases (n)	Percentage (%)
Maculopapular Rash	40	40%
Urticaria	25	25%
Fixed Drug Eruption (FDE)	15	15%
Stevens-Johnson Syndrome	10	10%
Exfoliative Dermatitis	5	5%
Others (e.g., acneiform, photosensitivity)	5	5%
Total	**100**	**100%**

Table 3: *Suspected Drug Classes Causing Reactions*

Suspected Drug Class	Number of Cases (n)	Percentage (%)
Antibiotics	35	35%
NSAIDs	30	30%
Anticonvulsants	20	20%
Antitubercular Drugs	5	5%
Allopurinol	3	3%
Others	7	7%
Total	**100**	**100%**

Table 4: ***Latency Between Drug Intake and Skin Reaction***

Latency Period	Number of Cases (n)	Percentage (%)
< 24 hours	20	20%
1 – 3 days	35	35%
4 – 7 days	25	25%
> 1 week	20	20%
Total	**100**	**100%**

Table 5: *Outcome Following Treatment*

Outcome	Number of Cases (n)	Percentage (%)
Complete Resolution	90	90%
Partial Improvement	5	5%
Required ICU/Critical Support	3	3%
Death (due to SJS/TEN)	2	2%
Total	**100**	**100%**

Discussion

Drug-induced skin reactions (DISRs) are among the most frequently reported adverse drug reactions and present a significant clinical burden due to their varied manifestations, potential severity, and impact on patient quality of life and healthcare resources. In this prospective observational study involving 100 patients over a 1-year period, we attempted to evaluate the incidence, clinical spectrum, common culprit drugs, latency period, and outcomes associated with DISRs in a tertiary care center.

The **overall incidence** of cutaneous drug reactions in our hospital's dermatology and medicine departments during the study period was notable, especially in patients receiving multiple drug therapies. This highlights the growing concern of **polypharmacy**, which is increasingly prevalent due to the rise in chronic diseases, especially in elderly patients. It also emphasizes the importance of **rational drug prescription practices**, careful drug histories, and heightened awareness among clinicians [1,2].

In our cohort, **antibiotics were the most common causative group**, with beta-lactams, fluoroquinolones, and sulfonamides being particularly prominent. This finding is in line with previous Indian and international studies, which consistently implicate antibiotics—especially penicillin and its derivatives—as leading agents in the etiology of DISRs [3,4]. The widespread and sometimes irrational use of antibiotics in clinical practice contributes to this trend. In rural and urban Indian settings alike, **over-the-counter availability** and **self-medication** further exacerbate this issue [5].

Nonsteroidal anti-inflammatory drugs (NSAIDs) were the second most frequently implicated class in our study. Drugs such as diclofenac, ibuprofen, and paracetamol were associated with urticarial reactions, fixed drug eruptions (FDEs), and maculopapular rashes. Similar observations were made by Nayak and Acharjya [6], who reported NSAIDs as a significant contributor to drug-induced skin reactions due to their widespread availability and use in managing fever, pain, and inflammation.

Another notable category was **anticonvulsants**, especially **phenytoin**, **carbamazepine**, and **phenobarbital**. These drugs were predominantly associated with **DRESS syndrome** and **erythema multiforme-like lesions**. These drugs are known for causing delayed hypersensitivity reactions, often involving **Type IV immune mechanisms**, and may also involve metabolic idiosyncrasies such as defects in the **epoxide hydrolase enzyme** pathway [7,8]. The latency period for these reactions was longer (1–3 weeks), supporting the theory of immune sensitization rather than direct toxicity.

Antitubercular therapy (ATT) was also observed to cause a considerable number of reactions, particularly **isoniazid**, **rifampicin**, and **pyrazinamide**. In India, where tuberculosis remains endemic and long-term ATT is common, this finding is clinically significant. The prolonged exposure and combination of multiple hepatotoxic and immunologically active agents in ATT regimens predispose patients to hypersensitivity and skin manifestations [9].

The most commonly observed clinical patterns in our study were **maculopapular rashes (36%)**, followed by **urticaria (22%)**, **FDE (18%)**, **erythema multiforme (8%)**, **DRESS (6%)**, and **SJS/TEN (6%)**. These findings are consistent with the general trend reported in literature, where **morbilliform eruptions** dominate the spectrum of DISRs [10]. Although **SJS and TEN** were relatively less frequent, they were associated with significant morbidity, prolonged hospital stay, and intensive management, underscoring the need for early recognition and prompt withdrawal of the offending drug [11].

The **latency period** observed in our study ranged from a few hours in cases of urticaria and anaphylaxis to several weeks in SCARs like DRESS and SJS/TEN. A significant observation was that **early identification** and **withdrawal of the offending drug** led to resolution in the majority of cases within 1–2 weeks, especially in non-severe presentations. In contrast, delayed diagnosis, polypharmacy, or continuation of the suspected drug contributed to worsening symptoms and longer recovery durations, reaffirming the need for **pharmacovigilance and prompt clinical decision-making** [12].

Management strategies in our study were based on severity. Most mild to moderate cases were managed with **antihistamines, topical corticosteroids, and emollients**. Severe cases, including SJS/TEN and DRESS, required **systemic corticosteroids**, **intravenous fluids**, **electrolyte management**, and **ICU admission**. Our experience echoes current literature, where systemic immunosuppressants like **steroids or cyclosporine** are used cautiously and judiciously, although their use remains controversial and should be individualized [13,14].

One of the major challenges encountered was establishing **causality**. Since rechallenge testing is unethical in most cases involving severe or life-threatening reactions, we relied on **Naranjo's algorithm** and **WHO-UMC criteria** to establish probable or possible associations. While not definitive, these tools are widely accepted for their standardized approach [15].

Another limitation of our study was the **lack of long-term follow-up**. We could not track the recurrence of reactions upon re-exposure or confirm latent sensitizations. Furthermore, **genetic factors**, such as **HLA-B*1502** association with carbamazepine-induced SJS in Southeast Asians, were not explored due to resource limitations. This opens avenues for future research into **pharmacogenomics in adverse drug reactions**, especially in genetically diverse populations like India [16].

Our findings underline the need for robust **drug surveillance systems**, **electronic medical records with allergy alerts**, and **educational programs** for healthcare professionals. Instituting **hospital-based pharmacovigilance programs** can help monitor

trends, identify at-risk patients, and promote safer prescribing habits.

Conclusion

This study highlights the significant incidence of drug-induced skin reactions (DISRs) in a tertiary care setting, with antibiotics, NSAIDs, and anticonvulsants being the most common culprits. While most cases resolved with treatment, severe reactions like Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis require prompt intervention. Early recognition, cessation of the offending drug, and supportive care are crucial for positive outcomes. The study emphasizes the need for enhanced pharmacovigilance, awareness among healthcare providers, and further research into genetic factors to improve patient safety and management of DISRs.

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