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Clinical, demographic, and histopathological profile of drug-induced cutaneous reactions in a Mexican tertiary hospital: a nine-year retrospective study

Perfil clínico, demográfico e histopatológico de reações cutâneas induzidas por medicamentos em um hospital terciário mexicano: estudo retrospectivo de nove anos

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RESUMO

As reações cutâneas adversas a medicamentos (RCAMs) constituem um desafio relevante na prática dermatológica pela ampla heterogeneidade clínica, potencial gravidade e dificuldade diagnóstica. Apesar de sua importância, dados latino-americanos permanecem escassos. Este estudo observacional retrospectivo teve como objetivo descrever os perfis clínico, demográfico e histopatológico das RCAMs em um centro terciário mexicano ao longo de nove anos. A pesquisa foi conduzida no Departamento de Dermatologia do Instituto Nacional de Ciências Médicas e Nutrição Salvador Zubirán (INCMNSZ) entre janeiro de 2015 e dezembro de 2024, com extração de dados de prontuários eletrônicos e laudos histopatológicos, incluindo informações demográficas, fármacos suspeitos, apresentações clínicas, achados microscópicos, comorbidades e gravidade. No total, 345 casos foram incluídos. O exantema maculopapular foi a apresentação mais frequente (37,4%), seguido por reações liquenoides (8,7%) e Reação a Fármaco com Eosinofilia e Sintomas Sistêmicos (DRESS) (7,2%). Formas graves, como síndrome de Stevens-Johnson/necrose epidérmica tóxica (SSJ/NET), ocorreram em 3,8% dos pacientes. Antibióticos, especialmente vancomicina, sulfonamidas e beta-lactâmicos, foram a classe farmacológica mais implicada (24.9%), seguidos por alopurinol (17.1%). Em 30,7% dos casos, o agente causal não pôde ser identificado. Mais de 80% dos pacientes apresentavam comorbidades, sobretudo condições crônicas e hematológicas. Os achados reforçam a necessidade de estratégias de farmacovigilância ativa, detalhamento rigoroso da história medicamentosa e avaliação dermatológica precoce, especialmente em populações polimedicadas e clinicamente vulneráveis.

Palavras-chave: Hipersensibilidade a medicamentos; Reações cutâneas adversas; Farmacovigilância; Epidemiologia.

ABSTRACT

Cutaneous adverse drug reactions (CADRs) represent a significant challenge in clinical practice due to their wide clinical spectrum, potential severity, and diagnostic complexity. Despite their clinical relevance, epidemiological data from Latin America remain scarce. This retrospective observational study aimed to characterize the clinical, demographic, and histopathological profiles of CADRs in patients evaluated over a nine-year period at a national tertiary care center in Mexico. Conducted at the Dermatology Department of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) between January 2015 and December 2024, data were collected from electronic medical records and histopathology reports, including patient demographics, suspected drugs, clinical presentations, histological findings, comorbidities, and severity. A total of 345 cases were analyzed. Maculopapular exanthema was the most frequent manifestation (37.4%), followed by lichenoid reactions (8.7%) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (7.2%). Severe reactions, such as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), occurred in 3.8% of cases. Antibiotics, particularly vancomycin, sulfonamides, and beta-lactams, were the most commonly implicated drug class (24.9%), followed by allopurinol (17.1%). In 30.7% of cases, the causative drug could not be identified. Over 80% of patients had at least one comorbidity, predominantly chronic and hematologic conditions. This study provides a comprehensive overview of CADRs in a high-complexity clinical setting and underscores the need for enhanced pharmacovigilance, detailed drug histories, and early dermatological assessment. Findings support the implementation of targeted preventive strategies and individualized risk evaluations, particularly in vulnerable and polymedicated populations.

Keywords: Drug hypersensitivity; Cutaneous adverse drug reactions; Pharmacovigilance; Epidemiology.

INTRODUCTION

Adverse drug reactions (ADRs) are unintended and harmful events that may occur following the administration of a pharmaceutical agent at doses employed for therapeutic, prophylactic, or physiological-modifying purposes. In Mexico, the Official Mexican Standard NOM-220-SSA1-2002 defines ADRs as: "Any harmful and unintended response to a drug that occurs at doses normally used in humans for prophylaxis, diagnosis, or treatment of disease, or for the modification of a physiological function" (Diario Oficial de la Federación, 2017).

At the international level, the World Health Organization (WHO), through its International Drug Monitoring Programme (Uppsala Monitoring Center), defines an adverse drug reaction (ADR) as serious when it meets one or more of the following criteria: results in the patient's death; poses a life-threatening risk; requires hospitalization or prolongs an existing hospital stay; results in significant, persistent, or permanent disability; leads to a congenital anomaly or birth defect; is deemed clinically significant, that is, necessitates medical intervention to prevent any of the aforementioned outcomes.

This distinction between serious and non-serious reactions is critical in pharmacovigilance, as it enables the prioritization of ADRs that pose the greatest risk to patient safety and therefore carry the highest clinical and epidemiological relevance.

Cutaneous Adverse Drug Reactions (CADRs)

CADRs, also referred to as drug eruptions or drug-induced dermatologic reactions, account for approximately 15% of all ADRs, according to data from the World Health Organization (World Health Organization, 1971). Their incidence in hospitalized adult populations is estimated to range between 1% and 3%, but can reach up to 5% in certain clinical settings, particularly within

dermatology and internal medicine (Bigby, 2001; Vora et al., 2023).

Clinical Spectrum and Severity of Cutaneous Adverse Drug Reactions

CADRs encompass a broad and heterogeneous clinical spectrum, with over 30 morphological patterns described in the medical literature, underscoring the diagnostic complexity and the necessity of a systematic approach. Although many of these reactions lack pathognomonic signs that would allow a definitive causal association with a specific drug, the most frequently observed manifestations include maculopapular exanthema, urticaria, and erythema multiforme, typically classified as mild to moderate reactions (Roujeau, 1993).

In contrast, severe forms account for approximately 2% to 6.7% of reported CADRs and are associated with significant morbidity, life-threatening potential, and the need for hospitalization. These include drug-induced erythroderma, blistering disorders such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) (Bettuzzi, et al., 2024; Del Pozzo-Magaña; Liy-Wong, 2024; Mockenhaupt et al., 2008).

Pharmacological Agents Most Frequently Implicated in Cutaneous Adverse Drug Reactions

The drugs most frequently implicated in CADRs include antibiotics (particularly beta-lactams and sulfonamides), analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, antipsychotics, and chemotherapeutic agents. The prevalence of these pharmacological groups in CADRs can vary significantly depending on the demographic, clinical, and therapeutic characteristics of the population studied (Barbaud et al., 2014; Marzano et al., 2016).

CADRs represent a major cause of dermatological morbidity and are often associated with unplanned hospital admissions, the need for discontinuation of the causative treatment, and impairment of patients' quality of life. Additionally, they impose a substantial burden on healthcare systems by increasing healthcare costs, prolonging hospital stays, and negatively impacting treatment adherence (Pirmohamed et al., 2004).

Risk Factors and Epidemiological Impact of CADRs

Although any patient may develop a CADR, several well-established risk factors have been identified that increase individual susceptibility. These include female sex, extremes of age, immunosuppression (including HIV infection and immunosuppressive therapy), polypharmacy, autoimmune diseases, and prolonged hospitalization (Montané, 2020; Mockenhaupt et al., 2008).

In the United States, ADRs are estimated to contribute to over 100,000 deaths annually, ranking among the leading causes of iatrogenic mortality (Lazarou et al., 1998). However, the specific burden attributable to CADRs remains underrecognized, particularly in middle-income countries such as Mexico, where epidemiological studies are still limited.

Local Data and Rationale for the Present Study

In Mexico, available data on CADRs originate primarily from tertiary care centers. In 2006, the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) reported a CADR prevalence of 0.7% among hospitalized patients, with a mortality rate of 16.6% in those presenting with severe forms. CADRs were more common in immunocompromised individuals and in patients with systemic lupus erythematosus (Hernández-Salazar et al., 2006).

Subsequently, a cross-sectional study was conducted in 2011 at Hospital General Dr. Manuel Gea González reported a prevalence of 0.6%, with a predominance in female patients (65.1%). The most frequently implicated drugs were trimethoprim-sulfamethoxazole (12.3%), piroxicam (10.7%), and carbamazepine (7.6%). The most common clinical manifestations included maculopapular exanthema (25%), fixed drug eruption

(16%), and photosensitivity (16%). The most prevalent comorbidities were systemic arterial hypertension (28.5%) and type 2 diabetes mellitus (12.5%) (Hernández-Salazar et al., 2011).

In a retrospective analysis published in 2014, Chávez-Lemus et al. reported that 34.4% of hospitalized patients evaluated by the Dermatology Department at the Centro Médico Nacional de Occidente (IMSS, Guadalajara) developed CADRs over an eight-year period. The most prevalent clinical entities were toxic epidermal necrolysis (32%) and Stevens–Johnson syndrome (14%), with epilepsy (16.1%) and diabetes mellitus (15%) as notable comorbid conditions (Chávez Lemus et al., 2014).

Given the increasing use of pharmacological agents in clinical practice, the limited local characterization of CADRs, and the need to strengthen pharmacovigilance strategies, this study aimed to characterize the clinical, demographic, and histopathological profiles of patients diagnosed with CADRs by the Dermatology Department at INCMNSZ, between January 1, 2015, and December 31, 2024, including both inpatient and outpatient populations.

METHODS

A retrospective observational study was conducted and approved by the Research Ethics Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), under protocol number DER-5723-25-25-1.

During the study period, a total of 45,360 dermatologic evaluations were performed. Through a systematic and comprehensive review of electronic medical records and histopathology reports, 448 cases with a presumptive or confirmed diagnosis of CADR were initially identified. After applying inclusion and exclusion criteria, 345 cases were selected for final analysis.

Inclusion and Exclusion Criteria

Patients were included if they were 18 years of age or older at the time of medical evaluation, had a complete clinical record with an institutional registration number, and received a clinical diagnosis of a CADR. The diagnosis was established based on a clear temporal correlation between drug administration and the onset of cutaneous lesions, supported by a specialist dermatologic evaluation and histopathological confirmation whenever a biopsy was available.

Cases were excluded if medical records were incomplete or if there was insufficient information to confirm or characterize the reaction. Exclusion also applied when a definitive diagnosis could not be established after clinical and histopathological review, when applicable, or when the cutaneous manifestations were not attributable to drug exposure, including those of infectious, autoimmune, idiopathic, or other alternative etiologies.

Diagnostic Strategy

The diagnosis of CADRs was based on the clinical morphology and distribution of the skin lesions, supplemented with histopathological examination when required. Suspected drug identification was guided by the type of reaction, the temporal pattern of symptom onset following drug exposure, and reference to causality assessment tools specific to each type of CADR. The likelihood of the causative agent was subsequently corroborated through literature review.

When a single drug had a clear temporal association with the reaction, it was considered the most probable causative agent. In cases of polypharmacy with no clear dominant suspect, a list of implicated drugs was compiled based on their timing and previously documented associations.

This assessment was routinely performed during the specialized dermatological consultation. For the purposes of this study, data were extracted from the medical notes contained in the electronic health records of patients with clinical documentation of suspected or confirmed CADR. It is important to note

that due to the retrospective nature of the study, not all records contained complete information, which constitutes an inherent limitation of the study design.

Case Selection and Data Collection

All cases recorded during the study period with sufficient clinical information for analysis were included, without applying formal statistical sampling. This approach was justified by the retrospective study design and the institutional access to complete medical records.

The Dermatology Department at INCMNSZ provides specialized care for complex dermatological conditions referred both from internal services and external institutions. It primarily serves an adult population with multiple comorbidities and handles approximately 4,500 dermatologic consultations annually.

The following variables were systematically and consistently extracted from each clinical record: age and sex; relevant comorbidities; suspected causative drugs; route of drug administration (when available); latency period between drug exposure and onset of reaction; clinical type of cutaneous reaction; histopathological findings (if biopsy was performed); prescribed treatments and clinical outcome (when documented).

This methodology enabled the construction of a representative sample of CADRs diagnosed in a tertiary care hospital setting, within a real-world clinical context characterized by patients with multiple predisposing factors.

Statistical Analysis

Descriptive statistics were used for data analysis. Categorical variables were expressed as absolute frequencies and proportions (%), while continuous variables were described using measures of central tendency (median) and dispersion (minimum and maximum values).

RESULTS

Study Population

A total of 448 patients evaluated by the Dermatology Department of the INCMNSZ between January 1, 2015, and December 31, 2024, were initially identified. After applying the inclusion and exclusion criteria, 345 patients were included in the final analysis.

Of these, 202 (58.6%) were female and 143 (41.4%) were male, with an estimated median age of 50 years. The most affected age groups were 29–39 years (18.6%), 50–59 years (17.7%), and 18–28 years (17.4%), indicating a predominance of cases among young and middle-aged adults. The distribution is detailed in Table 1.

Table 1. Age distribution of patients diagnosed with adverse cutaneous drug reactions (n= 345)

AGE GROUP (YEARS)	N	%
18–28	60	17.4%
29–39	64	18.6%
40–49	43	12.5%
50–59	61	17.7%
60–69	54	15.7%
70–79	*43*	*12.5%*
80–89	*15*	*4.3%*
90–99	*5*	*1.4%*

Morphological Classification of Reactions

According to clinical morphology, the most common reaction was maculopapular exanthema (129 cases, 37.4%), followed by lichenoid reactions (8.7%) and DRESS syndrome (7.2%). In 48 cases (13.9%), the morphology was not classifiable due to insufficient documentation. The full distribution is presented in Table 2.

Table 2: Clinical types of adverse cutaneous drug reactions (n= 345)

REACTION TYPE	N	%
Maculopapular exanthema	129	37.4%
Lichenoid reaction	30	8.7%
DRESS	25	7.2%
Urticaria	21	6.1%
Erythema multiforme	19	5.5%
Pityriasiform reaction	*12*	*3.5%*
SJS	*11*	*3.2%*
Erythroderma	*8*	*2.3%*
Vasculitis	*8*	*2.3%*
Fixed drug eruption	*9*	*2.6%*
Erythema annulare centrifugum	*7*	*2.0%*
SDRIFE	*6*	*1.7%*
Psoriasiform reaction	*6*	*1.7%*
AGEP	*4*	*1.2%*
TEN	*2*	*0.6%*
Unspecified	*48*	*13.9%*

Note: "Unspecified" indicates cases in which the specific clinical pattern of the cutaneous reaction was not clearly documented in the medical record due to the retrospective nature of the study.

Drugs, comorbidities and severity:

Implicated Drugs

In 30.7% of cases (106/345), the causative drug could not be identified due to insufficient documentation or exposure to multiple potential agents. Among the identified drugs, antibiotics were the most frequently implicated (24.9%), with the following subclass distribution: vancomycin (31.4%), beta-lactams (24.4%), sulfonamides (16.3%), other classes (18.6%), and quinolones (9.3%). Within beta-lactams, cephalosporins accounted for 10.5% of the total cases.

Allopurinol was the second most frequently involved agent (17.1%) (Table 3). Other pharmacologic groups collectively accounted for 16.5% of reactions and included antiretrovirals, antiangiogenics, antihypertensives, antifungals, and immunomodulators. NSAIDs, antitubercular drugs, and anticonvulsants were implicated in 2.9%, 1.4%, and 1.7% of cases, respectively. In 4.6% of patients, more than one drug was suspected.

Table 3: Drug classes associated with adverse cutaneous drug reactions (n= 345)

DRUG CLASS	N (CASES)	%
Antibiotics	86	24.9%
Allopurinol	59	17.1%
NSAIDs	10	2.9%
Anticonvulsants	6	1.7%
Antitubercular agents	5	1.4%
>1 drug involved	*16*	*4.6%*
Other drugs*	*57*	*16.5%*
Unspecified	*106*	*30.7%*

**Includes antihypertensives, anticoagulants, hypoglycemics, antiretrovirals, antiangiogenics, antifungals, monoclonal antibodies, beta-blockers, immunomodulators, corticosteroids, vaccines, and antivirals.*

Comorbidities

Among the 345 patients included in the study, a total of 523 comorbidities were documented, corresponding to an average of 1.5 comorbidities per patient. Chronic degenerative diseases were the most prevalent (28.1%), followed by hematologic malignancies (15.1%) and kidney diseases (9.6%). These percentages are not mutually exclusive, as individual patients could present with multiple comorbid conditions. This highlights the substantial burden of coexisting diseases in this population (Table 4).

Table 4: Comorbidities in patients with drug-induced skin reactions

COMORBIDITY	N	%
Chronic degenerative diseases	97	28.1%
Hematologic malignancies	52	15.1%
Kidney diseases	33	9.6%
Lupus	30	8.7%
Solid malignancies	29	8.4%
Hepatic diseases	*27*	*7.8%*
COVID-19 (prior)	*26*	*7.5%*
Thyroid disorders	*24*	*6.9%*
Cardiac diseases	*21*	*6.1%*
Dermatologic diseases	*18*	*5.2%*
Post-transplant	*10*	*2.9%*
Others	*156*	*45.2%*

** Multiple comorbidities were recorded per patient; therefore, total N exceeds cohort size*

Severity and associated drugs

Antibiotics were the pharmacological group most frequently associated with drug-induced dermatological reactions. These reactions displayed a wide clinical spectrum, including urticaria, maculopapular exanthema, erythema multiforme, SJS, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), fixed drug eruption, erythroderma, lichenoid and pityriasiform eruptions, among others.

The Table 5 summarizes the frequency, severity, and suspected drugs for each type of pharmacodermia. TEN and SJS were the most severe reactions, though infrequent (0.6% and 3.2%, respectively). They were associated with antibiotics, NSAIDs, allopurinol, and anticonvulsants. Moderate severity reactions included DRESS (7.2%), erythroderma (2.3%), vasculitis (2.6%), and AGEP (1.2%), frequently related to antibiotics and other agents. Maculopapular exanthema (37.4%) and unspecified reactions (13.6%) were the most common and generally mild.

Table 5: Severity and associated drugs by type of adverse cutaneous drug reaction (n= 345)

PHARMACODERMIA	N	%	SEVERITY	ASSOCIATED DRUG CLASSES
Toxic Epidermal Necrolysis (TEN)	2	*0.6%*	*Very high*	Antibiotics, NSAIDs, allopurinol, unspecified, other
Stevens-Johnson Syndrome (SJS)	11	*3.2%*	*Very high*	Antibiotics, NSAIDs, anticonvulsants, allopurinol, multiple
DRESS	25	*7.2%*	*High*	Multiple, unspecified
Erythroderma	8	*2.3%*	*High*	Antibiotics, other, unspecified
Vasculitis	9	*2.6%*	*High*	Anticonvulsants, antibiotics, allopurinol, unspecified
AGEP	*4*	*1.2%*	*Moderate*	*Antibiotics, antipyretics, anticonvulsants, unspecified, multiple*
Fixed drug eruption	*9*	*2.6%*	*Moderate*	*Unspecified*
Lichenoid reaction	*30*	*8.7%*	*Moderate*	*Antibiotics, unspecified, multiple*
Psoriasiform reaction	*6*	*1.7%*	*Moderate*	*Unspecified*
Pityriasiform reaction	*12*	*3.5%*	*Moderate*	*Antibiotics, other*
Erythema multiforme	*19*	*5.5%*	*Moderate*	*Antibiotics, other*
Urticaria	*21*	*6.1%*	*Moderate*	*Antibiotics, unspecified*
Erythema annulare centrifugum	*7*	*2.0%*	*Low*	*Other, unspecified*
Maculopapular exanthema	*129*	*37.4%*	*Low*	*Allopurinol, antibiotics, other, unspecified*
SDRIFE	*6*	*1.7%*	*Low*	*Other, unspecified*
Unspecified	*47*	*13.6%*	*Not applicable*	*Antibiotics, allopurinol, anticonvulsants, other, unspecified*

**DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms. *AGEP: Acute Generalized Exanthematous Pustulosis. *SDRIFE: Symmetrical Drug-Related Intertriginous and Flexural Exanthema*

Note: "Unspecified" indicates cases in which the specific clinical pattern of the cutaneous reaction was not clearly documented in the medical record due to the retrospective nature of the study.

This distribution highlights the clinical heterogeneity of drug-induced skin reactions, and the variety of drugs involved, with implications for diagnosis, monitoring, and individualized treatment decisions.

DISCUSSION

This study provides an updated characterization of CADRs in a Mexican population treated at a national tertiary care center over a nine-year period. As a national referral institution, the patient population includes individuals with multiple comorbidities and substantial pharmacological burden, potentially modifying the patterns typically observed in primary or secondary care settings.

Non-severe reactions, particularly maculopapular exanthema (37.4%), were the most frequent findings, consistent with national and international reports (Duong et al., 2017). In contrast, severe reactions were less common (12.8%), and no drug-related mortality was observed—unlike previous studies where DRESS-related mortality reached up to 10%, and SJS/TEN exceeded 20% (Sekula et al., 2013).

One of the most relevant findings was the high proportion of CADRs attributed to antibiotics (25%), particularly vancomycin (31.4% of antibiotic-related cases), sulfonamides, and beta-lactams. This underscores the importance of vigilant use, especially in empirical regimens or prolonged treatments. Although less frequent, quinolones were also associated with severe manifestations, warranting close clinical monitoring. Allopurinol was the second most commonly implicated drug (17%), reinforcing its strong association with hypersensitivity syndromes such as DRESS and SJS/TEN, particularly in patients with metabolic or renal disorders (Van Nguyen et al., 2019; Hershfield et al., 2013).

A significant limitation was the inability to identify the causative drug in 30.7% of cases, reflecting a methodological challenge inherent to retrospective designs, particularly in the context of polypharmacy, where establishing specific causal associations is difficult. Unlike other studies that have employed controlled re-exposure testing as a diagnostic tool (ROUJEAU, 1993), our institution did not perform such tests due to ethical considerations and the potential risk to patients. This limitation has also been noted in other hospital-based cohorts (Mockenhaupt et al., 2008).

Furthermore, confirmatory laboratory tests such as lymphocyte transformation testing or patch testing were not available. Although these may offer diagnostic value in selected cases, they are not standardized for all drugs and are generally unavailable in routine clinical practice (Barbaud, 2014; Pichler, 2003).

From an epidemiological perspective, a female predominance (58.5%) was identified, in line with studies suggesting greater immunological susceptibility in women (Montané, et al., 2020; Pavlos et al., 2012). Over 80% of patients presented with at least one comorbidity, with chronic degenerative and hematologic conditions being the most prevalent. These findings reinforce the clinical impact of CADRs in patients with high clinical vulnerability.

Additionally, the study included patients evaluated during the COVID-19 pandemic, which may have influenced the number of cases observed as well as the comorbidity profile, as several individuals had a history of SARS-CoV-2 infection (Carrión-Álvarez et al., 2021).

In terms of clinical severity, serious reactions such as SJS/TEN, DRESS, and vasculitis were primarily associated with antibiotics, allopurinol, and anticonvulsants. Moderate reactions were linked to a broader range of drugs, including combination regimens. This distribution highlights the importance of individualized risk assessment prior to initiating potentially high-risk medications.

The wide spectrum of clinical manifestations, from urticarial lesions to life-threatening exfoliative syndromes, emphasizes the need for prompt dermatological evaluation. Although 76% of cases included a diagnostic skin biopsy, the initial clinical suspicion remains fundamental, particularly in severe presentations.

CONCLUSIONS

This study provides a comprehensive and updated characterization of CADRs in a Mexican tertiary referral center over a nine-year period. Most reactions were non-severe, with maculopapular exanthema being the predominant pattern, while severe forms, including Stevens–Johnson syndrome and toxic epidermal necrolysis, were uncommon but clinically significant. Antibiotics, particularly vancomycin, sulfonamides, and beta-lactams were the most frequently implicated agents, reaffirming the critical need for dermatologic surveillance during antimicrobial therapy. Allopurinol emerged as the second most common culprit drug, often linked to severe hypersensitivity syndromes such as DRESS and SJS/TEN.

The inability to identify a clear causative agent in nearly one-third of cases underscores the urgent need to enhance pharmacovigilance systems, obtain detailed drug histories, and strengthen clinical documentation. The high prevalence of comorbidities, especially chronic and hematologic conditions, further highlights the importance of individualized risk assessment prior to initiating potentially high-risk pharmacologic treatments.

Our findings emphasize the pivotal role of early clinical suspicion, accurate dermatologic assessment, and standardized classification of CADRs, particularly in vulnerable and polymedicated populations. Integrating pharmacovigilance tools, comprehensive drug histories, and specialized dermatologic evaluations in high-complexity clinical settings is essential for timely intervention, prevention of severe complications, and improvement of patient safety.

Finally, this study underscores the importance of continued epidemiologic surveillance and supports the need for prospective, multicenter studies to refine diagnostic algorithms, strengthen pharmacovigilance practices, and inform national health policies aimed at reducing the burden of CADRs in Latin American populations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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