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Drug hypersensitivity reactions in adults: clinical patterns and drug profile

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ABSTRACT

Aims: Drug hypersensitivity reactions (DHRs) are immunologically mediated adverse drug reactions increasingly reported in recent years. This study aimed to assess the demographic characteristics and self-reported clinical features of adults presenting with suspected DHRs to two tertiary centers in Konya, Türkiye, and to examine the distribution of reactions attributed to β-lactam antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs).

Methods: This retrospective study included 138 patients who presented with suspected DHRs between 1 April and 30 October 2025 and had complete demographic and clinical data. Only reactions compatible with immunological mechanisms and occurring within the first 6 hours after drug intake were evaluated. Demographic variables, culprit drugs, reaction timing and type, and coexisting allergic diseases were extracted from electronic medical records.

Results: The median age was 40 years, and 73.9% were female. Cutaneous manifestations were the predominant presentation (89.1%), and 65.9% of reactions occurred within the first hour. β-lactams (43.5%) and NSAIDs (40.6%) were the main implicated drugs. The anaphylaxis rate was 19.6%, and 69.6% required hospitalization. Reactions within the first hour were associated with higher rates of anaphylaxis (28.6% vs. 2.1%; p<0.001), loss of consciousness (19.8% vs. 6.4%; p=0.038), and hospitalization (75.8% vs. 57.4%; p=0.026) than reactions at 1–6 hours. Anaphylaxis was more frequent in β-lactam reactions than NSAIDs (30.5% vs. 12.5%; p=0.006). NSAID reactions appeared at 1–6 hours, while β-lactam ones were largely within the first hour (p<0.001). Younger patients (<45 years) more frequently exhibited itching, urticaria, and abdominal pain (p=0.042; 0.042; 0.014, respectively).

Conclusion: β-lactam antibiotics and NSAIDs are the leading causes of reported DHRs in adults. β-lactams are particularly associated with early-onset reactions and anaphylaxis. Detailed assessment of clinical features is essential when evaluating drug allergy based on patient history. Regional data may contribute to developing more standardized diagnostic and management approaches for DHRs.

Keywords: Anaphylaxis, drug allergy, drug hypersensitivity, nonsteroidal anti-inflammatory drug, penicillin allergy

INTRODUCTION

Adverse drug reactions (ADRs) are unexpected effects that occur at therapeutic doses of medications.[1] Reactions that are unpredictable and associated with immunologic or genetic mechanisms account for approximately 15–20% of all ADRs and represent a significant cause of morbidity in clinical practice.[2] Drug allergy (DA), which falls within this category, has a broad impact on healthcare due to misdiagnosis and unnecessary drug restrictions. With the increasing availability of therapeutic options, the incidence of such cases is expected to rise in the future.[3]

The true incidence of DA remains unknown.[2] Approximately 10% of individuals receiving healthcare report a DA. Additionally, around 20% of anaphylaxis cases presenting to the emergency department are drug-induced, and 15–20% of hospitalized patients report a history of DA. In DA, the absence of reliable biomarkers and standardized definitions complicates the diagnostic process. Both underdiagnosis and overdiagnosis are common, leaving inadequately managed patients vulnerable to life-threatening reactions.[4]

The most commonly reported drug allergies are directed against antibiotics, opioids, and non-steroidal anti-inflammatory drugs (NSAIDs).[5] Among β-lactam antibiotics, penicillin ranks first among reported drug allergies.[1] However, penicillin allergy is often indistinguishable from rashes associated with viral infections, and unverified past reactions can remain recorded as "allergy" for years, making the true prevalence appear higher than it actually is. Moreover, the waning of immunoglobulin E (IgE)-mediated sensitization over time further diminishes the clinical relevance of historical reports. Studies have shown that sensitization disappears within five

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years in approximately half of patients and in over ten years in around 80% of cases.[6]

Self-reported DA is more common in adults, and the majority of cases presenting to hospitals due to DA are adults. In immediate-type ADRs, urticaria, itching, and angioedema have been reported as the most frequent manifestations.[5] The primary causes of hospital admissions related to DA include early-onset reactions such as anaphylaxis and delayed-type reactions such as severe cutaneous adverse reactions.[4] However, not every clinical manifestation directly reflects a specific immune mechanism; both IgE-mediated and non–IgE-mediated pathways can present with similar phenotypes.[5]

Repeated and prolonged exposure to a drug increases the likelihood of sensitization, thereby elevating the risk of DA. The extent of drug exposure varies globally due to differences in treatment costs and accessibility.[4] This variability in exposure frequency directly affects the reported rates of DA in populations, highlighting the critical importance of accurately documenting allergy histories. Therefore, the correct recording of drug hypersensitivity labels is essential for patient safety. However, a significant proportion of patient-reported DA histories do not reflect true hypersensitivity, often leading to mislabeling.[5] In patients who are mislabeled, avoidance of standard therapies can lead to the use of less effective alternative drugs, increased treatment costs, and, particularly in the case of antibiotics, contribute to the development of antimicrobial resistance.[3]

In order to enable more consistent definitions and classifications, establishing the prevalence of DA in a reliable manner is crucial for clinical practice. This study aimed to evaluate the self-reported prevalence of DA in an adult population presenting to two healthcare centers in Konya, with a particular focus on the distribution of reported allergies to β-lactam antibiotics and NSAIDs, as well as the characterization of reported reaction types. We anticipate that the findings will contribute to delineating the regional profile and support the development of more consistent diagnostic and management strategies for drug hypersensitivity.

METHODS

Ethics

Ethical approval for this study was obtained from the Non-interventional Clinical Researches Ethics Committee of Konya City Hospital (Date: 08.12.2025, Decision No: 2025/251). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Study Design

The medical records of patients presenting with suspected DA to the Allergy and Immunology Outpatient Clinics of Konya City Hospital and Beyhekim Training and Research Hospital between April 1 and October 30, 2025, were retrospectively reviewed. A total of 163 patients were initially evaluated. Patients who refused testing, whose reactions were assessed as non-allergic, or who reported reactions occurring more than 6 hours after drug intake were considered non-immediate and excluded from the study. Among the remaining patients, those who had clearly specified at least one suspected drug at presentation and had complete demographic and clinical data were included, resulting in a final study cohort of 138 patients.

Data Collection and Variables

For each patient, an allergy specialist reviewed all clinical information and investigations related to the suspected reaction. Culprit drugs were identified based on the medications reported in the patient's medical records and available alternative treatment options. Patients were evaluated in accordance with the recommendations of European Network of Drug Allergy/European Academy of Allergy and Clinical Immunology.[7] Data were obtained from electronic medical records and patient files. Recorded variables included demographic characteristics (age, sex), reaction type (urticaria, angioedema, anaphylaxis, etc.), suspected drugs, time to reaction onset, time elapsed since the reaction, and coexisting allergic comorbidities.

Reaction Timing Classification

This study was designed to evaluate only immediate drug reactions, which are highly likely to be mediated by immunological mechanisms. Immediate drug reactions are typically reported to occur within the first hour after drug administration, although in some drugs, they may extend up to 6 hours. Therefore, patients who developed reactions within the first 6 hours after drug intake were included in the study. Reaction timing was analyzed in two groups: (1) reactions occurring within the first hour, and (2) reactions occurring between 1 and 6 hours.

Statistical Analysis

Data entry and statistical analyses were performed using SPSS for Windows, version 18.0 (SPSS Inc. Chicago, IL, USA) package program. Continuous variables were assessed for normality using visual methods (histograms, Q-Q plots) and the Shapiro–Wilk test. Non-normally distributed continuous variables are presented as medians with interquartile ranges (IQR), and categorical variables are expressed as frequencies (n) and percentages (%). Comparisons between two independent groups were performed using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics of Patients

A total of 138 patients presenting with suspected DA were included in the study. The median age of the cohort was 40 years, and the majority were female (73.9%). Drug reactions most commonly manifested with cutaneous findings (89.1%). The majority of reactions occurred within the first hour following drug intake (65.9%). Regarding age distribution at the time of reaction, 63.8% of patients were younger than 45 years.

The most frequently implicated drug classes were β-lactam antibiotics (43.5%) and NSAIDs (40.6%). Within the β-lactam group, penicillins (32.6%) and cephalosporins (10.9%) were

the most commonly reported. A substantial proportion of patients required hospitalization due to the reaction (69.6%). Coexisting allergic diseases were present in 28.3% of patients. Detailed demographic and clinical characteristics of the cohort are presented in Table 1.

Table 1. General description of study population (n=138)

Variables	n (%) or median (IQR)
Age, years	40 (29-50)
Female sex	102 (73.9%)
Age at allergic reaction, years	38 (25-47)
Time to onset of reaction	
Within the first hour	91 (65.9%)
1-6 hour	47 (34.1%)
Reaction symptoms	
Cutaneous reaction	123 (89.1%)
Itching	89 (64.5%)
Angioedema	92 (66.7%)
Drug-related urticaria	81 (58.7%)
Dyspnea/wheezing/cough	58 (42%)
Anaphylaxis	27 (19.6%)
Loss of consciousness	21 (15.2%)
Abdominal pain	10 (7.2%)
Age at time of allergic reaction	
<45 years	88 (63.8%)
≥45 years	50 (36.2%)
Time passed drug reaction	
<1 year	79 (57.2%)
1-10 years	34 (24.6%)
>10 years	25 (18.1%)
Suspected drug	
Beta-lactams	60 (43.5%)
Penicillins	45 (32.6%)
Cephalosporins	15 (10.9%)
Macrolides	1 (0.7%)
Quinolones	5 (3.6%)
NSAID	56 (40.6%)
Local anesthetics	6 (4.3%)
General anesthetics	1 (0.7%)
Radiocontrast agents	1 (0.7%)
Iron preparations	5 (3.6%)
Vitamin B12	1 (0.7%)
Proton pump inhibitors	2 (1.4%)
Hospital admission for reaction	96 (69.6%)
Number of drug allergies	2 (1-2)
Coexisting allergic diseases	39 (28.3%)
Asthma	12 (8.7%)
Allergic rhinitis	23 (16.7%)

NSAID: Non-steroidal anti-inflammatory drugs, IQR: Interquartile range

Patient Characteristics and Clinical Features According to Reaction Timing

Clinically, anaphylaxis (28.6% vs. 2.1%) and loss of consciousness (19.8% vs. 6.4%) were more frequently observed within the first hour after drug intake. Regarding drug class distribution, penicillin-induced reactions were more common within the first hour (45.1%), whereas NSAID-induced reactions were more frequently observed after the first hour (74.5%). Among patients who developed reactions within the first hour, 75.8% required hospital admission (p=0.026), and the median number of reported drug allergies was 2 (IQR: 1–2; p=0.003). No significant differences were found between reaction timing and the presence of coexisting allergic diseases. Additional detailed data are presented in Table 2.

Table 2. Comparison of drug reactions occurring within the first hour and after one hour

Variables	Reaction within 1 hour (n=91)	Reaction within 1-6 hour (n=47)	p-value
Age, years	40 (28-52)	40 (33-49)	0.478
Female sex	69 (75.8%)	33 (70.2%)	0.477
Age at allergic reaction, years	36 (25-46)	38 (28-49)	0.405
Reaction symptoms			
Anaphylaxis	26 (28.6%)	1 (2.1%)	**<0.001**
Loss of consciousness	18 (19.8%)	3 (6.4%)	**0.038**
Cutaneous reaction	80 (87.9%)	43 (91.5%)	0.522
Angioedema	61 (67%)	31 (66%)	0.899
Itching	55 (60.4%)	34 (72.3%)	0.166
Drug-related urticaria	52 (57.1%)	29 (61.7%)	0.606
Dyspnea/wheezing/cough	39 (42.9%)	19 (40.4%)	0.784
Abdominal pain	10 (11%)	0	-
Age at allergic reaction			
<45 years	59 (64.8%)	29 (61.7%)	0.717
≥45 years	32 (35.2%)	18 (38.3%)	
Time passed drug reaction			
<1 year	48 (52.7%)	31 (66%)	
1-10 years	25 (27.5%)	9 (19.1%)	0.329
>10 years	18 (19.8%)	7 (14.9%)	
Suspected drugs			
Beta-lactams	51 (56.1%)	9 (19.1%)	**<0.001**
Penicillins	41 (45.1%)	4 (8.5%)	**<0.001**
Cephalosporins	10 (11%)	5 (10.6%)	0.950
Macrolides	0	1 (2.1%)	-
Quinolones	4 (4.4%)	1 (2.1%)	0.499
NSAID	21 (23.1%)	35 (74.5%)	**<0.001**
Local anesthetics	6 (6.6%)	0	-
General anesthetics	1 (1.1%)	0	-
Radiocontrast agents	1 (1.1%)	0	-
Iron preparations	5 (5.5%)	0	-
Vitamin B12	1 (1.1%)	0	-
Proton pump inhibitors	1 (1.1%)	1 (2.1%)	0.632
Hospital admission for reaction	69 (75.8%)	27 (57.4%)	0.026
Number of drug allergies	2 (1-2)	2 (1-4)	0.003
Coexisting allergic diseases	26 (28.6%)	13 (27.7%)	0.910

Data are presented as n (%) or median (interquartile range [IQR]). p values were calculated using the Mann–Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate. Bold values indicate p<0.05
NSAID: Non-steroidal anti-inflammatory drugs

Comparison of Patients with and without Drug-Induced Anaphylaxis

Anaphylaxis was observed significantly more frequently in penicillin-induced reactions (63% vs. 25.2%, p<0.001). In patients who developed anaphylaxis, reactions most commonly occurred within the first hour after drug intake (96.2%). Clinically, loss of consciousness, dyspnea, and abdominal pain were significantly more frequent in the anaphylaxis group (p≤0.001). Among patients without anaphylaxis, reactions occurring within the past year were more frequently observed (p=0.019). Hospital admission was required in 92.6% of patients with anaphylaxis (p=0.004). No significant association was observed between the presence of coexisting allergic diseases and anaphylaxis. Detailed data are presented in Table 3.

Drug Reactions and Clinical Findings According to Age Groups

When age groups (<45 years and ≥45 years) were compared, no significant differences were observed for most drug-related

Table 3. Demographic and clinical associations of patients with and without drug-induced anaphylaxis

Variables	With anaphylaxis (n=27)	Without anaphylaxis (n=111)	p value
Age, years	40 (30-48)	40 (29-51)	0.855
Female, sex	17 (63%)	85 (76%)	0.149
Age at allergic reaction, years	39 (20-43)	37 (26-48)	0.370
Time to onset of reaction			
Within the first hour	26 (96.2%)	65 (58.5%)	**<0.001**
1-6 hours	1 (3.7%)	46 (41.4%)	
Reaction symptoms			
Cutaneous reaction	23 (85.2%)	100 (90.1%)	0.493
Itching	16 (59.3%)	73 (75.8%)	0.526
Angioedema	19 (70.4%)	73 (65.8)	0.649
Drug related urticaria	14 (51.9%)	67 (60.4%)	0.421
Dyspnea/wheezing/cough	21 (77.8%)	37 (33.3%)	**<0.001**
Loss of consciousness	17 (63%)	4 (3.6%)	**<0.001**
Abdominal pain	6 (22.2%)	4 (3.6%)	**0.001**
Age at allergic reaction			
<45 years	19 (70.4%)	69 (62.2%)	0.426
≥45 years	8 (29.6)	42 (37.8%)	
Time passed drug reaction			
<1 year	9 (33.3%)	70 (63.1%)	
1-10 years	10 (37%)	24 (21.6%)	**0.019**
>10 years	8 (29.6%)	17 (15.3)	
Suspected drug			
Beta-lactams	18 (66.7%)	43 (37.8%)	0.023
Penicillins	17 (63%)	28 (25.2%)	<0.001
Cephalosporins	1 (3.7%)	14 (12.6%)	0.182
Macrolides	0	1	-
Quinolones	0	5 (4.5%)	-
NSAID	7 (25.9%)	49 (44.1%)	0.084
Local anesthetics	0	6 (5.4%)	-
General anesthetics	0	1 (0.9%)	-
Radiocontrast agents	0	1 (0.9%)	-
Iron preparations	1 (3.7%)	4 (3.6%)	0.669
Vitamin B12	1 (3.7%)	0	-
Proton pump inhibitors	0	2 (1.8%)	-
Hospital admission for reaction	25 (92.6%)	71 (64%)	0.004
Coexisting allergic diseases	5 (18.5%)	34 (30.6%)	0.210

Data are presented as n (%) or median (interquartile range [IQR]). p values were calculated using the Mann–Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate. Bold represent: p<0.05
NSAID: Non-steroidal anti-inflammatory drugs

and clinical characteristics (p>0.05). However, itching (70.5% vs. 53.1%, p=0.042), drug-related urticaria (64.8% vs. 46.9%, p=0.042), and abdominal pain (11.4% vs. 0%, p=0.014) were more frequently observed in younger patients. Detailed data are presented in Table 4.

Clinical Characteristics and Reaction Timing According to Causative Drug Groups

The frequency of anaphylaxis was significantly higher in patients with β-lactam–induced reactions compared to those with NSAID-induced reactions (30.5% vs. 12.5%; p=0.006). Similarly, drug-related urticaria was more common in the β-lactam group than in the NSAID group (71.2% vs. 44.6%; p=0.008). Most reactions in the β-lactam group occurred within the first hour after drug intake (83.1% vs. 39.2%), whereas NSAID-induced reactions predominantly developed within 1–6 hours (p<0.001). Detailed data are presented in Table 5.

Table 4. Comparison of clinical characteristics in patients under 45 years and 45 years or older

Variables	<45 years, n (%) (n=88)	≥45 years, n (%) (n=50)	p-value
Suspected drug			
Beta-lactams	38 (43.2%)	22 (44%)	0.869
Penicillin	29 (33.0%)	16 (32.0%)	0.971
Cephalosporin	9 (10.2%)	6 (12%)	0.717
Macrolides	-	1 (2%)	0.179
Quinolones	3 (3.4%)	2 (4%)	0.841
NSAID	34 (38.6%)	22 (44%)	0.475
Reaction symptoms			
Anaphylaxis	19 (21.6%)	8 (16%)	0.458
Cutaneous reaction	78 (88.6%)	44 (88%)	0.835
Itching	62 (70.5%)	26 (52%)	0.042
Drug-related urticaria	57 (64.8%)	23 (46%)	0.042
Dyspnea/wheezing/cough	36 (40.9%)	22 (44%)	0.651
Abdominal pain	10 (11.4%)	0	0.014
Time of reaction			
<1 hour	59 (67%)	31 (62%)	0.813
1–6 hours	29 (33%)	18 (36%)	

Data are presented as n (%) or median (interquartile range [IQR]). p values were calculated using the Mann–Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate. Bold values indicate p<0.05.
NSAID: Non-steroidal anti-inflammatory drugs

Table 5. Comparison of demographic and clinical characteristics between β-lactam– and nonsteroidal anti-inflammatory drug–induced hypersensitivity reactions

Variables	Beta-lactam, n (%) (n=59)	NSAID, n (%) (n=56)	p-value
Female sex	43 (72.9%)	38 (67.9%)	0.195
Age at allergic reaction			
<45 years	38 (64.4%)	34 (60.7%)	0.475
≥45 years	21 (35.6%)	22 (39.3%)	
Reaction symptoms			
Anaphylaxis	18 (30.5%)	7 (12.5%)	0.006
Loss of consciousness	11 (18.6%)	11 (19.6%)	0.349
Cutaneous reaction	55 (93.2%)	33 (58.9%)	0.174
Angioedema	44 (74.6%)	34 (60.7%)	0.327
Itching	42 (71.2%)	33 (58.9%)	0.140
Drug-related urticaria	42 (71.2%)	25 (44.6%)	0.008
Dyspnea/wheezing/cough	24 (40.7%)	24 (42.9%)	0.733
Abdominal pain	7 (11.9%)	7 (12.5%)	0.074
Time of reaction			
<1 hour	49 (83.1%)	22 (39.2%)	<0.001
1–6 hours	10 (16.9%)	34 (60.7%)	

Data are presented as n (%) or median (interquartile range [IQR]). p values were calculated using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Bold represent: p<0.05
NSAID: Non-steroidal anti-inflammatory drugs

DISCUSSION

In this adult cohort, β-lactam antibiotics and NSAIDs were the most commonly reported triggers of immediate drug hypersensitivity, and the majority of reactions occurred within the first hour after drug intake. Early-onset reactions were strongly associated with more severe clinical outcomes, including higher rates of anaphylaxis, loss of consciousness, and hospital admission. Penicillin derivatives showed a particularly strong association with anaphylaxis, whereas NSAID-related reactions more often appeared after the first hour and demonstrated a broader clinical spectrum. Younger adults (<45 years) reported more cutaneous manifestations such as itching, urticaria, and abdominal pain. Notably, nearly 70% of patients required hospital admission, and more than half of the reactions had occurred within the past year, indicating that most presentations reflected recent events.

Despite the lack of age-related differences in culprit drug distribution, β-lactam antibiotics emerged as the leading cause of anaphylaxis in our population, with the anaphylaxis rate being more than double that of NSAIDs. This finding is consistent with previous literature, which repeatedly identifies β-lactams as the most frequent culprits of severe immediate reactions in both adult and elderly patients. Within the β-lactam group, the predominance of penicillin over cephalosporins in our cohort may partly explain this trend, since penicillins are well-known to form highly immunogenic hapten–protein complexes capable of inducing robust IgE-mediated responses.[8,9] The strong association between β-lactams and anaphylaxis underscores the immunologic potency of these agents, likely related to these well-characterized mechanisms.

Although the present study focused on clinically immediate reactions, NSAID-induced hypersensitivity reactions may present as immediate events despite being mediated through non–IgE-dependent pathways. In this context, NSAID-induced reactions often follow non–IgE-mediated pathways, including cyclooxygenase-1 inhibition–driven overproduction of cysteinyl-leukotrienes, mast-cell activation through alternative pathways, and pseudoallergic mechanisms.[10] These mechanisms may contribute to a relatively lower rate of anaphylaxis and a tendency toward more delayed or multi-organ symptoms, as reflected in our data where NSAID reactions were less frequently associated with severe immediate outcomes. This mechanistic distinction helps explain the clinical divergence between β-lactam and NSAID reactions seen in our cohort and in prior studies. Beyond mechanistic differences, variations in clinical patterns have also been reported across regional cohorts. In comparison with our findings, where β-lactam antibiotics were the leading cause of anaphylaxis, a tertiary-center cohort from Turkiye demonstrated a different distribution, reporting NSAIDs as the most common overall culprits of drug hypersensitivity and showing a high frequency of type 1 reactions among NSAID-exposed patients.[11] Although both drug classes were implicated in anaphylaxis, the higher baseline prevalence of NSAID hypersensitivity in that cohort likely shifted the anaphylaxis burden toward NSAIDs. Comparable heterogeneity has also been reported internationally. In large population-based analyses from China, cephalosporins were identified as a more frequent cause of drug-induced anaphylaxis than penicillins, highlighting a distinct β-lactam distribution in that region.[12] In contrast, an electronic health-record study from Boston including nearly 20,000 anaphylaxis cases demonstrated that penicillins were the most prevalent triggers of drug-induced anaphylaxis.[13] Similarly, in a Spanish cohort evaluating approximately 4,500 drug hypersensitivity reactions, NSAIDs were the most common overall culprits; however, β-lactam antibiotics remained the leading cause of immediate-type reactions occurring within the first hour.[14] These differences may reflect variations in prescribing habits, regional drug-use patterns, referral characteristics, or population-level susceptibility.

Our findings demonstrate that reactions occurring within the first hour were strongly associated with severe clinical outcomes, including markedly higher rates of anaphylaxis, loss of consciousness, and hospital admission.[15] This aligns with prior literature indicating that early-onset symptoms are a key predictor of IgE-mediated reactions and severe systemic involvement.[16] Several studies have emphasized that rapid symptom onset reflects a more robust immunologic response, often driven by high-affinity IgE and rapid mast cell activation.[17,18] Therefore, documenting the exact timing of symptom onset is clinically crucial, both for risk stratification and for guiding diagnostic testing. The relatively high hospitalization rate observed in our cohort likely reflects the tertiary-care and referral-based nature of the participating centers. In addition, the presence of clinically significant reactions, including anaphylaxis, lowered the threshold for inpatient observation.

Although culprit drug distribution did not differ by age, younger adults reported higher frequencies of cutaneous symptoms—particularly itching, urticaria, and abdominal pain. Similar patterns have been reported in younger populations with more robust cutaneous mast-cell responsiveness, whereas older adults may present with less florid cutaneous signs despite comparable immunologic mechanisms.[19,20] The absence of significant age-related differences in anaphylaxis frequency in our cohort suggests that reaction timing and drug class may be stronger predictive markers than age alone.

Limitations

A major strength of our study is the inclusion of a real-life population from two tertiary centers, allowing the capture of clinically relevant presentations across a broad spectrum. Limiting inclusion to reactions occurring within the first six hours improved mechanistic homogeneity by enriching for true immediate reactions. Moreover, detailed electronic record verification minimized recall bias compared with self-report–only studies. While these strengths enhance the interpretability of our findings, several limitations should be acknowledged. Drug triggers were derived from patient-reported histories without confirmatory testing, which introduces the possibility of misclassification, although this approach reflects real-world clinical practice. In addition, a formal causality assessment was not performed in patients who may have been exposed

to more than one drug at the time of the reaction, which may have limited definitive identification of the culprit agent in some cases. Reported culprit medications were additionally verified through the national e-Prescription system to ensure accuracy. This combined approach improves reliability while acknowledging the inherent limitations of retrospective data. In a population with high rates of severe reactions and anaphylaxis, confirmatory testing carries substantial risk and is generally not performed, further explaining the reliance on clinical history. Moreover, full penicillin skin testing—including both the major determinant (penicilloyl-polylysine) and the minor determinant mixture— is not available in our country, which limits confirmatory testing options but does not affect the primary aim of this clinical cohort analysis. limiting the ability to perform comprehensive confirmation of suspected β-lactam allergy. The retrospective design may also lead to incomplete documentation, particularly regarding the precise timing of symptoms. Even so, the overall consistency of reaction patterns across subgroups supports the robustness and internal validity of our findings.

CONCLUSION

In this real-life adult cohort, β-lactam antibiotics were the leading triggers of early-onset anaphylaxis, while NSAIDs exhibited a more heterogeneous clinical profile with both immediate and later-onset presentations. Early symptom onset was strongly associated with clinical severity, underscoring its value as a practical risk indicator in everyday practice. Notably, rates of hospitalization and anaphylaxis were high across all age groups, highlighting that severe immediate reactions are not confined to older or more vulnerable populations. Regional prescription preferences may influence the relative distribution of culprit drugs, yet the underlying reaction patterns and the prominence of specific drug groups tend to remain consistent across different settings. Recognizing these region-specific trends is important for interpreting epidemiologic data within the appropriate context and for guiding local diagnostic and management strategies.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this study was obtained from the Non-interventional Clinical Researches Ethics Committee of Konya City Hospital (Date: 08.12.2025, Decision No: 2025/251).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: FAA; Design: FAA; Control: TÖ; Data Collection and/or Processing: FAA, TÖ; Analysis and/or Interpretation: FAA; Literature Review: FAA; Article Writing: FAA; Critical Review: All authors

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