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Antituberculosis drug-induced hypersensitivity: clinical characteristics and risk factors

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Abstract
Background: Antituberculosis drugs can cause hypersensitivity reactions that interrupt treatment and increase morbidity. Early identification and management are essential to prevent complications and drug resistance.
Objective: To evaluate the clinical characteristics, risk factors, and outcomes of antituberculosis drug-induced hypersensitivity reactions over a 10-year period in a tertiary referral center.
Methods: We retrospectively analyzed 449 patients hospitalized for antituberculosis drug-induced hypersensitivity between 2015 and 2024. A control group of 478 tuberculosis patients without hypersensitivity was included. Demographic features, comorbidities, hypersensitivity types, causative drugs, and treatment outcomes were compared.
Results: The prevalence of hypersensitivity was 12.1%. Female gender, older age, Turkish nationality, and history of other drug allergies were significant risk factors. Type 1 reactions (77.7%) were more common and associated with shorter treatment interruption and higher cure rates. Pyrazinamide was the most frequently implicated drug. Desensitization was successful in the majority of patients.
Conclusion: This large cohort study highlights key risk factors and clinical outcomes in tuberculosis drug hypersensitivity. Close monitoring of high-risk patients in the early treatment phase may reduce delays and improve outcomes.

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Introductıon

Tuberculosis is one of the leading causes of mortality worldwide. It is an infectious agent transmitted through the respiratory tract, and it requires multiple drugs and long-term use. One of the side effects of the treatment is drug hypersensitivity reaction.[1] Hypersensitivity interrupts tuberculosis treatment. The drugs can be started again after hypersensitivity has been treated. In tuberculosis treatment, compliance with treatment is very important for both treatment success and preventing the development of drug resistance.[2] Different rates of antituberculosis drug hypersensitivity reactions have been reported.[3,4] The first-line drugs are used for 6 months. If first-line drugs cannot be used because of hypersensitivity, the duration of treatment and therefore treatment costs increase. If second-line drugs are started, it is necessary to use more drugs for a longer period. There are articles suggesting that initiation of first-line drugs with provocation tests is a waste of time and that all drugs should be given individually with desensitization.[5-7] We recommend starting the drugs one by one with desensitization doses that have been described and then re-confirmed in a large series in our country.[6,8] We have previously presented the characteristics of patients who were evaluated for antituberculosis drug allergy in our clinic.[7,9-11] Our hospital is a tertiary referral hospital; patients with drug resistance and difficult treatment management are referred.

The aim of this study is to analyze the demographic and clinical characteristics of the patients in detail. We wanted to share our experiences over a period of 10 years.

Methods

The control group was selected from patients hospitalized for reasons other than drug hypersensitivity during the same period. These patients were chosen consecutively without formal matching but from the same hospital and time frame to reduce selection bias.

The following five main topics were determined for the study:

1. Demographic characteristics: age, gender, and nationality.
2. Comorbidities: allergic diseases, another group of drug allergy, and comorbid diseases.
3. Tuberculosis disease characteristics: diagnosis of tuberculosis, organ involved, previous treatment, drug resistance, initial tuberculosis treatment, treatment outcome, and duration of treatment.
4. Hypersensitivity characteristics: development time of hypersensitivity reaction, reaction finding, index reaction severity classification, results of tests for responsible drug, and desensitization success.
5. Laboratory parameters when hypersensitivity develops were analyzed.

The patient was evaluated by an allergist. Hypersensitivity reaction was grouped as immediate and non immediate. Immediate type was grouped as pruritis, urticaria, angioedema, urticaria+ angioedema and anaphylaxis. Non immediate type was grouped as maculopapular drug eruption, lichenoid drug eruption, drug reaction with eosinophilia and systemic symptoms, erythema multiforme, acute generalised exanthematous pustulosis, Stevens-Johnson syndrome, toxic epidermal necrolysis.[12] Immediate type hypersensitivity reactions were grouped according to Brown and Ring Mesmmer classification. Ring-Messmer classification: Grade 1: isolated skin involvement; Grade 2: skin involvement with dyspnoea, tachycardia, hypotension, arrhythmia; Grade 3: Grade 2 and bronchospasm, cyanosis, shock; Grade 4: respiratory and cardiac arrest. Brown classification Grade 1: one system is affected; Grade 2: two systems are affected; Grade 3: two systems are affected and vital signs are altered. (13) DRESS was classified in 3 groups as mild, moderate and severe.[14,15,16] Skin prick test and intradermal test were used for ımmediate type hypersensitivity reactions; intradermal test and patch test were used for non immediate reactions.Desensitisation was performed after the treatment of ınıtıal hypersensitivity reactions. In desensitisation, drug doses were planned recommended by Buhari et al. and used in our clinic.[6,8,9,11]

Ethics Committee approval was obtained prior to the study at University of Health Sciences, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital (2024-43).

Statistical analysis

The data obtained from the study were transferred to the computer and analyzed with Statistical Package for Social Sciences (SPSS) 25.0 package programme. In descriptive analyses, frequency data were expressed as number (n) and percentage (%), and numerical data were expressed as mean±standard deviation or median (interquantile range). Pearson Chi-square test and Fisher Exact test were used to compare categorical data. Normality distribution of numerical data was analyzed by the Kolmogorov–Smirnov test. The distribution of numerical data in two independent groups was evaluated by an independent samples *t*-test, and the distribution of data that did not fit the normal distribution was evaluated by Mann–Whitney U Test. Statistical significance level was accepted as $p<0.05$ for all tests.

Results

In this study, all patients who developed hypersensitivity because of antituberculosis treatment between 2015 and 2024 and were hospitalized and those who consulted the Allergy-Immunology clinic were examined. A total of 449 patients underwent desensitization. The control group consisted of 478 patients hospitalized for reasons other than hypersensitivity during the same years. Of the 3701 tuberculosis patients evaluated at that time, 449 were found to have drug hypersensitivity. The prevalence of drug allergy was calculated as 12.1%.

The distribution of demographic data between hypersensitivity and control groups is given in Table 1. The attributes like age ($p = 0.003$), female gender ($p<0.001$), history of hypersensitivity with other drugs ($p<0.001$), and

being a Turkish citizen (p = 0.002) were higher in patients who developed hypersensitivity compared to the control group. When comorbidities were divided into three groups as autoimmune, malignancy, and rheumatological, a difference was found between the groups (p = 0,017). In the group with hypersensitivity, the rate of autoimmune disease and malignancy was higher and the rate of rheumatological disease was lower compared to the control group.

The distribution of data in the hypersensitivity group is given in Table 2. It was determined that 96.9% of the patients were from the European Region; 43.4% (n = 195) were smear positive; 78% had pulmonary tuberculosis; and the most common extrapulmonary involvement was lymph node with 10.9%. RIF-resistant tuberculosis was recorded in 8% (n = 36) and INH-resistant tuberculosis was recorded in 15 patients. It was determined that 87.8% of the patients were initially treated with isoniazid, rifampicin, ethambutol, and pyrazinamide (HRZE). Hypersensitivity reactions developed a median of 8 (2-22) days after the start of treatment; 77.7% (n = 349) of the patients developed Type 1 hypersensitivity and 22.3% (n = 100) developed Type 4 hypersensitivity reactions.

The distribution of reactions according to gender in the hypersensitivity group is given in Table 3.

The distribution of the agent responsible for hypersensitivity and the type of reaction is presented in Table 4. The responsible agent was pyrazinamide in 64.8% (n = 83) and rifampicin in 14.1% (n = 18) of patients with type 1 hypersensitivity. The responsible agent was pyrazinamide in 59.5% (n = 94) and rifampicin in 18.4% (n = 18) of patients with type 4 hypersensitivity.

The distribution of hypersensitivity reaction characteristics according to reaction type is given in Table 5. Treatment completion time was found to be shorter in patients with type 1 hypersensitivity reaction (p<0.001). Treatment success rate was higher in patients with type 1 reaction (p = 0.001). It was noted that 97.7% of patients who developed Type 1 hypersensitivity reaction were Brown Grade 1, and 98% (n = 341) were Ring Mesmmer 1. Around 73.7% of patients who developed Type 4 had mild DRESS and 10.5% (n = 2) had severe DRESS. The number of consultations and desensitization completion time were statistically higher in patients with type 4 reactions (p<0.001).

The distribution of laboratory parameters according to reaction type in patients with hypersensitivity is shown in Table 6. Lymphocyte percentage was statistically higher in patients with type 1 reaction (p = 0.044). There is no statistical difference in other laboratory parameters (p>0.05).

Discussion

This study is the largest series conducted in the literature with regard to antituberculosis drug allergy. It was

Table 1 The distribution of demographic data between hypersensitivity and control groups.

		Hypersensitivity groups (n = 449)	Control groups (n = 478)	Total (n = 927)	p
Age (year)		51.67±17.98	48.06±19.27	49.81±18.73	**0.003***
Gender (female)		222 (49.4)	149 (31.2)	371 (40.0)	**<0.001****
Allergic diseases		55 (12.3)	19 (8.9)	74 (11.2)	0.198**
Allergic diseases	Asthma	31 (55.4)	1 (5.0)	32 (42.1)	
(n=76)	Rhinitis	6 (10.7)	7 (35.0)	13 (17.1)	-
	Asthma+ rhinitis	7 (12.5)	11 (55.0)	18 (23.7)	
	Urtıcarıa	9 (16.1)	0	9 (11.8)	
	Urticaria-angioedema	2 (3.6)	0	2 (2.6)	
	Atopic dermatitis	1 (1.8)	1 (5.0)	2 (2.6)	
Heart disease		103 (23.1)	67 (20.1)	170 (21.8)	0.320**
Use of B blockers		45 (10.1)	36 (10.9)	81 (10.5)	0.739**
Use of ACE inhibitors		53 (11.9)	47 (14.2)	100 (12.9)	0.361**
Comorbid disease	Autoimmune	11 (24.4)	2 (9.5)	13 (19.7)	
(n=66)	Malignancy	27 (60.0)	9 (4.5)	36 (54.5)	0.017**
	Rheumatological	7 (15.6)	10 (47.6)	17 (25.8)	
Immunosuppression		26 (5.8)	18 (5.4)	44 (5.6)	0.792**
Diabetes mellitus		66 (14.8)	61 (18.4)	127 (16.3)	0.176**
History of hypersensitivity with other drugs		20 (4.5)	2 (0.4)	22 (2.4)	**<0.001****
Previous drug allergy	Nonsteroidal anti-				0.515***
(drug group) (n=22)	inflammatory drug (NSAID)	8 (40.0)	0	8 (36.4)	
	antibiotics	12 (60.0)	2 (100.0)	14 (63.6)	
Cıtızen	Turkish	412 (91.8)	408 (85.4)	820 (88.5)	**0.002****
	Others	37 (8.2)	70 (14.6)	107 (11.5)	

*Independent Samples *t*-test.
**Pearson Chi-square Test.
***Fisher's Exact Test.

Table 2 The distribution of data in the hypersensitivity group.

			Total (n=449)
Natıonalıty	Turkish Other		412 (91.8)
		Syria	7 (1.6)
		Uzbekistan	6 (1.3)
		Azerbaijan	4 (0.9)
		Pakistan	3 (0.7)
		Russia	3 (0.7)
		Turkmenistan	3 (0.7)
		Georgia	3 (0.7)
		Iran	2 (0.4)
		Kyrgyzstan	2 (0.4)
		Lebanon	1 (0.2)
		Haiti	1 (0.2)
		China	1 (0.2)
		Chechnya	1 (0.2)
WHO	European region		435 (96.9)
country	Eastern mediterranean region		9 (2.0)
classification	South East Asia region		3 (0.7)
	Americas region		1 (0.2)
	Western Pacific region		1 (0.2)
Diagnostic Indicator	Smear		195 (43.4)
	Histopathologic		90 (20.0)
	Culture		80 (17.8)
	Molecular		53 (11.8)
	Clinic		31 (6.9)
Organ	Pulmonary		350 (78.0)
involvement	Extrapulmonary	Lymph node	49 (10.9)
		Pleura	33 (7.3)
		Urinary	5 (1.1)
		Bone	4 (0.9)
		Pericardium	3 (0.7)
		Peritoneum	2 (0.4)
		Colon	1 (0.2)
		Breast	1 (0.2)
		Thyroid	1 (0.2)
Prior treatment	No		426 (94.9)
	Yes	Relapse	20 (4.5)
		Treatment failure	2 (0.4)
		Patient lost to follow-up	1 (0.2)
Drug resistant	Unknown		31 (6.9)
	Sensitive		54 (12.0)
	Resistant	RIF-resistant Tbc/MDR Tbc	36 (8.0)
		INH resistance	15 (3.3)
		Extensively drug-resistant tuberculosis	2 (0.4)
		Pre-extensively drug-resistant tuberculosis	1 (0.2)
Inıtıal treatment	HRZE		394 (87.8)
	Non-HRZE		55 (12.2)
Change in treatment after desensitization			205 (45.7)
Treatment after	HRZE		211 (47.0)
desensitization	Non-HRZE		238 (53.0)
Hypersensitivity reaction time (days)			8 (2–22)
Hypersensitivity	Type 1		349 (77.7)
Reaction	Type 4		100 (22.3)

Table 3 The distribution of reactions according to gender.

		Female n (%)	Male n (%)	Total n (%)
Type 1 (n=349)	Pruritis	81 (45.0)	109 (64.5)	190 (54.4)
	Urticaria	75 (41.7)	49 (29.0)	124 (35.5)
	Angioedema	4 (2.2)	3 (1.8)	7 (2.0)
	Urticaria-Angioedema	13 (7.2)	7 (4.1)	20 (5.7)
	Anaphylaxis	7 (3.9)	1 (0.6)	8 (2.3)
Type 4 (n=100)	Maculopapular drug eruption	22 (52.4)	39 (67.2)	61 (61.0)
	DRESS	12 (28.6)	9 (15.5)	21 (21.0)
	Lichenoid drug eruption	5 (11.9)	5 (8.6)	10 (10.0)
	Erythema multiforme	2 (4.8)	1 (1.7)	3 (3.0)
	Fixed drug eruption	1 (2.4)	2 (3.4)	3 (3.0)
	SJS	0	2 (3.4)	2 (2.0)

Table 4 The distribution of the agent responsible for hypersensitivity.

Responsible drug	Type 1			Type 4			Total
	Female n (%)	Male n (%)	Total n	Female n (%)	Male n (%)	Total n	
Isoniazid	6 (8.2)	5 (9.1)	11 (8.6)	2 (14.3)	1 (6.3)	3 (10.0)	14 (8.9)
Rifampicin	12 (16.4)	6 (10.9)	18 (14.1)	6 (42.9)	5 (31.3)	11 (36.7)	29 (18.4)
Ethambutol	3 (4.1)	2 (3.6)	5 (3.9)	1 (7.1)	0	1 (3.3)	6 (3.8)
Pyrazinamide	44 (60.3)	39 (70.9)	83 (64.8)	3 (21.4)	8 (50.0)	11 (36.7)	94 (59.5)
Moxifloxacin	2 (2.7)	1 (1.8)	3 (2.3)	0	0	0	3 (1.9)
Amikacin	1 (1.4)	0	1 (0.8)	0	0	0	1 (0.6)
Rifampicin + pyrazinamide	3 (4.1)	1 (1.8)	4 (3.1)	0	0	0	4 (2.5)
İzoniyazid + pyrazinamide	0	1 (1.8)	1 (0.8)	0	0	0	1 (0.6)
Isoniazid + rifampicin	2 (2.7)	0	2 (1.6)	1 (7.1)	0	1 (3.3)	3 (1.9)
PAS	0	0	0	1 (7.1)	0	1 (3.3)	1 (0.6)
Cycloserine	0	0	0	0	1 (6.3)	1 (3.3)	1 (0.6)
Amikacin + PAS	0	0	0	0	1 (6.3)	1 (3.3)	1 (0.6)

conducted retrospectively with the approval of the ethics committee in our tertiary referral hospital. Two groups were included in the study. Hypersensitivity group: 449 patients who developed hypersensitivity because of tuberculosis treatment and underwent desensitization were included. The control group consisted of 478 tuberculosis patients hospitalized for reasons other than hypersensitivity. Older age, female gender, history of hypersensitivity with other drugs, and being a Turkish citizen were seen as risk factors. Treatment completion time was found to be shorter, treatment success rate was higher, and the number of consultations and desensitization completion time were statistically lower in patients with type 1 hypersensitivity reaction. The prevalence of drug allergy was calculated as 12.1%. It is also very important because it gives the prevalence of tuberculosis drug allergy in hospitalized patients.

According to Liu et al., the incidence of antituberculosis drug hypersensitivity is 2.9%.[3] We think that the prevalence is higher because we are a reference hospital and a special group of patients with complaints about drugs are hospitalized among all patients who are started on tuberculosis treatment.

Age is statistically higher in the hypersensitivity group. In a study in Switzerland, electronic medical records of 192,444 patients were checked, and older age was determined as a risk factor for drug allergy (for all drug groups).[17] Especially for tuberculosis treatment, older age has been associated with hypersensitivity in many studies.[7,18,19]

Many studies have been conducted on this subject in our center.[7,9-11] Type 1 hypersensitivity reactions were seen more in females.[9] Type 4 was seen more in males.[11] However, it did not reach statistical significance. In this study, the number of patients is much higher. In our study, female gender was determined as a statistically significant risk factor. Supporting our study, the female gender has been identified as a risk factor in many studies.[3,20,21]

Being a Turkish citizen has been considered a risk factor. In our study, we thought that it was related to the high number of patients from Turkey.

In the literature, we did not notice any association between malignancy, rheumatological disease, and

Table 5 The distribution of hypersensitivity reaction characteristics according to reaction type.

	Type 1 n (%)	Type 4 n (%)	Total n (%)	p
Determination of the responsible drug after desensitization	126 (36.3)	27 (27.0)	153 (34.2)	0.084*
Reaction treatment				
Antihistamines	92 (27.1)	1 81.0)	93 (21.3)	-
Methylprednisolone	14 (4.1)	3 (3.1)	17 (3.9)	
Antihistamine + Methylprednisolone	234 (68.9)	93 (95.9)	327 (74.8)	
Number of desensitization	1 (1-1)	1 (1-2)	1 (1-1)	0-346***
Treatment completion time (month)	7 (6-9)	9 (6-8)	9 (9-9)	**<0-001*** **
Treatment duratıon				
Treatment completion	176 (51.2)	40 (40.8)	216 (48.9)	**0,003***
cure	120 (34.9)	31 (31.6)	151 (34.2)	
Under treatment	32 (9.3)	12 (12.2)	44 (10.0)	
Nonfollow-up	15 (4.4)	15 (15.3)	30 (6.8)	
Dead	1 (0.3)	0	1 (0.2)	
End of treatment				
Treatment success	296 (86.0)	71 (72.4)	367 (83.0)	**0.001***
Under treatment	32 (9.3)	12 (12.2)	44 (10.0)	
Nonfollow-up	15 (4.4)	15 (15.3)	30 (6.8)	
Dead	1 (0.3)	0	1 (0.2)	
Cutaneous signs	349 (100.0)	100 (100.0)	449 (100.0)	-
Respiratory signs	8 (2.3)	0	8 (1.8)	0.209**
Cardiovascular signs	2 (0.6)	0	2 (0.4)	1.000**
Gastrointestinal signs	1 (0.3)	0	1 (0.2)	1.000**
Brown classificatıon				
Grade 1	341 (97.7)	-	341 (97.7)	-
Grade 2	8 (2.3)		8 (2.3)	
Ring mesmmer				
1	342 (98.0)	-	342 (98.0)	-
2	7 (2.0)		7 (2.0)	
3	0		0	
4	0		0	
DRESS				
Mild	-	14 (73.7)	14 (73.7)	-
Moderate		3 (15.8)	3 (15.8)	
Severe		2 (10.5)	2 (10.5)	
Number of consultations	6 (5-9)	9 (6-15)	7 (5-10)	**<0.001*** **
Time from treatment interruption to completion of desensitization (days)	12 (7-22)	27 (13-54)	13 (7-27)	**<0.001*** **

*Pearson Chi-square Test.
**Fisher's Exact Test.
***Mann-Whitney U Test.

autoimmune diseases for antituberculosis drug hypersensitivity. However, when we look at it in terms of antibiotic allergy, it is mentioned that comorbid diseases (allergic and nonallergic) are seen more in patients with antibiotic allergy.[3,22] In our study, for the first time, hıstory of hypersensitivity with another group of drugs was also identified as a risk factor.

Drugs can develop either type 1 or type 4 hypersensitivity reactions. The largest percentage consists of pruritis, urticaria, and angioedema. However, an important point is that serious drug allergies are quite rare. Serious drug reactions can manifest differently depending on the hypersensitivity type: anaphylaxis is typically associated with type I reactions, whereas Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS) are linked to type IV reactions. According to Liu et al., the most prominent hypersensitivity reaction was pruritis.[3]

When type 4 hypersensitivity develops, the first step is to stop treatment and give systemic steroids and identify the responsible drug.[19] In this study, all patients who developed type 1 and type 4 hypersensitivity were included. Therefore, antihistamine administration is more frequent.

Table 6 The distribution of laboratory parameters according to reaction type.

	Tip 1 n (%)	Tip 4 n (%)	Toplam n (%)	p
Eosinophils (10^3/μL)	0.17 (0.09-0.31)	0.2 (0.09-0.4)	0.18 (0.09-0.34)	0.092*
Eosinophils (%)	3.0 (1.0-4.0)	3.0 (1.3-6.0)	3.0 (1.0-4.02)	0.140*
Neutrophil (10^3/μL)	4.31 (3.28-6.22)	4.57 (3.33-7.29)	4.36 (3.29-6.32)	0.234*
Neutrophils (%)	62 (55-71)	64 (56-73)	62 (55-71.25)	0.519*
Lymphocytes 10^3/μL)	1.72 (1.3-2.2)	1.74 (1.28-2.20)	1.72 (1.29-2.20)	0.579*
Lymphocyte (%)	25 (18-31)	22 (15-29)	24.50 (17-30)	0.044*
Platelets (10^3/μL)	263 (214-410)	276 (209-367)	266 (213.75-343.5)	0.442*
ALT (U/L)	16 (11-27)	16 (11-25)	16 (11-26.5)	0.795*
AST (U/L)	21 (17-29)	21 (17-29)	21 (17-29)	0.838*
T Bilirubin (mg/dL)	0.3 (0.2-0.5)	0.4 (0.2-0.6)	0.3 (0.2-0.5)	0.240*
Urea (mg/dL)	2 7 (20-34)	25 (21-32)	26 (20.25-34)	0.413*
Creatinine (mg/dL)	0.6 (0.6-0.8)	0.7 (0.55-0.8)	0.6(0.6-0.8)	0.810*
HbA1C (mmol/mol)	5.4 (5.1-5.9)	5.15 (5.0-5.8)	5.3 (5.0-5.9)	0.260*
HIV positive	5 (1.4)	4 (4.0)	9 (2.0)	0.118**
Hepatitis B positive	3 (0.9)	-	3 (0.7)	1.000**

*Mann-Whitney U Test.
**Fisher's Exact Test.

It is recommended to wait 4-6 weeks to determine the culprit drug and restart treatment.[19] In our study, similar to the literature, the initiation of treatment was later in patients who developed type 4 hypersensitivity. The time required for the development of hypersensitivity and the initiation of desensitization was calculated as a mean of 13 (7-27) days in the all groups. In the group that developed type 4 hypersensitivity, the time required to restart treatment was a mean of 27 (13-54) days.

If drugs are started one by one with provocation instead of desensitization, treatment must be paused again when hypersensitivity develops. These long intervals increase disease transmission, treatment failure, and cause drug resistance. Therefore, same as Bermingham, we recommend that all drugs be given with desensitization.[5]

The most common causative agent in patients with both type 1 and type 4 hypersensitivity was pyrazinamide. According to Smahdi et al., the agent most frequently responsible for hypersensitivity is pyrazinamide.[23] The most common causative agent in DRESS patients was rifampin.[19] Nine patients showed hypersensitivity reactions with two different drugs. The most common combinations among them were pyrazinamide and rifampin. Multiple drug hypersensitivity syndrome (MDHS) is also mentioned in the literature. Ethambutol and rifampin are mentioned as the most common combination. [24] We think that just as the agent responsible for hypersensitivity changes, MDHS will also change according to the population studied.

In patients who develop type 1 hypersensitivity, the duration of treatment and ınterruptıon of treatment are shorter, and the number of consultations is lower. These data have reached statistical significance. Hepatotoxicity and eosinophilia are seen in type 4 reactions, especially in severe cases. Therefore, recovery takes longer.[19]

In a study conducted in Korea, it is mentioned that peripheral blood eosinophil count/percentage is a guide for DRESS.[25] In our study, there is a minimal increase in eosinophil count and percentage in the type 4 hypersensitivity group, but it is not statistically significant. It is also mentioned that peripheral blood eosinophilia is associated with poor liver function, long-term corticosteroid use, and longer hospital stays.[26] For this reason, the treatment period is longer in the group that develops type 4 reactions. Increases in eosinophil counts and liver enzyme values have been reported frequently, especially in DRESS cases.[26-28] However, detailed studies are needed on the blood values of patients who develop type 1 hypersensitivity. Data on this subject are limited.

The first limitation is being a retrospective study, which may lead to incomplete or missing data. In addition, the study was conducted in a single center, and only hospitalized patients were included. This may limit the generalizability of the findings to outpatient populations or to other geographic settings.

Older age, female gender, history of hypersensitivity with another drugs, and being a Turkish citizen were seen as risk factors. Because hypersensitivity reactions develop mainly on the eighth day, patients at risk can be monitored more closely in the initial stages of treatment.

Ethics Approval and Consent to Participate

Ethics Committee approval was obtained prior to the study at Health Sciences University, Süreyyapaşa Training and Research Hospital.

Authors' Consent for Publication

All authors approved this manuscript to be submitted to the Journal.

Availability of Data and Materials

The data that support the findings of this study are not publicly available as they contain information that could compromise the privacy of research participants. They are available from ZYK, İB, AB.

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Authors Contributions

ZYK, İB, AB were involved in the conceptualization and methodology of the study. ZYK, İB, AB were involved in the writing of the original article. ZYK, İB, AB, MK, FMT contributed to data collection. The writing and reviewing process involved ZYK, İB, AB. ZYK, İB, AB were responsible for project supervision.

Conflict of Interest

The authors declare that they have no conflict of interest.

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