

The Analysis of Bee Allergy Patients in Van, Türkiye

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ABSTRACT

Bee allergies cause a significant health risk due to the potential for severe, life-threatening reactions and they negatively an individual's quality of life. We aimed to investigate prevalence and characteristics of bee and wasp sting allergies in Van province of Türkiye.

Patients who experienced allergic reactions after any bee stings between 2021 and 2024 were evaluated. The study assessed patients', Apis-specific immunoglobulinE (IgE), Vespula-specific IgE, total IgE and tryptase results, in addition to demographic characteristics such as age, gender, time of bee sting, and severity of allergic reaction.

A total of 139 patients with venom allergy were included. The median age was 33 years and 53% of the patients were male. While 21% of the patients reported an allergy to honeybees, 62% reported an allergy to wasps, and 17% reported an allergy to both honeybees and wasp. Allergy tests were found negative in one of the four patients. Total IgE levels were significantly higher in those with positive allergy tests ($p=0,001$). Additionally, the positivity rate in allergy tests was found to be significantly higher for wasps than for honeybees ($p=0,001$).

We found that the prevalence of wasp allergy in our geographical region is higher than honey bee allergy although beekeeping activities are widespread. This may be due to the strict adherence to protective measures in the beekeeping sector and the fact that the city center is concentrated in a small area within the rural region.

Keywords: Bee allergy, Wasp allergy, Hymenoptera, Venom allergy, Specific IgE

Introduction

Hymenoptera venom allergy (HVA) can present with a broad spectrum of symptoms, ranging from mild skin reactions to severe, life-threatening conditions such as unconsciousness and cardiac arrest (1). Allergy test results can sometimes be misleading, as individuals with high skin test reactivity and elevated specific Immunoglobulin E (sIgE) levels are not always at risk for severe systemic sting reactions (SSRs). On the other hand, some patients with weakly positive or even negative test results can still experience severe SSRs(2). However, all patients who experience moderate to severe reactions should perform venom immunotherapy (VIT). It may also be considered for patients with generalized skin symptoms if their quality of life is notably affected (1-2).

The global prevalence of allergic reactions caused by Hymenoptera stings remains incompletely understood. Previous studies reported a prevalence of Hymenoptera sensitization ranging from 15% to 25%, while more recent research shows that the allergic reactions to Hymenoptera stings varies between 0.15% and 21.4%, indicating regional differences (3-6).

In recent years, beekeeping and honey production have become increasingly profitable industries in Türkiye. Approximately 80% of honey production in Türkiye is provided by mobile beekeepers, with over 140,000 families depending on this industry for their livelihoods (7). Several studies in Türkiye have assessed the prevalence of Hymenoptera venom allergies in adults. In these studies, specific populations, including factory workers, beekeepers, and hospital patients, were chosen to assess the prevalence of venom allergies in Türkiye. It was seen that bee allergy was investigated using questionnaires administered to factory workers in Afyon, individuals applying for a driver's license in Van, families of primary school children in Ankara, and patients via telephone interviews in Istanbul (7-12). Among Hymenoptera hypersensitive patients in Ankara and analysed by skin test and allergen-specific IgE, Vespula(wasp) was responsible for 52.3% of reactions and Apis(honey bee) for 27.7% of reactions according to Hymenoptera species (13). Van is a region where beekeeping is widespread and a city with many rural areas. There was no study which exactly analyzed the distribution of bee allergy in adult patients in the province of Van. In this study, we aimed to evaluate the types of bee allergies in the region and the general

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characteristics of the patients, in addition to the severity of anaphylaxis and laboratory results.

Materials and Methods

The study included patients with a history of immediate hypersensitivity reactions (HSRs) after venom stings between January 2021 and December 2024. The diagnosis of bee sting related reactions was made by anamnesis, physical examination and serum specific IgE tests (with bee venom allergens). The patients were confirmed with bee photographs to identify the type of bee in detailed history. Demographic features such as age, gender, history of honey bee or wasp stings, the type of allergic reaction, presence of asthma or mastocytosis, total IgE, tryptase, *Apis* and *Vespula*-specific IgE were screened from patients' medical records and the hospital data system, retrospectively. Serum allergen-specific IgE levels to *Apis* and *Vespula* venom were measured with the immunoCAP system (PhadiaAB, Uppsala, Sweden) according to the manufacturer's instructions. Bee venom skin prick test could not be performed due to operational reasons experienced with prick solutions supply in our country at that time. Systemic reactions were categorized based on the classification by Ring and Messmer, while the definitions of systemic reactions were aligned with the recent position paper from the European Academy of Allergy and Clinical Immunology (EAACI) (14-15).

Grouping according to specific IgE concentration was determined as outlined in Table 1 (16). Patients were grouped as completely compatible; if venom-specific IgE was positive with the type of bee stung in the patient's history compatible but double test positive; if venom-specific IgE was positive with another bee other than the bee in the patient's history, compatible but deficient test positive; if there was only one venom-specific IgE positivity although there was a history of two different bee stings. The characteristics of cases with positive allergy tests and those with negative allergy tests were compared.

This study protocol was reviewed and approved by [Van Training and Research Hospital ethical committee], approval number [GOKAEK-2024-19]. The study was realised in line with the principles set out in the Declaration of Helsinki. The patients who participated in the study provided written informed consent.

Statistical Analyses: Statistical analyses were conducted using SPSS 21.0 (SPSS Inc., Chicago, IL). Descriptive statistics for the variables were presented as frequency (%). Number of cases and percentages were used for categorical variables. Non parametric variables were expressed as

medians and interquartile ranges (IQR). The variables were evaluated by using analytical methods (Kolmogorov-Smirnov and/or Shapiro-Wilks test) to determine whether they were normally distributed. The Chi-square test was applied to compare categorical proportions in different groups. The Mann-Whitney U test was used to compare numerical data from two groups that do not follow a normal distribution. A p-value of $<0,05$ was considered to show a statistically significant result.

Results

A total of 139 patients were included in the study, with a median age of 33 years (range: 19–74). More than half of the patients were male ($n=74$, 53%). All patients had a history of HSRs in 1 hour after venom stings. A total of 86 (62%) patients reported a history of *Vespula* venom stings, 29 (21%) had a history of *Apis* venom stings, and 24 (17%) had been stung by both *Vespula* and *Apis* species. About a quarter of patients had negative allergy tests ($n=32$, 23%). Among the 107 patients with positive test results, 82% ($n=88$) were fully compatible, 12% ($n=13$) were compatible but double test positive, and 4% ($n=5$) were compatible but deficient-test positive. Although one patient reported an allergy to wasp in his history, only honeybee was found positive in his tests. When the according to severity reactions were evaluated; 4(3%) patients were Grade 1 reactions, 36(26%) patients were Grade 2 reactions and 99 (71%) patients were Grade 3 reactions. The median time between the patients' reaction and the time of testing was 24 (12-60) months and 55 (40%) had a history of venom stings in the last 1 year. A total of 12 (9%) patients had asthma, and 2(1%) patients were diagnosed with mastocytosis. The median baseline tryptase value was 3.9 (0.05-25) $\mu\text{g/L}$ and the median total IgE level was 1532 IU/mL (6-2500). *Apis*-specific IgE median value was 0.001 (0.001-0.507), *Vespula*-specific IgE median value was 1.5 (0.001-5.58). The highest specific IgE concentration was observed in Grade 3 in the *Apis* group and in Grade 5 in the *Vespula* group. Details are provided in Table 2.

In bee species, a higher rate (66%) of allergy test positivity was observed in *Vespula*, while more allergy test negativity (44%) was found in honey bee ($p=0,001$). In addition, total IgE was higher in patients with positive allergy test than in patients with negative allergy test (186 vs. 76, $p=0,001$). Comparisons of patients with positive and negative allergy tests are summarized in Table 3.

Table 1: Classification According to Specific IgE Concentration (16)

Venom Specific IgE level(IU/mL)		
Grade 0	<0.35	negative
Grade 1	0.35-0.7	weak positive
Grade 2	0.7-3.5	positive
Grade 3	3.5-17.5	positive
Grade 4	17.5-52.5	strong positive
Grade 5	52.5-100	strong positive
Grade 6	>100	strong positive

*IgE:Immunoglobulin E,

Table 2: Classification Of Bee Species With Positive Allergy Test According To Specific Immunoglobulin E Concentration

	Apis n=36	Vespula n=92
Grade 1 n (%)	5 (13.9)	11 (11.9)
Grade 2 n (%)	11 (30.5)	37 (40.2)
Grade 3 n (%)	15 (41.6)	28 (30.4)
Grade 4 n (%)	0	9 (9.7)
Grade 5 n (%)	0	7 (9.8)
Grade 6 n (%)	0	0

*Grades are arranged according to the results in Table 1.

Table 3: Comparison of the Characteristics of The Cases According to Whether the Venom Allergy Test Was Positive or Negative

	PositiveAllergy Test n =107	NegativeAllergy Test n =32	p value
Age,years median (IQR)	33 (27-44)	33 (29-46)	0,663
Gender (Female/Male)	46/61	19/13	0,103
Presence of asthma, n (%)	8 (8)	4 (14)	0,472
Types of bee, n (%)			
Apis	15 (14)	14 (44)	0,001
Vespula	71 (66)	15 (47)	
Apis+Vespula	21 (20)	3 (9)	
Severity of reaction, n (%)			
Grade 1	4 (4)	0 (0)	
Grade 2	28 (26)	8 (25)	0,524
Grade 3	75 (70)	24 (75)	
Total IgE IU/ mL, median (IQR)	186 (106-397)	76 (25-149)	0,001
Baseline Tryptase µg/L, median (IQR)	3.8 (2.3-6.5)	4.2 (2.9-7.0)	0,250

* IQR: Interquartile range, IgE:Immunoglobulin E,

** Chi-square analysis was applied for gender, asthma presence, bee type, and reaction severity, while the Mann-Whitney U test was utilized for the remaining variables

Discussion

To the best of our knowledge, this is the first study to evaluate bee allergies in Van by confirming them with allergy tests. One of the main results of the study was that the incidence of allergies to wasps was higher than to honeybees. Additionally, the rate of positive allergy tests was higher for *Vespula*. Another important finding was that in patients with high total IgE values, allergy tests are more likely to show bee allergy.

According to reports from the Ministry of Agriculture and Rural Affairs, Türkiye ranks as the fourth largest country in the world for the number of beehives and honey production, with annual honey production continuously increasing (17). While bee stings are typically considered a major issue in rural areas, in our country, they also constitute a significant public health concern in urban areas. The first study on venom allergy in Van was conducted on 709 healthy individuals who consecutively visited the University Hospital to obtain a medical report for a driving license (9). The frequency of allergic sting reactions was investigated using an interviewer-administered questionnaire. This study revealed that the rate of HSRs caused by *Vespula* (53.1%) was higher than that caused by honeybees (38.8%). In this study, HSRs were reported by healthy individuals who were evaluated based solely on their medical history when applying for a health report. No skin or laboratory tests were performed on any of the patients (9). On the other hand, we evaluated only the people who had allergic reactions in more detailed history and also confirmed them with allergy tests. Therefore, our study shows the bee allergy profile in the Van region more accurately and objectively.

In this study, the gender distribution in the study population was found to be approximately half-and-half. In one of the previous studies, 301 beekeepers were included in the study and the majority were male (18,19). In previous studies, the reason for the higher male ratio involved in beekeeping was attributed to the fact that beekeeping is predominantly a male-dominated occupation. On the other hand, the equality of male and female populations in our research is attributable to the inclusion of both beekeepers and the general population. Some previous studies have also emphasised the higher incidence of *Vespula* hypersensitivity (13,20,21). Similarly, in line with the literature; the most of the patients had a history of HSRs with *vespula* in our study. We included not only beekeepers but also the

general population in our study. However, beekeepers may have a lower incidence because they pay attention to protection against allergic reactions.

Serum findings revealed that the concentration of Apis- and *Vespula*-specific IgE was mainly at grade 3 vs grade 2 level respectively. In patients with compatible history, Apis-specific IgE level was maximum grade 3, while *Vespula*-specific IgE antibodies could be as high as grade 5. In a questionnaire-based study of 786 subjects conducted by Kalyoncu et al. it was observed that venom-specific IgE levels were mostly at class 1 and class 2 levels (8). In the study of Kalyoncu et al. a history of bee sting in the past year was 20.3%, whereas it was 39.5% in our study. Specific IgE concentrations were considered higher in patients with a history of bee sting in the last 1 year and due to sensitisation (22). In addition, we showed that the total IgE level was statistically higher in patients with positive allergy test (venom specific IgE) and was more common in the *Vespula* than in the Apis. Venom hypersensitivity can be driven by immunologic mechanisms, such as IgE-mediated or non-IgE-mediated venom allergies, as well as by non-immunologic mechanisms (14). Therefore, the specific IgE level may have been negative in 23% of the patients. The detection of venom-specific IgE-antibodies to identify the responsible species is very important for perform a VIT (23).

The presence of atopic diseases may increase the risk of systemic reaction incidence as described previously (24). Kalyoncu et al; previously reported that asthma in Turkish beekeepers were associated with SSRs (8). There were 12 (9%) patients with coexisting asthma in our study population whereas the other had no history of allergic disease. In our study, no significant association was found between asthma and the incidence of systemic reaction risk. The small sample size in our study may have contributed to this finding. A recent study suggests that 65% of hymenoptera venom allergic patients with elevated serum tryptase levels and a history of SSRs have an underlying mast cell disorder (25). Two patients with elevated basal serum tryptase levels were diagnosed with mastocytosis in our study. In line with the literature, two patients had a history of anaphylaxis without skin manifestations (26). In one of these two patients, total IgE level was 10.7IU/ mL and tryptase level was 7.80µg/L. This patient had a history of grade 3 allergic reaction. She had a history of honey bee HSRs but specific IgE test was negative. In the other patient, total

IgE level was 37IU/ mL and tryptase level was 25 µg/L. This patient also had a history of grade 3 allergic reaction. He had a history of HSRs with both honey bee and wasp, but honey bee specific IgE concentration was grade 1 (weak positive) and wasp specific IgE concentration was grade 2 (positive). Identification of concomitant Hymenoptera venom allergy in mast cell disease has been difficult to detect clinically due to the low sensitivity of venom-specific IgE levels and the possibility of non-IgE-mediated mast cell stimulation (27); therefore, diagnostic sensitivity was improved with a lower threshold for venom-specific IgE levels (IgE > 0.17 kUA/L) (28). Furthermore, although patients experienced more severe reactions, specific IgE values did not differ significantly among Grades 1, 2, and 3, suggesting that non-IgE-mediated mast cell activation may be responsible (29).

Although our study had valuable results, it had some limitations. Firstly, no prick test was performed on the patients. Unfortunately, there was a problem of access to bee allergen prick test solutions throughout our country at that time. Nevertheless, since specific IgE tests were performed on all patients and the specific IgE test is more sensitive than prick tests, the results are thought to be consistent (13,30). Secondly, component-resolved diagnostic tests could not be performed on double-positive patients. However, this test would be necessary in only 12% of patients for the decision of VIT (31,32). This test was not needed because the specific IgE tests for the bee type in the history of these patients were more significantly high.

In conclusion, hymenoptera venom allergy is a significant and often overlooked public health concern, posing a risk of life-threatening systemic reactions. Although beekeeping is widespread in this region, it was found that honey bee allergy is less common when precautions are taken and strategies should be developed in terms of measures against wasps to reduce the prevalence and incidence of wasp allergy. In addition, allergy tests were negative in one of 4 patients, indicating that new tests showing non-IgE stimulation of mast cells are needed to confirm allergy in these patients.

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