Allergol Immunopathol (Madr). 2023;51(3):68–79 eISSN:1578-1267, pISSN:0301-0546

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.all-imm.com

ORIGINAL ARTICLE



# Aeroallergen sensitization in school-age children with allergic rhinitis: What has changed during the COVID-19 pandemic?

**Nursen Cigerci Gunaydin[a]*, Ceren Tanc[b], Ezgi Tanburoglu Celiker[b], Sule Guler Kacmaz[b], Nedim Samanci[b], Aysin Nalbantoglu[b], Burcin Nalbantoglu[b]**

[a]*Department of Pediatrics, Division of Pediatric Allergy and Immunology, Faculty of Medicine, Tekirdağ Namık Kemal University, Tekirdağ, Turkey*

[b]*Department of Pediatrics, Faculty of Medicine, Tekirdağ Namık Kemal University, Tekirdağ, Turkey*

Received 5 February 2023; Accepted 27 February 2023
Available online 1 May 2023

**KEYWORDS**
aeroallergens;
allergic rhinitis;
children;
COVID-19 pandemic;
skin prick test

**Abstract**

*Background:* Pandemic period may affect aeroallergen sensitization.

*Objective*: The study aimed to investigate changes in allergen sensitivities of skin prick test (SPT) in patients with allergic rhinitis (AR) during pandemic and to evaluate relationship with disease severity.

*Methods*: In all, 164 AR patients with or without asthma, aged 6–17 years, who have undergone SPTs prior to the pandemic and after October 1, 2021 (18th month of the pandemic), were evaluated retrospectively. The wheal size of allergens in performed SPTs during and prior to the pandemic were compared. Detected changes in allergen sensitivities via SPT results were compared with changes in the disease severity parameters (AR severity, asthma severity, and the number of asthma exacerbations per year), frequency of upper respiratory tract infections and antibiotic use, laboratory parameters, demographic characteristics, and visual analogue scores (VAS).

*Results*: House dust mites (HDMs), cat, pollen, *Artemisia*, and *Cupressus* sensitization increased in AR patients during the Coronavirus disease 2019 (COVID-19) pandemic. HDM, mold, and pollen wheal diameters increased in SPTs. Proportion of polysensitization increased during the pandemic, compared to pre-pandemic period (9.1% vs 3%; $P < 0.001$), and number of non-sensitized patients decreased during the pandemic period compared to the pre-pandemic period (7.9% vs 22.6%; $P < 0.001$). An increase in HDM sensitivity in SPTs was correlated with VAS for nasal blockage, and an increase in cat sensitivity was correlated with VAS for all nasal symptoms.

*Conclusion*: We believe that inhalant allergen sensitization might have been affected by the lifestyle changes of patients during the pandemic. Hence, it is important to evaluate patients for allergen sensitization, especially patients with moderate/severe AR, to revise disease control measurements.



***Corresponding author**: Nursen Cigerci Gunaydin, MD, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Faculty of Medicine, Tekirdağ Namık Kemal University, Namık Kemal Kampüs, Street No. 1, Suleymanpasa, Tekirdağ 59030, Turkey. *Email address*: drnursen@hotmail.com

https://doi.org/10.15586/aei.v51i3.832

## Introduction

Prevalence of allergic diseases has increased globally for the last 30 years; and asthma and allergic rhinitis (AR) are the most common allergic respiratory diseases.[1] Being exposed to allergens is reported to cause development of allergen sensitization in atopic children and exacerbation of existing symptoms.[2,3] Allergen sensitizations vary globally, depending upon various geographical, climatic, and cultural factors.[4] According to different studies, the most common inhalant allergens are house dust mites (HDMs) and grass pollen.[5-7]

A new type of human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in Wuhan City, Hubei Province of China in December 2019, and was named the coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). In March 2020, WHO declared COVID-19 as a pandemic.[8-10]

In Turkey, the first COVID-19 patient was identified on March 11, 2020, and precautions for the pandemic were initiated.[10] Within the scope of these precautions, face-to-face education was suspended on March 13, 2020, and lockdown period was introduced on April 3, 2020. Online learning period continued until June 2021, and face-to-face education restarted in September 2021 with various precautions such as wearing mask and social distancing. During this period, children stayed at home for a prolonged period and increased exposure to indoor inhalant allergens.

Exposure and sensitization to indoor allergens is an important risk factor for asthma and airway diseases.[11] Exposure of sensitized patient to allergens may increase the symptoms of AR and asthma by triggering airway inflammation and hyperreactivity. During the quarantine period, decreased social interactions may be thought to decrease the physical activity levels of children, decrease exposure to airway viruses, and increase the number of families having pets. All these lifestyle alterations during this period may have caused some changes in allergen sensitization of children with AR or asthma.

The aim of this study was to evaluate changes in aeroallergen sensitization during the pandemic and to investigate their association with severity of the disease in children with AR in the Tekirdağ province of Turkey.

## Methods

### *Patient selection*

In all, 164 AR patients with/without asthma who were followed up in the pediatric allergy outpatient clinic and had skin prick tests (SPT) prior to and during the pandemic (after 1 October 2021) were included in the study. Patients with severe asthma and patients that changed their living environment during the pandemic were excluded from the study. The study was conducted in the Faculty of Medicine of Tekirdağ Namık Kemal University, Turkey.

### *Ethical committee approval*

All parents provided their written informed consent for the study. The study was performed according to the Declaration of Helsinki, and was approved by the Tekirdağ Namık Kemal University Ethical Committee (2022.31.02.15).

### *Data collection*

Demographic, clinical, and laboratory data of the patients were collected retrospectively. Frequency of upper respiratory tract infections (URI) and antibiotic usage, severity of asthma, frequency of asthma exacerbations, severity of AR, and laboratory parameters and SPT results prior to and during the pandemic were recorded from patient files. Visual Analogue Scores (VAS) were also recorded together with the SPT performed during the pandemic.

### *Assessment of asthma and allergic rhinitis symptoms*

Severity of asthma was assessed in patients with asthma according to Global Initiative for Asthma (GINA) guidelines.[12,13] VAS were used to assess disease control in patients with AR.[14] VAS was evaluated between “no symptom” (score = 0) and “as bad as it could be” (score = 10) for each AR symptom (nasal itching, sneezing, nasal blockage, nasal discharge, and eye symptoms). AR was diagnosed based on the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, and AR severity was graded as mild and moderate/severe.[15]

### *Skin prick test*

Medicines that may affect SPT results were discontinued at appropriate time prior to test. Positive control (histamine, 10 mg/mL), negative control (0.9% sodium chloride [NaCl]), and standardized commercial allergen solutions were used in SPTs (ALK-Abelló, Horsholm, Denmark). Following allergens were applied to perform SPTs: HDMs (Dermatophagoides farinae [*D. farinae*] and Dermatophagoides pteronyssinus [*D. pteronyssinus*]); mold (*Alternaria alternata*); 6 grass pollen mixture; weed pollen mixture; 9 tree pollen mixture; animal epithelium (cat and dog); cockroach (*Blattella germanica*); *Cupressus*; English plantain; *Artemisia vulgaris*; and olive and latex allergen extracts. A wheal diameter of ≥3 mm longer than the negative control was considered as allergen sensitivity.[16] Sensitization with five or more allergens was considered as polysensitization.[17]

### *Study protocol*

Allergen wheal diameters in SPTs of the patients performed during the pandemic were compared to the results of tests performed prior to the pandemic. Changes in allergen sensitization of SPTs were compared to changes in disease severity, demographical characteristics, laboratory results, and VAS.

### *Statistical analysis*

Statistical analysis was performed using the IBM SPSS Statistics V25. Descriptive statistics for continuous variables were expressed as mean, standard deviation, median, and minimum and maximum values. Frequencies and percentage values were presented for categorical variables. The assumption of normality was tested using the Kolmogorov–Smirnov test or the Shapiro–Wilk test. The Mann–Whitney U test was performed to compare differences between two independent groups when the dependent variable was continuous but not normally distributed. The Kruskal–Wallis test was used to determine whether there were statistically significant differences and more groups of independent variables on a continuous or ordinal dependent variable. Spearman's rank correlation has been used as a scale for measuring the degree of association between two variables. The Wilcoxon signed-rank test was used to compare pre-pandemic and post-pandemic measurements. Association between VAS and SPT results was assessed using regression analysis, considering demographical characteristics of the patients. $P < 0.05$ was considered as statistically significant.

## Results

Mean age of the patients was 10.1 ± 3.1(6–17) years, and 57.3% (n = 94) of the patients were boys. Mean disease follow-up duration was 5.4 ± 2.5 years, and 70% (n = 115) of the patients had concomitant asthma. A family history of atopy was discovered in 46.3% and passive smoking in 51.2% of the patients. A 2.5-fold increase was determined in bird ownership and 4-fold increase in cat ownership during the pandemic (Table 1). The mean Asthma Control Test Score of patients having concomitant asthma was 20.9 ± 4.3 (9–25) during the pandemic.

### *Aeroallergen sensitization*

Distribution of aeroallergen sensitization prior to the pandemic according to SPT results was as follows: 52.4% (n = 86) *D. pteronyssinus*, 49.4% (n = 81) *D. farinae*, 20.1% (n = 33) 6 grass pollen, 11.6% (n = 19) *Alternaria*, 8.5% (n = 14) cat epithelium, 6.7% (n = 11) cockroach, 6% (n = 10) dog epithelium, 4.3% (n = 7) 9 tree mix, 3.6% (n = 6) olive, 3% (n = 5) *Cupressus*, 1.2% (n = 2) weed mix, 1.2% (n = 2) English plantain, and 0.6% (n = 1) *Artemisia*.

Distribution of aeroallergen sensitization in SPTs performed during the pandemic were as follows: 60.4% (n = 99) *D. pteronyssinus*, 54.2% (n = 89) *D. farinae*, 28.6% (n = 47) 6 grass pollen, 17% (n = 28) *Alternaria*, 28% (n = 46) cat epithelium, 8.5% (n = 14) *Cupressus*, 5.5% (n = 9) cockroach, 5.5% (n = 9) 9 tree mix, 5.5% (n = 9) *Artemisia*, 6.7% (n = 11) olive, 5.5% (n = 9) weed mix, 3.6% (n = 2) English plantain, and 3.6% (n = 6) dog epithelium. During the pandemic, a significant increase was detected in the presence of sensitivities to HDMs ($P < 0.01$), cat ($P < 0.01$), grass pollen ($P = 0.01$), *Artemisia* ($P < 0.01$), and *Cupressus* ($P = 0.01$) (Figure 1).

Most of the patients had sensitization to 2–4 allergens prior to (52.4%) and during (59.1%) the pandemic. An increase in polysensitized patients (from 3% to 9.1%) and a decrease in non-sensitized patients (from 22.6% to 7.9%) were observed ($P < 0.01$) (Figure 2).

While wheal diameters because of HDMs, *Alternaria*, and 6 grass pollen increased significantly during the pandemic ($P < 0.01$), other allergens showed no difference ($P > 0.05$) (Figure 3).

During the pandemic, patients experienced fewer URI ($P < 0.01$), used antibiotics less frequently ($P < 0.01$), had higher total ımmunoglobulin E (IgE) levels ($P < 0.01$), had more allergen sensitivity in SPTs ($P < 0.01$), and more patients presented with an allergen sensitivity ($P < 0.01$), compared to the period prior to the pandemic. Moderate/severe AR was more frequent during the pandemic (55.5%), compared to prior to the pandemic (38.4%; $P < 0.01$). While patients having concomitant asthma (n = 115) experienced fewer asthma exacerbations during the pandemic (2.2/year), compared the prior to the pandemic (3.6/year); asthma severity was the same as prior to the pandemic. While there was no difference between eosinophil count ($P = 0.9$) and percentage values ($P = 0.84$), specific ımmunoglobulin E (sIgE) for HDMs increased during the pandemic ($P < 0.01$) (Table 2).

There was no relation between AR severity and distribution of diagnoses ($P = 0.73$), gender ($P = 0.45$), family

**Table 1** Clinical and demographical characteristics of patients.

| | |
|---|---|
| Diagnosis | 30% (n = 49) AR only; 70% (n = 115) allergic rhinitis (AR) and asthma |
| Gender | 57.3% (n = 94) boys, 42.7% (n = 70) girls |
| AR follow-up duration (years) | 5.1 ± 2.1 (3-13) |
| Asthma follow-up duration (years) | 5.4 ± 2.5 (3-13) |
| Family history of atopy | 46.3% (n = 76) present |
| Number of household members | 4 ± 0.8 (2-7) |
| Presence of passive smoking | 51.2% (n = 84) present |
| Presence of cat in home | Prior to the pandemic: 4.8% (n = 8)<br>During the pandemic: 18.9% (n = 31) present |
| Presence of dog in home | Prior to and during the pandemic: 3.7% (n = 6) |
| Presence of a pet bird at home | Prior to the pandemic: 10.3% (n = 17)<br>During the pandemic: 26.8% (n = 44) |

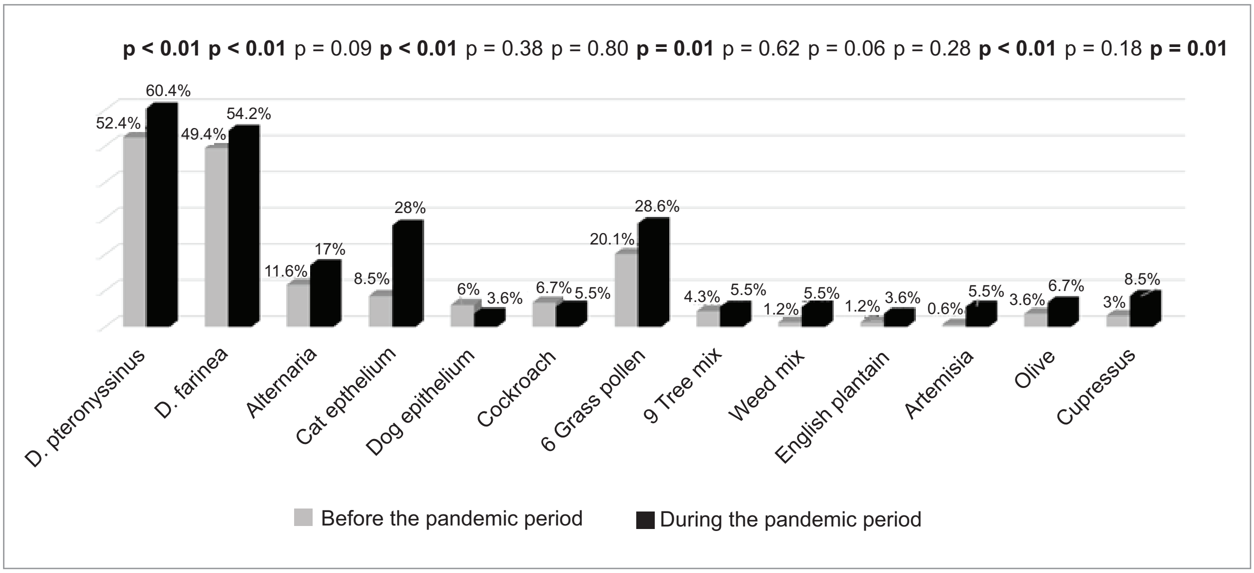


**Figure 1** Distribution of aeroallergen sensitization in skin prick test prior to and during the pandemic.

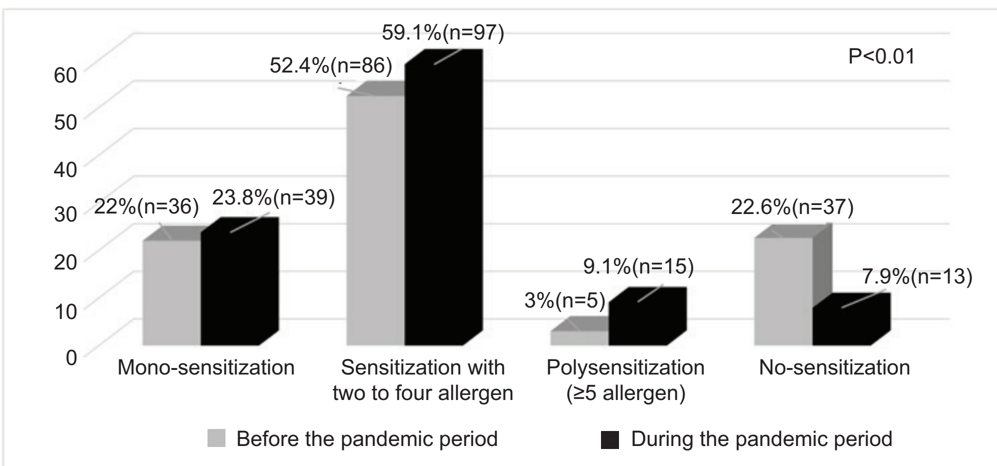


**Figure 2** Distribution of allergen sensitivity prior to and during the pandemic.

history of atopy (P = 0.09), passive smoking (P = 0.53), duration of having a pet (P = 0.4), and presence of a bird as a pet at home (P = 0.35). Patients having a pet cat at home (n = 31) had more severe AR (80.6%, n = 25 moderate/severe; 19.4%, n = 6 mild) than patients who do not have a cat (n = 133) (49.6%, n = 66 moderate/severe; 50.4%, n = 67 mild; P = 0.02) (data not shown).

A positive correlation was discovered between the changes in *D. farinea and D. pteronyssinus* wheal sizes, and total IgE and HDMs-sIgE levels (P < 0.001). Change in *Alternaria* wheal size in SPT was negatively correlated with the frequency of URI and positively correlated with total IgE levels (eTable 1).

Distribution of VAS recorded during the pandemic is shown in eFigure 1. The association between VAS and allergen wheal sizes prior to and during the pandemic was assessed. A positive correlation was discovered between VAS for nasal discharge and increase in HDMs wheal size in SPT (P < 0.01) (Table 3). Increase in cat wheal size was shown as positively correlated to VAS for nasal blockage, sneezing, and nasal itching (P < 0.05) (Table 3).

While mild and severe AR patients had no significant differences in allergen wheal diameters prior to the pandemic; patients with moderate/severe AR had significantly larger wheal diameters for HDMs than in patients with mild AR during the pandemic.

No significant association was discovered between AR severity and other allergens in SPT (Table 4).

No significant association was discovered between the mean allergen wheal sizes and the severity of the disease in patients with asthma prior to and during the pandemic (P > 0.05; eTable 2).

Five different components of VAS (nasal itching, sneezing, nasal blockage, nasal discharge, and eye symptoms)

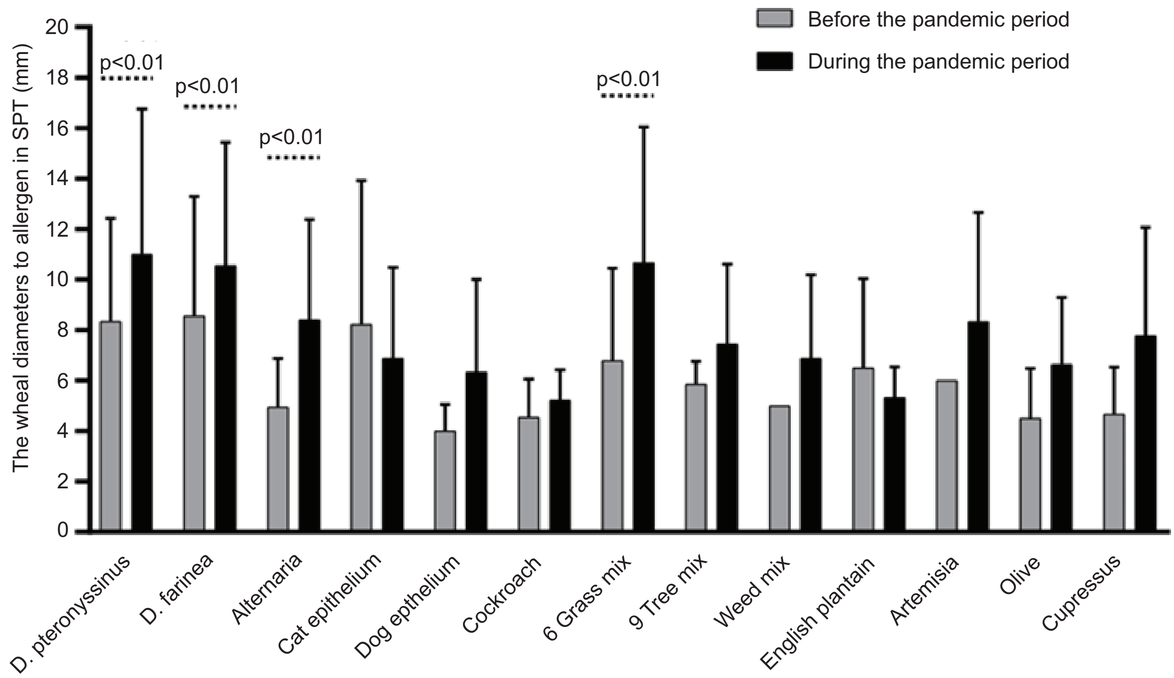


**Figure 3** Comparison of allergen wheal diameters in skin prick tests prior to and during the pandemic.

**Table 2** Comparison of clinical and laboratory parameters of patients prior to and during the pandemic.

| | Prior to the pandemic | During the pandemic | P |
|---|---|---|---|
| Number of URI (/year) | 5.6 ± 2.4 (1-12) | 3.3 ± 2.9 (0-12) | <0.01 |
| Number of antibiotic use (/year) | 4.6 ± 1.9 (1-12) | 2.3 ± 2.5 (0-10) | <0.01 |
| AR severity | 61.6% (n = 101) mild<br>38.4% (n = 63) moderate/severe | 44.5% (n = 73) mild<br>55.5% (n = 91) moderate/severe | <0.01 |
| Asthma severity | 68.7% (n = 79) mild<br>31.3% (n = 36) moderate | 57.4% (n = 66) mild<br>42.6% (n = 49) moderate | 0.08 |
| Number of asthma exacerbation/year | 3.6 ± 3.3 (0-10) | 2.2 ± 2.1 (0-15) | <0.01 |
| Presence of allergen sensitivity in skin prick tests | 77.4% (n = 127) present<br>22.6% (n = 37) absent | 92.1% (n = 151) present<br>7.9% (n = 13) absent | <0.01 |
| Number of sensitized allergens | 1.7 ± 1.5 (0-9) | 2.3 ± 1.5 (0-9) | **<0.01** |
| Total IgE (median) | 143 (0-4914) | 199 (0-2500) | **<0.01** |
| Eosinophil count | 332 ± 210 (60-1090) | 337 ± 258 (30-730) | 0.9 |
| Eosinophil percentage (%) | 4.2 ± 2 (0-10) | 4.0 ± 2.4 (0.6-13.4) | 0.84 |
| *D. pteronyssinus* IgE (median) | 0.50 (0.1-100) | 2.8 (0.1-221) | **<0.01** |
| *D. farinae* IgE (median) | 8 (3-21) | 10 (3-222) | **<0.01** |

AR: allergic rhinitis; *D. farinae*: Dermatophagoides farinae; *D. pteronyssinus*: Dermatophagoides pteronyssinus; IgE: ımmunoglobulin E; sIgE: specific ımmunoglobulin E; URI: upper respiratory tract infections.

and five different regression models were estimated along with statistically significant demographic variables investigated by the stepwise regression method.

Accordingly, the VAS of those who kept cats at home were found to be significantly higher for all nasal components than those who did not have cats, and only the visual analogue nasal blockage scores were significantly higher in those who kept birds at home, compared to those who did not own birds.

When we evaluated the relationship between VAS and changes in SPT results during the pandemic, a relationship was discovered between HDM wheal diameters and VAS for nasal blockage, and between cat wheal diameters and VAS for all nasal symptoms at a significance level of 5% (eTable 3).

## Discussion

Compulsory lifestyle changes during the COVID-19 pandemic might have altered the sensitivities of people against certain allergens. This study is important because it evaluates

**Table 3** Association between VAS and skin prick test results.

| | VAS (nasal blockage) | VAS (sneezing) | VAS (nasal discharge) | VAS (nasal itching) | VAS (eye symptoms) | D. farinea wheal diameter in SPT | D. pteronyssinus wheal diameter in SPT | Alternaria wheal diameter in SPT | 6 Grass pollen wheal diameter in SPT | Cat wheal diameter in SPT |
|---|---|---|---|---|---|---|---|---|---|---|
| Visual analogue score (nasal blockage) | 1.000 | — | — | — | — | — | — | — | — | — |
| Visual analogue score (sneezing) | 0.586*** | 1.000 | — | — | — | — | — | — | — | — |
| Visual analogue score (nasal discharge) | 0.617*** | 0.735*** | 1.000 | — | — | — | — | — | — | — |
| Visual analogue score (nasal itching) | 0.577*** | 0.740*** | 0.749*** | 1.000 | — | — | — | — | — | — |
| Visual analogue score (eye symptoms) | 0.183** | 0.276*** | 0.259*** | 0.278*** | 1.000 | — | — | — | — | — |
| D. farinea wheal diameter in SPT | 0.206*** | 0.072 | 0.068 | 0.083 | −0.002 | 1.000 | — | — | — | — |
| *D. pteronyssinus* wheal diameter in SPT | 0.253*** | 0.155 | 0.129 | 0.116 | 0.095 | 0.688*** | 1.000 | — | — | — |
| *Alternaria* wheal diameter in SPT | 0.062 | 0.093 | 0.093 | 0.058 | 0.021 | −0.017 | 0.003 | 1.000 | — | — |
| 6 Grass pollen wheal diameter in SPT | 0.049 | 0.135 | 0.136 | 0.078 | 0.037 | −0.067 | 0.116 | 0.153** | 1.000 | — |
| Cat wheal diameter in SPT | 0.188** | 0.174** | 0.149 | 0.158** | 0.023 | 0.087 | 0.240*** | −0.047 | 0.194** | 1.000 |

*D. farinae*: Dermatophagoides farinea; *D. pteronyssinus*: Dermatophagoides pteronyssinus; SPT: skin prick test; VAS: visual analogue score.
Significant correlations at the significance levels of 1% (P < 0.01)*** and 5% (P < 0.05).**

**Table 4** Association between severity of allergic rhinits (AR) and allergen wheal size in skin prick tests prior to and during the pandemic.

| | Prior to the pandemic | | | | During the pandemic | | | |
|---|---|---|---|---|---|---|---|---|
| | Allergic rhinits | n | Mean ± SD | *t*-test* | Allergic rhinits | n | Mean ± SD | *t*-test* |
| D. farinea wheal diameter in SPT | Mild | 101 | 3.891 ± 5.1 | −1.000 | Mild | 73 | 4.43 ± 5.7 | −2.388** |
| | Moderate/severe | 63 | 4.761 ± 5.8 | | Moderate/severe | 91 | 6.758 ± 6.7 | |
| *D. pteronyssinus* wheal diameter in SPT | Mild | 101 | 4.13 ± 5.1 | −0.759 | Mild | 73 | 5.26 ± 6.6 | −2.290** |
| | Moderate/severe | 63 | 4.761 ± 5.1 | | Moderate/severe | 91 | 7.74 ± 7.1 | |
| *Alternaria* wheal diameter in SPT | Mild | 101 | .63 ± 1.8 | 0.277 | Mild | 73 | 1.3 ± 3.4 | −0.591 |
| | Moderate/severe | 63 | .55 ± 1.6 | | Moderate/severe | 91 | 1.63 ± 3.8 | |
| 6 Grass pollen wheal diameter in SPT | Mild | 101 | 1.24 ± 3.1 | −0.419 | Mild | 73 | 2.48 ± 4.7 | −1.176 |
| | Moderate/severe | 63 | 1.46 ± 3.3 | | Moderate/severe | 91 | 3.51 ± 6.2 | |
| Cat wheal diameter in SPT | Mild | 101 | 0.65 ± 2.3 | −1.381 | Mild | 73 | 1.53 ± 3.2 | −1.442 |
| | Moderate/severe | 101 | 0.65 ± 2.3 | −1.381 | Moderate/severe | 73 | 1.53 ± 3.2 | −1.442 |

*D. farinae*: Dermatophagoides farinae; *D. pteronyssinus*: Dermatophagoides pteronyssinus; SD: standard deviation; SPT: skin prick test.
**t*-test was used to evaluate whether the mean skin prick test measurements changed according to disease severity prior to and during the pandemic.
Significant correlations at the significance levels of 1% (P < 0.01)*** and 5% (P < 0.05).**

changes in allergen sensitivities during the pandemic using SPT and investigates the association of these changes with the severity of allergic diseases and the effects of various factors.

Atopic sensitization is a risk factor for development of upper and lower respiratory symptoms.[18] Visitsunthorn et al. reported an allergen sensitivity rate of 67% by SPT in AR patients.[19] Patients in our study had an allergen sensitivity rate of 77.4% prior to the pandemic, and the rate increased to 92.1% during the pandemic. Most common allergens were HDMs, mold, grass pollen, and cat epithelium.

The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines report that asthma is present in approximately 15–38% of AR patients, with nasal symptoms being present in 6–50% of asthma patients.[15] In our study, asthma was highly frequent in patients with AR (70%). There was no difference in the aeroallergen sensitivities of patients according to the presence or absence of asthma.

Factors such as passive smoking, industrialized city lifestyle, gender, atopy history, increased total IgE, and aeroallergen polysensitization have been reported to be the risk factors for asthma and AR.[20] A study reported that patients with AR were 31.1% monosensitized and 21.5% polysensitized against allergens.[21] While polysensitization rates were low in our patients, an increase in the proportion of polysensitized patients (3–9.1%) and a decrease in the proportion of non-sensitized patients (22.6–7.9%) during the pandemic were remarkable.

Another study showed that passive smoking was associated with AR.[22] No association between the disease severity and passive smoking was discovered in our study, URI frequency, atopy history, gender, and total IgE.

Sensitization of children against indoor allergens during pre-school and school periods was associated with exposure to allergens.[23] It was believed that during the pandemic, implemented lifestyle changes around the world and long periods spent indoors at home increased exposure to indoor allergens, although their effects on allergic children have not been known yet. Yucel et al. showed that nasal symptoms were significantly worsened in HDM-sensitized AR patients during the lockdown period of March–May 2020, compared to March–April-May 2019.[24]

In this study, it was found that HDMs were the most commonly found allergens during the pandemic as they were prior to the pandemic. Additionally, it was showed that the rates of sensitization to HDMs increased during the pandemic (52.4–60.4% for *D. pteronyssinus* and 49.4–54.2% for *D. farinae*), and wheal sizes in SPT increased in the patients already sensitized.

Allergen exposure and sensitization are reported to have a strong dose-dependent relation, especially for HDMs.[25] HDMs are strongly associated with the AR and asthma pathogenesis, and the importance of assessing the allergen sIgE levels for HDMs has been reported in evaluating risk of allergic diseases.[26,27] In this study, sensitization against HDMs increased, which was positively correlated to total IgE and sIgE levels.

A strong evidence was determined that indoor allergens played important roles in triggering allergy and asthma symptoms.[28] Our study demonstrated that increase in wheal size in the SPT results of HDM sensitive patients increased VAS for nasal blockage, thus revealing a relationship between increase in allergen sensitization in SPT and AR severity.

According to the results of regression analysis, this finding suggested that increase in HDM wheal diameters in SPT during the pandemic increased VAS for nasal blockage.

Baumann et al. reported that exposure to common indoor aeroallergens was correlated to AR.[29] In this study, while there was no relation between the allergen wheal sizes and the severity of AR prior to the pandemic; moderate/severe AR was more frequent in patients with larger HDM wheal diameters during the pandemic. This result suggests that an increase in allergen sensitivities affected the frequency of moderate/severe AR. There was no difference between the change in allergen sensitivities in SPT and the severity of asthma or the frequency of asthma attacks in patients.

Exposure to pets, such as cats and dogs, has been associated to increase sensitivity to these animals and other inhaled allergens. Pet-associated allergy through sensitization gains importance where pets are present frequently. However, it has been reported that being a cat ownership in early childhood may be important in the prevention of sensitization against the cats and in decreasing the prevalence of AR.[20] Patients in our study frequently had birds (26.8%) and cats (18.9%). It was shown that cat ownership during the pandemic increased by four-fold, with increase in the number of cat-sensitized patients. In addition, increase in cat sensitivity in SPT increased VAS for all nasal symptoms. This is believed to be caused by the fact that children spent more time indoor with their cats because of decreased social interaction during the pandemic. In addition, presence of a pet cat at home was found to increase VAS.

Fungus spores are also one of the important indoor allergens. Weinmayr et al. reported that exposure to humidity and fungi was associated with the development and exacerbations of AR and asthma.[30-32] A study conducted in Bangkok concerning changes in allergen sensitivities after the flood reported that sensitivity decreased to certain species of cockroaches, grass, and fungi, while sensitivity increased in the case of *Alternaria* and dog.[19] *Alternaria spp.* grow in humid areas. These are indoor fungal allergens that reside in carpets, clothes, and on flat surfaces of residential buildings.[19] Tekirdağ province of Turkey has coasts on both the Marmara Sea and the Black Sea, with a subhumid climate. In our study, an increase in the wheal size of the patients sensitive to *Alternaria* during the pandemic was thought to be caused by the geographical characteristics of Tekirdağ— with sea coasts—and indoor characteristics of houses. Disease severity in our study was not associated to *Alternaria* allergen sensitivity most probably because of the limited number of patients with *Alternaria* sensitivity.

Cockroach is an important indoor allergen that triggers respiratory allergies. In a study conducted in the United States, the cockroach allergens were detected in 71% of dust samples taken from schools and daycare centers.[33] In the present study, prevalence of cockroach sensitivity was not high (6.7%) and even did not increase during the pandemic (5.5%).

Grass pollens are the most important allergen group discovered in our country and many other countries. In a study, *Artemisia vulgaris* and *Ambrosia artemisiifolia* pollen sensitivities were shown to be associated with the development of AR.[34] In the present study, an increase in grass pollen sensitivity rate and wheal sizes was observed. These might have been caused by the increased periods spent in house gardens accessible because of the socioeconomic and geographical characteristics of this region, or because of allergic sensitization that could have increased in time as a part of patient's natural atopic process. However, increase in pollen wheal sizes did not affect disease severity in our study.

## Limitations

This study has certain limitations. First, this was a single-center retrospective study. Even though it was believed that exposure to indoor allergens increased with long periods of stay at home, unavailability of indoor allergen measurements was the second limitation. Another limitation was that even though the presence of a bird as a pet at home was considered in the study, an SPT was not performed for bird sensitization. Inability to perform a spirometry in asthma patients was a limitation caused by the pandemic conditions.

## Conclusion

This study determined that during the COVID-19 pandemic, sensitivity rates increased for HDMs, cat, pollen, *Artemisia*, and *Cupressus*. Further, HDM, mold, and pollen wheal sizes in SPT increased in patients with AR. Regarding AR severity, it was demonstrated that VAS for nasal blockage increased with increased HDM sensitization, and VAS for all nasal symptoms increased with increased cat sensitization.

We believe that changes in the lifestyles of patients during the pandemic might have affected inhalant allergen sensitization. Therefore, reevaluation of altered allergen sensitizations, especially in the patients with moderate/severe AR, to revise disease control measurements is important.

## Funding

No external funding was secured for this study.

## Conflict of Interest

No conflict of interest was declared by the authors.

## Author Contributions

Nursen Cigerci Gunaydin designed the research, followed up patients, performed data collection, wrote the paper, analyzed the results, and edited the paper. Ceren Tanc followed up patients, performed data collection, and wrote the paper. Ezgi Tanburoglu Celiker designed the methodology, and performed data collection; Sule Guler Kacmaz performed data collection and wrote the paper. Nedim Samanci designed the research, and edited the paper. Aysin Nalbantoglu performed data collection, wrote the paper, and analyzed the results. Burcin Nalbantoglu designed the methodology, performed data collection, analyzed the results, and edited the paper.

## References

1. Asher MI, Montefort S, Björkstén B, Lai CK, Stranchan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phase one and three repeat multicountry cross-sectional surveys. Lancet. 2006;368(9537):733–43. https://doi.org/10.1016/S0140-6736(06)69283-0
2. Li J, Huang Y, Lin X, Zhao D, Tan G, Wu J, et al. Influence of degree of specific allergic sensitivity on severity of rhinitis and asthma in Chinese allergic patients. Respir Res. 2011;12(1):95. https://doi.org/10.1186/1465-9921-12-95
3. Tham EH, Lee AJ, Bever HV. Aeroallergen sensitization and allergic disease phenotypes in Asia. Asian Pac J Allergy Immunol. 2016;34(3):181–9.
4. Salo PM, Sever ML, Zeldin DC. Indoor allergens in school and day care environments. J Allergy Clin Immunol. 2009;124(2):185–94. https://doi.org/10.1016/j.jaci.2009.05.012
5. Farrokhi S, Gheybi MK, Movahed A, Tahmasebi R, Iranpour D, Fatemi A, et al. Common aeroallergens in patients with asthma and allergic rhinitis living in southwestern part of Iran: Based on skin prick test reactivity. Iran J Allergy Asthma Immunol. 2015;14(2):133–8.
6. Ozkaya E, Sogut A, Kucukkoc M, Eres M, Acemoglu H, Yuksel H, et al. Sensitisation pattern of inhalant allergens in children with asthma who are living different altitudes in Turkey. Int J Biometeorol. 2015;59(11):1685–90. https://doi.org/10.1007/s00484-015-0975-0
7. Sahiner UM, Civelek E, Yavuz ST, Buyuktiryaki AB, Tuncer A, Sekerel BE. Skin prick testing to aeroallergen extracts: What is the optimal panel in children and adolescents in Turkey? Int Arch Allergy Immunol. 2012;157(4):391–8. https://doi.org/10.1159/000329870
8. Wu Z, McGoogan JM. Characteristics of and ımportant lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239. https://doi.org/10.1001/jama.2020.2648
9. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: Classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020;5(4):536–44. https://doi.org/10.1038/s41564-020-0695-z
10. World Health Organization. Global-Turkey. Available from: https://covid19.who.int/region/euro/country/tr. Accessed November 30, 2020.
11. Platts-Mills TA, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: Report of the third ınternational workshop. J Allergy Clin Immunol. 1997;100:2–24. https://doi.org/10.1016/S0091-6749(97)70292-6
12. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: A survey for assessing asthma control. J Allergy Clin Immunol. 2004;113(1):59–65. https://doi.org/10.1016/j.jaci.2003.09.008
13. Global İnitiative for Asthma (GINA). Global strategy for asthma management and prevention. NHLBI/WHO workshop

report. Bethesda, MD: National Institute of Health, and National Heart, Lung and Blood Institute; revised 2020.
14. Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Daures JP, et al. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. Allergy. 2007;62(4):367-72. https://doi.org/10.1111/j.1398-9995.2006.01276.x
15. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines - 2016 revision. J Allergy Clin Immunol. 2017;140(4): 950-8. https://doi.org/10.1016/j.jaci.2017.03.050
16. Meltzer EO, Blaiss MS, Derebery MJ, Mahr TA, Gordon BR, Sheth KK, et al. Burden of allergic rhinitis: Results from the Pediatric Allergies in America survey. J Allergy Clin Immunol. 2009;124(3):43-70. https://doi.org/10.1016/j.jaci.2009.05.013
17. de Jong AB, Dikkeschei LD, Brand PL. Sensitization patterns to food and inhalant allergens in childhood: A comparison of nonsensitized, monosensitized and polysensitized children. Pediatr Allergy Immunol. 2011;22(1):166-71. https://doi.org/10.1111/j.1399-3038.2010.00993.x
18. Platts-Mills TA, Wheatley LM, Aalberse RC. Indoor versus outdoor allergens in allergic respiratory disease. Curr Opin Immunol. 1998;10(6):634-9. https://doi.org/10.1016/S0952-7915(98)80081-2
19. Visitsunthorn N, Chaimongkol W, Visitsunthorn K, Pacharn P, Jirapongsananuruk O. Great flood and aeroallergen sensitization in children with asthma and/or allergic rhinitis. Asian Pac J Allergy Immunol. 2018;36(2):69-76.
20. Testa D, DI Bari M, Nunziata M, Cristofaro G, Massaro G, Marcuccio G, Motta G. Allergic rhinitis and asthma assessment of risk factors in pediatric patients: A systematic review. Int J Pediatr Otorhinolaryngol. 2020;129:109759. https://doi.org/10.1016/j.ijporl.2019.109759
21. Baatenburg de Jong A, Dikkeschei LD, Brand PLP. Sensitization patterns to food and inhalant allergens in childhood: a comparison of non-sensitized, monosensitized, and polysensitized children: Sensitization patterns to food and inhalant allergens. Pediatr Allergy Immunol. 2011;22(2):166-71. https://doi.org/10.1111/j.1399-3038.2010.00993.x
22. Dogru M. Investigation of asthma comorbidity in children with different severities of allergic rhinitis. Am J Rhinol Allergy. 2016;30(3):186-9. https://doi.org/10.2500/ajra.2016.30.4315
23. Gruchalla RS, Pongracic J, Plaut M, Evans R, Visness CM, Walter M, et al. Inner City Asthma Study: Relationships among sensitivity, allergen exposure, and asthma morbidity. J Allergy Clin Immunol. 2005;115(3):478-85. https://doi.org/10.1016/j.jaci.2004.12.006
24. Yucel E, Suleyman A, Demirkale ZH, Guler N, Tamay ZU, Ozdemir C. “Stay at home”: Is it good or not for house dust mite sensitized children with respiratory allergies? Pediatr Allergy Immunol. 2021;32(5):963-70. https://doi.org/10.1111/pai.13477
25. Tovey ER, Almqvist C, Li Q, Crisafulli D, Marks GB. Nonlinear relationship of mite allergen exposure to mite sensitization and asthma in a birth cohort. J Allergy Clin Immunol. 2008;122(1):114-8. https://doi.org/10.1016/j.jaci.2008.05.010
26. Davies JM, Weber RW.A. Aerobiology of outdoor allergens. In: Burks AW, Holgate ST, O’Hehir RE, Brodie DH, Bacharier LB, Hershey GKK, Peebles RS, editors. Middleton’s allergy principles and practice, 9th ed. Philadelphia, PA: Elsevier; 2020. Vol. 1., pp. 428-50.
27. Gabet S, Ranciere F, Just J, Blic J, Lezmi G, Amat F, et al. Asthma and allergic rhinitis risk depends on house dust mite specific IgE levels in PARIS birth cohort children. World Allergy Organ J. 2019;12(9):100057. https://doi.org/10.1016/j.waojou.2019.100057
28. Langley SJ, Goldthorpe S, Craven M, Morris J, Woodcock A, Custovic A. Exposure and sensitization to indoor allergens: association with lung function, bronchial reactivity, and exhaled nitric oxide measures in asthma. J Allergy Clin Immunol. 2003;112 (2):362-8. https://doi.org/10.1067/mai.2003.1654
29. Baumann LM, Romero KM, Robinson CL, Hansel NN, Gilman RH,Hamilton RG, et al. Prevalence and risk factors for allergic rhinitis in two resource-limited settings in Peru with disparate degrees of urbanization. Clin Exp Allergy. 2015;45(1):192-9. https://doi.org/10.1111/cea.12379
30. Weinmayr G, Gehring U, Genuneit J, Buchele G, Kleiner A, Siebers R,et al. Strachan, dampness and moulds in relation to respiratory and allergic symptoms in children: Results from phase two of the international study of asthma and allergies in childhood (ISAAC phase two). Clin Exp Allergy. 2013;43(7):762-74. https://doi.org/10.1111/cea.12107
31. Caillaud D, Leynaert B, Keirsbulck M, Nadif R. Indoor mould exposure, asthma and rhinitis: Findings from systematic reviews and recent longitudinal studies. Eur Respir Rev. 2018;27(148):170137. https://doi.org/10.1183/16000617.0137-2017
32. Plaza V, Serrano J, Picado C, Cosano J, Ancochea J, de Diego A, et al. Clinical characteristics of the fatal and near-fatal asthma in *Alternaria alternata* sensitized patients. Med Clin (Barc). 2003;121(19):721-4. https://doi.org/10.1016/S0025-7753(03)74076-7
33. Chew GL, Correa JC, Perzanowski MS. Mouse and cockroach allergens in the dust and air in northeastern United States inner-city public high schools. Indoor Air. 2005;15(4):228-34. https://doi.org/10.1111/j.1600-0668.2005.00363.x
34. Li J, Sun B, Huang Y, Lin X, Zhao D, Tan G, et al. A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. Allergy. 2009;64 (7):1083-92. https://doi.org/10.1111/j.1398-9995.2009.01967.x

## Supplementary

**Table S1** Association between the skin prick test results and the clinical/laboratory parameters prior to and during the pandemic.

| | *D. farinea* wheal diameter in SPT | *D. pteronyssinus* wheal diameter in SPT | Alternaria wheal diameter in SPT | 6 Grass pollen wheal diameter in SPT |
|---|---|---|---|---|
| **URI frequency** | 0.052 | 0.071 | −**0.159**** | 0.065 |
| **Antibiotic use frequency** | −0.011 | 0.014 | −0.116 | −0.012 |
| **Asthma exacerbation frequency** | 0.020 | 0.095 | −0.003 | 0.037 |
| **Total IgE** | **0.206***** | **0.230***** | **0.168**** | 0.073 |
| **Eosinophil percentage (%)** | 0.024 | −0.025 | 0.131 | −0.056 |
| **Eosinophil cell count** | 0.048 | −0.016 | 0.100 | −0.103 |
| ***D. pteronyssinus*s IgE** | **0.452***** | **0.573***** | 0.012 | 0.122 |
| ***D. farinea*s IgE** | **0.607***** | **0.543***** | 0.057 | 0.042 |

*D. farinae*: Dermatophagoides farinae; *D. pteronyssinus*: Dermatophagoides pteronyssinus; IgE: ımmunoglobulin E; sIgE: specific ımmunoglobulin E; SPT: skin prick test; URI: upper respiratory tract infection.
Difference between the measured values prior to and after the pandemic was calculated for every variable, and the association between these differences was analyzed using Spearman's rank correlation analysis. Significant correlations at the significance levels of 1% (P < 0.01)*** and 5% (P < 0.05).**

**Table S2** Association between asthma severity and skin prick test wheal sizes during the pandemic.

| **Allergen wheal diameters in SPT** | **Prior to the pandemic** | | | | **During the pandemic** | | | |
|---|---|---|---|---|---|---|---|---|
| | **Asthma severity** | **n** | **Mean ± SD** | ***t*-test*** | **Asthma severity** | **n** | **Mean ± SD** | ***t*-test*** |
| D. farinea | Mild | 79 | 3.55 ± 4.9 | −1.132 | Mild | 66 | 5.08 ± 5.9 | −1.447 |
| | Moderate | 36 | 4.75 ± 5.8 | | Moderate | 49 | 6.8 ± 6.7 | |
| *D. pteronyssinus* | Mild | 79 | 4.26 ± 4.8 | 0.381 | Mild | 66 | 5.7 ± 6.3 | −1.586 |
| | Moderate | 36 | 3.89 ± 5.1 | | Moderate | 49 | 7.9 ± 7.9 | |
| *Alternaria* | Mild | 79 | 0.8 ± 2.1 | 1.202 | Mild | 66 | 1.38 ± 3.4 | −1.201 |
| | Moderate | 36 | 0.42 ± 1.3 | | Moderate | 49 | 2.29 ± 4.6 | |
| 6 Grass pllen | Mild | 79 | 1.07 ± 3 | −0.451 | Mild | 66 | 2.51 ± 5 | 0.299 |
| | Moderate | 36 | 1.36 ± 3.4 | | Moderate | 49 | 2.33 ± 5 | |

*D. farinae*: Dermatophagoides farinae; *D. pteronyssinus*: Dermatophagoides pteronyssinus;
SD: standard deviation; SPT: skin prick test.
**t*-test was used to evaluate whether the mean skin prick test measurements changed according to disease severity prior to and during the pandemic.

**Table S3** Regression analysis for association between skin prick test results and VAS.

| Independent variables | Model 1 | Model 2 | Model 3 | Model 4 | Model 5 |
|---|---|---|---|---|---|
| **Dependent variable: VAS (nasal blockage)** | | | | | |
| Constant | 3.999*** | 3.948*** | 4.124*** | 4.159*** | 4.276*** |
| Cat at home | 1.149*** | 0.999** | 1.186*** | 1.192*** | - |
| D. farinea in SPT | 0.105*** | - | - | - | - |
| *D. pteronyssinus*in SPT | - | 0.103*** | - | - | - |
| *Alternaria* in SPT | - | - | 0.026 | - | - |
| 6 Grass pollen in SPT | - | - | - | -0.007 | - |
| Cat in SPT | - | - | - | - | 0.115** |
| **Dependent variable: VAS (sneezing)** | | | | | |
| Constant | 4.305*** | 4.246*** | 4.287*** | 4.285*** | 4.461*** |
| Cat at home | 1.026** | 0.942*** | 1.069** | 0.883** | - |
| D. farinea in SPT | 0.032 | - | - | - | - |
| *D. pteronyssinus* in SPT | - | 0.054 | - | - | - |
| *Alternaria* in SPT | - | - | 0.067 | - | - |
| 6 Grass pollen in SPT | - | - | - | 0.056 | - |
| Cat in SPT | - | - | - | - | 0.105** |
| **Dependent variable: VAS (nasal discharge)** | | | | | |
| Constant | 4.489*** | 4.245*** | 4.245*** | 4.299*** | 4.664*** |
| Cat at home | 1.055** | 0.942** | 1.086** | 0.916** | - |
| Bird at home | - | 0.751** | 0.854** | 0.759** | - |
| D. farinea in SPT | 0.040 | - | - | - | - |
| D. pteronyssinus in SPT | - | 0.057 | - | - | - |
| *Alternaria* in SPT | - | - | 0.086 | - | - |
| 6 Grass pollen in SPT | - | - | - | 0.045 | - |
| Cat in SPT | - | - | - | - | 0.103** |
| **Dependent variable: VAS (nasal itching)** | | | | | |
| Constant | 4.243*** | 4.216*** | 4.273*** | 4.271*** | 4.408*** |
| Cat | 1.004** | 0.935** | 1.033** | 0.934** | - |
| D. farinea in SPT | 0.044 | - | - | - | - |
| *D. pteronyssinus* in SPT | - | 0.047 | - | - | - |
| *Alternaria* in SPT | - | - | 0.035 | - | - |
| 6 Grass pollen in SPT | - | - | - | 0.029 | - |
| Cat in SPT | - | - | - | - | 0.110** |
| **Dependent variable: VAS (eye symptoms)** | | | | | |
| Constant | 1.635*** | 1.587*** | 1.634*** | 1.612*** | 1.660*** |
| D. farinea in SPT | -0.004 | - | - | - | - |
| *D. pteronyssinus* in SPT | - | 0.024 | - | - | - |
| *Alternaria* in SPT | - | - | -0.003 | - | - |
| 6 Grass pollen in SPT | - | - | - | 0.007 | - |
| Cat in SPT | - | - | - | - | -0.018 |

*D. farinae*: Dermatophagoides farinae; *D. pteronyssinus*: Dermatophagoides pteronyssinus; SPT: skin prick test; VAS: visual analogue score.

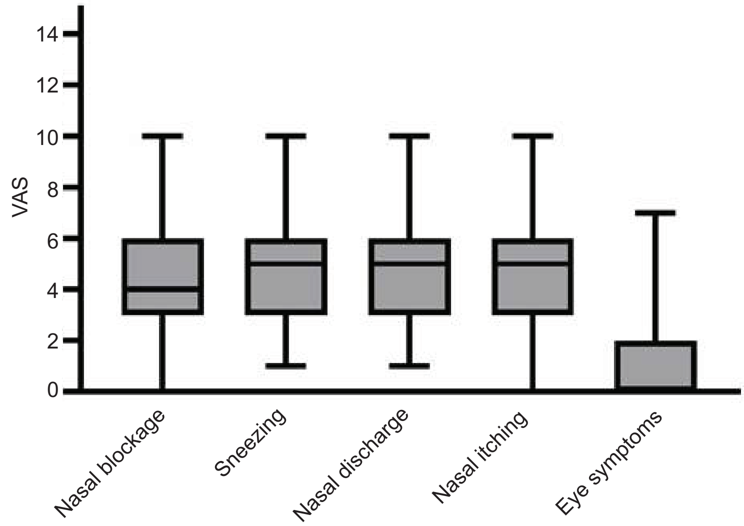


**Figure S1** VAS during the pandemic.