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Genetic predisposition and increased environmental allergen exposure in cat allergy: The pandemic is a very good example

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Abstract
Objective: Domestic cats are among the most common sources of indoor allergens. There was an increase in indoor allergen exposure, especially cats and house dust mites, as people spent more time at home during the COVID-19 pandemic lockdowns. In this study, our aim was to examine the frequency of cat sensitization and ownership after the COVID-19 pandemic and its relationship with other indoor and pollen allergen sensitizations.
Methods: The data of patients who applied to our clinic between 2018 and 2022, with a history of hypersensitivity reaction after contact with cats and diagnosed with cat allergy by positive skin test or specific immunoglobulin E (sIgE) level, were examined retrospectively. Skin test was performed in accordance with the manufacturer's instructions. sIgE levels against cat allergens were measured using The Phadia CAP System FEIA method.
Results: There has been an increase in the rate of cat ownership (P < 0.001) during the COVID-19 pandemic. The prevalence of cat allergy in 2020 and beyond (5.89%) was significantly higher than the pre-COVID period (4.53%; P < 0.001). The prevalence of concomitant df (dermatophagoides farinae) (1.53-1.58%), dp (dermatophagoides pterynossinus) (1.53-1.48%), and pollen (3.47-3.62%) hypersensitivity before COVID-19 did not differ significantly after COVID, but the prevalence of "penicillium" hypersensitivity before COVID (= 8/5825) was found to be significantly lower (0.14-1.28%).
Conclusion: During the pandemic period, both the increase in cat ownership and spending more time indoors seem to have led to an increase in cat allergy. No increase in indoor allergen sensitization other than penicillium accompanying cat allergy was detected.

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Introduction

Domestic cats are among the most common sources of indoor allergens, and cat allergy in humans is the most common mammalian immunoglobulin E (IgE)-mediated hypersensitivity.[1] The frequency of cat ownership is increasing in the general population, although the exact rate is unknown. An online study with 27,000 respondents from 22 countries revealed that on average 23% had cats, with cat ownership ranging from 6% in South Korea to 57% in Russia.[2] In Europe, about 26% of people consulted for a possible allergy to inhaled allergens are sensitized to cats.[3] Studies on the prevalence of cat allergy in our country are limited.[4] In a study, pet hypersensitivity (cat/dog) was detected in 54 of 209 atopic subjects (25.8%).[5]

Patients with cat hypersensitivity experience a range of allergic symptoms, such as conjunctivitis, rhinitis, asthma, urticaria-angioedema, or rarely anaphylaxis. The diagnosis of cat allergy is based on a compatible medical history and physical examination, confirmed by a positive skin prick test result or specific IgE (sIgE).[6]

Severe acute respiratory syndrome coronavirus 2 (SARSCoV2) is a new coronavirus that was identified at the end of 2019, causing death by infecting millions of people all over the world.[7,8] Various protection methods, including home isolation, have been recommended by the World Health Organization (WHO) to prevent transmission during the coronavirus disease 2019 (COVID-19) pandemic.[9] In accordance with these recommendations, long-term lockdowns were implemented. An increase in sensitivity to indoor allergens due to increased time spent at home has been confirmed in various studies[10,11]; however, there are very few studies in the literature examining the effects of the COVID-19 pandemic on cat sensitization.[11–13]

Considering the increase in pet ownership rates during the pandemic period and the increase in allergen exposure due to the lockdown, we initiated this study with the hypothesis that both situations may have increased cat hypersensitivity in our region. In this study, our aim was to examine all patients with cat hypersensitivity detected in our clinic in the last 5 years and to evaluate whether there is an increase in the frequency of cat sensitization and ownership after the COVID-19 pandemic, and if there is an increase, its relationship with other indoor and pollen allergen sensitizations.

Material and Methods

The medical records of the patients who were referred to the immunology and allergy polyclinic of our university hospital between 2018 and 2022 with atopic symptoms were reviewed retrospectively. Individuals who previously experienced hypersensitivity reactions (e.g., rhinitis and/or asthma) following exposure to cat allergens and proven with positive skin prick test or sIgE measurements against cat allergens were included in the study.

Measurement of sIgE

sIgE measurements against cat hair were measured using the Phadia CAP System FEIA method (Phadia, Uppsala, Sweden), and patients with a level more than 0.35 kUA/L on their test were deemed positive.

Skin prick test

Allergen extract drops were first applied to the forearm. This was followed by pricking the skin with a special lancet (Heinz Herenz Hamburg, Germany). A distance of more than 2 cm was ensured between different allergen extracts. At the end of 20 minutes, the induration size that was ≥ 3 mm larger than the size of the induration resulting from a negative control was considered positive.

Statistical Analyses

Data were analyzed using the Statistical Package for Social Sciences (SPSS) program (Version 23.0. NY). Descriptive statistics of the measurements were calculated as mean, standard deviation (SD), median, 25th and 75th quartiles, number, and percentage frequencies. The compliance of numerical type features obtained by measurement with normal distribution was examined with the Kolmogorov-Smirnov test; it was determined that they did not comply with normal distribution. Differences in cat prick sizes according to years were examined with Kruskal-Wallis analysis and significant differences were determined with post hoc Dunn test. The distribution of cat numbers according to years was examined with the Pearson chi-square test. The significance of the change in prevalence values according to years and the differences before and after COVID-19 were examined with the t-test for the difference between proportions. The relationship between the change in cat allergy over the years and sensitivity to indoor allergens was evaluated with Pearson correlation analysis. Statistical significance level was accepted as P <= 0.05.

Results

Patient characteristics

By screening 14,190 prick tests performed in our clinic and examining the positive sIgE values against cat allergens, 755 patients with cat allergy were identified. Table 1 presents the baseline characteristics of these patients. Among them, the majority (n = 493; 74.8%) were women. The median age of patients was 27.0 (22–37). While 55 of the patients were diagnosed with only positive sIgE, 14 patients had both skin prick test and sIgE positivity. In the majority of patients, cat-specific IgE was not tested; however, in those who were tested, median prick size was 5.0 mm (3.0–6.5). Allergic rhinitis was the most typical clinical manifestation (n = 742; 98%). The most common concomitant allergen sensitization was pollen (n = 506; 72.4%) in the patients with cat hypersensitivity.

Change in cat hypersensitivity and cat ownership rates over the years

These results indicate that the frequency of cat ownership at home has changed significantly over the years (2018 and

2019 was used to represent the pre-COVID period and 2020, 2021, and 2022 to represent the during COVID period). Especially in the during COVID years of 2021 and 2022, there has been an increase in the rate of cat ownership (P < 0.001) (Table 2).

When examined on a yearly basis, it is seen that the prevalence of cat allergy is higher, especially in recent years, although not in general (Figure 1). In addition, it was determined that the prevalence of cat allergy in 2020 and beyond (5.89%) was significantly higher than the pre-COVID period (before 2020 it was 4.53%) (P < 0.001) (Table 3).

The official cat adoption rates (obtained from the province environment and urbanization directorate) peaked in 2021, when lockdowns were common during the pandemic; the lowest rate was observed in 2023 (Figure 2).

Table 1 Demographic characteristics of the patients with cat hypersenisitivity.

Parameter	Value
Age, years (median)	27.0 (22-37)
Gender (f/m)	493/755
Family history of allergic diseases	105/755
Concomitant allergic diseases	
Allergic rhinitis	742/757 (98%)
Asthma	95 (12.5%)
Drug hypersensitivity	33 (4.4%)
Food allergy	23 (3.0%)
Venom allergy	10 (1.3%)
Atopic dermatitis	38 (5.0%)
Urticaria angioedema	43 (5.7%)
Allergic contact dermatitis	12 (1.6 %)
Eosinophil count, cells/μl (median)	240 (140-390)
Eosinophil percentage (median)	3.3 (2.10-5.2)
Total IgE, kuA/L (median)	164 (62.8-376.2)
Concomitant hypersensitivity to other allergens	
df*	222/702 (31.6%)
dp**	214/702 (30.5%)
Aspergillus	97/650 (14.9 %)
Penicillium	115/702 (16.4%)
Germanica	265/702 (37.7%)
Pollen	506/699 (72.4%)

*dermatophagoides farinae; **dermatophagoides pterynossinus.

The correlation between the frequency of cat ownership and cat allergy prevalence by year was calculated and a good correlation of 0.60 was observed. Due to the small number of years (k = 5), this relationship was not found to be statistically significant (P 0.285).

Cat allergy and co-sensitization to other allergens

The prevalence of concomitant df (dermatophagoides farinae) (1.53-1.58%), dp (dermatophagoides pterynossinus) (1.53-1.48%), and pollen (3.47-3.62%) hypersensitivity before COVID-19 did not differ significantly after COVID, but the prevalence of "penicillium" hypersensitivity before COVID (= 8/5825) was found to be significantly lower (0.14-1.28%).

The prevalence of "germanica" before COVID-19 (2.37% = 138/5825) was found to be significantly higher than the prevalence of "germanica" after COVID (1.52% = 127/8365) Table 3.

The relationships between cat allergy rates determined by years and sensitivity rates to indoor allergens are given in Table 4. There is a positive significant correlation between the prevalence of cat allergy and the prevalence of df, dp prevalence, and pollen prevalence, respectively. This result shows that as the rate of cat allergy increases, df, dp, and pollen allergies also increase; however, there is no significant change in the prevalence of aspergillus, penicillium, and germanica with the change in cat prevalence.

Discussion

In our study, we showed that the prevalence of cat allergy and cat ownership increased significantly during the COVID-19 pandemic compared to before; except for penicillium, we did not observe an increase in hypersensitivity to other concomitant indoor allergens in people with cat allergy.

There are rare studies in literature investigating the prevalence of cat allergy before and during COVID-19.[12,13] Furthermore, there is no study examining its relationship with indoor allergens.

Exposure time required for sensitization to an allergen is unclear. Due to the intermittent lockdowns lasting more than 1 year during the COVID-19 pandemic, people spent more time indoors and the duration of exposure to indoor allergens increased. According to certain research, exposure to cats in the first year of life may reduce the likelihood of developing allergic asthma when combined with other genetic and environmental risk factors,[14,15]

Table 2 Distribution of the frequency of cat ownership by years in patients with cat allergy.

		Years										Total
		2018		2019		2020		2021		2022		
		n	%	n	%	n	%	n	%	n	%	
Cat ownership	Yes	22	16.2%	27	21.1%	29	27.6%	53	33.8%	75	32.5%	206
	No	9	6.6%	9	7.0%	9	8.6%	28	17.8%	53	22.9%	108
Total		136		128		105		157		231		757

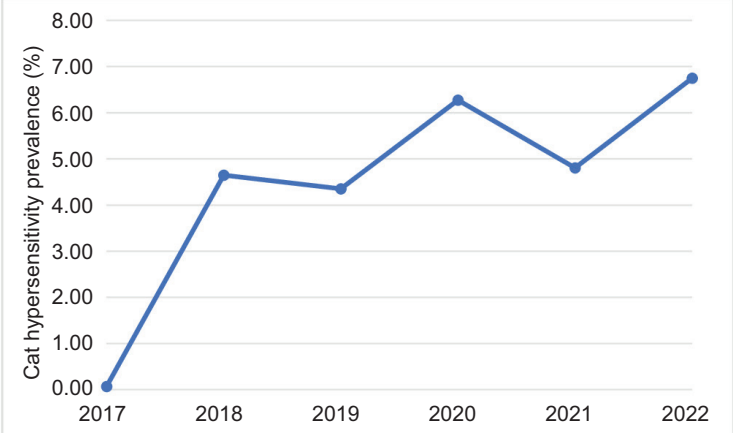

Figure 1 Change in cat allergy prevalence over the years.

Table 3 Change in sensitivity rates to other allergens concomitant to cat allergy over the years.

Years	Total Number of Patients Tested	Total number of positive cat prick tests and positive cat-specific igE value			df		dp		Mold		Germanica		Pollen	
		n	%	Prevalence before 2020 and after 2020 (%)	n	%	n	%	n	%	n	%	n	%
2018	2884	136	4.7	4.53	56	1.94	49	1.70	1	0.03	72	2.50	103	3.57
2019	2941	128	4.35		33	1.12	40	1.36	7	0.24	66	2.24	99	3.37
2020	1674	105	6.27	5,89	37	2.21	32	1.91	38	2.27	27	1.61	57	3.41
2021	3268	157	4.80		41	1.25	35	1.07	44	1.35	40	1.22	106	3.24
2022	3423	231	6.75		54	1.58	57	1.67	25	0.73	60	1.75	140	4.09

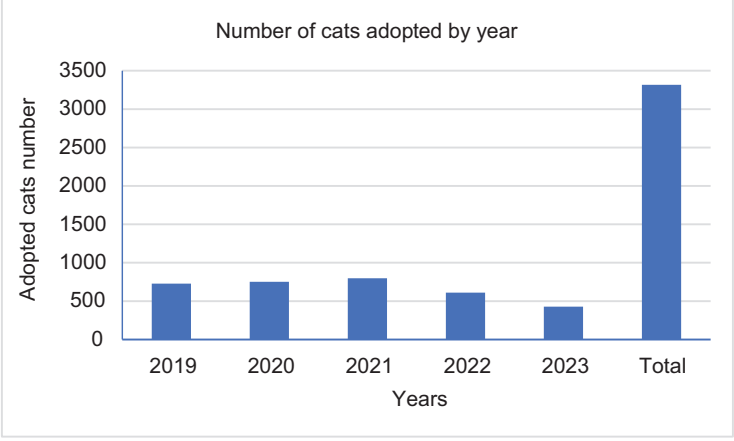

Figure 2 Change in official cat adoption rates over the years.

Table 4 Relationships between cat allergy and sensitization to other allergens.

		df Prevalence	dp Prevalence	Aspergillus Prevalence	Penicillium Prevalence	Germanica Prevalence	Pollen Prevalence
Cat hypersensitivity prevalence	r	879	930	236	578	702	951
	P	021	007	653	230	120	004

while there are studies showing that early exposure to cats and dogs increases sensitivity and allergic diseases. This genetic predisposition may vary on an individual basis by changing the Th2 or Th1 balance, depending on allergen and endotoxin exposure.[16] Although controversial, if the parent is atopic, early pet exposure may lead to allergic sensitization and diseases.[17]

When we compared the prevalence of co-sensitizations to other indoor allergens in the patients with cat allergy before and during COVID-19, we observed that the prevalence of house dust mites (HDMs) did not change and only the prevalence of penicillium increased significantly compared to before COVID-19. No significant change was observed in the prevalence of co-sensitization to pollen as an outdoor allergen. The increase in the prevalence of cat hypersensitivity may be due to the increase in the rate of cat ownership rather than spending more time indoors. Owning a cat is a risk factor for new onset cat sensitization.[18] As a matter of fact, in our study, we observed an increase in the cat ownership rate during COVID-19. When the data from official cat care homes of the last 5 years was examined, cat adoption rates peaked in 2021 when lockdowns were common and decreased dramatically in 2023 when the pandemic restrictions ended. This result is consistent with our increased ownership rates during and after COVID-19. Studies conducted before the COVID-19 pandemic also show that the prevalence of cat allergy is an increasing trend.[19] While the rate of cat allergy diagnosis in patients with symptoms of exposure to inhaled allergens in Europe is 26%,[3] in our clinic, according to the data of the last 5 years, this rate was 5.3%. This indirectly shows that cat exposure and ownership rates are lower in our country, although it has increased after COVID-19.

Since the structural properties of each allergen and the amount of presence in the environment are different, differences in sensitization times may cause this result. Cat allergens are smaller particles (2–15 μm) than other indoor allergens that easily rendered and remain airborne for several hours under normal ventilation.[20-22] It has been estimated that the amount of cat allergen inhaled daily in a home with a cat can reach up to 2 μg Fel d 1 (protein) per day, which is significantly greater than the daily exposure computed for dust mite or pollen allergens.[23] A study examining the properties of indoor allergens and emphasizing that these different properties (physical attributes, like the size, hydrophobicity, and charge of allergen particles, etc.) of these allergens affect the ability to stimulate the IgE response in genetically predisposed individuals has recently been published.[24] Another reason why the increase in the prevalence of cat allergy is not observed in other concomitant allergens is because in this period, the transfer of cat allergens from outside to inside actually decreased. Although it is speculative, we believe that other indoor allergens were already present in the home environment and people were already exposed to them; but those who did not have cats at home were not exposed to cat allergens, at least in the indoor environment. When cat ownership rate and exposure time indoor increase, sensitivity increases. Also, evolutionary distance of the allergens from humans is important, so the immune system's ability to discriminate between foreign and self-proteins is likely different for mammalian allergens versus arthropod allergens.[25]

Polysensitization is frequent in atopic individuals.[26] Coexistence of detectable cockroach and mold allergens are factors associated with increased dust mite exposure.[27] We planned to evaluate whether the same relationship exists between cats and other allergens. Although co-sensitization to HDM and pollen allergens do not differ before and during COVID-19, there was a positive significant correlation between the prevalence of cat allergy and the prevalence of df, dp, and pollen prevalence, respectively. According to our results, the most common concomitant allergen sensitization was pollen in the patients with cat hypersensitivity. Consistent with our findings, the frequency of cat sensitization was significantly higher in the patients in the timothy allergic group compared with those without timothy grass allergy (33.8% vs 12.3%; $P < 0.001$) in another study.[28] In a cross-sectional study with children sensitized to cat dander, 88% had co-sensitization to HDM and 93% had co-sensitization to grass pollen.[29] These rates were not this high in adults, according to our results. In another study, HDMs, cat, pollen, *Artemisia*, and *Cupressus* sensitization and proportion of polysensitization increased in AR (allergic rhinitis) patients during the COVID-19 pandemic compared to the pre-pandemic period (9.1% vs 3%; $P < 0.001$).[30] On the contrary, another study from China where the total positive rate of sIgE tests in AR patients significantly decreased after the COVID-19 epidemic compared to before emphasizes the importance of geographical differences even in the pandemic.[31]

One of the limitations of this study is that the actual cat adoption rates obtained from official institutions may not reflect reality due to the high number of unregistered adoptions. Also due to the retrospective design of the study, the cat ownership status of all patients was not clarified. Since this study included patients who were referred to our clinic due to atopic symptoms and underwent skin prick testing, it does not reflect the prevalence of the general population.

This is the first study comparing the changes in cat allergy prevalence before and during COVID-19 and its relationship with prevalence of other indoor and pollen allergens.

Our study reveals that cat ownership and cat hypersensitivity are an increasing trend. During the pandemic period, both the increase in cat ownership and spending more time indoors seem to have led to an increase in cat allergy. This seems to confirm the environmental part of the view of the integration of genetics and environmental exposures that explain the development of diseases such as allergic rhinitis and allergic asthma. In addition, our study shows that the more frequent and intense allergen exposure is, the easier the development of allergic disease may be in terms of cat allergy.

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Ethical Statement

Ethics approval was obtained from Erciyes University, Ethics Committee. (Date: 25.09.2023, No: 2023/630). This

retrospective study fully conformed to the principles of the Declaration of Helsinki. Due to its retrospective nature, the study was exempted from obtaining written informed consent by the ethics committee.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author, [author initials], upon reasonable request.

Authors Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Bahar Arslan, Gülden Paçacı Çetin and İnsu Yılmaz. The first draft of the manuscript was written by Bahar Arslan and all authors commented on previous versions of the manuscript. All authors read and approved the manuscript.

Conflict of Interest

The authors have no conflict of interests to declare that are relevant to the content of this article.

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