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Brief Communication

Pet Ownership Increases the Exhaled Nitric Oxide and Asthma Severity in Children With Atopic Asthma

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ABSTRACT

Exposure to pets can trigger symptoms in asthmatic children sensitized to pets. However, little is known about the association between pet ownership and asthma morbidity in children who are not sensitized to pets. We aimed to investigate the effect of pets on lung function, airway inflammation, and morbidity in children with asthma, and to determine whether the effect of exposure to pets vary based on pet sensitization status. A total of 975 asthmatic children, aged 5–15 years, were enrolled in the Korean Childhood Asthma Study. Pet ownership and asthma morbidity were evaluated by questionnaires or pediatrician evaluations. Pulmonary function, fractional exhaled nitric oxide (FeNO), and atopic status were assessed. FeNO levels were significantly higher in children with pets than in those without pets. Pet ownership significantly increased FeNO levels in atopic asthmatic children, irrespective of pet sensitization status. In children sensitized to pets, the geometric mean was 46.6 (range of 1 standard deviation, 26.9–81.5) for those with pets vs. 27.2 (13.8–53.6) for those without pets ($P < 0.001$). In children without sensitization to pets, the geometric mean was 37.3 (15.0–53.6) for pet owners vs. 25.2 (12.9–49.2) for non-owners ($P = 0.014$).

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The multiple regression analysis also revealed that pet ownership was significantly associated with increased FeNO levels and asthma severity in atopic asthmatic children. Pet ownership increased the FeNO levels and asthma severity, regardless of pet sensitization status, in children with atopic asthma. Exposure to pets could increase airway inflammation and disease severity even in atopic asthmatic children who are not sensitized to pets.

Keywords: Asthma; child; fractional exhaled nitric oxide testing; pets

INTRODUCTION

Asthma is a chronic airway inflammatory disease characterized by reversible airway limitation and bronchial hyperresponsiveness (BHR).[1] Although asthma is a heterogeneous disease, eosinophilic airway inflammation is a primary feature of childhood asthma, which results from exposure to allergens in sensitized children.[2] Exposure to allergens activates airway epithelial cells to produce pro-inflammatory cytokines and initiates a cascade that leads to the development of childhood asthma.[3]

Recently, the number of pets has been increasing,[4] and sensitization to cats and dogs has also increased among Korean children.[5] The association between early-life exposure to pets and the later risk of childhood asthma has been controversial.[6-8] A large birth cohort network reported that cat and dog ownership were not associated with pet sensitization, but sensitization to pets was linked to asthma in school-age children.[9] In addition, exposure to pet allergens was associated with increased asthma exacerbation and poor asthma control among children sensitized to them.[10,13]

However, there is little information on the effect of exposure to pets on asthma morbidity in children not sensitized to pets. In asthmatic children not sensitized to pets, pet ownership can lead to the development of new sensitization but does not affect asthma symptoms.[10] In contrast, exposure to dog allergens was associated with poor asthma control, regardless of sensitization status, in children with asthma.[14] Furthermore, little is known about the effect of exposure to pets on objective measures of airway inflammation and lung function other than symptoms in asthmatic children without sensitization to pets.

Hence, we aimed to investigate the effect of exposure to pets on airway inflammation and disease severity in asthmatic children based on sensitization status.

MATERIALS AND METHODS

Study design

A total of 975 asthmatic children (aged 5–15 years) were enrolled in the Korean Childhood Asthma Study, an ongoing nationwide observational prospective cohort study.[15] Asthma was diagnosed in patients with wheezing or cough, a significant bronchodilator response of forced expiratory volume in 1 second (FEV1) of greater than 12% from baseline on a pulmonary function test and/or a provocative concentration resulting in a 20% fall in FEV1 of ≤ 16 mg/mL on methacholine bronchial provocation tests.[16-18] Asthma severity was classified as mild intermittent, mild persistent, moderate persistent, or severe persistent according to the National Asthma Education and Prevention Program (NAEPP) recommendations.[19]

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Data of the participants' baseline characteristics were obtained using a set of questionnaires assessing pet ownership, asthma control and exacerbation. Pulmonary function, BHR, fractional exhaled nitric oxide (FeNO) levels, serum total IgE, and skin prick test (SPT) results for 18 common inhalant allergens were also evaluated. All participants continued to receive asthma medications in accordance with the NAEPP guidelines.[19] Participants' responses to treatment, including asthma control levels and exacerbation episodes, lung function, FeNO levels, and changes in demographic data and environmental factors, were evaluated every 6 months during regular visits. To investigate the effect of pets on asthma symptoms and airway inflammation according to the pet sensitization status, we included 811 children with data on both pet ownership and SPT results in the analysis. No significant difference was observed in the baseline characteristics between children included in the analysis and those who were not included (data not shown). Details of the study methods used to establish and track the cohort are provided elsewhere.[15,20] The Institutional Review Boards of all participating institutions approved the study protocol: Asan Medical Center (IRB No. 2016-0914); Seoul National University Hospital (IRB No. 1607-165-779); Pusan National University Yangsan Hospital (IRB No. 05-2016-121); Inha University Hospital (IRB No. 2016-07-016-008); Seoul National University Bundang Hospital (IRB No. 10-2017-036); Chonnam National University Hospital (IRB No. 2017-201); Korea University Anam Hospital (IRB No. 2015 AN 0310); Soonchunhyang University Hospital in Seoul (IRB No. 2017-01-011-002); Bucheon St. Mary's Hospital (IRB No. HC16SNMI0056); Sungkyunkwan University Samsung Changwon Hospital (IRB No. 2017-02-006-001); Kangdong Sacred Heart Hospital (IRB No. 2016-12-007-001); Catholic University of Korea, Uijeongbu St. Mary's Hospital (IRB No. UC16ONMI0113); Chungbuk National University Hospital (IRB No. 2016-09-003); Dankook University Hospital (IRB No. 2017-02-013); Korea University Guro Hospital (IRB No. 2016GR0336); Inje University Seoul Paik Hospital (IRB No. 2016-314); CHA Gangnam Medical Center (IRB No. GCI-16-37); National Health Insurance Service Ilsan Hospital (IRB No. NHIMC 2017-02-008); and Soonchunhyang University School of Medicine in Bucheon (IRB No. 2016-08-007-009). Written informed consent was obtained from both the patient and the caregiver.[15]

Statistical analysis

The clinical asthma outcome variables, including severity, control, exacerbation, pulmonary function, and FeNO level were compared. The χ^2 test or Fisher's exact test was used for analyzing categorical variables, while the independent *t*-test, one-way analysis of variance, Mann–Whitney test, and Kruskal–Wallis test were used for analyzing continuous variables, as appropriate. Multiple comparisons of more than 2 groups were adjusted using the Bonferroni correction. A multiple regression analysis was performed using the enter method. For FeNO (continuous outcome) measured over time, a linear mixed effects model with the patient as a random effect and pet ownership as a fixed effect was applied. For asthma severity, a generalized linear mixed effects model was used to calculate the odds ratio for repeated measures. Data management and statistical analyses were performed using the R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). All reported *P* values were two-sided, and a *P* value of < 0.05 was considered statistically significant.

RESULTS

Patients' characteristics

The study consisted of 811 participants, of whom 518 were male and 293 were female. The mean age of the participants was 9.6 ± 2.6 years. A total of 290 (35.8%) patients had mild

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Table 1. Baseline characteristics of children included in the analysis

Variables	Participants (n = 811)
Sex	
Male	518 (63.9)
Female	293 (36.1)
Age (yr)	9.6 ± 2.6
Height (cm)	136.6 ± 15.5
Weight (kg)	36.2 ± 14.2
Asthma severity	
Mild intermittent	290 (35.8)
Mild persistent	311 (38.4)
Moderate persistent	203 (25.1)
Severe persistent	5 (0.6)
Asthma controller medication	
None	195 (24.2)
LTRA monotherapy	77 (9.6)
ICS monotherapy	155 (19.2)
ICS + LTRA	150 (18.6)
ICS + LABA	84 (10.4)
ICS + LTRA + LABA	145 (18.0)
Other allergic diseases	
Allergic rhinitis	616 (76.2)
Atopic dermatitis	162 (20.0)
Pet ownership	
Dog	88 (10.9)
Cat	27 (3.3)
Both	9 (1.1)
None	686 (84.7)
No. of emergency visits within 1 year	
None	655 (81.4)
≥ 1	150 (18.6)
No. of admission within 1 year	
None	681 (84.7)
≥ 1	123 (15.3)
No. of steroids used within 1 year	
None	522 (66.6)
≥ 1	262 (33.4)
Frequency of asthma symptoms within 3 months	
< 2 per week	666 (84.5)
≥ 2 per week	122 (15.5)
Frequency of bronchodilator use within 3 months	
< 2 per week	670 (85.0)
≥ 2 per week	118 (15.0)
ACT score	21.0 ± 4.3
FEV1 % predicted	90.2 ± 16.7
FeNO	25.2 (12.2–52.3)

Data are expressed as number (%), mean ± SD, or geometric mean (range of 1 SD).
LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; LABA, long-acting β-agonist; ACT, asthma control test; FEV1, forced expiratory volume in 1 second; FeNO, fractional exhaled nitric oxide; SD, standard deviation.

intermittent asthma, 311 (38.4%) had mild persistent asthma, 203 (25.1%) had moderate persistent asthma, and 5 (0.6%) had severe persistent asthma. Approximately 15.3% of the participants owned a pet, with 88 (10.9%) owning a dog, 27 (3.3%) owning a cat, and 9 (1.1%) owning both. The participants' characteristics are summarized in **Table 1**.

Differences in pulmonary function, airway inflammation, and asthma outcome variables at enrollment according to the pet ownership status

Participants with pets had more severe asthma than those without pets ($P = 0.003$). Moreover, participants with pets had a significantly higher rate of asthma controller

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medication use, including combination therapy with long-acting β-agonist and leukotriene receptor antagonist, compared to those without pets ($P = 0.004$). The prevalence of admission due to asthma exacerbation in the previous 12 months was significantly higher in participants with pets (22.0%) than in those without pets (14.1%) ($P = 0.004$). Participants with pets had significantly higher FeNO levels (geometric mean, 36.4; range of 1 standard deviation, 16.0–83.1) than those without pets (23.8, 11.9–47.5) ($P < 0.001$). The levels of FEV1 were significantly lower in participants with pets (87.2 ± 18.3% pred) than in those without pets (90.7 ± 16.3% pred) ($P = 0.049$, **Table 2**).

Table 2. Comparison of pulmonary function, airway inflammation, and other asthma outcome variables based on pet ownership status

Variables	Pet ownership	
	Yes (n = 124)	No (n = 687)
Sex		
Male	75 (60.5)	443 (64.5)
Female	49 (39.5)	244 (35.5)
Age (yr)	10.9 ± 2.8***	9.3 ± 2.5
Height (cm)	144.5 ± 16.0	135.2 ± 14.9
Weight (kg)	42.7 ± 16.6	35.0 ± 13.4
Asthma severity		
Mild intermittent	30 (24.2)**	260 (38.0)
Mild persistent	49 (39.5)	262 (38.2)
Moderate persistent	45 (36.3)	158 (23.1)
Severe persistent	0 (0.0)	5 (0.7)
Asthma controller medication		
None	24 (19.5)**	171 (25.0)
LTRA monotherapy	8 (6.5)	69 (10.1)
ICS monotherapy	14 (11.4)	141 (20.6)
ICS + LTRA	25 (20.3)	125 (18.3)
ICS + LABA	19 (15.4)	65 (9.5)
ICS + LTRA + LABA	33 (26.8)	112 (16.4)
Other allergic diseases		
Allergic rhinitis	93 (75.0)	523 (76.5)
Atopic dermatitis	21 (16.9)	141 (20.6)
No. of emergency visits within 1 year		
None	95 (76.6)	560 (82.2)
≥ 1	29 (23.4)	121 (17.8)
No. of admission within 1 year		
None	96 (78.0)	585 (85.9)
≥ 1	27 (22.0)*	96 (14.1)
No. of steroids used with 1 year		
None	80 (67.2)	442 (66.5)
≥ 1	39 (32.8)	223 (33.5)
Frequency of asthma symptoms within 3 months		
< 2 per week	101 (84.2)	565 (84.6)
≥ 2 per week	19 (15.8)	103 (15.4)
Frequency of bronchodilator use within 3 months		
< 2 per week	103 (84.4)	567 (85.1)
≥ 2 per week	19 (15.6)	99 (14.9)
ACT score	20.3 ± 4.5	21.2 ± 4.2
FEV1 % predicted	87.2 ± 18.3*	90.7 ± 16.3
FeNO	36.4*** (16.0–83.1)	23.8 (11.9–47.5)

Data are expressed as number (%), mean ± SD, or geometric mean (range of 1 SD).
LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; LABA, long-acting β-agonist; ACT, asthma control test; FEV1, forced expiratory volume in 1 second; FeNO, fractional exhaled nitric oxide; SD, standard deviation.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, compared with participants without pets.

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Differences in pulmonary function, airway inflammation, and other asthma outcome variables according to atopy and pet ownership status

Atopic asthmatic children with pets had a significantly higher asthma severity than atopic asthmatic children without pets ($P = 0.046$). In addition, atopic asthmatic children with pets had a significantly higher rate of asthma controller medication use than atopic asthmatic children without pets ($P = 0.028$). Moreover, atopic asthmatic children with pets had significantly higher FeNO levels (42.3, 20.2–88.5) than atopic asthmatic children without pets (25.9, 13.2–50.7) ($P < 0.001$). Pet ownership also decreased FEV1 levels in atopic asthmatic children (86.8 ± 17.2% pred vs. 91.0 ± 15.8% pred) ($P = 0.011$). However, no significant difference was observed in the asthma outcome variables among non-atopic asthmatic children based on pet ownership status (**Table 3**).

Table 3. Comparison of lung function, airway inflammation, and other asthma outcome variables based on atopy and pet ownership status

Variables	Pet ownership			
	Atopic asthmatic children (n = 634)		Non-atopic asthmatic children (n = 177)	
	Yes (n = 92)	No (n = 542)	Yes (n = 32)	No (n = 145)
Sex				
Male	57 (62.0)	356 (65.7)	18 (56.3)	87 (60.0)
Female	35 (38.0)	186 (34.3)	14 (43.7)	58 (40.0)
Age (yr)	11.0 ± 2.6***,‡‡‡	9.4 ± 2.5†	10.7 ± 3.1‡‡	9.0 ± 2.5
Height (cm)	145.0 ± 15.5	135.5 ± 14.8	142.9 ± 17.7	134.0 ± 15.5
Weight (kg)	42.8 ± 17.1	35.2 ± 13.3	42.6 ± 15.3	34.6 ± 13.6
Asthma severity				
Mild intermittent	26 (28.3)*	229 (42.4)†,‡‡‡	4 (12.5)	31 (21.4)
Mild persistent	33 (35.9)	193 (35.7)	16 (50.0)	69 (47.6)
Moderate persistent	33 (35.9)	115 (21.3)	12 (37.5)	43 (29.7)
Severe persistent	0 (0.0)	3 (0.6)	0 (0.0)	2 (1.4)
Asthma controller medication				
None	19 (20.9)*,‡‡‡	147 (27.3)††,‡‡‡	5 (15.6)	24 (16.7)
LTRA monotherapy	5 (5.5)	54 (10.0)	3 (9.4)	15 (10.4)
ICS monotherapy	11 (12.1)	121 (22.4)	3 (9.4)	20 (13.9)
ICS + LTRA	12 (13.2)	64 (11.9)	13 (40.6)	61 (42.4)
ICS + LABA	17 (18.7)	59 (10.9)	2 (6.3)	6 (4.2)
ICS + LTRA + LABA	27 (29.7)	94 (17.4)	6 (18.8)	18 (12.5)
Other allergic diseases				
Allergic rhinitis	78 (84.8)††,‡‡‡	447 (82.8)†††,‡‡‡	15 (46.9)	76 (52.8)
Atopic dermatitis	19 (20.7)	116 (21.5)	2 (6.3)	25 (17.2)
No. of emergency visits with 1 year				
None	71 (77.2)	443 (82.3)	24 (75.0)	117 (81.8)
≥ 1	21 (22.8)	95 (17.7)	8 (25.0)	26 (18.2)
No. of admission with 1 year				
None	69 (75.8)	469 (87.2)	27 (84.4)	116 (81.1)
≥ 1	22 (24.2)	69 (12.8)	5 (15.6)	27 (18.9)
No. of steroids used with 1 year				
None	59 (65.6)	349 (66.2)	21 (72.4)	93 (67.4)
≥ 1	31 (34.4)	178 (33.8)	8 (27.6)	45 (32.6)
Frequency of asthma symptoms with 3 months				
< 2 per week	74 (84.1)	458 (86.1)	27 (84.4)	107 (78.7)
≥ 2 per week	14 (15.9)	74 (13.9)	5 (15.6)	29 (21.3)
Frequency of bronchodilator use with 3 months				
< 2 per week	76 (84.4)	450 (85.2)	27 (84.4)	117 (84.8)
≥ 2 per week	14 (15.6)	78 (14.8)	5 (15.6)	21 (15.2)
ACT score	20.0 ± 4.4	21.4 ± 4.0	21.0 ± 4.6	20.6 ± 4.9
FEV1 % predicted	86.8 ± 17.2*,‡	91.0 ± 15.8	88.5 ± 21.5	89.6 ± 18.4
FeNO	42.3***,†††,‡‡‡ (20.2–88.5)	25.9†,‡‡‡ (13.2–50.7)	14.3 (6.8–29.9)	15.8 (8.3–30.1)

Data are expressed as number (%), mean ± SD, or geometric mean (range of 1 SD).
LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; LABA, long-acting β-agonist; ACT, asthma control test; FEV1, forced expiratory volume in 1 second; FeNO, fractional exhaled nitric oxide; SD, standard deviation.
$^{*}P < 0.05$, $^{***}P < 0.001$, compared with atopic asthmatic children without pets. $^{†}P < 0.05$, $^{††}P < 0.01$, $^{†††}P < 0.001$, compared with non-atopic asthmatic children with pets. $^{‡}P < 0.05$, $^{‡‡}P < 0.01$, $^{‡‡‡}P < 0.001$, compared with non-atopic asthmatic children without pets.

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Differences in pulmonary function, airway inflammation, and other asthma outcome variables based on the pet sensitization and ownership status in atopic asthmatic children

Pet ownership significantly increased FeNO levels in participants with sensitization to pets (pet ownership, 46.6 [26.9–81.5] vs. non-ownership, 27.2 [13.8–53.6]; $P < 0.001$). Likewise, pet ownership significantly increased FeNO levels in participants without sensitization to pets (pet ownership, 37.3 [15.0–53.6] vs. non-ownership, 25.2 [12.9–49.2]; $P = 0.014$) (**Table 4**).

Table 4. Comparison of pulmonary function, airway inflammation, and other asthma outcome variables based on pet sensitization and ownership status among atopic asthmatic children

Variables	Atopic asthmatic children (n = 634)			
	Sensitization to pet			
	Yes (n = 237)		No (n = 397)	
	Pet ownership			
	Yes (n = 51)	No (n = 186)	Yes (n = 41)	No (n = 356)
Sex				
Male	34 (66.7)	118 (63.4)	23 (56.1)	238 (66.9)
Female	17 (33.3)	68 (36.6)	18 (43.9)	118 (33.1)
Age (yr)	11.1 ± 2.5**,‡‡‡	9.7 ± 2.5†	10.9 ± 2.8	9.2 ± 2.5
Height (cm)	145.2 ± 15.3	137.9 ± 15.9	144.8 ± 15.9	134.2 ± 14.0
Weight (kg)	42.8 ± 18.6	37.2 ± 13.4	42.7 ± 15.3	34.1 ± 13.1
Asthma severity				
Mild intermittent	14 (27.5)	82 (44.6)	12 (29.3)	147 (41.3)
Mild persistent	17 (33.3)	58 (31.5)	16 (39.0)	135 (37.9)
Moderate persistent	20 (39.2)	43 (23.4)	13 (31.7)	72 (20.2)
Severe persistent	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.6)
Asthma controller medication				
None	10 (20.0)	49 (26.6)	9 (22.0)	98 (27.6)
LTRA monotherapy	2 (4.0)	14 (7.6)	3 (7.3)	40 (11.3)
ICS monotherapy	8 (16.0)	44 (23.9)	3 (7.3)	77 (21.7)
ICS + LTRA	4 (8.0)	17 (9.2)	8 (19.5)	47 (13.2)
ICS + LABA	10 (20.0)	28 (15.2)	7 (17.1)	31 (8.7)
ICS + LTRA + LABA	16 (32.0)	32 (17.4)	11 (26.8)	62 (17.5)
Other allergic diseases				
Allergic rhinitis	45 (88.2)*,‡	149 (80.1)	33 (80.5)	298 (84.2)
Atopic dermatitis	11 (21.6)*,‡	49 (26.3)	8 (19.5)	67 (18.9)
No. of emergency with 1 year				
None	37 (72.5)	158 (85.4)	34 (82.9)	285 (80.7)
≥ 1	14 (27.5)	27 (14.6)	7 (17.1)	68 (19.3)
No. of admission with 1 year				
None	38 (74.5)	166 (89.7)	31 (77.5)	303 (85.8)
≥ 1	13 (25.5)	19 (10.3)	9 (22.5)	50 (14.2)
No. of steroids used with 1 year				
None	33 (66.0)	130 (71.4)	26 (65.0)	219 (63.5)
≥ 1	17 (34.0)	52 (28.6)	14 (35.0)	126 (36.5)
Frequency of asthma symptoms with 3 months				
< 2 per week	41 (82.0)	161 (87.5)	33 (86.8)	297 (85.3)
≥ 2 per week	9 (18.0)	23 (12.5)	5 (13.2)	51 (14.7)
Frequency of bronchodilator use with 3 months				
< 2 per week	44 (86.3)	160 (87.4)	32 (82.1)	290 (84.1)
≥ 2 per week	7 (13.7)	23 (12.6)	7 (17.9)	55 (15.9)
ACT score	20.0 ± 4.0	21.5 ± 4.1	20.0 ± 5.0	21.3 ± 4.0
FEV1 % predicted	87.3 ± 17.8	90.6 ± 16.6	86.0 ± 16.5	91.2 ± 15.3
FeNO	46.9***,‡‡‡ (26.9–81.5)	27.2 (13.8–53.6)	37.3‡ (15.0–92.7)	25.2 (12.9–49.2)

Data are expressed as number (%), mean ± SD, or geometric mean (range of 1 SD).
LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; LABA, long-acting β-agonist; ACT, asthma control test; FEV1, forced expiratory volume in 1 second; FeNO, fractional exhaled nitric oxide; SD, standard deviation.
$^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, compared with children who are sensitized to pets but do not own pets. $^{†}P < 0.05$, compared with children who are not sensitized to pets but own pets. $^{‡}P < 0.05$, $^{‡‡‡}P < 0.001$, compared with children who are not sensitized to pets and do not own pets.

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Multiple regression model for FeNO and asthma severity

A multiple regression analysis of other factors that could affect FeNO levels and asthma severity was performed in atopic asthmatic children. Pet ownership significantly increased FeNO levels and asthma severity in atopic asthmatic children ($P < 0.001$, $P = 0.035$, respectively) (**Tables 5** and **6**).

Differences in FeNO and asthma severity based on the pet ownership status over 12-month study period in atopic asthmatic children

During the 12-month study period, the difference in FeNO levels between children having atopic asthma with and without pets remained significant at 6 months (pet ownership, 30.3 [13.1–69.7] vs. non-ownership, 22.9 [12.0–43.8]; $P = 0.009$), but was no longer significant at 12 months (pet ownership, 40.0 [13.3–72.3] vs. non-ownership, 24.8 [13.1–46.8]; $P = 0.071$) (**Supplementary Fig. S1**). Atopic asthmatic children with pets tended to have a higher proportion of persistent asthma than atopic asthmatic children without pets at both 6 and 12 months, though the difference was not statistically significant (pet ownership vs. non-ownership, 55.7% vs. 47.2% at 6 months; 56.8% vs. 46.8% at 12 months) (**Supplementary Fig. S2**).

Table 5. Multiple linear regression analysis for FeNO in atopic asthmatic children

Variables	FeNO	
	β	*P*
Sex		
Male vs. female	0.942	0.362
Age	1.091	< 0.001
Allergic rhinitis	0.939	0.454
Atopic dermatitis	1.221	0.006
Asthma severity		
Mild intermittent		
Mild persistent	1.115	0.191
Moderate persistent	1.144	0.211
Severe persistent	0.934	0.885
Asthma controller medication		
None (reference)		
LTRA monotherapy	0.955	0.727
ICS monotherapy	1.001	0.987
ICS + LTRA	0.813	0.110
ICS + LABA	0.766	0.034
ICS + LTRA + LABA	0.920	0.472
Sensitization to pets	1.054	0.407
Pet ownership	1.436	< 0.001

FeNO, fractional exhaled nitric oxide; LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; LABA, long-acting β-agonist.

Table 6. Multiple logistic regression analysis for asthma severity in atopic asthmatic children

Outcome variables	Asthma severity (intermittent vs. persistent)	
	aOR	*P*
Sex		
Male vs. female	1.22	0.339
Age	0.98	0.555
Sensitization to pets	0.69	0.073
Pet ownership	1.91	0.035
ICS		
None vs. use	14.38	< 0.001
Asthma onset		
< 6 yr vs. ≥ 6 yr	1.46	0.068

aOR, adjusted odds ratio; ICS, inhaled corticosteroid.

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DISCUSSION

Pet ownership increased FeNO levels and worsened clinical asthma outcomes, including severity, use of controller medications, and exacerbation, in all asthmatic children. After dividing the participants into atopic and non-atopic asthmatic children, we found that pet ownership increased FeNO levels, asthma severity, and the use of asthma medications in atopic asthmatic children. Furthermore, the effect of pets on FeNO levels in atopic asthma was independent of pet sensitization status. Multiple regression analysis confirmed the impact of pets on both FeNO levels and asthma severity, regardless of pet sensitization status in children with atopic asthma.

Owning pets increased FeNO levels in children with atopic asthma, but not in those with non-atopic asthma. Interestingly, the effect of pets on FeNO levels in children with atopic asthma was independent of pet sensitization status. In the general population, pet ownership or early-life exposure to pets has been associated with decreased FeNO levels,[21,22] while pet sensitization has been linked to increased FeNO levels.[23] These results suggest that early exposure to pets may help prevent allergies, possibly due to the diversity of the pet's host microbiome,[24] but pet sensitization may contribute to the development of airway inflammation. However, few studies have investigated the effect of exposure to pets on FeNO levels in asthma patients based on pet sensitization status. Among adolescents with asthma, exposure to a cat or dog increased FeNO levels in those sensitized to pets and not using steroid inhalers.[23] In asthmatic patients already sensitized to pets, exposure to pets triggers an allergic immune response, leading to airway inflammation. However, it is necessary to explain why pet ownership increased FeNO levels in atopic asthma children even without sensitization to pets. Considering that exposure to pets did not affect FeNO levels in non-atopic asthma children, it is possible that exposure to pets may exacerbate airway inflammation through interactions with allergic inflammation already induced and sustained by other allergens.

Moreover, this current study demonstrated that exposure to pets increased asthma severity as well as FeNO levels, regardless of pet sensitization status, among children with atopic asthma. Although other factors may influence asthma severity, the increased asthma severity may be a consequence of airway inflammation, as determined by the FeNO level. A previous study found that exposure to dog or cat allergens among sensitized individuals with asthma was associated with increased asthma morbidity.[10,25] In another study of inner-city children with asthma, exposure to dog allergens increased asthma morbidity regardless of sensitization status, which supports our findings. However, increased FeNO levels were only observed among sensitized participants in that study,[14] which differs from our results. The discrepancy may be due to differences in the study population, sensitization measurement, and unmeasured environmental factors.

This study has some limitations. First, data on various factors that could influence the results were not available. These include the number of pets, duration of indoor and outdoor exposure, and allergen concentration from pets. Additionally, information on pets other than cats and dogs was lacking, as well as potential confounders such as air quality, socioeconomic status, medication adherence, and respiratory infections. Another limitation is that participants were recruited solely from tertiary hospitals, which may limit the generalizability of the findings. Furthermore, some data were collected through questionnaires, making them susceptible to recall bias. Therefore, further studies are needed

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to clarify the underlying mechanisms by measuring pet allergen concentrations, particularly in house dust, and evaluating the indoor environment.

In conclusion, pet ownership increased FeNO levels and asthma severity irrespective of pet sensitization status among children with atopic asthma. This finding suggests that exposure to pets could increase airway inflammation and disease severity, even in atopic asthmatic children who are not sensitized to pets.

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SUPPLEMENTARY MATERIALS

Supplementary Fig. S1

The levels of FeNO between atopic asthmatic children with and without pets during 12 months.

Supplementary Fig. S2

Proportion of children with persistent asthma based on pet ownership during 12 months.

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