DIFFERENTIATION BETWEEN ALLERGIC AND NON-ALLERGIC RHINITIS IN CHILDREN WITH CHRONIC RHINITIS, ALLERGY CLINIC, PHRAMONGKUTKLAO HOSPITAL

Tanuntorn Songchitsomboon[*,**], *Anupong Sirisungreung*[***], *Yiwa Suksawat*[*]

***Division of Allergy and Immunology, Department of Pediatrics, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Bangkok, Thailand**
****Department of Pediatrics, Uthong Hospital, Suphanburi, Thailand**
*****Department of Military and Community Medicine, Phramongkutklao College of Medicine, Bangkok, Thailand**

ABSTRACT

Background: Chronic rhinitis in children is a common problem. Investigation to diagnose allergic rhinitis (AR) using a skin prick test for aeroallergens requires a specialist doctor, which is not simply performed in primary health care facilities. Therefore, diagnosing patients with AR and non-allergic rhinitis (NAR) is based on clinical symptoms essential for treatment planning. This study compared clinical symptoms between AR and NAR, comorbidities, disease severity, and common aeroallergen sensitization.

Methods: A retrospective descriptive study was conducted among participants aged between 2-18 years with chronic rhinitis who were treated at the Department of Allergy and Immunology, Division of Pediatrics, Phramongkutklao Hospital, between 2014 and 2018. The medical records were reviewed on clinical symptoms, allergic test results, environmental data, and the severity according to Allergic Rhinitis and its Impact on Asthma (ARIA) classification. If the patient tested positive for aeroallergen, the allergist diagnosed AR. NAR is characterized by the same symptoms but with a negative skin prick test.

Results: Three hundred and seven participants were included. Among these patients, 226 (73.6 %) were categorized as AR, and 81 (26.4%) were NAR. The AR group had a higher percentage of males than the NAR group. Nasal pruritus and ocular symptoms were more commonly found in AR than in NAR. Regarding comorbidities, both groups had similar snoring, sinusitis, asthma, and atopic dermatitis. The most common aeroallergens among AR patients were *Dermatophagoides pteronyssinus* (82.7%), *Dermatophagoides farinae* (81.4%), followed by American cockroaches (38.1%), and German cockroaches (37.6%). Cat owners were associated with cat sensitization in AR patients (OR =2.77; 95% CI = 1.27-5.88).

Conclusions: In this study, the proportion of AR was higher than NAR. Nasal pruritus, ocular symptoms, or both strongly supported AR. The most common aeroallergen sensitization was house dust mites, followed by cockroaches. Initial treatment with antihistamine and other drugs can improve the severity of the disease.

Keywords: Chronic rhinitis, Allergic rhinitis, Non-allergic rhinitis, Thai children, Aeroallergen

J Southeast Asian Med Res 2022: 6(1):e0125
https://doi.org/10.55374/jseamed.v6i0.125

Correspondence to:
Suksawat Y, Division of Allergy and Immunology, Department of Pediatrics, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Bangkok 10400, Thailand
Email: yiwasuksawat@gmail.com

Received: 16 May 2022
Revised: 8 July 2022
Accepted: 20 July 2022

Introduction

Any inflammatory illness of the nasal mucosa is referred to as rhinitis. The development of one or more symptoms: rhinorrhea, sneezing, nasal itching, and nasal blockage, is clinically characterized as rhinitis.[1] Chronic rhinitis in children is a common problem in pediatric practice. The results of ISAAC Phase Three in Thai children revealed a significant increase in rhinitis symptoms in Bangkok and Chiang Mai.[2] Due to the prolonged period of this disease, it can affect daily activities such as academic performance, ability to work, and quality of life, leading to several indirect costs. Although allergic rhinitis (AR) is the most often recognized cause of chronic rhinitis in children, an alternative cause unrelated to allergic or infectious agents is known as non-allergic rhinitis (NAR). AR is caused by immunologic sensitization to aeroallergens resulting in the synthesis of specific IgE, which causes inflammatory processes leading to nasal symptoms. NAR is a chronic condition of the nasal mucosa with no evidence of allergic sensitization through skin prick tests (SPT) or specific IgE for aeroallergens.

A study of 660 children (aged 1 to 18 years) with chronic rhinitis in Singapore showed that AR was identified in 75.9 percent of cases, and NAR accounted for 24.1 percent of the total.[3] Previous research has shown that NAR patients would acquire more symptoms such as nasal obstruction and postnasal drip[4]; however, distinguishing between AR and NAR is less defined in children. Allergists will do further testing to diagnose allergic rhinitis using a skin prick test or specific IgE; however, it is difficult to carry out in primary care settings. As a result, diagnosing allergic rhinitis and non-allergic rhinitis by clinical symptoms before making treatment selections is essential. Gender disparities in the prevalence of atopic diseases are observed in many epidemiological studies. However, little is known about whether sex is more common among children and adolescents with rhinitis. A recent meta-analysis found sex-related differences in rhinitis prevalence, switching from a male to a female predominance around puberty. The male predominance from childhood seemed to persist in adolescence only in Asia[5]. This study aimed to describe the clinical profile of AR and NAR among children with chronic rhinitis diagnosis who visited a tertiary hospital's allergy clinics and had a skin prick test result. Furthermore, to evaluate the clinical difference and general characteristics between AR and NAR, the association between skin prick test results and area of residence, as well as how direct exposure as a pet owner contributes to the development of pet sensitization in allergic rhinitis patients.

Methods

The study protocol was approved by the Institutional Review Board, Royal Thai Army Medical Department (R045h/62). Data were collected retrospectively from patients aged 2-18 years diagnosed with chronic rhinitis between January 2014 to December 2018 at the Allergy and Immunology Clinic, Department of Pediatrics, Phramongkutklao Hospital. Diagnosis of chronic rhinitis was defined when patients had two or more of the following symptoms: rhinorrhea, nasal congestion, sneezing, or nasal itching that were present on most days for ≥ 4 weeks in the past year. Those who previously used some medications that could induce rhinitis symptoms were also excluded from the study. Patients with confirmed sinonasal disorders (such as a nasal

polyp, sinusitis, or nasal septum deviation that seriously impaired nasal cavity airflow) or pregnancy were excluded. All patients with neither contraindication for SPT nor active skin diseases were indicated for aeroallergen skin testing. SPT using stainless steel lancet was performed on all patients. Standard aeroallergen extracts including house dust mite [*Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df)], American cockroaches, German cockroaches, cat dander, dog epithelia, *Alternaria* spp., *Cladosporium* spp., mixed *Aspergillus* spp., *Curvularia* spp., Bermuda grass, Johnson grass, careless weeds, and acacia as well as positive and negative controls (histamine and saline, respectively) (ALK-Abello Pharmaceuticals Inc., Canada) were evaluated. An immediate reaction (wheal and erythema) was read after 15 minutes. The result of SPT was considered positive when the allergen wheal size was 3 mm or larger than the negative control. The allergists diagnosed a patient with AR if the test was positive for an aeroallergen. The same set of symptoms defined NAR but with a negative SPT.

The number of patients who participated in this study and underwent an aeroallergen SPT is shown in **Figure 1.** When the patients visited the Allergy Clinic, a symptom-based questionnaire adapted from ARIA guidelines was used to inquire about their symptoms and documented in the medical records. Age, sex, age at onset, family history of any atopic diseases, living area, and environmental data (presence of household pets and smoking) were collected. Patients' charts were reviewed for rhinitis symptoms (rhinorrhea, nasal congestion, nasal and eye itching or sneezing) and physician-diagnosed comorbidities; the severity of rhinitis according to ARIA classification and SPT result were recorded.

Statistical analysis

Continuous variables were summarized using mean and standard deviation, and categorical variables were summarized using counts and percentages. The association between allergic rhinitis status and baseline characteristics, including demographic data, clinical features, and comorbidities, were analyzed based on the distribution and expected values of data. Continuous data were assessed using Student's t-test, and categorical data were evaluated using the chi-square test and Fisher's exact test. Bivariate logistic regression was performed to estimate the association between aeroallergen sensitization profiles and living areas (Bangkok vs. other provinces). The association between pet sensitization test results and history of pet exposure was also explored using multivariable logistic regression adjusted by type of pet

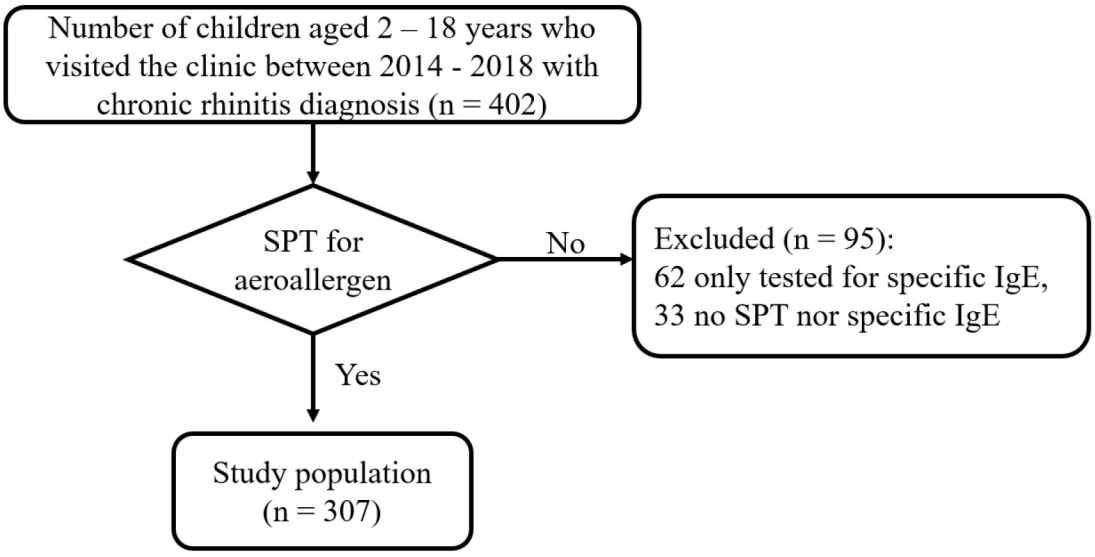


Figure 1. Number of patients who were assessed for chronic rhinitis and underwent skin prick test

exposure (cat, dog, others), age (years) at first diagnosis, and sex of patients. We assumed that age and sex were potential confounders between pet sensitization and history of pet exposure since age and sex are associated with allergy[5-7] and potentially related to pet exposure history. All analyses were performed using R version 4.0.2 software (R Core Team. R: A language and environment for statistical computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2020. Available from: http://www.R-project.org/).

Results

Characteristics of children with rhinitis

During the study, 402 children with rhinitis were assessed for symptoms of chronic rhinitis in the Pediatric Allergy Clinic, Phramongkutklao Hospital. Three hundred and seven patients had undergone SPT for aeroallergen. Among these patients with SPT results, 226 (73.6 %) were classified as AR, and 81 (26.4%) were NAR. Most of them were living in Bangkok (69.7%). The mean age of onset for patients was not different between AR and NAR; however, the mean age at first diagnosis for patients with AR was older than NAR (mean ages 7.53 vs. 6.39 years, p=0.012 (**Table 1**). Most patients in the AR group were male (65.0%), which differed from the NAR group in that males and females were equal. Most patients had no other medical conditions (72.6%), although we observed that 8% had attention deficit hyperactivity disorder (ADHD) before they were diagnosed with AR or NAR. Patients with NAR were more likely to clean the house every week than those with AR (p=0.005) (**Table 1**); however, there was not enough evidence to conclude the differences in the history of allergic disease in the family, passive smoking, presence of household pets, and rhinitis severity between AR and NAR patients.

Table 1. Baseline characteristics of allergic rhinitis and non-allergic rhinitis patients in the pediatric allergy clinic, Phramongkutklao Hospital, 2014–2018

Characteristics	Total (n = 307)	NAR (n = 81)	AR (n = 226)	*p*-value
Age of onset (years)				
Mean (SD)	5.36 (3.16)	5.06 (3.47)	5.47 (3.04)	0.308 [a]
Age at first diagnosis (years)				
Mean (SD)	7.23 (3.50)	6.39 (3.27)	7.53 (3.54)	0.012 [a]
Sex, n (%)				
Male	186 (60.6)	39 (48.1)	147 (65.0)	0.011 [b]
Family history of atopic diseases, n (%)				
No family history	122 (39.7)	35 (43.2)	87 (38.5)	
Allergic rhinitis	153 (49.8)	40 (49.4)	113 (50.0)	0.793 [c]
Asthma	21 (6.8)	4 (4.9)	17 (7.5)	
Others †	11 (3.6)	2 (2.5)	9 (4.0)	
Passive smoking, n (%) ‡	67 (22.2)	12 (15.2)	55 (24.7)	0.113 [b]
Household pets, n (%) ‡	92 (30.4)	20 (25.0)	72 (32.3)	0.283 [b]
Frequency of house cleaning, n (%)				
Every one week	169 (58.1)	55 (73.3)	114 (52.8)	0.005 [b]
Every two weeks	85 (29.2)	16 (21.3)	69 (31.9)	
Longer than two weeks	37 (12.7)	4 (5.3)	33 (15.3)	

Table 1. Baseline characteristics of allergic rhinitis and non-allergic rhinitis patients in the pediatric allergy clinic, Phramongkutklao Hospital, 2014–2018 (Cont.)

Characteristics	Total (n = 307)	NAR (n = 81)	AR (n = 226)	*p*-value
Severity of disease at baseline, n (%)				
Mild intermittent	20 (6.5)	8 (9.9)	12 (5.3)	0.059 [b]
Mild persistent	195 (63.5)	57 (70.4)	138 (61.3)	
Moderate to severe intermittent	2 (0.6)	1 (1.2)	1 (0.4)	
Moderate to severe persistent	90 (29.3)	16 (19.8)	74 (32.9)	
Living area, n (%)				
Bangkok	214 (69.7)	60 (74.1)	154 (68.1)	0.392 [b]

† Other family history included: atopic dermatitis, food allergy, chronic urticaria

‡ Missing passive smoking (n=5); missing household pet (n=4)

Statistical tests for *p*-value: a) t-test, b) chi-square, c) Fisher's exact

Clinical characteristics and comorbid disease

Table 2 shows the comparison of nasal symptoms between the two groups. The most prevalent symptom in both NAR and AR was rhinorrhea, followed by nasal congestion. The AR group had a higher proportion of nasal itching (52.2% vs 37.0%; $p = 0.027$) and ocular symptoms (50.9% vs 28.4%; $p = 0.027$) than NAR group. The proportions of rhinorrhea, nasal congestion, and sneezing were not different between the NAR and AR groups. Snoring and acute sinusitis were the most common comorbidities; nevertheless, comorbidities including snoring, acute sinusitis, asthma, and atopic dermatitis seemed to be similar between the two groups.

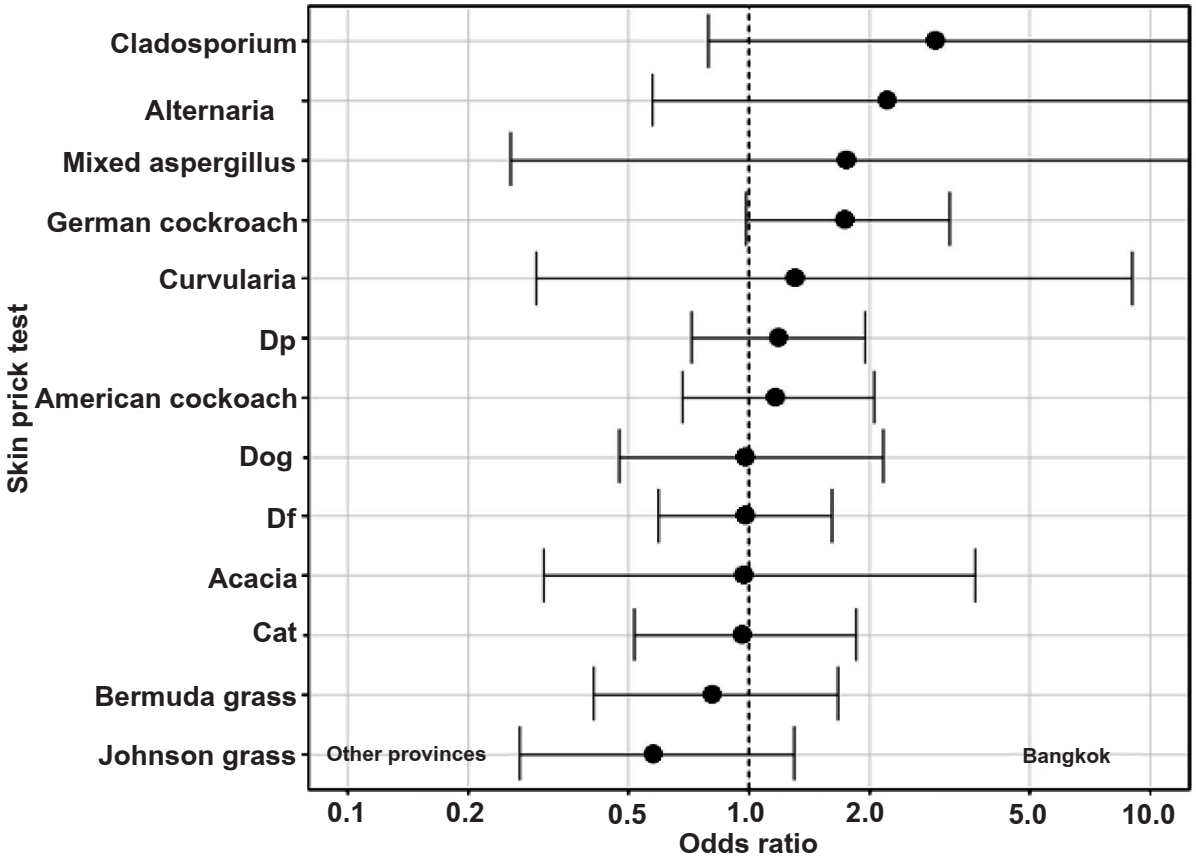
Table 2. Clinical symptoms and comorbidities between allergic rhinitis and non-allergic rhinitis patients in the pediatric allergy clinic, Phramongkutklao Hospital, 2014–2018

Clinical symptoms and comorbidities	NAR (n = 81)	AR (n = 226)	Chi-square *p*-value
Clinical symptoms, n (%)			
Rhinorrhea	70 (86.4)	193 (85.4)	0.968
Nasal congestion	57 (70.4)	160 (70.8)	1.000
Sneezing	39 (48.1)	125 (55.3)	0.328
Nasal itching	30 (37.0)	118 (52.2)	0.027
Ocular symptoms	23 (28.4)	115 (50.9)	0.001
Comorbidities, n (%)			
Snoring	19 (23.5)	50 (22.1)	0.927
Acute sinusitis	18 (22.2)	39 (17.3)	0.412
Asthma	11 (13.6)	41 (18.1)	0.443
Atopic dermatitis	2 (2.5)	22 (9.7)	0.065

NAR = non-allergic rhinitis, AR = allergic rhinitis

Aeroallergen sensitization profile in children with allergic rhinitis

The number of patients who lived in Bangkok was 214 (69.7%). **Figure 1** shows the prevalence of aeroallergen sensitization (based on SPT results) classified by patients who lived in Bangkok and other parts of Thailand. During the 4-year study period, Dp and Df were the most common aeroallergens sensitization (82.7% and 81.4%, respectively), followed by American cockroaches (38.1%), German cockroaches (37.6%), cat (24.3%), Bermuda grass (18.1%), dogs (15.9%), Johnson grass (12.8%), *Cladosporium* spp. (6.6%), acacia (5.8%), *Alternaria* spp. (5.3%), careless weed (3.5%), *Curvularia* spp. (3.5%), and mixed *Aspergillus* spp. (2.2%). Patients who lived outside of Bangkok seemed to have a higher chance of Bermuda grass sensitization (OR = 1.22; 95% CI = 0.61-2.46) than those who lived in Bangkok, similar to Johnson grass sensitization (OR = 1.71; 95% CI = 0.78-3.75), although their 95% CI were compatible with the null. On the other hand, patients who lived in Bangkok appear to have higher odds of aeroallergen sensitization profiles than those who lived outside Bangkok, for instance, *Cladosporium* (OR = 2.94; 95% CI = 0.79-19.07), *Alternaria* (OR = 2.23; 95% CI = 0.57-14.7), Mixed *Aspergillus* spp. (OR = 1.75; 95% CI = 0.25-34.53), German cockroaches (OR = 1.74; 95% CI = 0.99-3.17) and *Curvularia* spp. (OR = 1.31; 95% CI = 0.30-9.07) (**Figure 2**).



Dp = *Dermatophagoides pteronyssinus*, Df = *Dermatophagoides farinae*; could not determine odds ratio and 95% confidence interval for Careless weed due to sparse data.

Figure 2. Odd ratios and 95% confidence intervals for associations between aeroallergen sensitization profiles and area of living (Bangkok vs. other provinces)

Table 3. Association between household pets and pet allergen sensitizations among allergic rhinitis patients in the pediatric allergy clinic, Phramongkutklao Hospital, 2014–2018

	Skin prick test positive n (%)	Skin prick test negative n (%)	Adjusted OR†	95% CI†	*p*-value
Cat sensitization	55	252			
Cat ownership	14 (25.5)	25 (9.9)	2.77	1.27 - 5.88	0.009
Dog ownership	10 (18.2)	44 (17.5)	1.01	0.44 - 2.14	0.975
Dog sensitization	36	271			
Cat ownership	5 (13.9)	34 (12.5)	1.15	0.37 - 3.06	0.787
Dog ownership	9 (25.0)	45 (16.6)	1.63	0.67- 3.67	0.254

† OR = adjusted odds ratio, CI = confidence interval

Multivariable model logistic regression models included: type of pet ownership (cat, dog, others), age (years) at first diagnosis, and sex of patients

History of pet exposure in household and pet allergen sensitization

In this study, 30.4% of allergic rhinitis patients had pets in their houses. The proportion of cat sensitization (55/307=17.9%) was higher than dog sensitization (36/307=11.7%). The association between household pets and pet sensitization is shown in **Table 3**. After adjusting for type of pet exposure, age at first diagnosis, and sex of patients, the odds of sensitization to cats among rhinitis patients who were cat owners were 3.11 times that of those who did not own a cat. Using this statistical model, a plausible range of values for the odds ratio was 1.46 to 6.43 (95% CI=1.46-6.43).

Discussion

This study described the clinical characteristics of children with chronic rhinitis attending Phramongkutklao Hospital. The patients were divided into two groups: AR and NAR. The results revealed that children with AR were more common than NAR, similar to the findings of Vichyanond et al. [8], Visitsunthorn et al. [9], and Lee et al. [10] while differing from Westman et al. [11] and Lee et al.[12] However, our study could have a higher prevalence of AR than the general population because the patients were recruited from a pediatric specialist clinic. Since the symptoms of NAR were more severe than those of AR[13], patients with NAR went to see the doctor earlier. As a result, patients with NAR had a significantly lower age at first diagnosis than those with AR. Boys were shown to be more likely than girls to have AR in the children's age group, comparable to adulthood with chronic rhinitis, when men were also less likely to have NAR than females.[14] There were sex differences in the prevalence of AR over the life span, with boys having a greater frequency than girls during childhood, followed by an equal distribution in adolescence. [14]

Nasal itching and ocular symptoms were more frequent in AR than in NAR, similar to the study by Vichyanond et al. [8]; however, rhinorrhea, nasal congestion, and sneezing between the two groups were not different. Our study found that snoring was the most common comorbidity in children with AR and NAR. Snoring in these groups of patients might be due to adenoid hypertrophy or nasal congestion, affecting sleep quality. Patients with nasal congestion were more likely to have moderate to severe obstructive sleep apnea than allergic patients without nasal congestion.[15] Unfortunately, our questionnaires might be insufficient to assess sleep disorders,

and objective testing such as polysomnography should have been used to evaluate sleep disturbance accurately in the following study. Similar asthma prevalence in children with allergic and nonallergic rhinitis was consistent with previous studies.[16] Asthma was common comorbidity in children and adults with allergic rhinitis. Treatment for AR could reduce asthma symptoms; therefore, the clinician should look for other comorbidities and proper management if a patient presents with either AR or asthma symptoms.

House dust mites were shown to be the most frequent aeroallergen sensitization from studies in children with AR who lived in Bangkok[9] and Chiangmai Province[17], accounting for 80% of cases, similar to our study. House dust mite sensitization is relatively high because Thailand is located in a tropical environment. The temperature is generally warm and humid, favorable for mite proliferation. American cockroaches (*P. americana*) and German cockroaches (*B. germanica*) are common cockroach species found in people's homes, and their allergens can induce atopic diseases, particularly allergic rhinitis. In 2004, Tungtrongchitr et al. found that P. americana was the predominant cockroach species in the house of people who lived in Bangkok, followed by *B.germanica.*[18] We found more prevalence of German cockroach sensitization than American cockroach sensitization in children who lived in Bangkok, which differed from previous studies in Thailand.[9, 17] Furthermore, in this study, approximately 35% of children with AR in Bangkok were only sensitized to the German cockroach. A higher prevalence of German cockroach sensitization might be due to the increasing number of this type of cockroaches in Bangkok. We know that exposure to pet allergens is a significant risk factor for developing allergic sensitization and respiratory allergic diseases such as allergic rhinitis or allergic asthma. The presence of a pet at home is commonly regarded as the most significant risk factor for allergic sensitization. In previous studies, the association between cat ownership and sensitization to cats has remained questionable[19]; however, dog ownership was preventative for sensitization to dogs.[20] Our findings showed that cat ownership was strongly associated with cat sensitization in children with allergic rhinitis, opposite to dog ownership, which was not associated with dog sensitization. The timing of exposure, duration of the pets exposure, level of pet allergen exposure, or genetic risk seem to modify or induce pet sensitization.[21]

A strength of this study was the use of symptom-based questionnaires to collect medical data and SPT for aeroallergens, which were performed in most patients with chronic rhinitis to classify them into AR and NAR. However, a retrospective review was a significant limitation of this study; this data collection could not be as complete as in a prospective study. Patients with local allergic rhinitis (LAR) would have been indistinguishable in this study because NAR was differentiated from AR based only on rhinitis symptoms and the absence of negative SPT results. A systematic review of studies subjected to nasal allergen provocation tests (NAPT) has recently demonstrated local allergen reactivity in 16.1% of children previously considered NAR. [22] It is essential to use NAPT to evaluate rhinitis to identify LAR patients. The development of systemic atopy is not a common situation in LAR individuals. Nevertheless, LAR worsens rapidly with progressive rhinitis severity and impairment in quality of life. Therefore, a more accurate diagnostic test to define the type of chronic rhinitis is warranted to optimize patient management.

Conclusion

This study describes clinical characteristics between AR and NAR among children with chronic rhinitis. The proportion of AR was higher than NAR. The most common aeroallergen sensitization was house dust mites, followed by cockroaches. This information could benefit children who visit primary care for initial management and appropriate common allergen avoidance. Nasal pruritus or ocular symptoms strongly supported AR, of which additional allergy testing in those children may be required.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Acknowledgments

The authors would like to express gratitude to the patients and their families participating in this study. This study was supported by a Research Unit Grant from the Department of Pediatrics, Phramongkutklao Hospital and Phramongkutklao College of Medicine.

References

1. Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, Craig TJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol 2020; 146: 721-67.
2. Trakultivakorn M, Sangsupawanich P, Vichyanond P. Time trends of the prevalence of asthma, rhinitis and eczema in Thai children-ISAAC (International Study of Asthma and Allergies in Childhood) Phase Three. J Asthma 2007; 44: 609-11.
3. Chiang WC, Chen YM, Tan HK, Balakrishnan A, Liew WK, Lim HH, et al. Allergic rhinitis and non-allergic rhinitis in children in the tropics: prevalence and risk associations. Pediatr Pulmonol 2012; 47: 1026-33.
4. Mastin T. Recognizing and treating non-infectious rhinitis. J Am Acad Nurse Pract 2003; 15: 398-409.
5. Pinart M, Keller T, Reich A, Fröhlich M, Cabieses B, Hohmann C, et al. Sex-related allergic rhinitis prevalence switch from childhood to adulthood: a systematic review and meta-analysis. Int Arch Allergy Immunol 2017; 172: 224-35.
6. Collin SM, Granell R, Westgarth C, Murray J, Paul E, Sterne JA, et al. Pet ownership is associated with increased risk of non-atopic asthma and reduced risk of atopy in childhood: findings from a UK birth cohort. Clin Exp Allergy 2015; 45: 200-10.
7. Goldhahn K, Bockelbrink A, Nocon M, Almqvist C, DunnGalvin A, Willich SN, et al. Sex-specific differences in allergic sensitization to house dust mites: a meta-analysis. Ann Allergy Asthma Immunol 2009; 102: 487-94.
8. Vichyanond P, Suratannon C, Lertbunnaphong P, Jirapongsananuruk O, Visitsunthorn N. Clinical characteristics of children with non-allergic rhinitis vs with allergic rhinitis. Asian Pac J Allergy Immunol 2010; 28: 270-4.
9. 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: 69-76.
10. Lee KS, Yum HY, Sheen YH, Park YM, Lee YJ, Choi BS, et al. Comorbidities and phenotypes of rhinitis in Korean children and adolescents: a cross-sectional, multicenter study. Allergy Asthma Immunol Res 2017; 9: 70-8.
11. Westman M, Stjärne P, Asarnoj A, Kull I, van Hage M, Wickman M, et al. Natural course and comorbidities of allergic and nonallergic rhinitis in children. J Allergy Clin Immunol 2012; 129: 403-8.
12. Lee SH, Choi JH, Suh JD, Chung S, Hong SC, Kim JK, et al. Natural course of allergic and nonallergic rhinitis after 2 years in Korean children. Clin Exp Otorhinolaryngol 2016; 9: 233-7.
13. La Mantia I, Andaloro C. Demographics and clinical features predictive of allergic versus non-allergic rhinitis in children aged 6-18 years: A single-center experience of 1535 patients. Int J Pediatr Otorhinolaryngol 2017; 98: 103-9.
14. Fröhlich M, Pinart M, Keller T, Reich A, Cabieses B, Hohmann C, et al. Is there a sex-shift in prevalence of allergic rhinitis and comorbid asthma from childhood to adulthood? A meta-analysis. Clin Transl Allergy 2017; 7: 44.
15. Young T, Finn L, Kim H. Nasal obstruction as a risk factor for sleep-disordered breathing. The University of Wisconsin Sleep and Respiratory Research Group. J Allergy Clin Immunol 1997; 99: S757-62.
16. Chawes BL, Bønnelykke K, Kreiner-Møller E, Bisgaard H. Children with allergic and nonallergic rhinitis have a similar risk of asthma. J Allergy Clin Immunol 2010; 126: 567-73.e1-8.

17. Waithayawongsakul K, Lao-Araya M. Time trends of skin prick test reactivity to inhalant allergens among allergic children in Chiang Mai. Chiang Mai Med J 2021; 60: 475-86.
18. Tungtrongchitr A, Sookrung N, Munkong N, Mahakittikun V, Chinabut P, Chaicumpa W, et al. The levels of cockroach allergen in relation to cockroach species and allergic diseases in Thai patients. Asian Pac J Allergy Immunol 2004; 22: 115-21.
19. Simpson A, Custovic A. Pets and the development of allergic sensitization. Curr Allergy Asthma Rep 2005; 5: 212-20.
20. Van Gysel D, Govaere E, Verhamme K, Doli E, De Baets F. Exposure to pets and the association with sensitization and allergic disease in Belgian schoolchildren. Allergy 2009; 64: 663-4.
21. Kim HY, Shin YH, Han MY. Determinants of sensitization to allergen in infants and young children. Korean J Pediatr 2014; 57: 205-10.
22. Hamizan AW, Rimmer J, Alvarado R, Sewell WA, Kalish L, Sacks R, et al. Positive allergen reaction in allergic and nonallergic rhinitis: a systematic review. Int Forum Allergy Rhinol 2017; 7: 868-77.