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Pattern of allergic sensitization in chronic rhinitis: A 19-year retrospective study

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Abstract

Background: The pattern of allergic sensitization provides data for physicians to take appropriate care of allergic patients.

Objective: To analyze the long-term pattern of allergen skin prick test (SPT) sensitization at a single tertiary care hospital in Thailand.

Methods: Medical records of adult rhinitis patients during 1998 to 2017 were reviewed. Inclusion criteria were chronic rhinitis with positive SPT to at least one aeroallergen in the test panel. Outcome measures were SPT results, clinical symptoms, and their effect on patient quality of life (QoL). Descriptive statistics were used to demonstrate the pattern of sensitization. Multivariate linear regression was used to identify association between evaluated factors and patient QoL.

Results: Six thousand five hundred and seventeen adult patients were included in this study. Mean age was 36.4 ± 13.8 years. A majority of patients (59.4%) had positive SPT, and 83.7% of those had polysensitization. *Dermatophagoides pteronyssinus* and sedge were the most common indoor (54.8%) and outdoor allergens (37.7%), respectively. Compared among the various periods of data collection over a 19-year period, there was no major change in the pattern of sensitization. Considering the most recent data from 2013-2017, the prevalence of sensitization increased from 66.8% to 73.7% ($p < 0.001$). Clinical symptoms, except sneezing and allergen sensitization, affect QoL of chronic rhinitis patients ($p < 0.001$).

Conclusion: House dust mite and sedge are the most common indoor and outdoor allergens. There was no major change in the pattern of sensitization. Almost all allergic symptoms significantly affect QoL.

Key words: Allergy, skin prick test, allergic rhinitis, allergic sensitization, chronic rhinitis.

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Introduction

One of the most commonly observed diseases in the outpatient department is rhinitis. Immunoglobulin E (IgE)-mediated nasal inflammation plays a major role in chronic rhinitis. Effective management of allergic rhinitis (AR) requires a precise diagnosis which is the identification as inflammatory process of immunoglobulin E – mediated. In routine clinical practice, initial treatment by pharmacotherapy with avoidance of suspected causative allergens is the standard of care.[1] When the initial treatment does not provide significant improvement, precise diagnosis of allergic rhinitis by skin prick test (SPT) is the principle modality.[2]

SPT is considered a standard diagnostic method because of its accuracy, reproducibility, and affordability.[3] SPT requires good quality allergen extracts, and extracts that are appropriate for each geographic area. The pattern of SPT sensitization varies depending on the region.[4-16]

In addition to the characteristics of the pattern of allergic sensitization in each region, changes in the allergic sensitization pattern need to be periodically evaluated. Allergic sensitization patterns may change due to level of industrialization, climate change, and global warming, which may affect dissemination of allergens – especially pollen.[17,18] Clinical profile,

severity of quality of life (QoL), and comorbidities have been proposed as having association with SPT pattern.[19-21]

Allergic sensitization pattern of SPT vary according to area. For example, in Europe, the principle major burden allergens are birch or ragweed.[5,12,13,22] In tropical regions, the major allergen is house dust mite.[4,7] Moreover, some allergens may also contribute for the clinical burden, such as molds and mosquito.[23,24]

In addition to differences in allergic sensitization pattern by geographical area, the allergic sensitization pattern may change over time. Several factors can affect a change in pattern, especially environmental effect.[18] Allergic status also affects patient QoL.[19-21] Updated allergic sensitization pattern data will help to guide effective allergy management. The objective of this article was to analyze the long-term pattern of allergen skin prick test (SPT) sensitization at a single center in Thailand, and to identify symptoms and other factors that significantly associate with patient QoL.

Methods

A retrospective chart review of patients that attended the outpatient allergy clinic of the Department of Otorhinolaryngology, Siriraj Hospital was conducted. Data was collected during 1998 to 2017. Patients with chronic rhinitis who had symptoms for more than one year and who had positive skin prick test (SPT) were included. Rhinitis was defined as the presence of 2 or more of the following symptoms: itching, sneezing, rhinorrhea, and/or nasal obstruction for more than 1 hour per day.[25] Exclusion criteria were nasal polyposis, nasal tumors, and rhinitis medicamentosa.

The following data were extracted from the medical record: age, sex, result of SPT, presenting allergic symptoms, and comorbidities.

The SPT extracts were "Siriraj Allergen Vaccine (SAV)", which has been tested for Thai Food and Drug Agency (FDA) standard and allergenic potency (Greater Pharmaceutical Co. Ltd).[26] The criterion of positive is size of wheal larger than 3mm with accompanying flare. The extract panels were: *Dermatophagoides pteronyssinus*, American cockroach (*Periplaneta americana*), cat, dog, mosquito (*Aedes aegipti*), mold (*Aspergillus spp.*, *Penicillium spp.*, *Cladosporium spp.*), Bermuda grass (*Cynodon dactylon*), para grass (*Brachiaria mutica*), sedge (*Cyperaceae*), careless weed (*Amaranthus palmeri*), and kapok (*Ceiba pentandra*). The positive and negative controls were histamine and normal saline, respectively.

The pattern of allergic sensitization of each allergen was displayed as percentage of subjects who have positive skin reaction comparing to the number of subjects who have been SPT. The sensitization of SPTs was categorized into monosensitization and polysensitization (positive SPT for equal to or more than two allergens). The pattern of allergic sensitization was also grouped into indoor allergen or outdoor allergen sensitization.

To determine their effect on QoL, most recent clinical data from the 2013 to 2017 period were analyzed. That data set was also analyzed to compare the prevalence rate of sensitization. A questionnaire for allergic rhinitis, which was validated by our team, was used to determine QoL.[21]

Statistical analysis

Data analysis was performed using PASW Statistics (SPSS Inc, Chicago, IL, USA). Demographic data and other categorical variables are presented. Data are presented as frequency and percentage for categorical data, and as mean plus or minus standard deviation and range for continuous data. Clinical symptoms and SPT sensitization were evaluated for association with QoL using linear regression analysis. Factors with a *p*-value less than 0.2 in univariate analysis were included in multivariate analysis by stepwise method. The results of multivariate analysis are shown as regression coefficient and 95% confidence interval. To compare the prevalence of allergic sensitization during 2013 to 2017, 'Chi-square for trend' method was used. A *p*-value less than 0.05 was considered statistically significant.

The local ethical committee approved this study with COA # 242/2559(EC1).

Results

Demographic and clinical data are shown in **Table 1**. The clinical symptoms of subjects with SPT positive (AR) were statistically difference from the subjects with SPT negative except the perennial symptoms. The onset of rhinitis and family history of atopy in AR group are statistically difference from NAR. The pattern of allergic sensitization stratified by time period is shown in **Table 2**. All patients were positive for at least one allergen. *Dermatophagoides pteronyssinus* and sedge were the most common indoor (54.8%) and outdoor allergens (37.7%), respectively. (**Figure 1**)

Table 1. Demographic and clinical characteristics of patients during 1998-2017 (N = 6,517)

Characteristics	n (%)	Skin test positive	Skin test negative	*p*-value
Age (years)				
Mean (SD)	36.4 (13.8)	34.3	39.0	< 0.001
Range	7 to 81	7 to 78	7 to 81	
Sex				
Male	2,359 (36.2%)	1,394 (59.1%)	965 (40.9%)	< 0.001
Female	4,158 (63.8%)	2,171 (52.2%)	1,987 (47.8%)	< 0.001
Allergic sensitization		3,871 (59.4%)	2,646 (40.6%)	< 0.001

Table 1. (Continued)

Characteristics	n (%)	Skin test positive	Skin test negative	*p*-value
Polysensitization		3,240 (83.7%)		
Itchy nose	3,788 (58.1%)	2,354 (60.8%)	1,434 (54.2%)	< 0.001
Sneezing	3,352 (51.4%)	2,101 (54.3%)	1,251 (47.3%)	< 0.001
Running nose	4,146 (63.6%)	2,593 (67.0%)	1,553 (58.7%)	< 0.001
Stuffy nose	4,106 (63%)	2,524 (65.2%)	1,582 (59.8%)	< 0.001
Itchy eye	2,825 (43.3%)	1,835 (47.4%)	990 (37.4%)	< 0.001
Cough	2,081 (31.9%)	1,142 (29.5%)	939 (35.5%)	< 0.001
Snoring	1,851 (28.4%)	1,049 (27.1%)	802 (30.3%)	0.005
Perennial symptoms	2,732 (41.9%)	1,618 (41.8%)	1,114 (42.1%)	0.80
Family history of atopy	3,214 (49.3%)	1,978(51.1%)	1,236 (46.7%)	< 0.001
Onset of rhinitis (years)	28.37	25.4	35.3	< 0.001
Quality of Life (SD)	72.8 (17.6)	72.8 (18.0)	73.0 (16.0)	0.78

Table 2. Pattern of allergen sensitization during 1998-2017 (N = 3,871)

Years 1998-2017 (N = 3,871)			
Years 1998-2004 (n = 1,197)	**Years 2005-2009 (n = 995)**	**Years 2010-2012 (n = 779)**	**Years 2013-2017 (n = 900)**
Top 3 Indoor Allergens			
1. Mite 40.1% (n = 994)	1. Mite 50.6% (n = 696)	1. Mite 59.3% (n = 753)	1. Mite 44.1% (n = 614)
2. Cockroach 11.4% (n = 283)	2. Dog 37.4% (n = 515)	2. Cockroach 42.5% (n = 539)	2. Cockroach 35.0% (n = 488)
3. Dog 8.2% (n = 203)	3. Cockroach 31.0% (n = 427)	3. Cat 40.4% (n = 513)	3. Cat 32.5%(n = 453)
Top 3 Outdoor Allergens			
1. Sedge 18.5% (n = 458)	1. Sedge 38.1%(n = 487)	1. Sedge 47.4%(n = 604)	1. Sedge 38.1%(n = 386)
2. Bermuda 13.64% (n = 337)	2. Para grass 36.3%(n = 482)	2. Para grass 44.6%(n = 584)	2. Bermuda 30.9% (n = 408)
3. Para grass 11.14% (n = 275)	3. Bermuda 36.0%(n = 446)	3. Bermuda 41.5%(n = 548)	3. Para grass 26.4% (n = 354)

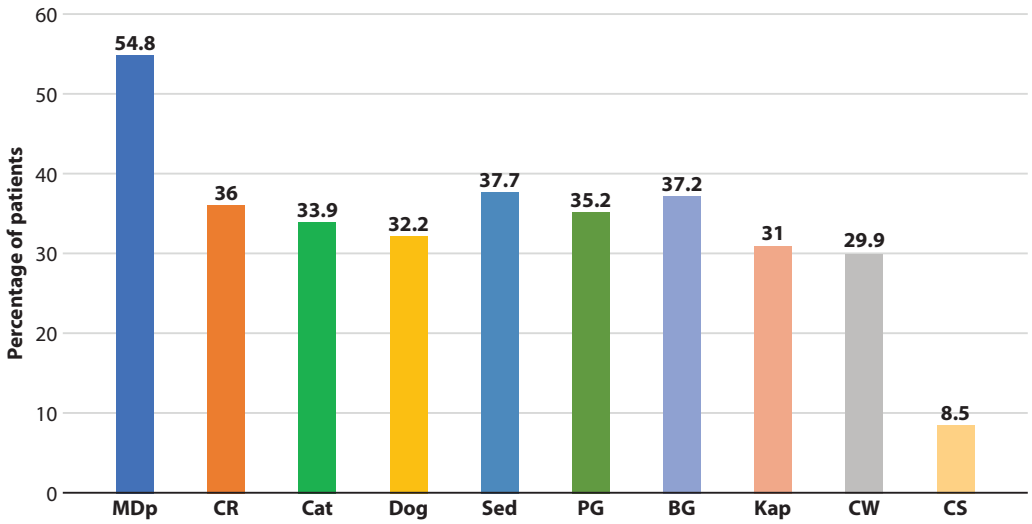

Figure 1. Pattern of allergen sensitization during 19 years (1998–2017)
Abbreviations: MDp (Mite/*Dermatophagoides pteronyssinus*), CR (Cockroach), Sed (Sedge), PG (Para grass), BG (Bermuda grass), Kap (Kapok), CW (Careless weed), CS (*Cladosporium spp.*).

During the most recent period (2013 to 2017), the data from 1,457 chronic rhinitis patients were used for inferential statistical analysis. The mean age was 37.2 years, and the majority of patients were female. Mite with cockroach is the common pattern of polysensitization.

During the most recent five-year period, the prevalence of overall allergen sensitization significantly increased from 66.8% to 75.7% (chi-square test for trend: $p = 0.006$). The prevalence of indoor allergen sensitization also significantly increased from 59.6% to 72.3% (chi-square test for trend: $p = 0.001$). The prevalence of outdoor allergen sensitization did not change significantly (chi-square test for trend: $p = 0.097$). (**Figure 2**)

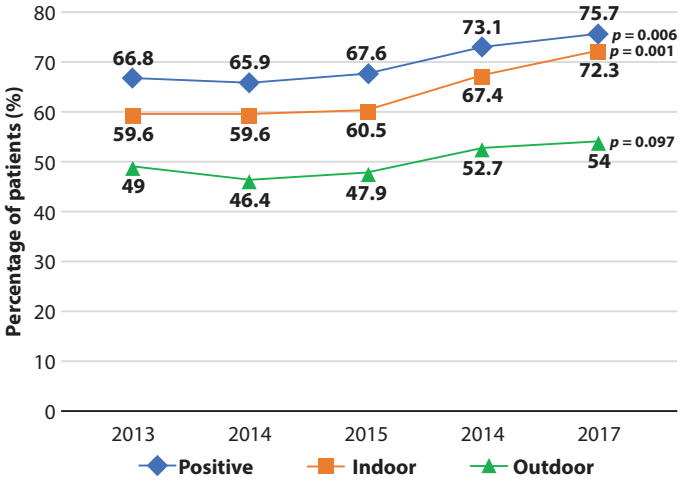

Figure 2. Trend change of allergen sensitization during 2013–2017 (N = 1,457)

Figures 3 show the trend of allergic sensitization pattern for individual allergens during the most recent five-year period. Mite was also found to be the most common indoor sensitization (44.1%), and sedge was the most common outdoor sensitization (31.3%). The sensitization of fungal allergens was less than the sensitizations from the other groups.

During that time period, the trend changes show house dust mite as the most common sensitization. Cockroach and dog alternately manifested as the second and the third most common allergic sensitization. Dog remained as the fourth most common indoor sensitization. For the outdoor allergens, sedge remained the most common sensitization during most years. The sensitization of careless weed decreased, and the sensitization of para grass remained stable.

Regarding the issue of burden of AR symptoms, the correlation between mean wheal diameter of SPT and rhinitis symptoms was determined by Pearson's correlation coefficient. Only the degree of wheal of mite and dog sensitization showed statistical significant with AR symptoms ($p < 0.0001$, r = 0.1), but there was no statistical significant with the other allergen. Clinical characteristics, sex, and sensitization status were evaluated to identify factors that significantly associate with patient QoL. Univariate analysis revealed clinical symptoms and sex to be statistically significantly related to QoL, but no significant relationship was found for sensitization. Multiple linear regression analysis revealed that all rhinitis symptoms, except sneezing, adversely affect patient QoL (**Table 3**). Sensitization also did not remain statistically significant in multivariate analysis. Itchy nose and itchy eyes were the symptoms that had the most pronounced effect on QoL, with regression coefficients of 5.08 (95% confidence interval [CI]: 3.18-6.98) and 5.2 (95% CI: 3.29-7.10), respectively.

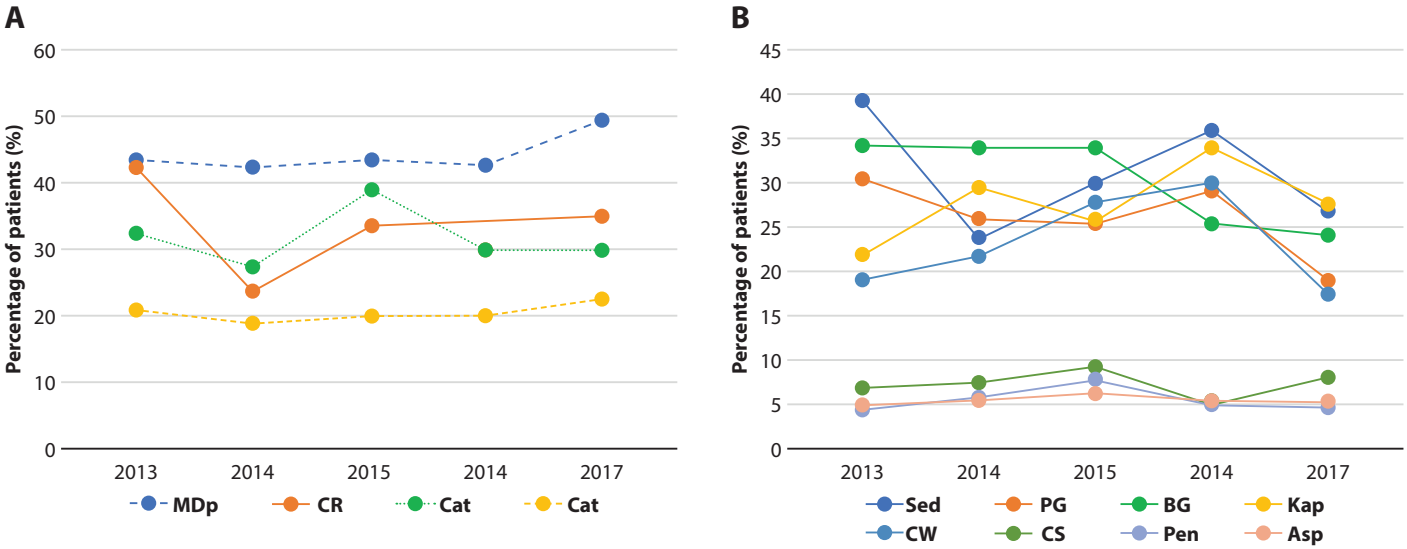

Figure 3. Trend change of indoor (Figure 3A), outdoor allergens and molds (Figure 3B) during 2013–2017 (N = 1,457)
Abbreviations: MDp (Mite/*Dermatophagoides pteronyssinus*), CR (Cockroach), Sed (Sedge), PG (Para grass), BG (Bermuda grass), Kap (Kapok), CW (Careless weed), CS (*Cladosporium spp.*), Pen (*Penicillium spp.*), Asp (*Aspergillus spp.*).

Table 3. Factors that affect patient quality of life (QoL) (N = 1,457)

Factor	n	Univariate analysis p-value	Multivariate linear regression	
			Regression coefficient (95% CI)	*p*-value
Sex				
Male	524			
Female	933	< 0.001*	2.00 (0.13:3.86)	0.036*
Ichy nose				
No	645			
Yes	785	< 0.001*	5.08 (3.18:6.98)	< 0.001*
Sneezing				
No	735			
Yes	695	< 0.001*	-	
Rhinorrhea				
No	553			
Yes	877	< 0.001*	2.44 (0.53:4.34)	< 0.001*
Nasal congestion				
No	546			
Yes	884	< 0.001*	4.12 (2.32:5.92)	< 0.001*
Ichy eyes				
No	825			
Yes	605	< 0.001*	5.20 (3.29:7.10)	< 0.001*
Cough				
No	417			
Yes	1013	< 0.001*	3.22 (1.33:5.11)	0.001*
Snoring				
No	404			
Yes	1026	< 0.001*	3.50 (1.59:5.42)	< 0.001*
Perennial symptoms				
No	653			
Yes	777	< 0.001*	3.79 (2.07:5.52)	< 0.001*
Weather change				
No	413			
Yes	1,017	< 0.001*	3.09 (1.11:5.06)	0.002*
Sensitization				
Negative	434			
Positive	996	0.742	-	

Discussion

The main finding of this 19-year study (1998 to 2017) is that house dust mite and sedge remain the most common indoor and outdoor allergens. The second and third most common indoor allergens, which are cockroach and cat. Mosquito has been reported for the allergens of dermatologic manifestations in in the study of allergy clinic of Internal Medicine Department.[23] Its contribution for the respiratory allergic symptoms remains questionable. So, we did not display the sensitization of mosquito in the analysis chart. Sedge, para grass, and Bermuda grass were the most common allergens in our outdoor allergens group. A recent study from another tertiary care center in Thailand reported the most common outdoor allergens to be Bermuda grass and timothy grass.[6]

Regarding the associated symptoms, ophthalmologic symptoms were found in 43.3% of patients, which is consistent with the finding from the aforementioned study from Thailand. We also found that 28.4% of patients suffer from snoring, and that 31.9% of patients have coughing symptoms. This finding supports the concept of one airway – one disease.[27]

In order to quantitatively compare the trend of sensitization prevalence, we utilized the data from the latest five-year period (2013 to 2017). This data set was also used to determine the effect of clinical symptoms and allergic status on patient QoL.

During the 2013 to 2017 period, the percentage of sensitization showed a statistically significant increase from 66.8% to 75.7%. The sensitization pattern of change was found to be greater in indoor allergens (59.6% to 72.3%) than in outdoor allergens (49% to 54%). This finding supports the global trend of epidemiologic study that suggests that allergic sensitization is affected by environmental factors, such as increasing level of industrialization, climate change, and global warming, which may affect dissemination of allergens.[13,18]

House dust mite remained the most common indoor allergen during the 2013 to 2017 period, and sedge remained the most common in the outdoor group. Careless weed assumed a lessor role during the recent period in our study. A study from Singapore reported Bahia grass to be the most common allergen.[28] A recent study from the Philippines found Bermuda grass to be the most common outdoor allergen.[7] *Cladosporium spp*. was the most common in our fungus group. A report from Poland showed *Alternaria spp*. to be the most common, and *Cladosporium spp*. to be the second most common.[24]

We used linear regression multivariate analysis to determine the effect of clinical characteristics and sensitization status on patient quality of life. Similar to previous reports, all of the clinical parameters significantly affect patient QoL in univariate linear regression.[21,29] However, sneezing symptom did not remain significantly associated with QoL in multivariate analysis. Also and surprisingly, sensitization status did not show significant association with QoL. This may be explained by the fact that some patients that have rhinitis symptoms for many years can have either a negative or positive skin prick test. Moreover, there may be a subgroup of patients with local IgE (local allergic rhinitis) who have a negative skin prick test.[30] Regarding the finding of sex as the factor that affects QoL, the finding can also be postulated by the tendency of health awareness of female comparing to male especially when determining the effect of allergic symptoms to QoL.

The notable limitation of this study is its retrospective design. Consistent with this limitation, some data were found to be missing or incomplete. However, all SPT procedures were performed according to uniform technique by trained technicians. Importantly, this study had a large enough sample size to perform multivariate linear regression analysis to identify significant associations between evaluated factors and patient QoL.

Conclusion

The results of this study revealed an increasing prevalence of allergy sensitization. The increase is more pronounced in indoor allergens than in outdoor allergens. House dust mite remains the most comment indoor allergen, and sedge is the most common outdoor allergen. A change in sensitization pattern was found for cockroach, bermuda grass, and para grass. Patient quality of life is affected by all clinical symptoms, except sneezing and allergen sensitization.

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Conflict of interest declaration

All authors declare no personal or professional conflicts of interest relating to any aspect of this study.

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