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Brief communication (Original)

Prevalence of impaired lower airway function in Thai patients with allergic rhinitis

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Background: Allergy is a chronic inflammatory disease, which may affect the upper and lower airway in reversible airflow obstruction or asthma. Spirometry is a noninvasive way to assess lower airway function routinely and to detect reversible airflow obstruction.

Objectives: To determine the prevalence of abnormal spirometry in Thai patients with allergic rhinitis (AR) who did not have lower airway symptoms.

Methods: Spirometry and bronchodilation testing were performed in AR patients.

Results: We included 153 patients aged from 20 to 60 years who had AR (diagnosed by clinical data and positive skin prick test) and who fulfilled the study criteria. Twenty-three patients with AR (15%) showed decreased forced expiratory volume in 1 s (FEV_1) compared with normal values (FEV_1 <80% of predicted value). Four patients with AR (3%) showed reversible airflow obstruction. Thirty-seven patients with AR (24%) showed decreased forced expiratory flow during 25-75 s ($FEF_{25–75}$) compared with the reference value ($FEF_{25–75}$ <80% of predicted value). The sensitization to both indoor and outdoor allergens was statistically and significantly associated with the decreased FEV_1 (odds ratio (OR) = 7.79, 95% confidence interval (CI) 1.08-55.91, $P = 0.03$). The duration of AR was more than 10 years significantly affected $FEF_{25–75}$ (adjusted OR = 2.6; 95%CI = 1.01-6.72, $P = 0.04$).

Conclusions: Impaired lower airway function and reversible airflow obstruction in patients with AR are not uncommon. Spirometry should be performed to detect lower airway impairment early in patients with AR, especially those sensitized to indoor and outdoor allergens.

Keywords: Allergic rhinitis, asthma, FEV_1, reversible airflow obstruction, spirometry

Allergic rhinitis (AR) and allergic asthma are two common allergic diseases. The prevalence of AR worldwide, including Thailand, is 20%-40% [1, 2]. Epidemiologic studies have shown that the prevalence of asthma in patients with AR is 19%-35%, which is higher than the prevalence of asthma in the normal population [3, 4].

There are various ideas about the linkage of upper and lower airways, such as sharing similar airway epithelial lining and pathophysiology, and both conditions respond to same treatment modalities [5-7]. AR may lead to the development of asthma or aggravate an asthmatic attack. The first hypothesis is nasobronchial reflex. This reflex is considered to arise because of evidence that nasal irritation can lead to bronchoconstriction [8]. The second hypothesis is that mouth breathing as a result of AR can lead to unconditioned (cold, dry) air that passes to the lower airway, resulting in bronchial hyperactivity [4]. The third hypothesis is related to the systemic inflammation after the local nasal allergy. Allergic inflammation in the nose leads to release of cytokines and mediators especially interleukin (IL)-5 from bone marrow [9]. The fourth hypothesis is chronic irritation of lower airway from postnasal drip [9].

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To evaluate the lower airway function, spirometry is the standard test. There are various studies from the west that have studied the prevalence of spirometric abnormalities in AR without asthmatic symptoms [10, 11]. Force expiratory volume in 1 s (FEV_1) and the forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25–75}$) have been proposed as early predictors of small airway hyperresponsiveness [11]. In those studies, the risk factors, such as age, sex, duration of symptoms, type of allergen sensitization and symptom severity have been shown to affect spirometric impairment in patients with AR.

In Thailand, the prevalence of asthma associated with AR mostly derives from history taking, implying that patients already have symptoms of asthma [12]. There are limited data of impaired spirometry in AR without asthma in Asians. Although there are several articles showing the relationship between AR and the lower airway, the majority describe AR with concurrent asthma or with aggravation/worsening of asthma symptoms [12-15]. Because of the different types of allergens (e.g. grass pollens) and different clinical manifestations of AR (e.g. seasonal vs. perennial), the objective of this study was to determine the prevalence and risk factors of abnormal spirometry in Thais with AR without lower airway symptoms.

Method

The present study was a cross-sectional examination of pulmonary function in patients with AR. The study was approved by the institutional review board of Siriraj hospital (certificate of approval No. Si224/2009). Written informed consent was obtained from all study participants. Patients with chronic (symptoms ≥1 year) rhinitis with positive allergic skin prick test (SPT) relevant to the history, 20-60 years old, and normal X-ray of the paranasal sinuses and the chest were included. SPT of common indoor allergens (house dust mite, cat, dog, and cockroach) and outdoor allergens (pollens and molds) was conducted. Once a diagnosis of AR was made, the severity of AR was classified according to the standard recommendations of the Allergic Rhinitis with its Impact on Asthma (ARIA) guidelines [16]. Exclusion criteria were pulmonary disease, asthma, current or previous smoking, severe cardiovascular disease, current use of β-blocker drugs, pregnancy, aneurysm in the chest, aorta, or brain, previous history of ophthalmologic, abdominal or thoracic surgeries, immunodeficiency, hepatitis, and gastroesophageal reflux (by history).

Spirometry was performed using a computer assisted spirometer (Koko Spirometer, Ferraris Respiratory, Louisville, CO, USA). Patients stopped medication that may affect the spirometric result before performing the test. The test was conducted by a single technician who is familiar with the technique recommended by the standard guidelines [17]. Two main values of spirometry including FEV_1 and reversible airflow obstruction were considered. Airflow obstruction was defined as FEV_1 values <80% of predicted [17, 18]. According to the guidelines, reversible airflow obstruction was defined as the increased FEV_1 ≥12% from baseline [19]. The association between each spirometric variable and AR parameters such as duration, severity, type of allergen sensitization were analyzed. The other variable of spirometry i.e. the force expiratory flow during 25-75 second ($FEF_{25–75}$), was also recorded and analyzed because some articles proposed this value as a predictor of early airway obstruction [20-22].

Statistical analysis

Data were analyzed using STATA software (STATA version 12.0, Stata Corp, College Station, TX, USA). Age of subjects was shown in mean ± standard deviation (SD). Other baseline characteristic data including sex, duration of rhinitis symptoms, and type of allergen sensitization are expressed in number or percent.

Logistic regression analysis between spirometry and each variable/baseline parameter was analyzed. *P* were based on 2-sides with significant level of < 0.05.

Results

We included 153 patients with AR in the present study. All patient participants fulfilled the criteria of symptoms of chronic rhinitis for one-year or more. None of them had any symptoms of asthma. Their characteristics are described in **Table 1**.

The mean ± SD of FEV_1 and $FEF_{25–75}$ was 98.89 ± 11.93 and 95.64 ± 22.42, respectively. Twenty-three cases (15%) had abnormal FEV_1 (**Table 2**). Four patients had a percent change of FEV_1 higher than 12%. Thirty-seven patients had abnormal $FEF_{25–75}$. (**Table 2**).

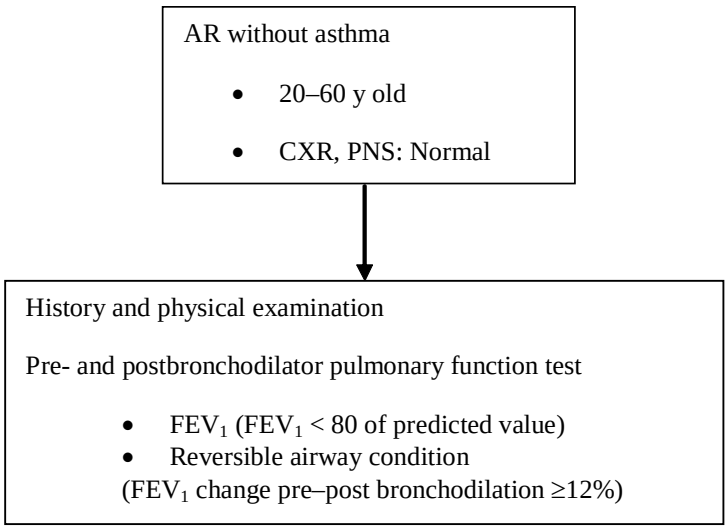

Figure 1. Study flow chart
AR = Allergic rhinitis, CXR = chest x-ray, PNS = film paranasal sinus, FEV_1 = force expiratory volume in 1 s.

Table 1. Patient characteristics

Characteristics	Number (percent)
Age (years)	
Mean ± standard deviation	34.4 ± 10.5 (range 20-59)
Sex	
Male/Female	46 (30%) / 107 (70%)
Duration of symptoms	
≤ 5 years	62 (41%)
5–10 years	52 (34%)
≥ 10 years	39 (26%)
Severity of allergic rhinitis	
Mild intermittent	38 (25%)
Moderate/severe intermittent	37 (24%)
Mild persistent	19 (12%)
Moderate/severe persistent	59 (39%)
Allergic to indoor allergens	25 (16%)
Allergic to outdoors allergens	16 (11%)
Allergic to both indoor and outdoor allergens	112 (73%)

Table 2. Prevalence of abnormal pulmonary function test results

	Number (percent)
Abnormal FEV_1	23 (15%)
Abnormal % change of FEV_1	4 (3%)
Abnormal $FEF_{25–75}$	37 (24%)

FEV_1 = Force expiratory volume in 1 second, $FEF_{25–75}$ = force expiratory flow during 25-75 s

In 23 patients who had FEV_1 less than 80% of predicted value, half had moderate to severe persistent symptom severity. The majority were sensitized to both indoor and outdoor allergens (**Table 3**).

The sensitization to both groups of allergens was significantly associated with FEV_1 abnormality (odds ratio = 7.79, 95% confidence interval (CI) 1.08-55.91, $P < 0.03$). There was no association between FEV_1 abnormality and other variables such as duration of allergy, symptom severity, sensitization to indoor allergens only and sensitization to outdoor allergens only (**Table 4**).

Four patients had the percent changes of FEV_1 ≥12% after bronchodilator administration. There was no association between abnormal percent change of FEV_1 and the duration of allergy, symptom severity, type of allergen sensitization (**Table 5**).

Thirty-seven patients had the value of $FEF_{25–75}$ <80% of predicted value. From the univariate analysis, moderate/severe intermittent symptom severity seemed to affect $FEF_{25–75}$. Therefore, in the multivariate analysis of symptom severity was not significant.

The duration of allergic symptoms >10 y significantly affected $FEF_{25–75}$. Multivariate analysis found duration significantly affected $FEF_{25–75}$ (adjusted OR = 2.07; 95%CI = 1.01-4.25, $P < 0.05$). There was no influence of abnormal percent change of $FEF_{25–75}$ on sensitization to indoor or outdoor allergens (**Table 6**).

Table 3. Prevalence of abnormal pulmonary function (Force expiratory volume in 1 s <80%), duration of allergy, severity of allergic symptoms, and sensitization to allergens

	Number	Prevalence (%)
Overall prevalence	153	23 (15)
Duration of allergy		
≤ 5 years	62	10 (16)
5–10 years	52	7 (14)
≥ 10 years	39	6 (15)
Severity of allergic symptoms		
Mild intermittent	38	4 (11)
Moderate/severe intermittent	37	5 (14)
Mild persistent	19	2 (11)
Moderate/severe persistent	59	12 (20)
Sensitization to indoor allergens	25	1 (4)
Sensitization to outdoor allergens	16	1 (6)
Sensitization to both indoor and outdoor allergens	112	21(19)

Table 4. Clinical characteristics and their relation to FEV_1

Characteristics	Total	Subject with FEV_1 < 80%	OR	95%CI	*P*
Duration of allergy (y)					
≤ 5	62	10 (16%)	1	-	
5–10	52	7 (14%)	0.83	0.34-2.04	0.691
≥ 10	39	6 (15%)	0.95	0.38-2.42	0.921
Severity of allergic symptoms				-	
Mild intermittent	38	4 (11%)	1	-	
Moderate/severe intermittent	37	5 (14%)	1.28	0.37-4.41	0.691
Mild persistent	19	2 (11%)	1	0.20-4.98	1.000
Moderate/severe persistent	59	12 (20%)	1.93	0.67-5.55	0.203
Sensitization to indoor allergens	59	1 (4%)	0.23	0.08-1.65	0.09
Sensitization to outdoor allergens	16	1 (6%)	0.39	0.06-2.69	0.29
Sensitization to indoor and outdoor allergens	112	21 (19%)	7.79	1.08-55.91	***0.03**

OR = odds ratio, CI = confidence interval, FEV_1 = force expiratory volume in 1 s, **P* < 0.05

Table 5. Clinical characteristics and their relation to percent changes of FEV_1

Characteristics	Total	Subject with percent change $FEV_1 \geq 12\%$	OR	95%CI	*P*
Duration of allergy (y)					
≤ 5	62	0 (0%)	-	-	
5–10	52	3 (5.8%)	-	-	0.06
≥ 10	39	1 (2.6%)	-	-	0.21
Severity of allergic symptoms					
Mild intermittent	38	1 (2.63%)	1	-	
Moderate/severe intermittent	37	1 (2.7%)	1.03	0.07-15.82	0.99
Mild persistent	19	0 (0%)	0	-	0.48
Moderate/severe persistent	59	2 (3.39%)	1.28	0.12-13.71	0.83
Sensitization to indoor allergens	25	2 (8%)	5.12	0.75-34.66	0.06
Sensitization to outdoor allergens	16	0 (0%)	0	0	0.48
Sensitization to indoor and outdoor allergens	112	2 (1.79%)	0.36	0.05-2.51	0.28

OR = Odds ratio, CI = Confidence interval, FEV_1 = force expiratory volume in 1 s

Table 6. Clinical characteristics and their relation to $FEF_{25–75}$

Characteristics	Total	Participant with $FEF_{25–75}$ <80%	OR	95%CI	*P*
Duration of allergy (y)					
≤ 5	62	10 (16%)	1	-	
5–10	52	14 (27%)	1.67	0.81-3.04	0.16
≥ 10	39	13 (33%)	2.07	1.01-4.25	***0.04**
Severity of allergic symptoms					
Mild intermittent	38	10 (26%)	1	-	
Moderate/severe intermittent	37	9 (24%)	0.92	0.42-2.01	0.04
Mild persistent	19	4 (21%)	0.80	0.28-2.21	0.66
Moderate/severe persistent	59	14 (24%)	0.90	0.44-1.81	0.77
Sensitization to indoor allergens	25	8 (32%)	1.41	0.73-2.71	0.31
Sensitization to outdoor allergens	16	6 (38%)	1.66	0.82-3.35	0.19
Sensitization to both indoor and outdoor allergens	112	23 (21%)	0.60	0.34-1.05	0.08

OR = odds ratio, CI = confidence interval, FEV_1 = force expiratory volume in 1 s, $FEF_{25–75}$ = force expiratory flow during 25–75 second, **P* < 0.05

Discussion

International Study of Asthma and Allergies in Childhood (ISAAC) standardized questionnaire showed that the prevalence of asthmatic symptoms ranged from 2.1% to 32.2% [2]. In Thailand, the ISAAC phase three survey showed that 13.9%–25% of children with rhinitis had asthma [1]. Recently, we reported 16.1% of our patients with AR treated at the ear, nose, and throat (ENT) allergy clinic had concomitant symptoms of asthma [12]. In that study, 15 percent of patients with AR (23 of 153 patients) had abnormal FEV_1 even though they did not have any lower airway symptoms. Our 15% prevalence of FEV_1 abnormality differs from the finding reported by Ciprandi et al. (8% prevalence) even though the standard criteria, the value of FEV_1 <80% of predicted value was used as the outcome parameter [11]. These 23 cases of our series have been followed up regularly in our ENT allergy clinic to monitor the possibility of lower airway involvement.

Because the definition of asthma is a reversible airway condition, some studies considered ≥12 percent change of FEV_1 after bronchodilator administration as another variable by which to diagnose asthma [23]. In our study, only 4 patients showed ≥12 percent changes of FEV_1.

Ciprandi et al. proposed the $FEF_{25–75}$ as an early indicator of lower airway involvement [20, 24, 25]. The various cut-off value of $FEF_{25–75}$ has been proposed, but the consensus of cut-off value has not yet been established. When using the criteria of $FEF_{25–75}$ less than 80% of predicted value as suggested [26], the prevalence of abnormal $FEF_{25–75}$ was 24.2% (37/153 patients) in our study. The prevalence of our abnormal $FEV_{25–75}$ was higher than the finding of Ciprandi et al. (11%) in 2009.

Several clinical parameters may influence the abnormality of spirometry. For example, duration of rhinitis had been shown to be moderately correlated (Pearson's correlation coefficient = 0.36) with the abnormality of FEV_1 [26]. Our data showed the longer duration of AR (especially a duration >10 y) affected the $FEF_{25–75}$. This data is consistent that reported by Ciprandi et al. in 2010, who found that patients with a long duration of AR were more likely to develop small airway obstruction [26].

The nasal symptom severity (as measured by total nasal symptom score) has been shown to affect nasal airflow and FEV_1 [27]. When nasal symptom severity was classified according to ARIA classification, the majority of our patients were categorized as the moderate–severe/persistent group [16, 28]. The symptom severity, according to ARIA classification, did not show influence on spirometric values either FEV_1, percent change of FEV_1 or $FEF_{25–75}$ in our study.

Spirometry can show sensitization to outdoor and indoor allergens. Ciprandi et al. [26] showed significant influence of pollen allergen ($P < 0.01$) and barely significant of perennial allergens ($P < 0.05$) on FEV_1 and $FEF_{25–75}$. In the present study, sensitization to indoor and outdoor allergens significantly influenced FEV_1 ($P < 0.05$). By contrast with the studies from Europe, pollen sensitization or allergy showed no influence on FEV_1 in our patient participants [29, 30].

An explanation for the differences in prevalence of spirometric abnormalities and risk factors between our present study and the various studies conducted in Europe are proposed as follows. First, allergens in Thailand differ from those in Europe or North America, for instance birch, hazel, and olive trees are rare in Thailand. Second, the severity of AR has been classified according to ARIA instead of a visual analog scale. Last, in tropical countries, a pattern of perennial AR is more prevalent than seasonal AR.

Although the present study provides information regarding the prevalence of abnormal spirometry results in patients with AR, it has some limitations. First, patients may not be presenting lower airway obstruction on the occasion of the examination, but on different occasions bronchospasm may develop. The application of allergen-specific nasal provocation tests in combination with spirometry in patients with AR showed that allergic nasal reactions may lead to the development of upper and/or lower ventilation obstruction in patients with AR and previously normal spirometry [31, 32]. Second, other spirometry variables such as forced vital capacity (FVC) or the ratio of FEV_1 to FVC were not included in the interpretation. Third, the possibility that other unrecognized lower airway conditions (such as occult bronchiectasis) might interfere with interpretation of spirometric abnormality cannot be excluded. Nevertheless, this study included the patients with AR without any lower airway symptoms, without abnormal chest x-ray, and who were nonsmokers. Moreover, all participants stopped antiallergic medication for one week before the day of spirometry, because of the allergen skin prick test was performed on the same day. These modalities would reduce the possibility of confounding factors affecting pulmonary function test interpretation.

Conclusion

In patients with AR who had no symptoms of lower airway, the prevalence of abnormal FEV_1 (<80% of predicted value) and abnormal percent change of FEV_1 (≥12%) after bronchodilator were 15% and 2.6% respectively. The early predictor of small airway obstruction ($FEF_{25–75}$) was abnormal in 24.2%. The sensitization to both indoor and outdoor allergens significantly affected FEV_1 abnormality. A duration of allergy more than 10 y significantly affected $FEF_{25–75}$. When patients with AR seek treatment, the lower airway status should always be evaluated. Awareness of upper and lower airway linkage will lead to early and proper treatment before significant deterioration of lower airway function occurs. A suspicion of bronchial asthma should be raised especially in patients from an AR subgroup.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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