Survey of Asthmatic Patients' Sensitization to House Dust Mites in Southwestern Taiwan

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Background: House dust mites (HDM) are one of the major risk factors for the development of bronchial asthma. The percentage of sensitization to HDM was reported to be 71.9% in Taipei City. In southwestern Taiwan, the percentage of sensitization to HDM has not been estimated. We retrospectively reviewed the medical records of asthmatic patients treated at the Chiayi branch of Chang Gung Memorial Hospital to investigate the percentage and associations with demographic characteristics.

Methods: We analyzed the data of 194 asthmatic patients diagnosed between January 2003 and July 2005. Sensitization to indoor allergens was identified by serum specific immunoglobulin E (IgE) of ImmunoCAP. Demographic characteristics of age, gender and residence were evaluated for associations with allergic sensitization.

Results: The percentage of sensitization to HDM was only 45.9% in patients in southwestern Taiwan. The majority of the studied group were elderly patients. The age variable significantly influenced the percentage of sensitization to HDM and cockroaches ($p < 0.001$ in both comparisons). The gender variable contributed to sensitization to cockroaches only ($p = 0.002$). For residential variables, there was no significant difference in the percentage of allergic sensitization to all tested indoor allergens among distinct areas of southwestern Taiwan.

Conclusion: The percentage of sensitization to HDM in asthmatic patients residing in southwestern Taiwan was lower than that in metropolitan patients. This discrepancy might be attributed to the larger proportion of aged patients.

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Key words: asthma, house dust mites, allergy, sensitization, Taiwan.

Asthma is an atopic disease, manifested by sensitization to environmental allergens. The development of asthma depends on an interaction between genetic factors and environmental allergens, especially house dust mites (HDM).[1,2] Allergic exposure leads to sensitization, and sensitization to HDM is an important risk factor for the development of asthma in childhood.[3] The prevalence of sensitization to HDM in atopic patients is around 70% to 90% worldwide.[4] In Taipei, Taiwan, HDM were also the

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most important allergens and Dermatophagoides pteronyssinus (Der p) was the dominant species found in house dust, with an incidence of about 78.8%.[5,6] The percentage of sensitization to HDM was 71.9%, estimated from the outpatient clinics of the Taipei branch of Chang Gung Memorial Hospital.[7] However, the percentage of sensitization to HDM has been shown to be different for those living in distinct regions, even in the same country. Some reports indicate that urbanization may influence the percentage of sensitization to HDM but its contribution is still controversial.[8,9] Climate conditions also affect the percentage but only relative humidity has been conclusively associated with sensitization and distribution of HDM.[10] In southwestern Taiwan, where most people reside in suburban and rural areas, the percentage of sensitization to HDM has not been estimated and may be different from that of urban areas of Taiwan. In order to elucidate the clinical significance of sensitization to HDM in asthmatic patients in southwestern Taiwan, we retrospectively reviewed the medical records of patients with asthma from outpatient clinics of the Chiayi branch of Chang Gung Memorial Hospital. The majority of patients in this hospital were from Chiayi County and neighboring counties, such as Yunlin and Tainan. In this report, we investigate the percentage of sensitization to HDM and other indoor allergens identified by serum allergen specific immunoglobulin E (IgE) and explore associations with demographic characteristics.

METHODS

The medical records of patients with bronchial asthma diagnosed between January 2003 and July 2005 were included for review. The diagnosis of asthma was based on the criteria of the 2002 Global Initiative for Asthma (GINA) guidelines.[11] All patients enrolled for analysis of percentage of sensitization to indoor allergens had positive results to the methacholine bronchial provocation test. There were 194 consecutive patients (78 females and 116 males) recruited. All of them received blood sampling for IgE assay of ImmunoCAP (Pharmacia CAP System; Pharmacia Diagnostics AB, Uppsala, Sweden).[12] The specific IgE levels of 6 indoor allergens were analyzed, including Der p, Dermatophagoides farinae (Der f) (to be changed to Blomia tropicalis (Blom t) after March 2004), Cat epithelium and dander (Cat), Dog dander (Dog), Cockroach German (Cockroach) and Candida albicans (Candida). The Pharmacia CAP system defines seven quantitative classes by the following criteria: class 0, below 0.35 kUA/l; class 1, 0.35 to 0.7 kUA/l; class 2, 0.7 to 3.5 kUA/l; class 3, 3.5 to 17.5 kUA/l; class 4, 17.5 to 50 kUA/l; class 5, 50 to 100 kUA/l; class 6, above 100 kUA/l. A value of 0.35 kUA/l or above is identified as a positive result and considered positive sensitization to allergen.[13-14] Some specimens were randomly sampled to be rechecked at Chang Gung Memorial Hospital in Taipei and the laboratory of Pharmacia Diagnostics AB (Taiwan), and no discrepancy was ever found.

The ImmunoCAP results were analyzed to investigate the percentage of sensitization to HDM (positive results of specific IgE assay for either Der p or Der f/Blom t) and the other five indoor allergens among asthmatic patients residing in southwestern Taiwan. Demographic characteristics including age, gender and residence were evaluated for associations with the percentage of allergic sensitization. The age category was divided into 4 age groups: < 21 years, 21-40 years, 41-60 years and > 60 years. The residential variables were classified as: Chiayi City, an urban area with a population of 267,000 (area C); the suburban areas of Chiayi County near the beaches (area S); the mountainous areas of Chiayi County (area M); Yunlin County, in the north of Chiayi County (area Y); Tainan County, in the south of Chiayi County (area T).

Statistical analysis

The chi-square test or Fisher's exact test were used to examine the percentage difference of sensitization to individual allergens within different age groups, gender and residential variables. The mean ages of patients sensitized and non-sensitized to HDM were compared by two-sample *t*-test. The chi-square test was used to compare the percentage difference of sensitization to HDM among age groups, gender and residence. In order to enhance the effect of demographic variables on allergic sensitization, we summed the CAP system classes of all indoor allergens in individual subgroups as an indoor allergic sensitization score. The comparison of scores between demographic variables was tested by one-way analysis of variance (ANOVA) for age groups and residences, and by two-sample t-test for gender.

In order to adjust type I error, the Bonferroni method was used for multiple comparisons within demographic variables with significantly different scores. A *p* value of less than 0.05 was regarded as statistically significant.

RESULTS

The demographic characteristics and allergic sensitization of the enrolled asthmatic patients are demonstrated in Table 1. There were a total of 194 asthmatic patients, 78 females and 116 males. Approximately 46.9% of the patients were over 60 years old and the percentage of those younger than 21 years was only 8.8%. The mean age was 53 years. There was no significant difference in mean age between female and male patients (54.47 vs. 52.47 years, respectively). Most of the patients in this study resided in areas S and Y (46.9% and 30.9%, respectively). The positive rate of ImmunoCAP for any of six indoor allergens (with a value of 0.35 kUA/l or above) was 56.2%. The percentage of sensitization to the indoor allergens was, in decreasing order, HDM 45.9%, Cockroach 24.7%, Candida 22.2%, Dog 8.8% and Cat 3.1%. The percentage of sensitization to HDM was obviously lower than the result (71.9%) from outpatient clinics at the Taipei branch of Chang Gung Memorial Hospital.[7] In addition, the demographic characteristics, including age, gender and residence, were analyzed for association with the percentage of sensitization to HDM and other indoor allergens. The results are summarized in Table 2. The percentage of sensitization to Der p, Der f/Blom t and Cockroach were significantly different among distinct age groups ($p < 0.001$ in three comparisons). The gender variables contributed to sensitization to Cockroach only and male patients had significantly higher frequency of sensitization than female patients (32.8% vs. 12.8%, respectively; $p = 0.002$).

We further focused on the percentage of sensitization to HDM and summarized the results for two species of dust mites for further analyses. As shown in Table 3, the patients with HDM sensitization were younger than those without sensitization (43 vs. 61 years, respectively). The percentage of sensitization to HDM was 88.3% in patients younger than 21 years and declined with aging. Regarding the effect of residential variables on the percentage, our data indicated that the distinct residence did not contribute to a significant difference in the percentage of sensitization to any indoor allergen including HDM. The univariate comparisons of indoor allergic sensitization scores, by sum of the CAP system classes for

Table 1. Demographic Characteristics and Allergic Sensitization of Asthmatic Patients in Southwestern Taiwan

Characteristic	n = 194	%
Age (mean±SD: 53.27±19.98; range: 8-85)		
<21 yr	17	8.8
21-40 yr	39	20.1
41-60 yr	47	24.2
>60 yr	91	46.9
Gender		
Female (mean age ±SD: 54.47 ±17.89)	78	40.2
Male (mean age ±SD: 52.47 ±21.30)	116	59.8
Residence		
Area C	8	4.1
Area S	91	46.9
Area M	19	9.8
Area Y	60	30.9
Area T	16	8.2
CAP		
Positive	109	56.2
Negative	85	43.8
HDM		
Positive	89	45.9
Negative	105	54.1
Cockroach		
Positive	48	24.7
Negative	146	75.3
Candida		
Positive	43	22.2
Negative	151	77.8
Dog dander		
Positive	17	8.8
Negative	177	91.2
Cat dander		
Positive	6	3.1
Negative	188	96.9

Abbreviations: SD: standard deviation; Area C: Chiayi City urban area; Area S: suburban areas of Chiayi County near the beaches; Area M: mountainous areas of Chiayi County; Area Y: Yunlin County north of Chiayi County; Area T: Tainan County south of Chiayi County; HDM: house dust mites, either Dermatophagoides pteronyssinus (Der p) or Dermatophagoides farinae/Blomia tropicalis (Der f/Blom t); CAP: specific IgE tests of six indoor allergens by ImmunoCAP, any of six indoor allergens with a value of 0.35 kUA/l or above (≧ class 1) equals a positive result; Cockroach: Cockroach German; Candida: Candida albicans; Cat dander: Cat epithelium and dander.

Table 2. Sensitization to Individual Indoor Allergens and Influence of Demographic Factors

Variable	Age					Gender			Residence					
	<21 yr (n = 17)	21-40 yr (n = 39)	41-60 yr (n = 47)	>60 yr (n = 91)	*p* value	Female (n = 78)	Male (n = 116)	*p* value	C (n = 8)	S (n = 91)	M (n = 19)	Y (n = 60)	T (n = 16)	*p* value
Der p														
N	2	12	25	72	< 0.001	47	64	0.483	4	54	11	32	10	0.925
P	15	27	22	19		31	52		4	37	8	28	6	
Der f/Blom t														
N	3	13	24	71	< 0.001	47	64	0.483	4	56	12	31	8	0.693
P	14	26	23	20		31	52		4	35	7	29	8	
Cockroach														
N	4	25	36	81	< 0.001	68	78	0.002	7	71	15	42	11	0.693†
P	13	14	11	10		10	38		1	20	4	18	5	
Candida														
N	12	34	34	71	0.345	65	86	0.131	8	69	15	49	10	0.290†
P	5	5	13	20		13	30		0	22	4	11	6	
Dog														
N	15	32	44	86	0.112†	72	105	0.665	7	83	16	57	14	0.405†
P	2	7	3	5		6	11		1	8	3	3	2	
Cat														
N	17	36	46	89	0.325†	76	112	1†	8	89	19	58	14	0.277†
P	0	3	1	2		2	4		0	2	0	2	2	

Abbreviations: Der p: Dermatophagoides pteronyssinus; Der f: Dermatophagoides farinae; Blom t: Blomia tropicalis; Cockroach: Cockroach German; Candida: Candida albicans; Dog: Dog dander; Cat: Cat epithelium and dander; N: negative result of allergen sensitization; P: positive result of allergen sensitization.
p value refers to comparison of percentage of sensitization to individual indoor allergens within different age groups, gender and residential variables to be tested by chi-square test or Fisher's exact test†.

Table 3. Percentage of Sensitization to House Dust Mites by Demographic Variables

Variable	HDM positive (n = 89)	HDM negative (n = 105)	*p* value
Age, yr (mean ± SD)	43.56 ± 20.05	61.5 ± 15.85	< 0.01‡
<21 yr	15 (88.2%)	2 (11.8%)	< 0.01
21-40 yr	28 (71.8%)	11 (28.2%)	
41-60 yr	24 (51.1%)	23 (48.9%)	
>60 yr	22 (24.2%)	69 (75.8%)	
Gender			0.413
Female	33 (42.7%)	45 (57.3%)	
Male	56 (48.3%)	60 (51.7%)	
Residence			0.907
Area C	4 (50%)	4 (50%)	
Area S	39 (42.9%)	52 (57.1%)	
Area M	8 (42.1%)	11 (57.9%)	
Area Y	30 (50%)	30 (50%)	
Area T	8 (50%)	8 (50%)	

Abbreviations: HDM: house dust mites; HDM positive: sensitization to house dust mites; HDM negative: non-sensitization to house dust mites.
‡ *p* value refers to the difference in mean age between HDM positive and HDM negative by independent *t*-test.
Other *p* values refer to the percentage difference of sensitization to HDM among age groups, gender and residences by chi-square test.

all six allergens, to demographic variables are shown in Table 4 and multiple comparisons within different age groups are demonstrated. Age and gender were significantly associated with indoor allergic sensitization scores. In the age category, younger patients had significantly higher scores than older patients ($p < 0.001$) and the score decreased with aging. Male patients had significantly higher scores than female patients (mean: 3.84 vs. 2.62, respectively; $p = 0.032$). The residential variables had no effect on allergic sensitization, even after enhancement by sum of CAP system classes for all allergens ($p = 0.802$).

DISCUSSION

The specific type of airborne allergens varies with the geoeconomic situation. In Taiwan, HDM were the most important allergens among respiratory allergies.[15] In the metropolis of Taipei City, the percentage of sensitization to HDM was as high as 71.9% among asthmatics.[7] In southwestern Taiwan, there was a markedly lower percentage of positive

Table 4. Univariate Comparisons of Indoor Allergic Sensitization Score* for Demographic Variables

Variable	n (194)	Score (Mean ± SD)	*p* value
Age			<0.001†
I: <21 yr	17	8.4706 ±5.1492	I>II, II, IV
II: 21-40 yr	39	4.9744 ±4.2950	II>IV
III: 41-60 yr	47	3.4468 ±3.6879	III>IV
IV: >60 yr	91	1.6484 ±2.8377	
Gender			0.032‡
Female	78	2.6154 ±3.3968	
Male	116	3.8448 ±4.5004	
Residence			0.802§
Area C	8	3.1250 ±3.9799	
Area S	91	3.0220 ±3.6116	
Area M	16	3.7895 ±5.5536	
Area Y	60	3.5000 ±4.1843	
Area T	16	4.2500 ±5.0794	

Abbreviations: Allergic sensitization score*: sum of the CAP system classes for all six indoor allergens; Area C: Chiayi City urban area; Area S: suburban areas of Chiayi County near the beaches; Area M: mountainous areas of Chiayi County; Area Y: Yunlin County north of Chiayi County; Area T: Tainan County south of Chiayi County.

p values refer to the difference among age groups† by one-way ANOVA followed by Bonferroni multiple comparisons, between gender‡ by two-sample t-test and among residences§ by one-way ANOVA.

sensitization to indoor allergens. The most common sensitization allergen in asthmatics was still HDM, with a percentage 45.9% which was lower than that in the metropolis. However, the interpretation of our data could be limited due to too small a patient population, data collection from one local hospital and unknown comorbidity of allergic rhinitis. Even though an entirely different result was expected, it may be worth trying to analyze the possible factors that contributed to the percentage difference.

Many factors have been reported to influence the prevalence of sensitization to HDM, including genetic variants, age, gender and environmental factors.[16-18] There have been many studies seeking an association between environmental factors and mite sensitization but most results remain controversial. Only climatic conditions and damp conditions are documented as increasing the percentage of sensitization.[19,20] The climatic records from the Central Weather Bureau of Taiwan show the mean monthly temperature is 22°C in Chiayi County, almost the same as in Taipei City. The mean monthly relative humidity is 82% in Chiayi County and 77% in Taipei City. Climatic conditions and relative humidity seem similar in these two regions, and may not provide any contribution to the percentage variance. In addition, the urbanization of distinct areas has been demonstrated to affect the percentage of sensitization to HDM but the results vary in different reports.[8,9] In the present study, the percentage of sensitization to HDM appeared similar among distinct residential areas with different degrees of urbanization. However, the interpretation of our data was limited due to unknown duration of residence and the residential subgroup in Chiayi City being too small in number to conclude that there was a different prevalence between urban and suburban areas in this region. Except for those in Chiayi City, most of our patients reside in suburban and rural areas. It seems reasonable that the lower percentage of sensitization to HDM in southwestern Taiwan compared with Taipei City might be caused by the variant urbanization. However, the term "urbanization" involves a number of more complicated conditions including different factors that have the effect of sensitization to HDM. It is not appropriate to take urbanization as the single reason for the difference in the percentage of sensitization to HDM.

On the other hand, some reports revealed that male gender had a higher frequency of sensitization to HDM.[18] In the present study, male gender contributed to significantly higher indoor allergic sensitization scores and significantly higher frequency of Cockroach sensitization, both of which are in accordance with a previous report.[21] However, our data did not show a higher percentage of sensitization to HDM among the male gender. Regarding the effect of aging on allergic sensitization, we were aware that serum IgE levels decreased significantly with aging for atopic individuals. Furthermore, some reports indicated that the frequency of sensitization to HDM showed a normal distribution curve, with a peak in young adults, and decreased with aging.[4,22] In our study, the change of percentage with aging revealed a similar trend i.e. higher in young patients but declining in elderly subjects. Moreover, we also found the same effect of aging on Cockroach sensitization.[23]

Elderly patients made up the majority of our asthmatic population and the mean age was 53 years. In Chiayi and Yunlin Counties, the indexes of aging

are 74.95% and 69.19%, respectively; both are markedly higher than that of 58.15% for Taipei City in 2003. (Index of aging is the percentage of the population aged above 65 years compared to the population aged 0-14 years. Data are from the Accounting and Statistics Office of Chiayi County Government, Accounting and Statistics Office of Yunlin County Government and Department of Budget, Accounting and Statistics of Taipei City Government.) Our older asthmatic population reflects the aging of the general population in this region. The higher percentage of aged patients and decreasing sensitization with aging contributed to the lower percentage of sensitization to HDM in southwestern Taiwan. Even though there was a lower percentage of sensitization to indoor allergens in the aged group, elderly asthmatics appeared to have more severe asthma and higher mortality.[24] Most studies focused on the development of child asthma because of the concept of the cohort effect to asthma, and the asthmatic pathogenesis of aged subjects has seldom been studied.[25] All of our asthmatic patients had a positive result for the methacholine bronchial provocation test, indicating the presence of bronchial hyperresponsiveness in nature. It has been known that bronchial hyperresponsiveness is associated with airway inflammation and atopy.[26,27] If this is so, how do we explain the lower percentage of sensitization to aeroallergens in elderly asthmatic patients? There might be two possible explanations: one is that allergens different from the major ones in young asthmatic patients associate with bronchial hyperresponsiveness in older subjects; another is that not allergens but irritants cause most airway inflammation in aged asthmatic patients.[28-30] Our data warrants further study regarding the development of bronchial asthma in aged patients, in particular those without sensitization to HDM. Additionally, a novel approach for primary and secondary prevention of asthma, conducted on the basis of the prevalence of sensitization to allergens and different populations, in individual regions is thus recommended.

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臺灣西南部氣喘病人塵蟎敏感調查

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背 景： 塵蟎是氣喘的主要危險因子之一。在台灣台北，氣喘及過敏性鼻炎病人對塵蟎敏感的比率約 71.9%。在台灣西南部，大部分的氣喘病人是居住在市郊或鄉下，而他們對於塵蟎敏感的比率目前尚未確知。我們從長庚紀念醫院嘉義分院的門診氣喘病患，去作回顧分析以調查塵蟎敏感比率，並探討影響塵蟎敏感比率的因素。

方 法： 我們回顧從 2003 年 1 月到 2005 年 6 月門診氣喘病人的病歷，共 194 個有激發測試陽性反應的氣喘病人；統計 ImmunoCAP 的室內過敏源敏感測試結果，並分析和居住地、年齡、及性別對過敏源敏感比率的相關性。

結 果： 台灣西南部氣喘病人塵蟎敏感比率只有 45.9%，明顯比台北低。而大多數本研究的病人年紀較大，平均年齡爲 53 歲。更進一部分析發現小於 21 歲的病人塵蟎敏感比率較高，年齡變項對於塵蟎和蟑螂的敏感有顯著影響 (p 值都小於 0.001)。而性別變項只對蟑螂敏感有影響 (p 值等於 0.002)，男性病人有較高的蟑螂敏感率。在不同居住地變項對所有測試的室內過敏源敏感的影響並沒有顯著差異。

結 論： 台灣西南部塵蟎敏感的比率只有 45.9%，明顯比都會台北的病人低，這樣偏低的塵蟎敏感率歸因於年紀大的病人佔該地區氣喘病人的大部份。

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關鍵詞： 氣喘，塵蟎，過敏，敏感，台灣。

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