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Indoor environmental risk factors and seasonal variation of childhood asthma

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Seasonality of asthma may result from varying exposures. This cross-sectional study was designed to examine the relationship between indoor environmental factors and seasonal childhood asthma. Study subjects were participants from the International Study of Asthma and Allergies in Childhood (ISAAC) in 2004, a population-based surveillance, which included school children aged 6–15 yr in south Taiwan. Cases included 1725 children who experienced asthma symptoms in the past 12 months and the references consisted of 19,646 children who reportedly have no asthma history. By using a moving average and principal component analysis, asthmatic children were grouped into four asthma subtypes: winter, spring, summer/fall, and perennial. Multivariate logistic regression was used to evaluate the effect of indoor environmental factors on seasonality of childhood asthma. For all asthma prevalence, a peak occurred in the winter and a nadir appeared in summer. Contributing factors of asthma for children, regardless of seasonality, included younger age, parental atopy, maternal smoking during pregnancy, breast feeding, and perceived air pollution. After adjusted for salient risk factors, water damage was significantly associated with all subtypes of asthma. Presence of cockroaches was related to the summer/fall asthma (adjusted odds ratio [aOR] = 1.65, 95% confidence interval [CI] = 1.12–2.55). Visible mold on the walls was associated with an increased occurrence of winter and spring asthma (aOR = 1.53, 95% CI = 1.26–1.85 and aOR = 1.34, 95% CI = 1.10–1.62, respectively). Passive smoking was shown to be related to spring and summer/fall asthma. Water damage is a possible risk for childhood asthma year-round. Cockroaches and visible mold on the walls may play essential roles for seasonality of childhood asthma in Taiwan. Plausible mechanisms and allergic effects should be further determined. Elimination of these allergens is necessary to help prevent the development of asthma.

Yueh-Ying Han[1], Yung-Ling Lee[2] and Yueliang Leon Guo[1,3]

[1]Department of Environmental and Occupational Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [2]Institute of Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan, [3]Department of Environmental and Occupational Medicine, National Taiwan University Hospital, Taipei, Taiwan

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Yueliang Leon Guo, PhD, MD, MPH, No. 17, Shyujou Rd., Rm339, Taipei 100, Taiwan
Tel.: +886 2 3322 8216
Fax: +886 2 2327 8515
E-mail: leonguo@ntu.edu.tw

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Asthma is a disease consisting of a cluster of symptoms, which may result from varying exposures. It is a major chronic disease among children. The prevalence of asthma has been reportedly increasing in children and young adults from Western and Asian countries (1). This increasing prevalence of childhood asthma was also remarkable in Taiwan over the past decades (2, 3). These unfavorable trends may partly be explained by changes in case ascertainment and diagnostic practice on asthma overtime (4). Atopic heredity is also related to the development of asthma (5), nevertheless, it is unlikely to account for the striking epidemic of childhood asthma. Environmental factors, including air pollutants, indoor allergens, gas cooking and nitrogen dioxide, environmental tobacco smoking (ETS), and urbanization, have been suggested to contribute to the increasing asthma occurrence (6, 7). Some lifestyles, dietary habits, and behavior changes may also contribute (8).

Although the etiology of childhood asthma is not well-established, a seasonal variation of asthma has been widely recognized. For instance, incidence and mortality of asthma, general practice episodes, and hospital admission all vary by seasons (9, 10). Additionally, seasonal patterns in climate changes (11), air pollutants (12), pollen counts (13), fungal spore (14), and dust mite populations (15) are reported to be associated with asthma seasonality. It is also considered that pollen is more likely related to seasonal asthma, whereas dust mites to perennial asthma. Indoor allergen exposure has been presumed as the most significant risk factor for childhood asthma, yet the specific allergens among seasons are uncertain. A better understanding of asthma risk factors according to seasons or climate conditions could be used for lifestyle improvement and asthma prevention. The purpose of this cross-sectional study is to examine the association between seasonal asthma and indoor environmental factors among children in Taiwan.

Methods

Study design

In 2004, this cross-sectional population-based study was conducted in five administrative districts of southern Taiwan, including Tainan County, Tainan City, Kaohsiung County, Kaohsiung City, and Pintung County (Fig. 1) School children were randomly selected from 20 of the 189 middle schools and 74 of the 627 elementary schools. Stratified sampling by grades was applied in each school. A modified Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was taken home by students and answered by their parents. A total of 22,545 children were selected from 30,082 participants aged 6–15 yr. We excluded 7537 children because of incomplete questionnaires and obtained an overall 75% response rate.

The study was approved by the Respiratory Health Screening Steering Committee of the Taiwan Department of Health and by the

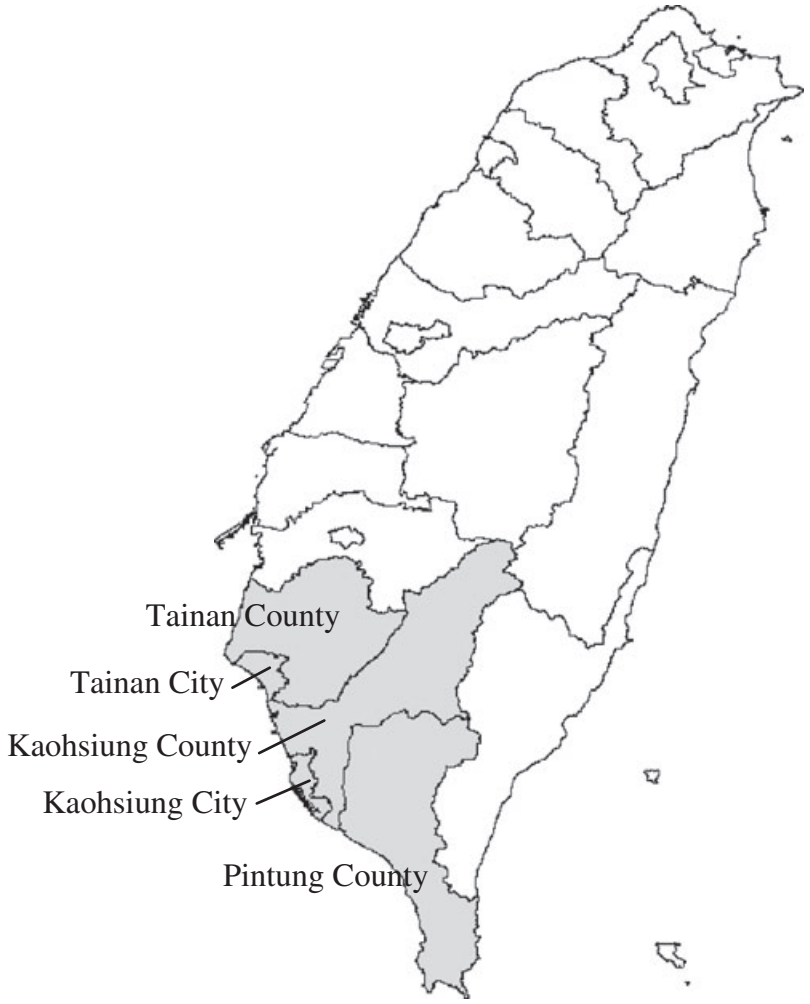

Fig. 1. Five administrative districts of the study in southern Taiwan.

Institutional Review Board at National Taiwan University Hospital. Informed consent was obtained from parents for each participant.

Outcome and exposure

The revised ISAAC questionnaire included information on demographic characteristics, health history, environmental exposures, hereditary factors, and potential confounders. The validity of the questionnaire was evaluated by pulmonologists and epidemiologists (16). The definition of current asthma was determined by the questions answered by the main caretaker, ''Has this child ever been diagnosed by a physician as having asthma?''(Q1) ''Has this child ever experienced dyspnea with wheezing in the chest?''(Q2) If the answers were ''yes'' to both above questions, he/she would be further asked, ''Has this child ever experienced dyspnea with wheezing in the chest in past 12 months?''(Q3) Those who reported ''yes'' to this question were defined as current asthma cases. A total 1725 children were identified as current asthma cases. A total of 19,646 children whose main caretaker answered ''No'' to both Q1 and Q2, and were grouped into the reference group.

Those who experienced asthma in the past 12 months were asked to identify the months of attacks. The month with asthma attack was given an original attack score of 1, and the month without attack given score of 0. Seasonality of asthma attacks was classified as follows: (i) Children were classified as having perennial asthma (n = 187), if they experienced asthma symptoms in at least one month of each season; (ii) For those without perennial asthma, a weighted moving average (WMA) approach was used to represent the monthly occurrences. The WMA attack score of each target month was calculated as (original attack score $\times 1$) + (original attack score of months before and after the target month $\times 0.5$) + (original attack score of 2 months before and 2 months after the target month $\times 0.25$). Moving average can effectively smooth out random fluctuations and the data could be more responsive to real changes. (iii) For each child, there is WMA attack score of each month, ranging from 0 to 2.5. Principal component analyses (PCA) were then used on these WMA scores to categorize asthma attack subtypes. The PCA yielded 3 rotated factors with Eigenvalues of > 1.0. Thus, those children with attacks in November, December, January, and February belonged to winter-attack asthma group (n = 590); those with attacks in March, April, May, and June belonged to spring-attack asthma (n = 629); those with attacks in July, August, September, and October belonged to summer/fall-attack asthma (n = 255). (iv) A total of 64 children with asthma could not be classified into any of above three seasonal attacks, nor perennial asthma, and were excluded when conducting multivariate analysis for risk factors by asthma subtype.

Indoor environmental factors at home included the presence of cockroaches, water damage, visible mold on the walls, incense burning, dehumidifier use, carpet use, pet ownership, and passive smoking. Parental atopy was defined as a history of maternal or paternal asthma, allergic rhinitis, or atopic eczema. Information about maternal smoking during pregnancy and breast feeding were obtained from the questionnaire. It has been shown the perception of indoor air quality is related to the load of air pollution. In addition, the perception of indoor air quality among allergic individuals is different from non-allergic ones (17). To adjust for outdoor air quality and susceptibility, information on perceived air pollution was also collected. Daily temperature data was obtained from Environmental Protection Agency (EPA) air pollution monitoring stations within the study areas. Monthly average for 2004 was calculated as the mean of daily temperature.

Statistical analysis

Bivariate analyses were conducted to evaluate each relative risk factor on childhood asthma. Statistical significant was set at $p < 0.05$ based on a two-sided calculation. Multivariate logistic regression model and calculation of adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were used to determine the effects of demographic characteristics and indoor environmental factors on asthma. For the four asthma subtypes, identical analytical methods were used to determine the indoor environmental risk factors.

Results

The prevalence of current asthma among school children was 8.1% (8.2% in boys and 8.0% in girls, data not shown) in southern Taiwan in 2004. Demographic characteristics of the study population are shown in Table 1. The prevalence of current asthma was not significantly different between boys and girls. The average age of asthmatic children was younger than non-asthmatic children (mean = 10.8 ± 2.3 and 11.2 ± 2.4, $p < 0.001$). Higher parental

Table 1. Demographic characteristics of study subjects

Characteristics	Asthma (%) (n = 1725)	Reference (%) (n = 19646)	p-value*
Sex			
Boy	50.4	49.9	0.643
Age (yr)			
Mean ± s.d.	10.8 ± 2.3	11.2 ± 2.4	<0.001†
≤ 9	34.2	29.2	<0.001
10–12	39.8	39.0	
≥13	26.0	31.8	
Highest parental education (yr)			
≤ 9	17.5	20.0	0.005
10–12	47.1	49.9	
≥13	33.5	30.1	
Family income (1000/yr)			
<400	37.6	39.6	0.171
400–1000	51.3	50.2	
>1000	11.1	10.1	
Parental atopy	52.5	29.6	<0.001
Maternal smoking during pregnancy smoking	4.4	2.4	<0.001
Breast feeding	44.7	40.7	0.001

*Pearson chi-square test.
†Calculated by *T*-test.

education, parental atopy, maternal smoking during pregnancy, and breast feeding were found significantly associated with current asthma. Family income was not significantly different between two groups.

Among the children with current asthma, 187 were classified as having perennial asthma, 590 having winter-attack asthma, 629 having spring-attack asthma, and 255 having summer/fall-attack asthma. Fig. 2 illustrates the number of children with asthma attack in each month, for all current asthmatics, and for each asthma subtype. In 2004, the average monthly temperature was highest in August and lowest in January. Overall, a peak in the number of all asthma cases appeared in December and the number of cases decreased as the temperature increased, to reach a nadir in August. This pattern was similar, but not identical with winter asthma. The temporal pattern of perennial asthma appeared to be flat over time. A peak of spring asthma was observed in March. Higher numbers of summer/fall asthma cases were observed in June and October.

By analyzing data according to case–control study methods and using a multivariate logistic regression model, variables including younger age, parental atopy, maternal smoking during pregnancy, breast feeding, and perceived air pollution were found to be significantly related to current asthma (Table 2). Among these risk factors, parental atopy showed the strongest effect (aOR = 2.50, 95% CI = 2.26–2.77). Indoor environmental factors, including presence of cockroaches (aOR = 1.24, 95% CI = 1.07–1.44), water damage (aOR = 1.43, 95% CI = 1.24–1.66), visible mold on the walls (aOR = 1.38, 95% CI = 1.23–1.56), and passive smoking (aOR = 1.25, 95% CI = 1.13–1.39) were independently associated with current asthma in school children. Incense burning, dehumidifier use, carpet use, and pet ownership were not statistically related to childhood asthma.

To estimate indoor risk factors associated with asthma seasonality, a separate multivariate logistic regression model was applied to each asthma subtype (Table 3). Compared with the reference group and adjusted for sex, age, highest parental education, parental atopy, maternal smoking during pregnancy, breast feeding and perceived air pollution, the presence of

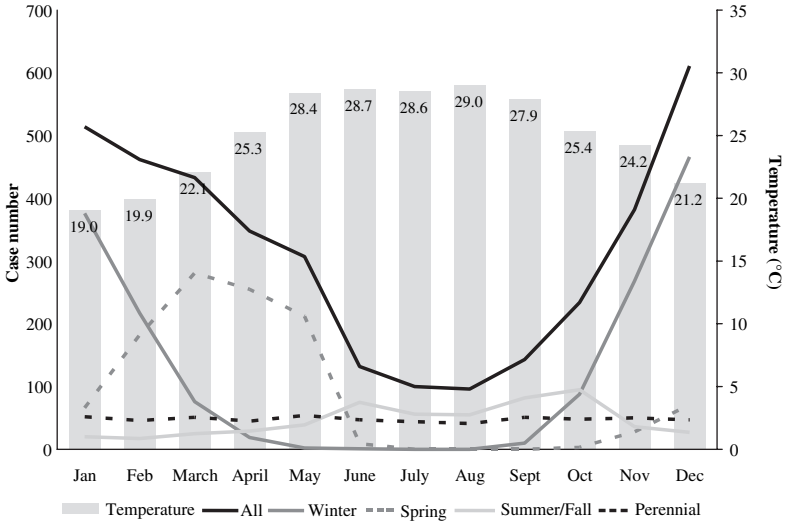

Fig. 2. Seasonal trends for asthma case number (person/time) by month. Black line represents all cases combined. Light grey bar represents average monthly temperature.

Table 2. Multivariate logistic regression analysis for childhood asthma in relation to suspected risk factors

Characters	Current asthma (n = 1725)	Reference (n = 19646)	aOR*	95% CI†
Sex				
Boy	870	9794	1.03	0.93–1.13
Girl	855	9852	1.00	
Age (yr)				
<10	590	5738	1.30	1.14–1.48
10–12	687	7666	1.20	1.05–1.36
≥13	448	6242	1.00	
Parental education (yr)				
≤ 9	307	3926	0.98	0.84–1.15
10–12	844	9799	0.94	0.84–1.06
≥13	574	5921	1.00	
Parental atopy				
Yes	906	5813	2.50	2.26–2.77
No	819	13,833	1.00	
Maternal smoking during pregnancy				
Yes	75	467	1.86	1.43–2.40
No	1650	19,179	1.00	
Breast feeding				
Yes	771	7997	1.11	1.00–1.23
No	954	11,649	1.00	
Perceived air pollution				
Yes	1232	12,307	1.27	1.13–1.42
No	493	7339	1.00	
Cockroaches				
Yes	1502	16,168	1.24	1.07–1.44
No	223	3478	1.00	
Water damage				
Yes	264	1982	1.43	1.24–1.66
No	1461	17,664	1.00	
Visible mold on walls				
Yes	426	3255	1.38	1.23–1.56
No	1299	16,391	1.00	
Incense burning				
Yes	1012	11,350	1.01	0.91–1.12
No	713	8296	1.00	
Dehumidifier use				
Yes	1059	11,456	1.06	0.95–1.17
No	666	8190	1.00	
Carpet				
Yes	175	1954	1.06	0.89–1.25
No	1550	17,692	1.00	
Pet				
Yes	572	6301	1.01	0.90–1.13
No	1153	13,345	1.00	
Passive smoking				
Yes	957	9759	1.25	1.13–1.39
No	768	9887	1.00	

*aOR, adjusted odds ratios;
†95 % CI = 95% confidence interval for odds ratio.

cockroaches (aOR = 1.65, 95% CI = 1.12–2.55) was noted as a risk factor for summer/fall asthma. Water damage was found statistically associated with all subtypes of asthma. Visible mold on the walls was shown to be a predictor of winter asthma and spring asthma (aOR = 1.53, 95% CI = 1.26–1.85 and aOR = 1.34, 95% CI = 1.10–1.62, respectively). Passive smoking was significantly associated with the subtype of spring and summer/fall asthma (aOR = 1.25, 95% CI = 1.05–1.47 and aOR = 1.64, 95% CI = 1.26–2.14, respectively). Incense burning, dehumidifier use, carpet use, and pet ownership were not shown to be related to any subtype of childhood asthma.

Discussion

This is the very first study on seasonality of asthma attacks in Taiwan. Using rather simple statistical approaches, we were able to classify current asthma into four seasonal categories according to the months of symptomatic attacks. Separation of asthmatic children into perennial, winter, spring, and summer/fall-attack asthma allows for further in depth investigation on environmental etiological investigations. Considering seasonal variations, this large scale cross-sectional study further examined the imperative risk factors, focusing on indoor environment, and asthma prevalence among school children aged 6–15 yr in southern Taiwan.

In this study, it was verified that age, parental atopy, maternal smoking during pregnancy, passive smoking, and home environment were associated with prevalent asthma in school children. The results were comparable with previous ISAAC studies in Taiwan (16). Adjusted for host characteristics and other factors, presence of cockroaches, water damage, visible mold on the walls and passive smoking were found to be independently linked to childhood asthma and may account for seasonal variation. Gene-environmental interactions of the asthma pathogenesis have augmented the discussion of asthma studies. It is likely that asthma-related symptoms result from the effect of environmental stimuli in susceptible individuals (18). In our study, parental atopy was shown to have the highest aORs compared to other risk factors. However, when the data were stratified by parental atopy, indoor environmental factors, including water damage and visible mold on walls, remained significant risk factors of asthma for children without parental atopy (data not shown). We found that breast feeding leads to a slightly increased occurrence of childhood asthma. Based on a cohort study, there was a U-shaped relation between duration of breast feeding and the risk of asthma and chronic respiratory symptoms with an optimal duration of 4–6 months (19). Future studies are needed to clarify the relationship between breast feeding and increased risk of childhood asthma.

The pattern of monthly asthma prevalence was lower in warm months and higher in cold

Table 3. Multivariate logistic regression analysis for seasonal childhood asthma in relation to indoor environmental risk factors

		Winter (n = 590)			Spring (n = 629)			Summer/fall (n = 255)			Perennial (n = 187)		
Risk factors	Reference (n = 19464)	Case (n)	aOR*	95% CI†	Case (n)	aOR*	95% CI†	Case (n)	aOR*	95% CI†	Case (n)	aOR*	95% CI†
Cockroaches													
Yes	16168	511	1.17	0.92–1.50	548	1.24	0.98–1.59	229	1.65	1.12–2.55	160	1.10	0.74–1.70
No	3478	79	1.00		81	1.00		26	1.00		27	1.00	
Water damage													
Yes	1982	89	1.46	1.14–1.84	92	1.33	1.04–1.67	44	1.61	1.13–2.23	31	1.66	1.09–2.45
No	17664	501	1.00		537	1.00		211	1.00		156	1.00	
Mold on the wall													
Yes	3255	156	1.53	1.26–1.85	151	1.34	1.10–1.62	60	1.31	0.96–1.75	43	1.21	0.85–1.71
No	16391	434	1.00		478	1.00		195	1.00		144	1.00	
Incense burning													
Yes	11350	332	0.94	0.79–1.12	384	1.10	0.93–1.30	155	1.04	0.80–1.35	101	0.87	0.65–1.17
No	8296	258	1.00		245	1.00		100	1.00		86	1.00	
Dehumidifier use													
Yes	11456	381	1.21	0.99–1.44	371	0.95	0.80–1.12	149	0.98	0.76–1.27	127	1.33	0.98–1.83
No	8190	209	1.00		258	1.00		106	1.00		60	1.00	
Carpet													
Yes	1954	46	0.80	0.58–1.08	71	1.21	0.93–1.56	30	1.18	0.79–1.72	22	1.22	0.76–1.89
No	17692	544	1.00		558	1.00		225	1.00		165	1.00	
Pet													
Yes	6301	184	0.96	0.80–1.14	216	1.05	0.88–1.25	89	1.04	0.80–1.35	63	1.08	0.79–1.47
No	13345	406	1.00		413	1.00		166	1.00		124	1.00	
Passive smoking													
Yes	9759	312	1.14	0.96–1.36	252	1.25	1.05–1.47	159	1.64	1.26–2.14	95	1.10	0.82–1.50
No	9887	278	1.00		277	1.00		96	1.00		92	1.00	

*aOR: adjusted odds ratio, adjusted for sex, age, parental education, parental atopy, maternal smoking during pregnancy, breast feeding, and perceived air pollution.
†95% CI = 95% confidence interval for odds ratio.

months. This pattern was similar to the asthma-related hospitalization and intensive care unit admissions (20). Increased asthma prevalence in cold season may be attributable to climate factors, air pollutants, and/or housing environments. Cold air has been known to be a precipitating factor, which exacerbates asthma occurrence. In the spring and winter, the weakness of continental high pressure and pressure gradient results in a less dispersed and a higher level of air pollutants in Taiwan (20). Higher concentration of house dust mites in the winter months has also been suggested (21). The increase of outdoor activities and higher temperatures may account for some of the reduction of asthma occurrence in the warm months. Considering the onset of summer/fall asthma, the augmented case numbers in June and October may reflect fluctuating temperatures during seasonal transition and therefore, varied mixes of exposures (Fig. 2).

The oceanic and tropical/subtropical monsoon climate in Taiwan keeps the temperatures, on a daily average, between 18 and 28°C in the winter and summer. The year-round warm temperature and high relative humidity (80%) results in a moist housing environment that has been associated with increased asthma risk. Studies in two Japanese cities with different climates indicated the prevalence of bronchial asthma was significantly higher in the city with the subtropical climate (22). Dampness in buildings may cause water damage, wet spots, visible molds and create suitable conditions for the growth of bacteria, fungi, and even viruses (23). The positive percentages of specific IgE antibodies to inhaled allergens was shown to be higher in the subtropical city than in the temperate city (24). In this and previous studies (25), water damage was found to be related to childhood asthma perennially. Eliminating dampness-related causative agents should be considered as primary step of asthma control in Taiwan.

A critical review, based on the meta-analysis of the scientific literatures, concluded that building dampness and molds were associated with approximately a 30–50% increase in respiratory and asthma-related health outcomes (26). Causal association between respiratory health effects and microtoxin produced by molds or fungi remains controversial. It has been suggested that

allergic responses to indoor molds may be immunoglobulin E (IgE)- or immunoglobulin G (IgG)-mediated. The most common form is immediate type hypersensitivity or IgE-mediated ''allergy'' to fungal proteins. This reactivity can lead to allergic asthma or allergic rhinitis, which is triggered by breathing in mold spores or hyphal fragments (27). By assessing the seasonal distribution of mold allergies, Corey et al. (28) suggested that mold allergy was diagnosed most frequently in the winter among atopic patients. In Taiwan, the total concentrations of microbial species have been shown to be twice as higher in the winter than in the summer (29). As a result, it is prudent for individuals who are sensitized in the cold season to reduce exposure to aeroallergens and to avoid high humidification that encourages the growth of molds. Clinicians should also be aware that removal of the fungal source is a key measure to be undertaken, as well as to decrease potential exposure of indoor mold allergens.

Cockroach-produced allergens have been identified as a major cause of childhood asthma in the home environment (30). However, research on the climatic effects on cockroaches is limited. Higher temperatures have been suggested to facilitate the passage of cockroaches between dwellings. Cockroach allergens can be derived from several sources, including saliva, fecal material, secretions, cast skins, debris, and dead bodies and the allergen levels remained elevated several months after the drop in the number of detected cockroaches (31). Levels of cockroach allergens, instead of presence of cockroaches at home, should be studied to identify its asthmatic effect on seasonal variation. Passive smoking has been discussed in the etiology of childhood asthma. It was reported that childhood exposure to passive smoking was associated with clinically significant childhood asthma. A dose–response effect between passive smoking and asthma severity was also evident. (32). Passive smoking was observed to notably increase asthma prevalence in the summer and fall while Ronchetti et al. (33) suggested smoking products most affect asthma in the winter. Levels of individual exposure and smoking behavior among families warrant further investigation to elucidate our findings.

Knowledge of allergen elimination among asthmatic patients might confound the casual relationship. Consequently, some lifestyle factors, such as incense burning, dehumidifier use, carpet use, and pet ownership might provide protective effects for asthmatic children. Other indoor allergens not included in our study should also be considered. In Taiwan, the home dust mite (HDM) concentration has seasonal variation, with the highest concentrations noted from July to November (34). As a result, HDM should be considered as a likely source of the exacerbation of seasonal asthma. To further support this, A parallel was found between seasonal variations of IgG4 antibodies and house dust mites, as well as skin prick test to pollen allergy (15, 35). We suggest that simultaneous evaluation of the level of antibodies and allergens would illuminate the causation between indoor factors and seasonal asthma among children.

Given that the participants in our study were selected from five connected districts with similar climates, this study was able to overcome the geographic differences in asthma occurrences and allergens distribution. Even so, misclassification is a potential limitation because the recognition of asthma symptoms may differ among individuals and the prevalence of asthma was reported by parents. Moreover, recall bias may have been introduced between cases and controls because parents who live with asthmatic children may be more prone to reporting their exposure although information has been collected in a uniform manner. Underreporting may also occur among the asthmatic cases because of parental avoidance of reporting illness of their children. Background information and seasonal changes of air pollutants, such as particulate matter (PM_{10}) and ozone, has been shown to affect childhood asthma and should also be considered. According to EPA air pollutant monitoring data in 2004, PM_{10} levels in winter (105 $\mu g/m^3$) were much higher than in summer (56 $\mu g/m^3$) in southern Taiwan. However, we did not observe much difference in ozone levels during summer months (29.8 p.p.b.) compared with winter months (30.2 p.p.b.). Finally, categorizing of seasonal subtype of asthma has been challenging. A more sophisticated classification should probably include immunological and biological information of the asthmatic children. Objective assessment of asthma diagnosis and measurement of home environment should also be incorporated in future studies when possible.

Conclusion

This study took an approach to subdivided current asthmatic children into seasonal subtypes according to the months of attacks. Indoor exposures, including presence of cockroaches and visible mold on the walls were found differentially contributing to different seasonal

subtypes of childhood asthma. While studying environmental factors for asthma, categorizing asthmatic children into seasonal subtypes may significantly enhance detection of causal links.

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