

Short communication

Birth month and sensitization to house dust mites in asthmatic children

Background: Early exposure to high quantities of allergen has an important role in the incidence of atopic sensitization. In fact, subjects sensitized to house dust mites (HDMs) have a significantly higher proportion of births in the season when HDMs are most abundant.

Objective: The aim of this study was to investigate whether birth month patterns differ for asthmatic patients sensitized only to HDMs and for those sensitized to HDMs and other allergen(s).

Methods: Among 2225 patients with asthma, aged 10–16 years, 1642 sensitized to HDMs were identified by skin prick testing. This group was composed of patients sensitized only to HDMs ($n = 715$) and patients sensitized to HDMs and other allergen(s) ($n = 927$). The birth month distributions of the group of HDM-sensitive asthmatics or its subgroups were compared with that of a reference population (total live births in the same years as the studied subjects). The risk ratio of a given birth month in relation to all the other months was calculated as an odds ratio (OR) with the corresponding 95% confidence interval (CI).

Results: A significant difference in birth month distribution was observed for HDM-sensitive asthmatics ($\chi^2 = 23.6$, $P = 0.015$), with higher rates of birth in August (OR: 1.23, 95% CI: 1.04–1.46) and September (1.24, 1.04–1.46).

When the two subgroups were analyzed separately, significantly more births were noted in August (1.34, 1.06–1.71) and September (1.34, 1.05–1.70) for those sensitized only to HDMs, whereas no such birth month preference was observed for those sensitized to HDMs and other allergen(s).

Conclusions: The HDM-positive asthmatics showed a greater proportion of births in August and September, which correspond to high HDM exposure. However, this birth month pattern was evident in asthmatic-sensitive only to HDMs, but was not observed in those sensitive to HDMs and other allergen(s).

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It has been suggested that the first few months of life constitute a sensitive period during which exposure to certain allergens may predispose an individual to the subsequent development of atopic disease (1). The quantity of allergen is also an important factor and there is evidence that exposure to high quantities of allergen during infancy is associated with an increased risk of sensitization to this kind of allergen (2). Several investigations have demonstrated that subjects sensitized to house dust mites (HDMs) have a significantly higher proportion of births in the season when HDMs are most abundant (3, 4), suggesting that early exposure to high quantities of allergen has an important effect on the incidence of atopic sensitization.

It is recognized that subjects with sensitivity to HDMs can be categorized as monosensitized (i.e. sensitized to only HDMs) or as polysensitized (i.e. sensitized to other classes of allergens in addition to HDMs) (5). It has been hypothesized that monosensitized subjects require greater

exposure to the sensitizing allergen than polysensitized subjects, before becoming sensitized (6). If this hypothesis is correct, the relationships between the month of birth and sensitization to HDMs may differ in these two subgroups, because exposure to high levels of HDM allergen during the first few months is likely to have a different impact.

We have studied the relationship between the month of birth and the type of sensitization in a series of 2225 children with asthma. The main purpose of the present study was to investigate whether there is a difference in birth month distributions of asthma patients sensitized only to HDMs and those sensitized to both HDMs and other allergen(s).

Methods

We collected the records of 2225 asthma patients (1423 boys and 802 girls, aged 10–16 years) that attended asthma clinics at the

Seoul National University Children's Hospital and at the Sanggye Paik Hospital, from January 2000 to December 2002. The patients had all lived in the Seoul Metropolitan area since birth, had undergone skin prick testing, and had no history of immunotherapy. A diagnosis of asthma was made clinically, if a subject had typical asthmatic symptoms (chronic cough with nocturnal exacerbation, wheezing, or dyspnea). About one-third (694) of the patients had undergone methacholine inhalation test, and most (676) of those tested showed bronchial hyperresponsiveness (methacholine $PC_{20} < 16$ mg/ml).

Skin prick testing was performed using 13 common aeroallergens, namely, HDMs (*Dermatophagoides pteronyssinus*, *D. farinae*), animal danders (cat epithelia, dog epithelia), pollens (mugwort, rye grass, ragweed, hazel, alder, oak), molds (*Aspergillus fumigatus*, *Alternaria alternata*), and cockroach (*Blattella germanica*). Histamine and isotonic saline were used as positive and negative controls. A mean wheal diameter of 3 mm or more in the absence of any reaction in the saline solution was considered as a positive reaction.

Subjects with sensitization to HDMs were designated as group 1 ($n = 1642$). Of these, about two-fifths showed exclusive sensitization to HDMs (group 1a, $n = 715$), and the remainder reacted to HDMs and other allergen(s) (group 1b, $n = 927$). Subjects with exclusive sensitization to allergen(s) other than HDMs were designated as group 2 ($n = 152$). Nonatopic asthmatic subjects were designated as group 3 ($n = 431$).

Birth month distribution of each patient group was compared with that of a reference population. As a reference population, we used all children born in the Seoul Metropolitan area, during the same period (from 1984 to 1992) as the patients under investigation, data upon which was available from the National Statistical Department.

Statistical analysis

Statistical analysis was performed using the chi-square test as a goodness-of-fit test and using the chi-square test with Yates (continuity) correction. Differences were regarded to be significant if P -value was < 0.05 . The expected distribution of the month of birth among the patients in each group was calculated from the distribution of birth month for the reference population. We compared the frequencies of observed births per month with the expected frequencies per month after defining the upper limit of expected births (ULEB) and the lower limit of expected births with a 95% confidence interval (CI). The risk ratio of a given birth month in relation to all the other months was calculated as an odds ratio (OR) with the corresponding 95% CI.

Results

The birth month distributions of each group were compared with that of the reference population (Table 1). A significant difference was found for group 1 ($\chi^2 = 23.6$, $P = 0.015$). The other groups had birth month distributions similar to that of the reference population. When the distributions of groups 1a and 1b were examined separately, a significant difference was noted for group 1a ($\chi^2 = 20.7$, $P = 0.037$), but not for group 1b ($\chi^2 = 7.3$, $P = 0.776$).

The distributions of observed births per month of group 1 and those of its subgroups were compared with the expected frequencies per month. Significantly more

Table 1. The birth month distributions of each studied group and that of the reference population

Birth month	Group 1			Group 2	Group 3	Reference population
	Subtotal	Group 1a	Group 1b			
January	152	67	85	15	44	160 506
February	158	63	95	16	44	168 993
March	117	50	67	12	37	118 411
April	114	46	68	11	36	114 125
May	115	51	64	12	37	115 101
June	119	48	71	14	31	110 430
July	130	56	74	15	28	117 882
August	157	74	83	11	29	120 564
September	161	75	86	11	31	122 832
October	158	74	84	12	37	128 741
November	140	60	80	11	39	124 324
December	121	51	70	12	38	121 772
Total	1642	715	927	152	431	1 523 681
χ^2	23.6	20.7	7.3	2.3	4.6	
P -value	0.015	0.037	0.776	0.997	0.950	

births were noted for August and September in group 1, 157 and 161 vs ULEBs of 151 and 153, respectively. When the two subgroups were examined separately, group 1a showed significantly more births for August and September, 74 and 75 vs ULEBs of 71 and 72, whereas no such birth month preference was observed in group 1b (data not shown).

Table 2 shows the ORs with 95% CIs of given birth months for observed patients in group 1 and its subgroups. In group 1, significantly increased ORs were noted in August (1.23, 95% CI: 1.04–1.46) and September (1.24, 1.04–1.46). An analysis of the two subgroups revealed similar results in group 1a (August: 1.34, 1.06–1.71; September: 1.34, 1.05–1.70). Again, no significant deviation according to the month of birth was observed in group 1b.

Table 2. Odds ratios (ORs) with 95% confidence intervals (CIs) of a given birth month for patients in group 1 and its subgroups

Birth month	Group 1		Group 1a		Group 1b	
	OR	95% CI	OR	95% CI	OR	95% CI
January	0.88	0.74–1.05	0.88	0.68–1.13	0.88	0.69–1.12
February	0.86	0.72–1.01	0.77	0.60–1.00	0.93	0.74–1.17
March	0.90	0.74–1.10	0.89	0.67–1.19	0.91	0.70–1.19
April	0.92	0.75–1.12	0.85	0.63–1.15	0.98	0.76–1.28
May	0.92	0.76–1.12	0.94	0.71–1.25	0.90	0.69–1.19
June	0.99	0.82–1.21	0.92	0.69–1.23	1.06	0.81–1.37
July	1.01	0.84–1.22	1.01	0.77–1.33	1.00	0.77–1.30
August	1.23	1.04–1.46	1.34	1.06–1.71	1.13	0.89–1.45
September	1.24	1.04–1.46	1.34	1.05–1.70	1.15	0.90–1.46
October	1.16	0.98–1.38	1.25	0.98–1.59	1.09	0.86–1.39
November	1.05	0.88–1.26	1.03	0.79–1.34	1.06	0.83–1.36
December	0.92	0.76–1.11	0.88	0.66–1.18	0.95	0.73–1.24

Discussion

Numerous prospective studies have examined the effect of the inhalant environment in early infancy on the subsequent manifestations of allergy (7, 8). Although some studies found no relationship between sensitization patterns and the month of birth (9), several investigations have found correlations between certain birth months and sensitization to pollen (10), mite (11, 12), and animal dander (13).

In the present study, we found a significant difference in birth month distributions between patients sensitized to HDMs (group 1) and the reference population. A greater proportion of HDM-sensitive asthmatics were born in August and September than was expected. An increased tendency for high births, although statistically not significant, was noted in October. Studies on the monthly distributions of HDM allergen levels in the Seoul Metropolitan area showed that highest levels were detected from August to October (14). Thus, asthmatic children with HDM sensitivity are more likely to have been born at the time of the year when HDM allergen levels are highest. Our results agree with those of previous studies in England (11) and Denmark (12), which showed that patients born in the season when HDMs are most abundant have an increased risk of developing HDM allergy. The novelties of the present study reside in that the birth month distributions were compared separately in patients sensitized only to HDMs (group 1a) and in patients sensitized to both HDMs and other allergen(s) (group 1b). A higher prevalence of birth in August and September was evident in the former group, but not in the latter group.

Several points merit consideration to interpret our data cautiously. First, the effects found were small ($OR < 2$). Secondly, the calculations were based on little differences in absolute numbers of children ($n = 3-8$). In this context, it may be argued that even small differences became statistically significant because of the rather large reference group. Furthermore, no correction was made for the multiple comparisons involved when testing for

differences between each of the 12 months. An additional complication was the observation made by Aalberse et al. (15) that not only for inhalant allergy, but also for egg white or cow's milk allergy a birth month variation was found. Therefore, the relationship between the month of birth and HDM allergy might not be purely a reflection of allergen exposure, and another seasonal factor may contribute.

The different birth month patterns in HDM-positive asthmatics according to the presence of concomitant sensitization to other allergen(s) may possibly be explained by a 'different sensitization threshold' hypothesis (6). Subjects with a low 'sensitization threshold' will probably develop sensitization not only to HDMs but also to other allergen(s) present at low concentrations (polysensitization). On the contrary, subjects with a high 'sensitization threshold' would require a higher exposure to the sensitizing allergen, and as a consequence, may develop allergy to only perennial and ubiquitous allergens-like HDMs (monosensitization). If this hypothesis is correct, the month of birth pattern would be manifested more definitively in asthmatic-sensitive only to HDMs than in asthmatic-sensitive to HDMs and other allergen(s), because exposure to high quantities of HDM allergen in the first few months of life may have a greater impact on the former group of patients.

In conclusion, HDM-positive asthmatics showed a greater proportion of births in August and September, when they would have high HDM exposure. This birth month pattern, however, was evident in asthmatic-sensitive only to HDMs, but not in those sensitive to HDMs and other allergen(s).

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References

1. Croner S, Kjellman NI. Predictors of atopic disease: cord blood IgE and month of birth. *Allergy* 1986;**41**:68-70.
2. Kihlstrom A, Lilja G, Pershagen G, Hedlin G. Exposure to birch pollen in infancy and development of atopic disease in childhood. *J Allergy Clin Immunol* 2002;**110**:78-84.
3. Businco L, Cantani A, Farinella F, Businco E. Month of birth and grass pollen or mite sensitization in children with respiratory allergy: a significant relationship. *Clin Allergy* 1988;**18**:269-274.
4. Karachaliou FH, Panagiotopoulou K, Manousakis M, Sinaniotis K, Papageorgiou F. Month of birth, atopic disease, and sensitization to common aeroallergens in Greece. *Pediatr Allergy Immunol* 1995;**6**:216-219.
5. Silvestri M, Rossi GA, Cozzani S, Pulvirenti G, Fasce L. Age-dependent tendency to become sensitized to other classes of aeroallergens in atopic asthmatic children. *Ann Allergy Asthma Immunol* 1999;**83**:335-340.
6. Silvestri M, Oddera S, Rossi GA, Crimi P. Sensitization to airborne allergens in children with respiratory symptoms. *Ann Allergy Asthma Immunol* 1996;**76**:239-244.
7. Sporik R, Holgate ST, Platts-Mills TA, Cogswell JJ. Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood. A prospective study. *N Engl J Med* 1990;**323**:502-507.

8. Lau S, Illi S, Sommerfeld C, Niggemann B, Bergmann R, von Mutius E et al. Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study. Multicentre Allergy Study Group. *Lancet* 2000;**356**:1392–1397.
9. Schafer T, Przybilla B, Ring J, Kunz B, Greif A, Uberla K. Manifestation of atopy is not related to patient's month of birth. *Allergy* 1993;**48**:291–294.
10. Carosso A, Ruffino C, Bugiani M. The effect of birth season on pollinosis. *Ann Allergy* 1986;**56**:300–303.
11. Morrison Smith J, Springett VH. Atopic disease and month of birth. *Clin Allergy* 1979;**9**:153–157.
12. Korsgaard J, Dahl R. Sensitivity to house dust mite and grass pollen in adults. Influence of the month of birth. *Clin Allergy* 1983;**13**:529–535.
13. Pearson DJ, Freed DL, Taylor G. Respiratory allergy and month of birth. *Clin Allergy* 1977;**7**:29–33.
14. Nahm DH, Park HS, Kang SS, Hong CS. Seasonal variation of skin reactivity and specific IgE antibody to house dust mite. *Ann Allergy Asthma Immunol* 1997;**78**:589–593.
15. Aalberse RC, Nieuwenhuys EJ, Hey M, Stapel SO. 'Horoscope effect' not only for seasonal but also for non-seasonal allergens. *Clin Exp Allergy* 1992;**22**: 1003–1006.