

The Association Between Birth Season and Future Development of Childhood Asthma

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Summary. The aim of this study was to examine a possible association between birth season (date of birth) and future development of asthma in children. A case-control study was designed to include asthmatic children aged 2–7 years, living in the city of Beer-Sheva, in southern Israel, registered in one pediatric center. Controls were healthy children matched for age and registered at the same clinic. Demographic data, past medical history, and asthma history and severity were collected using the computerized medical charts and asthma registry. A structured telephone questionnaire was used to complete the data. Children with a history of prematurity or chronic significant illness were excluded from the study. Sixty-six children and 69 controls were enrolled in the study. There were significantly more males in the asthmatic group compared to controls ($P = 0.003$). History of bronchiolitis or recurrent wheezing episodes in the first year, family history of asthma, and Middle-Eastern origin were significantly more common among asthmatic children than controls ($P < 0.001$). Asthmatic children were more likely to be born between March and June and least likely to be born between October and December, compared to controls ($P < 0.05$). Multivariate logistic regression analysis revealed three variables to be independent significant risk factors for development of asthma: birth season between March and June, acute bronchiolitis or recurrent wheezing episodes during first year of life, and male gender. Birth season during late winter and spring is associated with asthma during childhood. **Pediatr Pulmonol.**

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Key words: asthma; allergy; bronchiolitis; RSV; wheezing; birth season.

INTRODUCTION

Asthma is the most prevalent chronic illness among children, and its prevalence, burden, and morbidity have been on the rise in recent years.^{1–4} Some of the factors known to influence the development of asthma are male gender, positive family history, environmental hazards such as urban air pollution, allergies, smoking, and viral infections, mainly RSV bronchiolitis, which affect young infants.^{5–7} A significant percentage of infants who suffer from bronchiolitis will develop asthma.^{8–10} One explanation is that viral lower respiratory infections affecting the immature immune system of young infants can bring about recurrent wheezing and hence cause hyperactivity of the airways.¹¹ Since acute RSV bronchiolitis occurs during the winter season, namely December–February, we hypothesized that birth season (birth date) might have an effect on the risk of infants developing asthma, that is, infants who are born between June and October and, therefore, exposed to winter weather during the first 6 months of life would have a higher occurrence of asthma. This study addresses the association between birth season and later development of asthma.

METHODS

We conducted a case-control study comprised of Jewish children 2- to 7-years-of-age during the year 2003,

attending the Primary Care Pediatric Center in Beer-Sheva, in southern Israel. Most families attending the clinic came from middle and upper middle class urban populations.

Cases were children with active asthma as defined by their computerized medical charts and who had at least one exacerbation episode during the year before enrollment. Controls were children without asthma matched by age and attending the same clinic. They were selected using systematic random sampling. Consent was obtained from all parents. The study was approved by the local Helsinki Review Board. Children with history of prematurity, other chronic respiratory, cardiac, or kidney disease, or receiving corticosteroids for other illnesses were excluded from the study. Sociodemographic and

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asthma history data were collected using the computerized medical charts and asthma registry. A short structured telephone questionnaire was used to complete information missing in the charts. All questionnaires were analyzed anonymously.

Data were collected using EpiData package. Data analysis was carried out using the SPSS 12.0 package. Chi-square and Fisher exact test were used for categorical variables. *t*-test and Mann–Whitney were used for continuous variables. Logistic regression was used for multivariate analysis.

RESULTS

One hundred sixty children were eligible to enroll in the study: 71 cases and 89 controls. Complete data were obtained from 135 children (84.4%). There was no parental refusal to participate; 5 case children and 20 controls could not be reached for an interview. Complete data were obtained from 66 cases and 69 controls.

The demographic and environmental data of the two groups are described in Table 1. The groups differed regarding gender, country of origin, and family history of asthma. There were significantly more males among asthmatic children ($P = 0.003$). There were more children with Middle Eastern origin among the cases compared to children without asthma, whose parents were more frequently from western countries. Positive family history for asthma was more common among asthmatic children. No significant differences were found between cases and controls regarding exposure to smoking or to house pets.

The distribution of possible risk factors between the two groups is presented in Table 2. In contrast to our hypothesis, asthmatic children were more frequently born between January and May, compared to controls ($P < 0.05$). History of bronchiolitis and/or wheezing

episodes was more common among cases. Although a history of respiratory illnesses, mainly upper respiratory infection (URI), in the first year was more common among cases, both groups had a high prevalence of URIs. Surprisingly, no significant difference was detected in skin allergies, such as atopic dermatitis, between cases and controls.

In order to refine the results, the frequency of births of cases and controls in each month of the year was analyzed (Table 3). According to Figure 1, the peak frequency of births of children with asthma was between March and June (52.9% compared to 34.7% of controls, $P = 0.038$) with a declining trend, and the lowest frequency moving towards the late months of the year (October–December). This pattern becomes more evident when compared to the control group where there was no trend in the frequency of month of birth throughout the year. Children born during March–June had significantly higher rates of bronchiolitis in infancy (49.2% vs. 31.6%, $P = 0.038$). However, no synergetic effect of being born between March and June and having bronchiolitis in infancy was detected with respect to asthma in childhood. Multivariate analysis was performed to control for other risk factors for asthma (Table 4). Birth season (between March and June) was an independent risk factor (OR = 2.36, 95%CI: 0.99; 5.60) for asthma at 2- to 7-years-of-age, as well as other well-known risk factors such as history of bronchiolitis, family history of asthma, and male gender.

DISCUSSION

The rationale behind conducting this study was the evidence connecting RSV bronchiolitis during infancy and future development of asthma during the preschool period.^{8–10,12–16} Since the high season of RSV bronchiolitis occurs mainly during winter months (December–

TABLE 1—Demographic and Environmental Characteristics of the Study Groups

	Cases (n = 66)	Controls (n = 69)	P-value
Male gender (%)	48 (72.7)	33 (47.8)	0.003
Age in years, mean $\pm$ SD	4.6 $\pm$ 1.3	4.5 $\pm$ 1.3	0.589
Mother's country of birth			
Israel (%)	56 (84.4)	57 (82.6)	0.725
USA, Canada, and Europe (%)	4 (6.1)	9 (13.0)	0.169
Arab speaking countries, Asia, and Africa (%)	6 (9.1)	3 (4.4)	0.269
Maternal grandmother's country of birth			
Israel (%)	9 (13.6)	11 (15.9)	0.706
USA, Canada, and Europe (%)	7 (10.6)	18 (26.1)	0.021
Arab speaking countries, Asia, and Africa (%)	50 (75.7)	40 (57.8)	0.028
Family history of asthma			
In at least one first degree relative (%)	38 (57.6)	15 (21.7)	<0.001
Parents (%)	7 (10.6)	2 (2.9)	0.073
Brothers/sisters (%)	33 (50.0)	15 (21.7)	0.001
Exposure to passive smoking (at least one of the parents smoking)	22 (33.3)	32 (46.4)	0.122
Exposed to pets at home (%)	5 (7.6)	11 (15.9)	0.133

TABLE 2—Distribution of Risk Factors in Study Groups

	Cases (n = 66)	Controls (n = 69)	P-value
	n (%)	n (%)	
Infants born June–October	27 (40.9)	29 (42.0)	0.895
Infants born January–May	36 (54.5)	26 (37.7)	0.049
History of bronchiolitis	37 (56.1)	16 (23.2)	<0.001
History of wheezing during first year of life	59 (89.4)	26 (37.7)	<0.001
History of respiratory illness in the first year of life ¹	60 (90.9)	51 (73.9)	0.010
Currently suffering from allergies	6 (9.1)	5 (7.2)	0.695
Suffered or currently suffering from dermatologic diseases ²	25 (37.9)	17 (24.6)	0.097

¹The most frequent disease was upper respiratory infection; reported by 60 cases and 50 controls.

²The most frequent disease was atopic dermatitis reported for 21 cases and 14 controls.

February), we considered that infants born during the last quarter of the year would go through the high season of RSV bronchiolitis when they are at a very young age. The immune system during this period of life is immature and therefore they are at higher risk for allergic sensitization of their airways and eventually might develop hyperactive airways, namely asthma, in the future.⁴ In a very recent study by Yoo et al.,¹⁷ asthmatic children 10- to 16-years-of-age, sensitized to house dust mite (HDM), had a significantly higher proportion of births during August and September when HDMs are most abundant.

Surprisingly, in our study, more children with asthma were born at the end of the winter and early spring (March–June) compared to controls. It is noteworthy that those who were born between October and December were at a very young age during the RSV season and had a significantly lower risk for developing asthma. The birth season factor was still significant, even after controlling for other variables associated with asthma development. These differences in distribution of the month of birth between the two studies can be explained by the different asthma age group populations: the study by Yoo et al.

enrolled older asthmatic children (age 10–16 years), although in our study, the population age group was significantly younger (2–7 years). Asthma is a heterogeneous disease.¹⁸ The form associated with atopy is preponderant later in childhood, during school years, although the preschool form is associated with viral respiratory illnesses and more likely to have a history of RSV bronchiolitis.^{10,13,19} This observation may explain the insignificant differences between cases and controls in the prevalence of atopic disease in our study population. Another possible explanation for the differences in birth distribution among asthmatic children compared to controls may be based on the “Hygiene Theory.”^{9,20,21} This theory suggests that environmental changes in the industrialized world led to reduced contacts with some infectious agents, resulting in growing rates of atopy, asthma, and allergy.⁹ In our study, infants who were exposed to viral infection (most likely RSV bronchiolitis) at a very young age were more protected against the development of asthma, although those born at the end of the winter and early spring, who were exposed to RSV infection during the last quarter of their first year of life, might be at higher risk for developing asthma. Therefore, birth season and hence the timing of exposure to RSV bronchiolitis may be an important factor for future development of asthma. Other factors which may play an important role in development of asthma are family

TABLE 3—Distribution of Month of Birth Among Cases and Controls

	Cases (n = 66)	Controls (n = 69)
	n (%)	n (%)
January	5 (7.6)	5 (7.2)
February	5 (7.6)	3 (4.3)
March	11 (16.6)	7 (10.1)
April	10 (15.1)	4 (5.8)
May	5 (7.6)	7 (10.1)
June	9 (13.6)	6 (8.7)
July	5 (7.6)	7 (10.1)
August	6 (9.1)	7 (10.1)
September	4 (6.1)	5 (7.2)
October	3 (4.5)	4 (5.8)
November	2 (3.0)	7 (10.1)
December	1 (1.5)	7 (10.1)

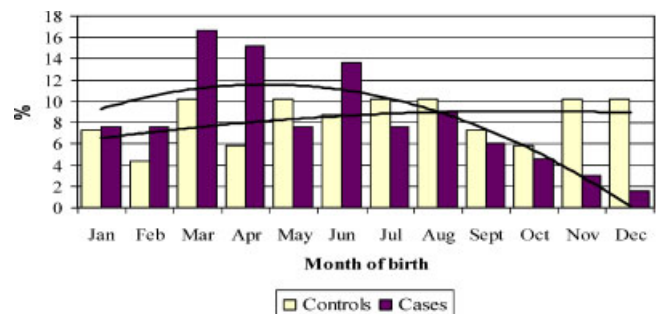
**Fig. 1. Distribution of month of birth among cases and controls.**

TABLE 4—Logistic Regression Model for Asthma in Children at 2- to 7-years-of-age

	OR (95%CI)	P-value
Born between March and June	2.36 (0.99; 5.60)	0.052
History of bronchiolitis and/or wheezing in the first year of life	10.44 (3.63; 30.04)	<0.001
Family history of asthma (first degree)	3.96 (1.64; 9.55)	0.002
Male gender	3.34 (1.40; 8.01)	0.007

history of asthma and allergy, smoking, and air pollution.^{7,22} Our results confirm these findings in relation to family history, but did not reach significance for parental smoking. In contrast to the study by Illi et al.,²³ repeated viral respiratory infections during early life were very common in both asthmatic and controls in our population. As expected, asthma was more common among male children and children with a family history of asthma.⁷ The limitations of this study are the relatively small sample size, and the fact that definitions of acute bronchiolitis and asthma were determined by the primary physicians at the clinic. Most cases of bronchiolitis were clinically diagnosed. RSV was measured only in a few cases. Nevertheless, most cases of bronchiolitis during the high winter season are due to RSV infections.^{9,24} A recently published study revealed that RSV+ as well as RSV− bronchiolitis in early infancy presented a significant risk for developing asthma later in childhood.²⁵

We conclude that birth season (month of birth) is associated with future development of early childhood asthma. Family planning is a possible recommendation for parents with a strong family history of asthma. RSV immunization might be considered for the high-risk group. Further larger prospective studies are needed to confirm this observation.

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