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Original Article

Asthma and risk factors in the first 6 years of life in a population-based cohort

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ABSTRACT

Background. The frequency of asthma increases in childhood and asthma is associated with risk factors varying across age groups. The aim of our study was to assess the prevalence of asthma and its associated risk factors in the first six years of life.

Methods. Within the scope of the Adana Pediatric Allergy and Risk Factor (ADAPAR) birth cohort study, 203 infants that had experienced at least one wheezing attack during the first year of life were followed for asthma development until the age of six years. Additionally, 223 infants that were followed within the scope of the same study and had no wheezing attacks in the first year of life were assigned to the control group.

Results. At the end of the sixth year, 46 (22.7%) infants were diagnosed with asthma and the use of antibiotics of the mother during pregnancy (OR: 2.98), the presence of allergic diseases in the mother (OR: 4.70) and sibling (OR:2.11), the presence of atopy (OR:4.76), and recurrence of wheezing in the first age (OR:17.35) were identified as risk factors for asthma.

Conclusions. The prevalence of asthma at six years of age was higher than that of other studies. Prevention of infections at an early age and during pregnancy can reduce the prevalence of asthma.

Key words: asthma, wheezing, childhood, risk factor.

Asthma is a common chronic respiratory disease in children.[1] The disease can be caused by numerous environmental and genetic factors and is associated with risk factors varying across age groups. Meaningfully, knowledge of these risk factors will help to prevent asthma development. Birth cohort studies can contribute substantially to the understanding of health and diseases. The aim of this study was to assess the incidence of asthma and associated risk factors in the first six years of life as a part of the Adana Pediatric Allergy and Risk Factor (ADAPAR) birth cohort study.

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Material and Methods

Study design

The prospective study was performed as a part of the ADAPAR birth cohort study. The study protocol was approved by Çukurova University local ethics committee (02.03.2018/75-46) and was performed in accordance with the Helsinki Declaration. The details of this birth cohort study has been described in detail elsewhere.[2] Within the scope of ADAPAR study, 203 infants who had at least one wheezing attack in the first year of life were included in this study. Additionally, 223 infants that were followed within the scope of ADAPAR birth cohort study and had no wheezing attacks in the first year of life were included into the control group. An informed parental consent was obtained from all the participants before inclusion.

Follow-up assessment

All the infants were followed at six-month intervals for a total period of six years. Cord blood samples were taken and a physical examination was performed after the birth for each participant. A baseline questionnaire that probed questions on pregnancy conditions, environmental exposures, and family history of allergic disorders was administered to the mothers after birth. Additionally, follow-up questionnaires were administered following physical examination at each visit to assess patients' allergic symptoms and environmental exposure. Each year, a skin prick test was performed using food allergens (egg, wheat, milk, peanut), and major inhalant allergens (Allergopharma, Germany) including dust mites (dermatophagoides pteronyssinus and D. Farinae), tree pollens (hazel, elm poplar, alder, and sallow), grass pollens (timothy, oat, barley, wheat grass, rye, orchard, meadow fescue, blue grass and velvet), and molds (Alternaria alternata, Fusarium moniliforme and Cladosporium herbarum). A wheezing attack was defined as an acute wheezing episode reported by parents . At the end of the sixth year, participants were evaluated for asthma development. Asthma was defined as presence of asthma symptoms within the last 12 months in the absence of a cold (respiratory distress, wheezing, wheezing or shortness of breath after exercise), 12% increase in forced expiratory volume in 1 second (FEV1) after bronchodilator, or receiving regular medication for asthma within the last one year.

Statistical analysis

Data were analyzed using SPSS for Windows version 22.0 (IBM Corp. Released 2013, Armonk, NY). Categorical data were compared using Chi-square test or Fisher's exact test. Continuous data were expressed as mean and 95% confidence interval (CI) or median and interquartile range (IQR) as appropriate. Skewed data were compared using Mann-Whitney U test. Unadjusted and adjusted odds ratios (OR) with 95% CI were determined. A p value of < 0.05 was considered significant.

Results

A total of 1,475 infants were born in the period between February 2010 and February 2011 at Çukurova University Medical Hospital. Of these, 98 infants were excluded due to insufficient parental knowledge of ADAPAR. Of the remaining 1,377 infants, 220 (15.9%) of them who had experienced at least one wheezing attack during the period between birth and the end of the first year of age were planned to be included in this study. However, 17 out of 220 infants were excluded since their family refused to enroll in the study and thus the remaining 203 children were included. Table I presents the evaluation of risk factors for wheezing at the end of first year of life.

At the end of the sixth year, 46 (22.7%) infants were diagnosed with asthma (Table II) and the risk factors for asthma were revealed as maternal use of antibiotics during pregnancy, presence of allergic diseases in the mother and sibling, presence of atopy, and recurrence of wheezing attacks in the first year of age (Table III).

Discussion

Wheezing is a common symptom in infants and it is difficult to predict whether wheezing symptoms will develop into asthma in later periods. Asthma prevalence in childhood has been reported to be 8-22%.[3-6] Children experiencing a wheezing attack during the first year of age have a higher risk of asthma development.[7]

Risk factors for the development of wheezing symptoms during the first year of age have been investigated in numerous studies.[8-11] In cohort studies, the incidence of wheezing during the first year of life has been reported to be 18-28%.[12-14] In our study, it was found to be 15.9% and it was revealed that 2.7% of the infants had two or more wheezing attacks. Accordingly, the wheezing prevalence in our study was lower than that of other studies. A previous study evaluated the wheezing symptoms described

Table I. Evaluation of risk factors for wheezing at the end of the first year.

Risk factors	N (%)	Infants who had a wheezing attack at least once in the first year		
		n (%)	OR (% 95 CI)	p
Gestational age (weeks)				
<37	219 (15.9)	46 (20.9)	1	0.002
≥37	1158 (84.1)	174 (79.1)	0.25 (0.10-0.59)	
Domestic pet at home				
No	1271 (92.3)	209 (95)	1	0.046
Yes	106 (7.7)	11 (5)	0.32 (0.10-0.97)	
Upper respiratory infection				
0	243 (17.6)	8 (3.6)	1	
1	648 (47)	90 (40.9)	4.74 (1.69-13.31)	0.003
2-3	440 (32)	103 (46.8)	9.47 (3.34-26.89)	0.001
≥ 4	46 (3.4)	19 (8.6)	24.91 (5.89-105.24)	0.001
Lower respiratory infection				
0	1280 (93)	151 (68.6)	1	
1	89 (6.4)	63 (28.6)	16.83 (7.31-38.75)	0.001
2-3	8 (0.6)	6 (2.8)	5.92 (0.59-58.93)	0.129
Food allergy				
No	1344 (97.6)	211 (96)	1	0.716
Yes	33 (2.4)	9 (4)	1.34 (0.26-6.75)	
Cord blood Ig-E			1.05 (0.43- 2.53)	0.910

by parents as in our study and reported that the risk factors for wheezing attacks within the first year included eczema in the child, damp housing and asthma in the mother or sibling, and family history of allergic disease. In our study upper and lower respiratory tract infections, presence of a pet at home, and birth before 37 weeks of pregnancy were established as risk factor for wheezing within the first year of age. However, although recurrent wheezing is presumed to be an atopic condition, no correlation was found between food allergy and this condition.

The investigators of RESPIR (Registro y Análisis Epi-demiológico de las Sibilancias y el Asma en una PoblaciónInfantil en La Ribera),7 ISAAC (International Study of Asthma and Allergies inChildhood),[15] and TCRS (Tucson Children's Respiratory Study)[16] reported the prevalence of asthma at six years of age as 12.8%, 9.6% and 9.8%, respectively. In our study, this prevalence was found to be 22.7%.

Alfonso et al.[7] determined the risk factors for school asthma as atopic dermatitis, at least one attack of wheezing within the first year of age, prematurity, and a family history of asthma. The authors also reported that experiencing one wheezing attack during the first age increased the risk of asthma at six years of age. In our study, however, more than one wheezing attack was found to increase the risk of asthma.

In the BAMSE (Barn/Children, Allergy and Milieu in Stockholm, an Epidemiological) study that evaluated children that experienced wheezing at the age of 2-8 years, Neuman et al.[17] defined wheezing and asthma in a similar way to our study and found the prevalence of asthma as 14% and also reported that increased frequency of wheezing was a risk factor for childhood asthma

Whether exposure to a pet at home is a protector or a risk factor for asthma remains controversial.[18] In our study, presence of a pet

Table II. Features of participants and relationship between asthma development and risk factors.

Variable	Asthma (+) n (%)	Asthma (-) n (%)	p
Gender			
Female	22 (11.5)	169 (88.5)	0.164
Male	39 (16.6)	196 (83.4)	
PRM at pregnancy			
No	59 (14.8)	341 (85.2)	0.556
Yes	2 (8)	24 (92)	
Use of antibiotics of during pregnancy			
No	45 (12.5)	314 (87.5)	0.022
Yes	16 (23.9)	51 (76.1)	
Tobacco smoke exposure during pregnancy			
No	50 (14.1)	304 (85.9)	0.618
Yes	11 (16.4)	61 (83.6)	
Tobacco smoke exposure at home			
No	45 (14.8)	260 (85.2)	0.406
Yes	16 (13.2)	105 (86.8)	
Allergic diseases of sibling			
No	38 (10.6)	322 (89.4)	0.001
Yes	23 (34.8)	43 (65.2)	
Allergic diseases of mother			
No	35 (9.9)	319 (90.1)	0.001
Yes	26 (36.1)	46 (63.9)	
Allergic diseases of father			
No	59 (14.3)	353 (85.7)	1.000
Yes	2 (14.3)	12 (85.7)	
Domestic pet at home			
No	52 (13.4)	336 (86.6)	0.091
Yes	9 (23.7)	29 (76.3)	
Dampness at home			
No	47 (12.9)	317 (87.1)	0.045
Yes	14 (22.6)	48 (77.4)	
Environment			
Countryside	8 (28.6)	20 (71.4)	0.045
Urban	53 (13.4)	345 (86.6)	
Day care attendance			
No	12 (8.7)	126 (91.3)	0.026
Yes	49 (17.1)	239 (82.9)	
Upper respiratory infection in first year			
No	7 (16.3)	36 (83.7)	0.650
Yes	54 (14.1)	329 (85.9)	
Use of antibiotics in first year			
No	5 (10.6)	42 (89.4)	0.658
Yes	56 (14.8)	323 (85.2)	
Wheezing attack in first year			
No	15 (6.7)	208 (93.3)	0.001
Yes	46 (22.7)	157 (77.3)	
Atopy			
No	31 (15.7)	166 (84.3)	0.001
Yes	16 (47.1)	18 (52.9)	

PRM: Premature rupture of membranes

Table III. Risk factors for asthma at the sixth year.

Risk factors	OR (95 % CI)	p
Use of antibiotics during pregnancy	2.98 (1.35-6.55)	0.007
Allergic diseases in sibling	2.11 (0.98-4.56)	0.057
Allergic diseases in mother	4.70 (2.29-9.64)	0.001
Presence of atopy	4.76 (2.19-10.33)	0.001
Wheezing attack at first age		
1	1	
2	15.53 (5.47-44.12)	0.001
≥ 3	17.35 (5.28-59.99)	0.001

in the house was found to be a risk factor for wheezing although no correlation was found between exposure to pet at home and asthma at the age of six. In contrast, a few studies indicated that exposure to a pet at home, particularly a cat, was a risk for asthma.[18-20]

A recent study conducted with children aged 9-12 years indicated that the use of antibiotics during the first six months of life is an independent risk factor for asthma, as shown in our study.[18] Another study showed that the use of antibiotics during the first weeks of life is a risk factor for asthma in the following years.[21] In our study, it was also revealed that maternal use of antibiotics during pregnancy is a risk factor for asthma. Stokholm et al.[22] reported that maternal use of antibiotics in pregnancy was associated with an increased risk of childhood asthma like in our study. On the other hand, it has been hypothesized that both the risk of allergic diseases and the methylation levels of imprinted genes increase with intrauterine antibiotic exposure.[23,24] In a similar way, a recent retrospective cohort study by Yoshida et al.[25] found a significant relationship between antibiotic exposure during fetal period and early development of asthma.

Our study was limited since no respiratory test was performed, which was due to the fact that young children are not suitable for the equipment used for lung function tests.

In conclusion, risk factors for asthma at six years of age were found to include maternal use of antibiotics during pregnancy, presence of allergic diseases in the mother and sibling, presence of atopy, and recurrence of wheezing and upper respiratory tract infection in the first year of life.

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Author contribution

The authors confirm contribution to the paper as follows: study conception and design: DÖ, DUA; data collection: DÖ; analysis and interpretation of results: AŞŞ, DÖ; draft manuscript preparation: AŞŞ.

Ethical approval

The study protocol was approved by Çukurova University local ethics committee (02.03.2018/75-46) and was performed in accordance with the Helsinki Declaration.

Conflicts of interest

There is no conflict of interest among the authors of this article.

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