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Factors associated with asthma control in children: findings from a national web-based survey

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Running Title

Factors associated with asthma control

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Abstract

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Factors associated with asthma control in children: findings from a national web-based survey

Abstract

Background: Although achieving and maintaining control of asthma is considered to be the goal of asthma treatment, determinants of asthma

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control are not fully understood. Our aim was to assess factors associated with asthma control among paediatric patients in the general population.

Methods: In June 2012, a web-based survey was conducted to identify Japanese children aged 6 to 11 years who currently have asthma and evaluate control of their disease using the Childhood Asthma Control Test (C-ACT). Associations were evaluated among uncontrolled asthma (C-ACT score <20) between environmental factors, demographics and comorbid allergic diseases.

Results: Among the 3,066 children with current asthma, 447 (14.6%) had uncontrolled asthma. Multivariable analysis identified factors such as low birth weight (adjusted OR 1.65, 95%CI 1.25-2.18), obesity (adjusted OR 1.44, 95%CI 1.05-1.99), and pet ownership before birth (adjusted OR 1.68, 95%CI 1.24-2.29) to be associated with uncontrolled disease. Comorbid allergic diseases, especially rhinitis were a significant risk of uncontrolled asthma (adjusted OR for severe rhinitis: 3.88, 95%CI 2.50-6.00). The severity of rhinitis symptoms was inversely correlated with the C-ACT score ($p < 0.001$).

Conclusions: A population-based web survey showed an association between several factors and the control of pediatric asthma. The assessment of these factors may help identify the children at risk with uncontrolled asthma.

Keywords

asthma; asthma control; Childhood Asthma Control Test; rhinitis; web survey

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Introduction

Asthma is one of the most common chronic pulmonary diseases of childhood and is a cause of poor quality of life (QOL) due to emergency department visits, school absences and impairment of daily activities (1). Achieving and maintaining asthma control has been identified as the goal of asthma treatment in current guidelines (2). This goal benefits patients not only in regard to improving quality of life, but also in reducing the risk of future exacerbations (3).

Studies suggest that a proportion of patients with asthma continue to have poorly controlled disease, despite advances in therapies such as inhaled corticosteroids. A worldwide study in 2004 showed that asthma patients who

report restriction of normal daily activities ranged from 17 to 68% (4), and later studies have reported similar results both in adults and children (5, 6).

Other than higher asthma severity, comorbidities such as allergic rhinitis and socioeconomic status are reported to have a role in disease control in adult and paediatric asthma patients (5, 7, 8). The relationship of asthma control with active or passive smoking and obesity has also been suggested (9, 10). However, determinants of asthma control are not fully understood. Moreover, few studies have evaluated multiple factors among the general population in paediatric asthma. Previous community-based surveys among children (11) are often conducted with limited sample sizes, that could be due to the method of sample collection.

Web-based surveys are regarded as a useful tool for allowing large numbers of participants to respond with a higher and faster response rate than conventional methods (12). These advantages have also been utilized recently in epidemiological surveys for allergic diseases. A national web-based survey administered in the United States in 2007 assessed 1,812 adult patients with moderate-to-severe asthma and reported that 55% had uncontrolled disease in a real-world setting (5).

The aim of this study was to evaluate the factors associated with uncontrolled paediatric asthma in the general population using a web-based survey.

Methods

Study population and participation

This study was conducted using the Macromill online research system (MACROMILL, Inc. Tokyo, Japan), which maintains one of the largest research panels in Japan.

In June 2012, we conducted the primary survey among parents with at least one child aged 6 to 18 years to evaluate the prevalence of allergic diseases. Parents filled in an online questionnaire regarding the child's general characteristics (such as age, sex, body weight, height, family history, and other environmental factors) and whether the child had symptoms of allergic diseases. This survey consisted of the ISAAC (International Study of Asthma and Allergies in Childhood) core questionnaire module for wheeze, eczema, and rhinitis (13). If a parent had two or more children satisfying this condition, they completed the questionnaire for each child.

We sampled children defined as asthma by the questionnaire of the primary survey, and conducted the secondary survey among them using a questionnaire regarding the child's medication and symptoms. Because this was completed by a parent, we used the official Japanese version of the Childhood Asthma Control Test (C-ACT), which is consisted of four

questions for the child and three questions for the caregiver, and scores range from 0 (poorest asthma control) to 27 (optimal asthma control). C-ACT has been developed and validated for children and their caregivers to answer to assess the level of asthma control for those aged 4 to 11 years (14). Thus, 6 to 11 year old children were included in the current analysis.

The study protocol was approved by the independent review board of the Tokyo Metropolitan Children's Medical Center. All parents were provided with an online explanation of the purpose and the procedure of the study, and gave informed consent by proceeding to the questionnaire.

Definitions and Classifications

The definitions used in this study are presented in Table 1. Current asthma was defined based on the ISAAC questionnaire and the use of medication for wheezing symptoms. A C-ACT score of 19 or less was classified as uncontrolled asthma (14). Current eczema, history of eczema, current rhinitis and the severity of rhinitis were defined according to the ISAAC questionnaire. History of food allergy was assessed by whether the child ever had a doctor diagnosis or was suspected of having this disease.

The child's body mass index (BMI) was categorised according to the reference BMI values for Japanese children (15). Children who were at the 95th

percentile or more were defined as obese. Birth weight of less than 2500 g was defined as low birth weight (LBW).

Statistical Analysis

All analyses were performed using the SPSS package version 21 (IBM Corp, Armonk, NY, USA). For comparison, unpaired *t*-tests were used for continuous variables; chi-square tests were used for categorical variables. Univariable logistic regression analysis was used to assess the association between each variable and asthma control. Variables were further analysed by multiple logistic regressions. All study variables were forced into the model. We used the Jonckheere-Terpstra test to assess trends for continuous variables. A *p*-value of <0.05 was considered statistically significant.

Results

Among the 35,000 parents, 32,163 (91.9%) responded to the primary survey for 49,096 children. The primary survey showed that the prevalence of current asthma among 6 to 18 year old Japanese children was 9.8%, and 3231 children were aged 6 to 11. Responses to the secondary survey were collected for 3,066 children, constituting a 94.9% response rate (Fig.1).

Uncontrolled asthma was found in 14.6% children with current asthma. Patients with well-controlled asthma and uncontrolled asthma

were not significantly different with regard to sex and age. The proportion of children using inhaled corticosteroids was 16.6% and 46.1% in the well-controlled asthma and the uncontrolled asthma groups, respectively (Table 2).

Table 3 shows the relationship of each study variable and asthma control. Children with low birth weight were significantly more likely to have uncontrolled asthma, and were at risk even after adjusting for other study variables (adjusted OR 1.65, 95%CI 1.25-2.18). Day care attendance during infancy and breastfeeding for at least 6 months did not show significant differences in the two groups. Annual income and paternal education were not significantly different, although maternal education level showed statistical significance in relationship with asthma control in the multivariable analysis (adjusted OR 1.33, 95%CI 1.02-1.73). Maternal smoking (adjusted OR 1.42, 95%CI 1.02-1.97), though not paternal smoking was an independent risk factor for uncontrolled disease.

Pet ownership had a significant relationship with asthma control depending on when it started. Pet ownership from before birth (adjusted OR 1.68, 95%CI 1.24-2.29) and before 12 months of age (adjusted OR 5.50, 95%CI 2.16-14.05) were both indicated as significant risk factors for uncontrolled asthma. Obesity was also a risk factor for uncontrolled disease (adjusted OR 1.44, 95%CI 1.05-1.99).

Comorbidities, such as current rhinitis, history of eczema, and history of food allergy, were each individually associated with uncontrolled asthma ($p<0.01$, $p<0.01$, $p=0.02$, respectively). The risk of having uncontrolled disease was higher when the rhinitis symptoms were severe (adjusted OR 3.88, 95%CI 2.05-6.00) than mild-moderate (adjusted OR 1.62, 95%CI 1.22-2.17).

The severity of rhinitis symptoms was inversely correlated with the C-ACT score ($p<0.001$; Fig.2).

Discussion

In this study, we were able to identify several factors associated with uncontrolled asthma in the general paediatric population. Our findings are mostly consistent with what is reported in the literature, but also add new insight for identifying children at increased risk for uncontrolled asthma.

LBW had a significant relationship with uncontrolled asthma in our analyses. Previous studies have shown that LBW is related to subsequent wheeze or asthma in childhood, which is possibly associated with reduced airway growth (16). Although controversy remains surrounding the role of LBW in asthma, a recent meta-analysis of 147,252 children in 31 birth cohort studies has reported that younger gestational age at birth was

associated with school-age asthma, and that the association of LBW with asthma is largely explained by gestational age at birth (17). Meanwhile, the association of LBW or prematurity with the control of asthma is less studied. The current analyses suggest that foetal development may be relevant not only for the development of asthma but also for the control of disease.

Pet ownership starting before birth and during infancy was significantly associated with uncontrolled asthma in our analyses. The results of previous reports regarding the association of pet ownership with the development of asthma or sensitisation are controversial (18). However, for patients who have developed asthma, pet allergen exposure has been reported to be associated with worsening symptoms similar to our results (19, 20). A study among school-aged asthmatic children showed that the severity of wheezing symptoms was significantly associated with the exposure to low levels of household cat and dog allergens for those who are sensitised (19). Several studies have indicated that the negative effect of pet allergen exposure may be significant for non-sensitised asthma patients as well (21, 22). The association of pet ownership with asthma control in our analyses differed depending on when it started. This fact might be due to the difference in the amount of the cumulative allergen exposure. Further exploration is probably difficult without the measurement of exposure and sensitisation and is expected in future studies. The possibility that children

with uncontrolled asthma avoid owning pets after developing symptoms also exists and would mask the negative effect of pet ownership starting after the first year.

Allergic rhinitis is widely accepted to have similar pathogenesis to asthma, and has been recognised as a cause of uncontrolled asthma in adults (7, 23). A nationwide survey among Japanese adult asthma patients showed that 68.5% had self-reported rhinitis, and significantly more of these patients had uncontrolled asthma than those without rhinitis (25.4% vs 18.0%) (23). The impact of rhinitis on the level of asthma control among children is less well studied, but we have recently conducted a large population-based nationwide study among more than 100,000 Japanese children and have reported that rhinitis symptoms is a risk factor of current asthma and severe asthma (24). Our current analyses have confirmed these results, and have also shown that the severity of rhinitis correlates with the degree of asthma control.

The major limitation of this study is that all data were self-reported and retrospectively obtained, lacking objective data such as IgE and lung function tests. Defining asthma and other allergic diseases mainly based on the ISAAC questionnaire may have resulted in over-diagnosis in some children, as previously reported (25). Since the information about asthma treatment was limited to the name of the medications prescribed, the exact treatment step could not be included in the assessment. The treatments of

rhinitis symptoms were also not evaluated. However, the strength of this study is that it has collected thorough data among a large number of children with asthma in the general population, and measured their symptom control by a widely-used tool. This has enabled the assessment of children without having regular follow-up by physicians and cannot be assessed by hospital-based studies.

It should also be noted that discrepancies of the assessment of asthma control has been reported between C-ACT and GINA criteria, showing that the generally used cut-off points may overestimate the proportion of children with controlled asthma as defined with GINA (26, 27). Nevertheless these tools have shown good correlation in these studies, and the cut-off score of 19 by C-ACT in our study has surely detected the children with uncontrolled asthma defined with GINA criteria.

Finally, the generalizability of this study is another concern because of the use of a web-based questionnaire. However, the Japanese Ministry of Internal Affairs and Communications has shown that the Internet diffusion rate among people aged 20-49 years exceeds 90%, which means that most parents of schoolchildren currently use the computer and the Internet in Japan(28). Furthermore, the web-based ISAAC questionnaire, ACT/C-ACT has been shown to be reproducible and comparable with the paper-based versions, even preferred by respondents (29, 30). Therefore, our current

web-based survey is likely to contain comprehensive and reliable information about the general paediatric population.

In conclusion, we found several factors associated with asthma control in a population-based study. Further understanding of these risk factors may lead to possible interventions to improve disease control.

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Conflict of interest

The authors declare no conflict of interest.

Figure legends

Figure 1 Flow chart of the study subjects.

Figure 2 Distribution of the C-ACT score based on the presence and the severity of the rhinitis symptoms

No rhinitis was defined as a negative answer to the question “In the past 12 months, has your child had a problem with sneezing, or a runny or blocked nose when he/she did not have a cold or the flu?” Rhinitis was defined as a positive answer to this question, and then the severity was assessed by the answer to the question “In the past 12 months, how much did this nose problem interfere with your child’s daily activity?” where possible answers were “not at all”, “a little”, “a moderate amount”, or “a lot”. Box and whisker plots represent median, 25% to 75% range, and 5% to 95% range.

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Table 1 Definitions of the variables included in the study.

Variable	Definition
Current asthma	Positive response to the question “Has your child ever had wheezing in the chest in the past 12 months?” or “Has your child been prescribed daily medication for wheezing symptoms in the past 4 weeks?”
Uncontrolled asthma	Current asthma with C-ACT score of 19 or less
Current eczema	Positive response to these two questions “Has your child had this itchy rash at any time in the past 12 months?” and “Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks or around the neck, ears or eyes?”
History of eczema	Positive response to the question “Has your child ever had atopic dermatitis?”
Current rhinitis	Positive answer to the question “In the past 12 months, has your child had a problem with sneezing, or a runny or blocked nose when he/she did not have a cold or the flu?”
Mild to moderate	Current rhinitis with answering “not at all”, “a little”, “a moderate amount” to the question “In the past 12months, how much did this nose problem interfere with your

rhinitis	child's daily activity?"
Severe rhinitis	Current rhinitis with answering "a lot" to the question "In the past 12 months, how much did this nose problem interfere with your child's daily activity?"
History of food allergy	Positive answer to the question "Has a doctor ever said the child had food allergy or the suspect of food allergy?"
Obese	Body mass index (BMI) at the 95 th percentile or more
Low birth weight (LBW)	Birth weight of less than 2500g

Table-2 Characteristics of the respondents of the secondary survey

	Total (n = 3066)	Controlled asthma (n = 2619)	Uncontrolled asthma (n = 447)	<i>P</i> value
Age (Y)				0.97
mean +/- SD	8.00 +/- 1.69	8.00 +/- 1.69	8.00 +/- 1.68	
Sex				0.91
Male	1818	1554 (59.3%)	264 (59.1%)	
Female	1248	1065 (40.7%)	183 (40.9%)	
Controller medication				<0.01
ICS use	641	435 (16.6%)	206 (46.1%)	
LTRA use	554	425 (16.2%)	129 (28.9%)	
β-stimulant only	221	176 (6.1%)	45 (10.1%)	
None	1650	1583 (60.4%)	67 (15.0%)	

ICS use: Inhaled corticosteroid alone or in combination with other medication

LTRA use: Leukotriene modifiers only or in combination with medication other than ICS

None: no medication or use of medication other than LTRA, ICS, β-stimulant

Table 3 Association between uncontrolled asthma and environmental factors, demographics and comorbid allergic diseases

Variable	(N)	Uncontrolled asthma % (n)	Crude OR (95%CI)	P value	Adjusted OR* (95%CI)	P value
Birth weight						
≥ 2500g	(2574)	13.6 (349)	1		1	
< 2500g	(472)	20.3 (96)	1.63(1.27-2.09)	<0.01	1.65 (1.25-2.18)	<0.01
Daycare during infancy						
No	(2810)	14.8 (417)	1		1	
Yes	(250)	12.0 (30)	0.78 (0.53-1.16)	0.22	0.64 (0.41-1.10)	0.06
Breast-feeding						
Less than 6mo	(1574)	15.7 (247)	1		1	
More than 6mo	(1408)	13.6 (192)	0.85 (0.69-1.04)	0.11	0.89 (0.71-1.11)	0.29
Annual income(yen)						
< 5million	(1151)	16.1 (185)	1		1	
≥ 5 <7.5 million	(994)	13.9 (138)	0.84 (0.66-1.07)	0.16	0.81 (0.62-1.05)	0.11
≥ 7.5 million	(670)	14.9 (100)	0.92 (0.70-1.19)	0.52	0.89 (0.66-1.20)	0.44
Paternal education level						
Less than college	(1484)	15.3 (227)	1		1	
Completed college	(1473)	14.1 (207)	0.91 (0.74-1.11)	0.34	0.98 (0.76-1.26)	0.87
Maternal education level						
Less than college	(2255)	14.1 (318)	1		1	
Completed college	(781)	16.1 (126)	1.17 (0.94-1.47)	0.17	1.33 (1.02-1.73)	0.04
Paternal smoking						
No	(2052)	13.0 (267)	1		1	
Yes	(1014)	17.8 (180)	1.44 (1.17-1.77)	<0.01	1.20 (0.94-1.54)	0.14

Maternal smoking						
No	(2677)	13.6 (363)	1		1	
Yes	(389)	21.6 (84)	1.76 (1.35-2.29)	<0.01	1.42 (1.02-1.97)	0.04
Paternal asthma						
No	(2603)	14.1 (367)	1		1	
Yes	(463)	17.3 (80)	1.27 (0.97-1.66)	0.08	1.13 (0.84-1.50)	0.43
Maternal asthma						
No	(2542)	14.0 (355)	1		1	
Yes	(524)	17.6 (92)	1.31 (1.02-1.69)	0.03	1.23 (0.93-1.63)	0.14
Pet ownership						
No	(2238)	13.0 (291)	1		1	
From before birth	(381)	22.0 (84)	1.89 (1.44-2.48)	<0.01	1.69 (1.24-2.29)	0.01
From infancy	(26)	42.3 (11)	4.91 (2.23-10.79)	<0.01	5.50 (2.16-14.05)	<0.01
From after age1	(404)	14.4 (58)	1.12 (0.83-1.52)	0.46	0.98 (0.70-1.38)	0.91
Body mass index						
< 95 percentile	(2704)	14.0 (379)	1		1	
≥ 95 percentile	(362)	18.8 (68)	1.42 (1.07-1.89)	0.02	1.44 (1.05-1.99)	0.03
Current rhinitis						
No	(791)	9.2 (73)	1		1	
Mild-moderate	(2090)	15.3 (320)	1.78 (1.36-2.33)	<0.01	1.62 (1.22-2.17)	0.01
Severe	(185)	29.2 (54)	4.05 (2.72-6.04)	<0.01	3.88 (2.50-6.00)	<0.01
History of eczema						
No	(2063)	12.1 (249)	1		1	
Yes	(1003)	19.7 (198)	1.79 (1.46-2.20)	<0.01	1.58 (1.25-2.00)	<0.01
History of food allergy						
No	(2010)	12.8 (257)	1		1	

Yes	(1056)	18.0 (190)	1.50 (1.22-1.84)	<0.01	1.31 (1.04-1.65)	0.02
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*Adjusted for sex, age and all variables shown. OR: odds ratio. CI: confidence interval.



