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Childhood asthma control in Japan: A nationwide, cross-sectional, web-based survey

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Abstract

Background: Recent surveys have shown that many patients with asthma experience uncontrolled symptoms and decreased quality of life due to their disease. However, few large population-based studies have evaluated asthma control in Japanese children.

Objective: To show the reality of asthma control and the pattern of asthma controller medication use among Japanese children.

Methods: In 2012, a web-based survey was conducted to identify children aged 6 to 11 years with asthma in Japan. Among children with current asthma, we collected information regarding their asthma controller medication use and evaluated the control level of asthma using the Childhood Asthma Control Test (C-ACT). In this study, a C-ACT score of 19 or less, 20 to 22, and over 22 were classified as uncontrolled asthma, well-controlled asthma, and optimally controlled asthma, respectively.

Results: Among the 3,033 children with current asthma, 442 (14.6%), 635 (20.9%), and 1,956 (64.5%) children had uncontrolled, well-controlled, and optimally controlled disease, respectively. In the past 1 month, 1,387 (45.7%) reported receiving at least 1 asthma controller medication with 638 (21.0%) reported receiving inhaled corticosteroid. Among the children with uncontrolled asthma, 67 (15.2%) were not receiving any asthma controller mediations. Among children receiving asthma controller medication, 27.0%, 31.4% and 41.5% had uncontrolled, well-controlled, and optimally controlled asthma, respectively.

Conclusions: Although more than half of children with current asthma had optimally controlled disease, some children without any controller medications and more than a quarter of the children receiving asthma controller medications had uncontrolled disease.

Keywords: asthma, asthma control, child, guidelines, treatment

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Introduction

Asthma is one of the most common non-communicable diseases in childhood, and has an impact on quality of life of the patients and their families.[1,2] Asthma in children is the main cause of school absence and poor school performance.[3,4] Furthermore, uncontrolled asthma imposes a far greater burden on the patients, their families, and society than well-controlled asthma.[5,6]

The goal of asthma management according to recently published guidelines are to achieve and maintain control of the disease such that there are no symptoms, or limitations on activities like attending school or engaging in sports. Clinical studies have shown that currently available, effective asthma controller medications, particularly inhaled corticosteroid (ICS), can archive good control in most patients with asthma.[7,8]

However, large community-based surveys in many regions have reported that the majority of patients experience a high rate of symptoms and disruption of life due to their disease.[9-11]

The Japanese pediatric guideline for the treatment and management of asthma (JPGL)[12] recommends higher levels of control and early intervention compared to other international guidelines such as the Global Initiative for Asthma (GINA) report and Japanese Guideline for Adult Asthma.[13,14] However, only few population-based studies have evaluated asthma control in Japanese children.[15] Here, we report data from a nationwide, web-based survey, conducted among more than 3,000 children with current asthma whose family had registered on an online research panel. The data provide important insights into the reality of asthma control levels and the pattern of asthma controller medication prescriptions for Japanese children.

Methods

Study design and populations

A survey was conducted using an online research system (MACROMILL, Inc. Tokyo, Japan). The method of the survey has been described in detail elsewhere.[16] We conducted the primary survey among parents with children aged 6 to 18 years to evaluate the prevalence of allergic diseases in July 2012. In the same month, we conducted the secondary survey among children identified as having current asthma in the primary survey. To evaluate the control of asthma, we used the Japanese version of the Childhood Asthma Control Test (C-ACT), which was developed for children aged 4 to 11 years and validated in a web–based version.[17,18] Thus, children aged 6 to 11 years were included in the current analysis.

The survey 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 definition of current wheeze, current rhinitis and current eczema were taken from the International Study of Asthma and Allergies in Childhood.[19] Current asthma was defined as current wheeze by ISAAC definition, or having a positive response to 'Has your child taken the controller medications for wheezing symptoms throughout the past 4 weeks?' in order to capture children having no symptoms due to using asthma controller medications. ICS, inhaled long-acting β stimulant (LABA), leukotriene receptor antagonist (LTRA), and the tulobuterol patch (TP) were defined as asthma controller medications as per JPGL.[12,20]

Evaluation of asthma control

Previous reports have used a C-ACT cut off score of 19 to identify uncontrolled asthma.[17] However, recent studies have shown that this cut–off point seems to underestimate the proportion of children with uncontrolled asthma.[21-23] Moreover, our study has shown that a cut off of 23 can identify children with well–controlled asthma having normal lung function.[24] Therefore, we divided the children with a score of 20 or more into 2 groups in this study: the well-controlled asthma group, which had a score of 20 to 22, and the optimally controlled asthma group, with a score over 22.

Statistical analysis

All analyses were performed using the SPSS package version 19 (IBM Corp, Armonk, NY, USA). For comparison, the chi-square test was used for categorical variables. Univariate and multivariate logistic regression analyses were used to assess the association between each variable and use of an ICS-containing regimen. $P < 0.05$ was considered statistically significant.

Results

Characteristics of the children in this study

Of the 3,231 children aged 6 to 11 years with current asthma invited to participate in the second survey, 3,066 responded (response rate: 94.9%). After omitting 33 children who failed data quality checks, 3,033 were analyzed in this study (**Figure 1**). Boys were more likely to have current asthma than girls. Of the children with current asthma, 2,576 (84.9%), 2,247 (74.1%) and 786 (25.9%) had current wheeze, current rhinitis and current eczema, respectively. In the past 1 month, 1,387 (45.7%) reported receiving at least 1 asthma controller medication. Among them, 21.0% reported receiving an ICS-containing medication, 29.5% reported receiving LTRA, and 18.3% reported receiving TP (**Table 1**).

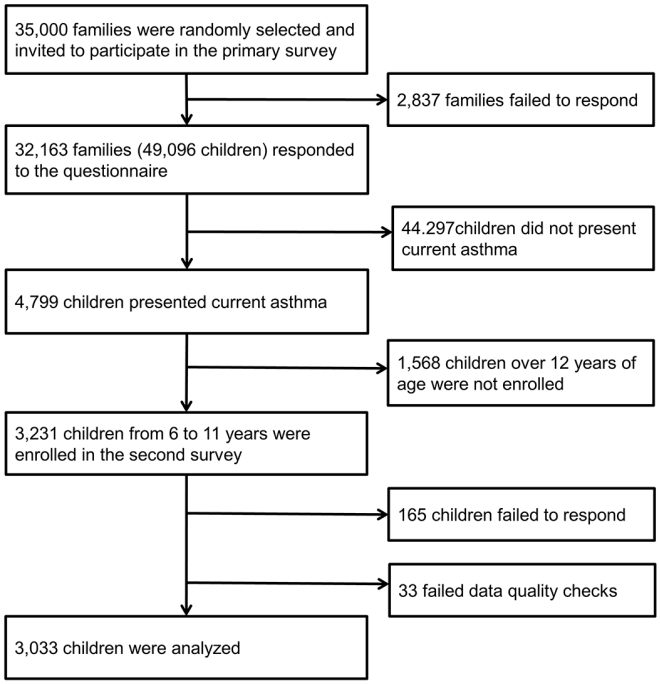

Figure 1. Flow chart of the study subjects

Table 1. Characteristics of children in this study

	n	%
Sex		
Boys	1797	59.2
Girls	1236	40.8
Age		
6 to 8 years	1730	57.0
9 to 11 years	1303	43.0
Comorbidities		
Current wheeze Current rhinitis	2576	84.9
Current rhinitis	2247	74.1
Current eczema	786	25.9
Familial History of Asthma		
Father	458	15.1
Mother	518	17.1
Passive smoking		
Father	1008	33.2
Mother	383	12.6
Annual income (yen)		
< 5 million	1139	37.6
≥5 <7.5 million	982	32.4
≥7.5 million	665	21.9
Regular controller in the past 1 month	1387	45.7
Any ICS-containing inhaler	638	21.0
(ICS only inhaler)	(445)	(14.7)
(ICS/LABA inhaler)	(193)	(6.4)
LTRA	894	29.5
Tulobuterol patch	555	18.3
LABA only inhaler	5	0.2

ICS: inhaled corticosteroid, LABA: long-acting β-agonist, LTRA: leukotriene receptor antagonist, TP: tulobuterol patch

Asthma control in children with current asthma

Of the children with current asthma, 442 (14.6%), 635 (20.9%), and 1,956 (64.5%) children had uncontrolled, well-controlled, and optimally controlled asthma, respectively (**Table 2**). Children receiving at least 1 asthma controller medication were more likely to have poor control compared to those not using any asthma controller medications ($p < 0.01$). The proportion of children receiving asthma controller regimens varied with the asthma control level in children (**Figure 2**). Among children with optimally controlled asthma, 70.6% were not receiving any asthma controller medications. Children with well-controlled disease were likely to be receiving a non-ICS-containing regimen (38.9%) and those with uncontrolled disease were likely to be receiving an ICS-containing regimen (46.4%). However, 53.6% of children with uncontrolled disease were not receiving ICS, 15.2% were not receiving any asthma controller medications, and 38.4% were receiving a non-ICS-containing regimen.

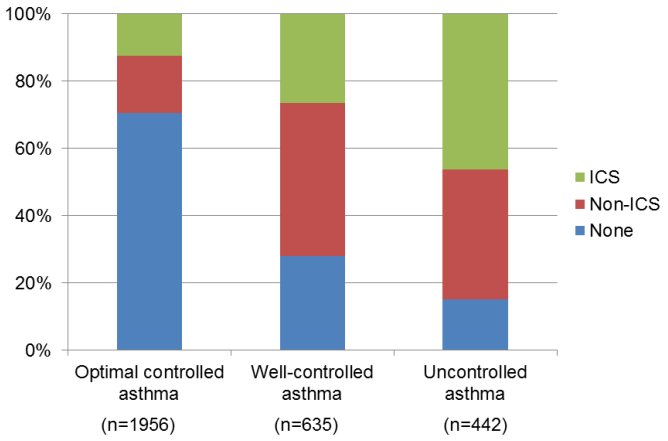

Figure 2. Asthma controller regimens for children with optimally controlled, well-controlled, and uncontrolled disease. ICS: ICS-containing regimens, Non-ICS: Non-ICS-containing regimens.

Asthma control in children receiving asthma controller medications

Among the 1,387 children receiving asthma controller medications, 375 (27.0%), 436 (31.4%), and 576 (41.5%) children had uncontrolled, well-controlled, and optimally controlled asthma, respectively (**Table 2**).

Children receiving an ICS-containing regimen were older and more likely to have a parental history of asthma and uncontrolled disease compared to those receiving a non-ICS-containing regimen even when adjusted for other variables ($p < 0.01$, $p = 0.01$ and $p < 0.01$, respectively: **Table 3**). **Table 4** shows the association between asthma controller regimens and the control of the disease in detail. The most common regimen was LTRA alone administered to the largest proportion of children with controlled disease (53.7%). TP alone and LTRA+TP were the next most common regimens. However, 37.4% of children receiving LTRA+TP had uncontrolled

Table 2. The control of asthma in children with current asthma

	Overall	The level of asthma control						p-value
		Uncontrolled (C-ACT score <20)		Well-controlled (C-ACT score 20-22)		Optimally controlled (C-ACT score >22)		
	n	n	%	n	%	n	%	
Total	3033	442	14.6	635	20.9	1956	64.5	
At least one asthma controller medication in the past 1 month								
No	1646	67	4.1	199	12.1	1380	83.8	<0.01
Yes	1387	375	27.0	436	31.4	576	41.5	

Table 3. Factors associated with receiving ICS–containing regimen

	ICS–containing regimen							
Variable	**%**	**(n/N)**	**Crude OR**	**(95%CI)**	**P-value**	**Adjusted OR†**	**(95%CI)**	**P-value**
Sex								
Boys	45.8	(392/856)	1			1		
Girls	46.3	(285/531)	1.00	(0.82-1.27)	0.87	1.02	(0.82-1.27)	0.86
Age								
6 to 8 years	42.1	(352/835)	1			1		
9 to 11 years	51.8	(266/552)	1.48	(1.19-1.83)	<0.01	1.47	(1.18-1.83)	<0.01
Current rhinitis								
No	46.6	(131/281)	1			1		
Yes	45.8	(507/1106)	0.97	(0.75-1.26)	0.84	0.89	(0.60-1.17)	0.40
Current eczema								
No	45.4	(443/975)	1			1		
Yes	47.3	(195/412)	1.08	(0.86-1.36)	0.56	1.08	(0.85-1.36)	0.54
Parental history of asthma*								
No	43.3	(410/947)	1			1		
Yes	51.8	(228/440)	1.41	(1.12-1.77)	<0.01	1.37	(1.09-1.73)	0.01
Parental smoking*								
No	46.5	(398/847)	1			1		
Yes	44.4	(240/540)	0.90	(0.73-1.12)	0.38	0.86	(0.69-1.07)	0.17
Annual income (yen)								
< 5 million	46.7	(246/527)	1			1		
≥5 <7.5 million	44.4	(194/437)	0.91	(0.70-1.18)	0.48	0.83	(0.53-1.29)	0.41
≥7.5 million	48.5	(157/324)	1.07	(0.81-1.42)	0.61	1.03	(0.78-1.37)	0.82
Unknown	41.4	(41/99)	0.81	(0.52-1.25)	0.34	0.89	(0.69-1.16)	0.40
Asthma control								
Optimal controlled	42.3	(244/576)	1			1		
Well-controlled	43.3	(189/436)	1.04	(0.81-1.34)	0.75	1.04	(0.81-1.34)	0.76
Uncontrolled	54.7	(205/375)	1.64	(1.26-2.13)	<0.01	1.62	(1.24-2.12)	<0.01

OR, odds ratio; CI, confidence interval
* At least 1 parent, † Adjusted for all variables shown

Table 4. The association between asthma controller regimens and the control of disease

		The level of asthma control		
Regimen	**n**	**Uncontrolled (%) (C-ACT score <20)**	**Well–controlled (%) (C-ACT score =20-22)**	**Optimally controlled (%) (C-ACT score >22)**
LTRA	356	15.4	30.9	53.7
TP	199	20.6	32.7	46.7
LTRA+TP	190	37.4	37.4	25.3
ICS+LTRA	169	29.6	27.2	43.2
ICS	164	18.3	30.5	51.2
ICS/LABA+LTRA	77	42.9	22.1	35.1
ICS+LTRA+TP	71	60.6	25.4	14.1
ICS/LABA	63	23.8	30.2	46.0
ICS+TP	41	24.4	41.5	34.1
Others	57	47.4	40.4	12.3

ICS: inhaled corticosteroid, LABA: long-acting β-agonist, LTRA: leukotriene receptor antagonist,
TP: tulobuterol patch

disease. ICS+LTRA and ICS alone were commonly used regimens among children receiving an ICS-containing regimen. More than half of children receiving ICS alone had optimally controlled asthma, whereas 60.6% of children receiving ICS +LTRA+TP had uncontrolled asthma. A few children received inhaled LABA without ICS.

Discussion

This cross-sectional study showed the reality of asthma control and the pattern of asthma controller medication use among Japanese children. Many children, especially those receiving asthma controller medications, did not have optimally controlled disease. Previous studies showed that children with a C-ACT score over 19 included those with uncontrolled disease as defined by GINA,[21-23] and that a cut off of 23 was able to identify children with well–controlled asthma having normal lung function.[24] Children with a score of 20 to 22 (about 20% of children with current asthma) required improvement of their symptoms to archive optimally controlled disease. The results in our study were similar with those in the Asthma Insights and Reality in Japan 2011 report showing that 17% of children under 11 years of age had uncontrolled disease.[15] The Asthma Insights and Reality in 12 Asian-Pacific areas in 2006 showed that 43.2% of children with current asthma had uncontrolled asthma as defined by C-ACT of 19.[22] Although we have shown that uncontrolled asthma is common in Japan along with these previous reports in the world, children with asthma might have a better controlled disease in Japan compared to other Asian regions.

Children receiving an ICS-containing regimen were older and more likely to have a parental history of asthma and poorly controlled asthma compared to those receiving a non-ICS -containing regimen. Children with a familial history of asthma also had a lesser chance of remission compared to those without a familial history.[25,26] ICS might be used with consideration for asthma control and prognosis. Although previous studies showed that the use of ICS for asthma in Japan is lower than in the west,[27] the use of ICS for childhood asthma (21% of children with current asthma) seems to show an increase compared with the findings of the aforementioned Asthma Insights and Reality in Japan, which reported the figures of 9% in 2000 and 12% in 2005.[28] However, more than half of children with uncontrolled disease were not receiving ICS, and would benefit from improved asthma management. It should also be noted that many children using ICS, especially in combination with other controller medications, still had poor controlled disease. This finding is in line with other community -based surveys.[10,11] While some of them might have refractory disease, it is possible that the efficacy of their treatments were affected by poor adherence or inaccurate inhaler technique.[29] Although unfortunately we did not evaluate adherence or inhaler technique, simplifying controller regimens and the sustained follow-ups after the prescription of ICS might bring better disease control for children with asthma in Japan.

Additionally, our study showed some concerns about TP, a long acting form of tulobuterol, which commonly used as LABA in Japan and other East Asian countries. Asthma guidelines have strongly discouraged LABA monotherapy because of its association with the risk of severe exacerbations and asthma -related deaths.[30] While only a few children in Japan received inhaled LABA monotherapy, many children received TP, a long acting form of tulobuterol, without any combination with anti-inflammatory controller medications. This result was also found in the analysis of the administrative claims database of the Japan Medical Data Center Co., Ltd. (Tokyo, Japan).[31] Furthermore, 37.4% of uncontrolled asthma was seen in children receiving LTRA and TP despite the availability of ICS. Although caregivers and children might prefer a transdermal application to inhaled drugs because of its convenience and concerns about side effects, clinicians need to prescribe anti -inflammatory medications for children who need asthma controller medications and use TP more carefully.

The study had a large sample with high response rate, and was able to assess both the level of asthma control and patterns of prescription of asthma controller medications for Japanese children. If the survey were repeated in the future, it would provide time-trends of the reality of asthma control and management among Japanese children. The major limitations of our study were those associated with online research. Respondents registering on an online research panel may not represent the general population. Moreover, all the data of our survey were reported by parents via online questionnaire. These responses could not be clinically verified, and the possibility of inaccurate responses due to poor recall cannot be excluded. In addition, our survey was not able to assess medication adherence and inhaler technique, important factors in uncontrolled asthma.[29] However, the same limitations would exist in other community-based survey methodologies, such as random-digit dialing and postal questionnaires. Because the traditional sampling methods have suffered from low response rates in past decades, many recent, community-based surveys have chosen online questionnaires if study population has a high level of internet access.

In conclusion, our study described the reality of asthma control and management among Japanese children. Although more than half of the children with current asthma had optimally controlled disease, more than a quarter of the children receiving asthma controller medications had uncontrolled disease.

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