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Uncontrolled asthma and its risk factors in Chinese children: A cross-sectional observational study

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Abstract

Objective: Asthma afflicts many children in China but information about asthma management among Chinese pediatric asthma patients is limited. This study aims to evaluate asthma control among Chinese pediatric patients and identify risk factors associated with uncontrolled asthma. **Methods:** A total of 4223 patients with persistent asthma aged 2–16 years from 42 tertiary hospitals across all regions of mainland China except Tibet were surveyed. Asthma Control Test (ACT), Childhood Asthma Control Test (C-ACT) and Global Initiative for Asthma (GINA) criteria were used to assess asthma control for children aged 12–16 years, 4–11 years and 2–3 years, respectively. Uncontrolled asthma was defined as ACT or C-ACT score ≤ 19 or GINA-defined uncontrolled asthma. Risk factors associated with uncontrolled asthma were identified using multivariate logistic regression models. **Results:** Asthma was uncontrolled in 19.9% of the subjects. High rates of uncontrolled asthma were found in subjects with treatment non-adherence (44.1%), concomitant allergic rhinitis (AR) (23.3%), disease duration ≥ 1.5 years (22.8%), and first-degree relatives with AR (21.5%). The risk of uncontrolled asthma was much higher in the treatment non-adherence group compared to the complete adherence group (OR = 5.79, $p < 0.001$). Concomitant AR, disease duration ≥ 1.5 years, and first-degree relatives with AR were also confirmed as risk factors associated with uncontrolled asthma. **Conclusions:** About 20% of Chinese pediatric asthma patients had uncontrolled asthma. Treatment adherence and AR were the most significant risk factors. Tailored measures aimed at improving treatment adherence and diagnosis and treatment of AR should be adopted to improve the level of asthma control in Chinese children.

Keywords

Asthma control, children, persistent asthma

History

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Introduction

Asthma is one of the most common chronic diseases throughout the world. Its prevalence has increased considerably over the past 20 years, especially in children [1,2]. Several studies have documented the increase in pediatric asthma in China. In 2000 a national survey of 43 cities in 31 provinces showed that the overall prevalence of asthma among children aged 0–14 years old was 1.97%, with the highest prevalence in Shanghai (4.6%) [3]. In 2005 a study carried out in 8 major cities in China reported asthma incidence of 3.3% among children aged 6–13 years old [4]. A third national survey, carried out in 43 cities in 27 provinces from September, 2009 to August, 2010 found asthma prevalence among children aged 0–14 years

old to be 3.02%, again with the highest prevalence in Shanghai (7.57%) [5].

Although the cause of asthma is not well understood, effective therapies and management guidelines are available. According to Global Initiative for Asthma (GINA) guidelines, the goal of asthma management is to achieve and maintain control of the clinical manifestation of the disease for prolonged periods [2]. Unfortunately, suboptimal control of asthma is still prevalent around the world [2], including in China. A study carried out in 29 cities in mainland China in 2009 reported that 66.0% of asthmatic children aged 0–14 years old had experienced asthma attacks in the past 12 months, 26.8% had visited the emergency department, and 16.2% had been hospitalized [6]. In recent years, several studies conducted among smaller populations also reported that uncontrolled asthma is prevalent in Chinese pediatric patients, with the rate of uncontrolled asthma ranging from around 20% to more than 50% [7–10]. However, no additional large population-based studies

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of asthma control status among pediatric patients in China have been conducted since 2009.

This study aims to provide updated information about asthma management among pediatric outpatients in mainland China, including the proportion of uncontrolled asthma and its impact on patients' daily activities, the potential risk factors associated with uncontrolled asthma, and controller medication usage. The results will provide information that can be used to implement and adjust asthma control strategies, and ultimately improve asthma control among Chinese pediatric patients.

Methods

Study design and patients

This nationwide cross-sectional observational study was conducted between October, 2012 and June, 2013. It involved 8873 asthma patients age 2 years and older who visited outpatient clinics of respiratory disease departments for treatment, prescription refill or consultation during the study period. Results from subjects aged ≥ 17 years old will be reported separately. Here we report the results of subjects 2–16 years of age. These subjects were enrolled from 42 tertiary general hospitals covering all territories and regions of mainland China except Tibet.

All participants had confirmed asthma with asthma duration of three months at least and had symptoms or took asthma medication during the past 12 months by the enrollment, based on medical chart review. For children 6–16-years-old, asthma was defined as the presence of relevant clinical history (i.e. history of recurrent dyspnoea, wheezing or cough episodes) and pulmonary function tests demonstrating variable airflow limitation by means of airway responsiveness testing or airway reversibility testing, which satisfied those of GINA [2]. For children under 5 years old, asthma was defined as the presence of relevant clinical history with support of pulmonary function tests or therapeutic trial or tests for atopy [11]. Disease and treatment duration were also collected through medical chart review. The study investigators consecutively screened eligible patients during their routine visits. Patients who had intermittent asthma, bronchitis, cystic fibrosis, pneumonia or whose parents or legal guardians were not able to fill in the questionnaires were not enrolled.

The study was initially approved by the Independent Ethics Committee of Beijing Children's Hospital, Capital Medical University. Other participating hospitals either accepted that decision or conducted a further independent ethics review, according to their own institutional policy. Informed consent was obtained from the parents or legal guardians of all study subjects.

Data collection

Socio-demographic and clinical data including family history of allergic disease, concomitant disease (e.g. rhinitis, allergic rhinitis), asthma symptoms when diagnosed, asthma duration since diagnosis, asthma related treatments and tests, asthma controller adherence were collected from medical chart review, and asthma symptoms in the previous four weeks (e.g. frequency, limitation on activity/sleep, use of reliever), participants' school absences, reason for non-adherence, extent

to limitation of physical activities (e.g. no physical activity, only mild activities, no strenuous activities, all physical activities), and loss of work days of their parents or caregivers due to asthma during the past 12 months were collected through patient or parent self-report during the interview with physicians.

Rhinitis was defined as nasal symptoms, including sneezing, nasal blockage, and itching of the nose, occurring during multiple consecutive days for more than 1 hour on most days and not caused by cold or flu [12]. On the basis of current nasal symptoms, allergic rhinitis (AR) was defined as rhinitis associated with IgE-mediated immune response confirmed by serum specific IgE or skin prick test [12]. Asthma controller adherence was assessed by physicians through review of prescription refill in the past 3 months (i.e. $\geq 90\%$, 70–89%, 50–69%, $< 50\%$) and was categorized into 4 groups: complete adherence, good adherence, poor adherence and non-adherence. Reason for non-adherence was asked through a closed list including but not limited to self-deemed relief, concern of side effect and concern on children's growth due to long term intake of medication.

The 5-item Asthma Control Test (ACT) and Childhood Asthma Control Test (C-ACT) questionnaires were used to assess the level of asthma control for children aged 12–16-years-old [13–15] and aged 4–11-years-old, respectively [16,17]. Both questionnaires in Chinese have been validated in other studies [14,17]. Using the ACT and C-ACT, the degree of asthma control was classified into two levels: controlled (ACT or C-CAT ≥ 20), and uncontrolled (ACT or C-CAT ≤ 19). All questions were completed by subjects or their caregivers and reviewed by physicians for completeness.

GINA criteria were used to assess the level of asthma control for children aged 2–3-years-old. According to GINA criteria for children under 5 years of age, asthma control level was classified into three levels: controlled, partly controlled and uncontrolled [3].

Quality control

All data from medical chart review and interview were collected using a uniform data collection form. All investigators were trained on the standardized study protocol and data collection form before initiation of the study. A Clinical Research Organization (CRO) was employed to monitor the quality of data collection and to manage the data. All data were input into a programmed database by two persons, independently, for statistical analysis.

Statistical analysis

We calculated sample size based on the estimation of uncontrolled asthma rate. Because the rate of uncontrolled asthma in Chinese children has not been well established, we used the reported rate of approximately 42% among adult Chinese asthma patients [18] to estimate the rate among Chinese children as 50%. The estimated sample size was 1537 for a 95% confidence level with margin of error at $\pm 2.5\%$. Since we planned to do stratification analysis on AR co-morbidity and other risk factors, we considered to amplify the sample size over 3000. Meanwhile, in order to maintain sample representative with consideration of geographic variation and feasibility for study site, we finally determined that each site enrolled

100 patients for 42 study hospitals, that is, 4200 patients as our sample size.

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were described by mean, median, standard deviation (SD), first and third quartiles (Q1 and Q3), minimum and maximum. Categorical variables were described by frequency and percentage.

Chi-square test was used to compare proportions of categorical variables between different subgroups. Wilcoxon rank test was used to evaluate the difference in number of days of school absences, loss of work days and limitation on physical activities between subjects with controlled and uncontrolled asthma.

To explore the potential risk factors associated with uncontrolled asthma, the level of asthma control was summarized into two categories: controlled asthma (ACT ≥ 20 or C-ACT ≥ 20 or GINA-defined controlled and partly controlled asthma) and uncontrolled asthma (ACT ≤ 19 or C-ACT ≤ 19 or GINA-defined uncontrolled asthma). The proportion of uncontrolled asthma in subjects with different characteristics was calculated and compared using Chi-Square test. To identify risk factors associated with uncontrolled asthma, univariate logistic regression was performed for each potential factor surveyed. Factors of statistical significance (*P* < 0.1) were then analyzed using multivariate logistic regression models. Correlation between factors was examined by calculating Spearman's rank correlation coefficient. If moderate or high correlation existed between two factors, only one of the two factors was entered into the multivariate logistic regression model. Sensitivity analysis was performed to test the stability of the results by replacing categorical age group with age in years in multivariate logistic regression model. Odds ratio (OR), the 95% confidence interval and *p* value of each factor from the multivariate logistic regression models was estimated and presented. A two-tailed *p* value of less than 0.05 was considered to be statistically significant.

Statistical analyses were performed using the SAS® System for Windows 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Subjects' demographic and clinical characteristics

A total of 4223 asthma patients aged 2–16 years were enrolled in this study. The average age of the subjects was 7.10 (±3.3) years old. As shown in Table 1, 18.4% were 2–3-years-old, 69.7% were 4–11-years-old and 11.9% were 12–16-years-old. Then, 67.8%, (2865/4223) of the subjects were male. Most of the subjects lived in cities (72.2%, 3047/4233). 49.3% (2081/4223) of the subjects lived with parents or caregivers who smoke, and among these, 57.1% (1189/2081) lived with parents or caregivers who smoke indoors. Then 55.1% (2326/4221) of the subjects' parents received a college education or beyond. The subjects' history of allergic disease and family history were displayed in Table 1.

Asthma manifestation

The median duration of asthma since diagnosis for the subjects was 18 months (Q1-Q3: 8.0–36.0) (Table 2). For most of the subjects, diagnosis of asthma was based on typical clinical manifestation. Approximately half of the subjects had pulmonary function test (spirometry or peak expiratory flow) to

Table 1. Uncontrolled asthma according to subject characteristics.

Factor	N (%*)	Uncontrolled Asthma n (%†)	<i>p</i> value#
Overall	4223	841 (19.9%)	
Age group (years)			
2–3	779 (18.4)	93 (11.9%)	<0.001
4–11	2943 (69.7%)	646 (22.0%)	
12–16	501 (11.9%)	102 (20.4%)	
Gender			
Male	2865 (67.8%)	560 (19.5%)	0.384
Female	1358 (32.2%)	281 (20.7%)	
Education level of parents/caregivers			
Junior high school or lower	803 (19.0%)	187 (23.3%)	0.009
Senior high school	1092 (25.9%)	226 (20.7%)	
College and above	2326 (55.1%)	428 (18.4%)	
Smoking status of parents/caregivers			
Non-smoker	2142 (50.7%)	412 (19.2%)	0.163
Outdoor smoker	892 (21.1%)	170 (19.1%)	
Indoor smoker	1189 (28.2%)	259 (21.8%)	
First-degree relatives with asthma			
No	3819 (90.4%)	744 (19.5%)	0.030
Yes	404 (9.6%)	97 (24.0%)	
First-degree relatives with AR			
No	2603 (61.6%)	493 (18.9%)	0.044
Yes	1620 (38.4%)	348 (21.5%)	
Concomitant AR			
No	3046 (72.1%)	567 (18.6%)	<0.001
Yes	1177 (27.9%)	274 (23.3%)	
Concomitant rhinitis			
No	2592 (61.4%)	441 (17.0%)	<0.001
Yes	1631 (38.6%)	400 (24.5%)	
History of eczema			
No	2247 (53.2%)	471 (21.0%)	0.069
Yes	1976 (46.8%)	370 (18.7%)	
Asthma duration since diagnosis more than 1.5 years			
No	2162 (51.2%)	372 (17.2%)	<0.001
Yes	2061 (48.8%)	469 (22.8%)	
Usage of asthma controller during the previous 4 weeks			
No	475 (11.2%)	146 (30.7%)	<0.001
Yes	3748 (88.8%)	695 (18.5%)	
Asthma controller adherence			
Complete adherence	2749 (65.1%)	353 (12.8%)	<0.001
Good adherence	794 (18.8%)	204 (25.7%)	
Poor adherence	396 (9.4%)	159 (40.2%)	
Non-adherence	281 (6.7%)	124 (44.1%)	

*Percentage was calculated using number of subjects with non-missing value of that factor as the denominator.

†Percentage was calculated using N on the same row as the denominator.

#*P* value was calculated using chi-square test by comparing the proportions of uncontrolled asthma across the subgroups classified based on the specific factor.

support the diagnosis, and about half of the subjects had therapeutic trial as diagnostic tool (Table 2). The proportion of subjects who had been given a skin prick test or serum specific immunoglobulin E (IgE) test was 49.4% (2086/4223) and 38.4% (1623/4223), respectively.

Cough and wheeze were the most common asthmatic symptoms among the study subjects at time of diagnosis, while breathlessness and chest tightness were relatively uncommon.

Table 2. Asthma diagnosis and symptoms of asthma when diagnosis made.

Subjects (N = 4223)	
Asthma duration since diagnosis (months)	
n	4223
Mean (SD)	26.6 (25.56)
Median	18.0
Q1~Q3	8.0, 36.0
Min~Max	3, 168
Diagnostic tools/tests for asthma	
Typical clinical manifestation of asthma	4132 (97.9%)
Pulmonary function test	2138 (50.6%)
Therapeutic trial bronchodilators inhaled	2067 (49.0%)
Other (atopy test)	202 (4.8%)
Primary symptom at time of diagnosis	
Cough	3740 (88.6%)
Wheeze	3324 (78.7%)
Breathlessness	1057 (25.0%)
Chest tightness	798 (18.9%)
Other	29 (0.7%)

Then 56.7% (2396/4223) of the subjects reported changes in asthmatic symptoms with the seasons and 13.2% (558/4223) of the subjects were diagnosed as having cough-variant asthma.

And 45.8% of the study subjects (1935/4223) reported having asthma symptoms during the previous 4 weeks through the interview with physician; 20.3% (859/4223) of the subjects had nocturnal symptoms/awakening, 18.2% (769/4223) had more than twice of daytime asthma symptoms per week, 12.8% (539/4223) were limited in daily activities, and 10.2% (431/4223) used reliever medication more than twice per week. More than half of the subjects (52.1%, 2200/4220) had asthma exacerbations during the past 3 months.

Asthma management

During the previous 4 weeks, asthma controller medications were taken by 88.8% (3748/4223) of the subjects. Most of the subjects (61.3%, 2587/4223) took combination therapies. Inhaled corticosteroids (ICS) plus long-acting β -agonists (LABA) fixed dose combination (ICS/LABA FDC) was the most common combined therapy, followed by ICS plus LTRA (leukotriene receptor antagonist), and ICS/LABA FDC plus LTRA (Table 3). About one third of the subjects (27.5%, 1161/4223) used monotherapies, with ICS being the most frequently used monotherapy (Table 3).

In all 38.0% (1603/4223) of the subjects used other medications or therapies, mainly including antibiotics (24.6%, 1039/4223) and Traditional Chinese Medicine (17.5%, 739/4223).

Overall, 65.1% (2749/4220) of the subjects had complete asthma controller adherence, 18.8% had good adherence, 9.4% had poor adherence, and 6.7% were non-adherent. Among all the subjects, 11.2% (475/4223) had not used any asthma controller during the previous 4 weeks. Of these subjects, 30.7% (146/475) had uncontrolled asthma. 67.9% (322/474) of the subjects who had not used asthma controller stopped doing so without consulting their physician and 66.1% (213/322) of these stopped because they thought their asthma symptoms had been relieved. 26.7% (86/322) stopped medication because of concern about side effect and 9.9% (32/322) because of concern about the effect of the medication on children's growth.

Table 3. Therapy pattern of subjects during the previous 4 weeks.

Asthma controller medications	Subjects (N = 4223)
Combination therapies	
ICS/LABA FDC	2587 (61.3%)
ICS+LTRA	879 (20.8%)
ICS/LABA FDC+LTRA	671 (15.9%)
ICS/LABA FDC+LTRA+Other	621 (14.7%)
ICS+LTRA+Other	80 (1.9%)
ICS+Other	52 (1.2%)
LTRA+Other	52 (1.2%)
Other	26 (0.6%)
Monotherapies	
ICS	206 (4.9%)
LTRA	1161 (27.5%)
Sustained-release Theophylline	904 (21.4%)
Mast cell stabilizers	231 (5.5%)
Other	9 (0.2%)
No any asthma controller was used	5 (0.1%)
	12 (0.3%)
	475 (11.2%)

Note: FDC = fixed dose combination; ICS = inhaled corticosteroids; LABA = long-acting beta agonists; LTRA = leukotriene receptor antagonists.

Uncontrolled asthma and its impact on daily activities

According to ACT criteria, 79.6% (399/501) of the 12–16-year-old subjects had controlled asthma and 20.4% (102/501) had uncontrolled asthma. Based on C-ACT criteria, the proportions of 4–11-year-old subjects with controlled and uncontrolled asthma were 78.0% (2297/2943), and 22.0% (646/2943), respectively. Based on GINA definitions, the proportions of 2–3-year-old subjects with controlled, partly controlled and uncontrolled asthma were 57.5% (448/779), 30.6% (238/779) 11.9% (93/779), respectively. Overall, uncontrolled asthma was detected in 19.9% (841/4223) of all the subjects.

The proportions of uncontrolled asthma among subjects with different characteristics are shown in Table 1. Regarding the relationship between asthma and treatment adherence, significantly higher proportions of uncontrolled asthma were found in subjects with poor asthma controller adherence (40.2%) or non-adherence (44.1%), or who did not take asthma controller during the previous 4 weeks (30.7%). Moreover, a significantly higher proportion of uncontrolled asthma was found in the study subjects with concomitant AR (23.3%), rhinitis (24.5%), family history of asthma (24.0%), or family history of AR (21.5%). A higher proportion of uncontrolled asthma was also observed in subjects with asthma duration since diagnosis of more than 1.5 years (22.8%).

Uncontrolled asthma had more severe limitation on daily physical activities to the study subjects in all age groups, compared to controlled asthma ($P < 0.001$, Table 4). This effect was most severe in the 12–16-year-old group. Furthermore, as shown in Table 4, in the 4–11-year and 12–16-year age groups significantly higher proportions of subjects with uncontrolled asthma missed school during the past 12 months than those with controlled asthma (69.0% vs 52.3%, 55.9% vs 32.8%, both $P < 0.001$). Similarly, same phenomenon on missed work days was found in both groups' parents or caregivers (Table 4). Among parents and caregivers with work absence, the median number of days of absence during the past 12 months was 10 for those with children in 4–11 age group and 7 for those with children in 12–16 age group, whether or not their children's asthma was controlled. However, more days of work absence

Table 4. Impact of asthma on physical activities of the subjects during the previous 12 months by age group and status of asthma control.

	Status of Asthma Control		<i>P</i> value*
	Controlled	Uncontrolled	
Physical activities			
2–3 years old			
Number of subjects	686	93	
No physical activity	1 (0.1%)	1 (1.1%)	<0.001
Only mild activities	24 (3.5%)	6 (6.5%)	
No strenuous activities	170 (24.8%)	41 (44.0%)	
All physical activities	491 (71.6%)	45 (48.4%)	
4–11 years old			
Number of subjects	2297	646	
No physical activity	17 (0.7%)	12 (1.9%)	<0.001
Only mild activities	96 (4.2%)	77 (11.9%)	
No strenuous activities	730 (31.8%)	284 (43.9%)	
All physical activities	1454 (63.3%)	273 (42.3%)	
12–16 years old			
Number of subjects	399	102	
No physical activity	4 (1.0%)	1 (1.0%)	<0.001
Only mild activities	33 (8.3%)	17 (16.7%)	
No strenuous activities	139 (34.8%)	50 (49.0%)	
All physical activities	223 (55.9%)	34 (33.3%)	
Subjects with missed school attendance <i>n</i> (%)			
2–3 years old	277 (40.4%)	38 (40.9%)	1.000
4–11 years old	1202 (52.3%)	446 (69.0%)	<0.001
12–16 years old	131 (32.8%)	57 (55.9%)	<0.001
Subjects whose parents or caregivers had missed any work day <i>n</i> (%)			
2–3 years old	339 (49.4%)	55 (59.1%)	0.078
4–11 years old	1109 (48.3%)	384 (59.4%)	<0.001
12–16 years old	129 (32.3%)	46 (45.1%)	0.016

Percentage was calculated using number of subjects with non-missing assessment as the denominator.

*for Physical activities, *p* value was calculated using Wilcoxon rank test; for others, *p* value was calculated using chi-square test.

were reported by parents and caregivers of children with uncontrolled asthma in 2–3 age group compared to those with controlled asthma (median days: 20 vs. 10, $P = 0.004$). Similarly, among the patients with at least one day of school absence, the median number of days of school absence was 10 days for children in 4–11 age group and 7 days for children in 12–16 age group, whether or not the children's asthma was controlled. In 2–3 age group, more days of school absence were reported for children with uncontrolled asthma compared to those with controlled asthma (median days: 20 vs. 10, $P = 0.001$).

Risk factors of uncontrolled asthma

Multivariate logistic regression was performed to identify risk factors for uncontrolled asthma (Table 5). All the factors shown in Table 1, except for “usage of asthma controller during the previous 4 weeks” and “concomitant rhinitis,” were included. These two factors were excluded from the model because “usage of asthma controller during the previous 4 weeks” was found to be moderately correlated with “asthma controller adherence” (Spearman's rank correlation coefficient = 0.415, $P < 0.001$), and “concomitant rhinitis” was highly correlated with “concomitant AR” (Spearman's rank correlation coefficient = 0.784, $P < 0.001$).

Table 5. Risk factors of uncontrolled asthma – multivariate logistic regression model 1.

Factor	Odds Ratio (95% CI)*	<i>p</i> value*
Age group (vs ‘2–3 years old’)		
4–11 years old	2.30 (1.78–2.96)	<0.001
12–16 years old	1.97 (1.40–2.77)	<0.001
Female (vs ‘male’)	1.08 (0.91–1.28)	0.376
Concomitant AR	1.26 (1.06–1.50)	0.011
Asthma duration since diagnosis more than 1.5 years	1.22 (1.03–1.44)	0.022
History of eczema	0.95 (0.81–1.12)	0.54
Smoking status of parents/caregivers (vs ‘nonsmoker’)		
Outdoor smoker	1.02 (0.83–1.26)	0.848
Indoor smoker	1.08 (0.90–1.30)	0.423
First-degree relatives with asthma	1.13 (0.87–1.46)	0.351
First-degree relatives with AR	1.19 (1.01–1.40)	0.042
Asthma controller adherence (vs ‘complete adherence’)		
Good adherence	2.41 (1.98–2.94)	<0.001
Poor adherence	4.87 (3.85–6.17)	<0.001
Non-adherence	5.79 (4.42–7.58)	<0.001
Education of parents/caregivers (vs ‘Junior high school or lower’)		
Senior high school	0.83 (0.66–1.04)	0.109
College and above	0.77 (0.63–0.96)	0.017

*Odds-ratio and *p* value were from a multivariate logistic regression model with uncontrolled asthma as the event and all factors listed in this table as the predictors.

As shown in Table 1, the rate of uncontrolled asthma increased dramatically as controller adherence decreased from complete adherence to non-adherence (12.8% vs. 44.1%, $p < 0.001$). Multivariate logistic regression analysis confirmed that the risk of uncontrolled asthma increased significantly as asthma controller adherence decreased ($P < 0.001$; Table 5). Compared with subjects with complete adherence, the odds ratio (OR) of uncontrolled asthma was 2.41 ($P < 0.001$) among subjects with good adherence, 4.87 ($P < 0.001$) among subjects with poor adherence, and 5.79 ($P < 0.001$) among subjects with non-adherence. Concomitant AR was also confirmed to significantly increase risk of uncontrolled asthma (OR = 1.26, $p = 0.011$), as well as family history of AR (OR = 1.19, $P = 0.042$) and asthma duration since diagnosis over 1.5 years was associated with increased risk of uncontrolled asthma (OR = 1.22, $P = 0.022$). High education level of parents and caregivers was a protective factor for asthma control.

A higher proportion of subjects in the 4–11-year and 12–16-year age groups had uncontrolled asthma compared to those in the 2–3-year group (Table 1, Table 5). To test whether risk of uncontrolled asthma increases linearly with age, a second multivariate logistic regression model was built by replacing age group with age in years as a continuous variable in the model. As shown in Table 6, the second model gave similar results to the first model, except that age was not identified as a significant factor, indicating that the relationship between age and asthma control is not linear.

Discussion

The results of this study show that 19.9% of pediatric asthma in China is currently uncontrolled. Insufficient treatment was

Table 6. Risk factors of uncontrolled asthma – multivariate logistic regression model 2.

Factor	Odds Ratio (95% CI)*	<i>p</i> value*
Age (years)	1.00 (0.97–1.03)	0.968
Female (vs ‘male’)	1.09 (0.92–1.29)	0.308
Concomitant AR	1.35 (1.13–1.61)	0.001
Asthma duration since diagnosis more than 1.5 years	1.40 (1.18–1.66)	<0.001
History of eczema	0.91 (0.77–1.07)	0.235
Smoking status of parents/caregivers (vs ‘non-smoker’)		
Outdoor smoker	1.02 (0.83–1.26)	0.832
Indoor smoker	1.08 (0.89–1.29)	0.44
First-degree relatives with asthma	1.14 (0.88–1.47)	0.318
First-degree relatives with AR	1.19 (1.01–1.40)	0.039
Asthma controller adherence (vs ‘complete adherence’)		
Good adherence	2.31 (1.90–2.81)	<0.001
Poor adherence	4.58 (3.62–5.78)	<0.001
Non-adherence	5.34 (4.10–6.96)	<0.001
Education of parents/caregivers (vs ‘Junior high school or lower’)		
Senior high school	0.84 (0.67–1.06)	0.144
College and above	0.80 (0.65–0.99)	0.036

*Odds-ratio and *p* value were from a multi-variate logistic regression model with uncontrolled asthma as the event and all factors listed in this table as the predictors.

found to be the most significant factor in uncontrolled asthma among the Chinese pediatric patients in this study. Then, 11.2% of the study subjects had not taken any asthma controller during the previous 4 weeks; and, of these subjects, 30.7% had uncontrolled asthma. Multivariate logistic regression analysis showed that poorer asthma controller adherence is a significant risk factor associated with uncontrolled asthma. Compared to subjects with complete adherence, the risk of uncontrolled asthma was 4.79 times higher in subjects with non-adherence, 3.87 times higher in subjects with poor adherence and 1.41 times higher in subjects with good adherence. Considering that 34.9% (1471/4220) of the subjects did not achieve complete asthma controller adherence, improving adherence should be a priority in the effort to improve asthma control status among Chinese pediatric patients.

Although usage of asthma controller during the previous 4 weeks was not included in the multivariate logistic regression models due to its moderate correlation with asthma controller adherence (Spearman’s rank correlation coefficient = 0.415, $P < 0.001$), it is still an important factor that provides insight into reasons for poor controller adherence. Among the subjects who had not used asthma controller during the previous 4 weeks, most stopped taking asthma medication on their own because they thought their asthmatic symptoms had been relieved. This finding showed that these subjects, or their parents, may have over-estimated the level of asthma control they had achieved. This is consistent with a study conducted in China in 2009, which revealed that parents’ knowledge about asthma control affected the control level their children achieved [6], implying that educating parents about asthma management could improve asthma control.

Concomitant AR was a risk factor associated with uncontrolled asthma in this study (OR = 1.26). This was consistent with findings from several other studies [9,19–21]. Considering that 27.9% of the subjects in this study had AR, adequate identification and treatment of AR in pediatric asthma patients in China is important to improve asthma control level. Subjects with concomitant rhinitis were also found to have a higher proportion of uncontrolled asthma than others (24.5% vs 17.0%, $P < 0.001$). Although rhinitis was not included in the multivariate logistic regression model due to high correlation between concomitant AR and rhinitis (Spearman’s rank correlation coefficient = 0.784, $P < 0.001$), the significant effect found in univariate analysis indicates that identification and treatment of rhinitis is as important as treating AR in asthma management. Family history of AR was also found to be significantly associated with uncontrolled asthma (OR = 1.19, $P = 0.042$), suggesting that more effort should be made with patients with a family history of AR to achieve good control of asthma.

This study showed that asthma duration over 1.5 years since diagnosis can also increase the risk of uncontrolled asthma (OR = 1.22, $P = 0.022$). This result was different from a previous study conducted among Chinese pediatric asthma patients which showed that long disease course was a protective factor in asthma control because children with a longer disease course may have better treatment compliance [6]. In contrast, a study conducted among adults in Poland reported that uncontrolled asthma occurred significantly more frequently in patients with longer disease duration [22]. The inconsistent results from these studies indicate that duration of asthma itself may not be a direct factor influencing asthma control. More attention should be paid to the significant and modifiable factors discussed above to improve asthma control in Chinese pediatric patients.

Very few studies have investigated the impact of asthma on children’s school absences and their parents’ loss of work days in China. This study showed that uncontrolled asthma has more severe impact on children’s school attendance and physical activities, and parents’ work absenteeism, than controlled asthma. This was consistent with a study conducted in France which showed an 8-fold risk of caregivers losing more than 5 workdays per year when their child’s asthma was poorly controlled [23]. Thus long-term consequences of uncontrolled asthma include lowering of pediatric patients’ academic performance and caregivers’ work productivity. Therefore, improving asthma control level could enhance not only the quality of life of the children but also promote their parents’ work productivity and promote competitiveness in the workplace. In the present study a considerable proportion of subjects with controlled asthma, as defined by ACT, C-ACT or GINA criteria reported missed school days, limitation in physical activities and missed work days of their parents. This is possible because the ACT, c-ACT and GINA definitions of controlled asthma allow minor symptoms or limitation on physical activities. Thus, to improve the quality of life of pediatric asthma patients and their parents, achieving ACT, c-ACT or GINA defined controlled asthma is the minimum goal.

The generally used cut-off point of 19 was employed with both the ACT and C-ACT to define uncontrolled asthma in this study. Several studies have analyzed the consistency of ACT and C-ACT defined uncontrolled asthma vs GINA

criteria defined uncontrolled asthma [24–26]. Overall, the consistency has been shown to be moderate. Nevertheless, ACT and C-ACT are useful tools to monitor the level of asthma control when lung function testing is not available or feasible, or in large-scale studies.

Because this study was a cross-sectional survey, no definite conclusion can be drawn about the causal relationship between risk factors and uncontrolled asthma. The enrolment of study participants depends on patients' clinical visit and their willingness to be surveyed which might result in selection bias. Also, since the participants all came from tertiary general hospitals, it is possible that the symptoms of asthma among these patients were more severe than ordinary asthma patients such as patients visiting lower grade hospitals or receiving medical care out of hospital. Moreover, the study mainly focused on persistent asthma which could bring significant disease burden in terms of quality of life and health resource utilization.

We excluded intermittent asthma because it does not necessarily need controller treatment and has limited negative impacts on patient's daily activity and sleep because of its symptoms less than once a week. Therefore, interpreting the results needs caution. The study was carried out between November and June of next year when the impact of rhinitis/allergic rhinitis on asthma control could be modified by the season. Rhinitis in this study was not differentiated further by either negative allergy test or without allergy tests conducted, which leads to potential under-diagnosed AR among rhinitis. Nevertheless, this study provided a comprehensive profile of the most recent asthma control status in Chinese pediatric patients. The results should serve as valuable references to guide further management of asthma control in China.

The results of this study revealed that the level of asthma control and the quality of life of pediatric asthma patients in China are still unsatisfactory. Poor asthma controller adherence was the most important risk factor contributing to uncontrolled asthma. Greater effort should be made to educate parents and caregivers of pediatric patients about asthma control and the importance of asthma controller adherence. Diagnosis and appropriate treatment of AR and rhinitis are also important.

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Declaration of interest

The authors declare that they have no conflicts of interest in relation to this article. The authors are responsible for the content and the writing of this article.

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