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Evaluation of the factors affecting lung function in pediatric patients with asthma

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ABSTRACT

Purpose: This study aimed to analyze the risk factors affecting lung function in children with asthma based on clinical data to advice on clinical treatment and prognosis.

Methods: This study included newly diagnosed patients with asthma admitted to the Respiratory Department of Chengdu Women's and Children's Central Hospital in Sichuan from July 2020 to June 2021. The factors associated with lung function were analyzed using univariate and multivariate linear regression with the forward method, while factors affecting lung ventilation function were analyzed using multivariate logistic regression.

Results: Sixty percent of the patients had normal lung function. Age was significantly negatively correlated with forced vital capacity (FVC)/FVC_{predicted} ($B = -1.385$, $p = 0.001$), FEV₁/FEV_{1predicted} ($B = -2.092$, $p < 0.001$), and FEV₁%/FEV₁%_{predicted} ($B = -0.834$, $p = 0.001$). Body mass index (BMI) for age Z score ($B = 1.661$, $p = 0.045$) and cesarean delivery ($B = 4.471$, $p = 0.013$) were significantly positively correlated with FVC/FVC_{predicted}. Birth weight was significantly positively correlated with FEV₁/FEV_{1predicted} ($B = 4.593$, $p = 0.027$). Multivariate logistic regression analysis revealed that age ≥ 6 years and cough variant asthma (CVA) were risk factors for abnormal lung function.

Conclusions: Age, BMI for age Z score, mode of delivery, and birth weight were significantly correlated with lung function in children with asthma. Furthermore, children with asthma and normal lung function were more likely to be overlooked. More attention should be given to children with asthma and normal lung function, and CVA.

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Asthma; factors; lung function; pediatric

Introduction

Asthma is the most common chronic respiratory disease characterized by abnormal and inflammatory airway mucosa, reversible airway obstruction, and airway hyperresponsiveness (1). In susceptible people, this inflammation can lead to recurrent coughing (especially at night or early morning), wheezing, dyspnea, and chest tightness (1). Asthma affects more than 300 million people worldwide (2). Children are more likely to develop asthma than adults because of problems such as different breathing patterns and immature respiratory and immune system (3). Lung function impairment in children with asthma is likely to persist into adolescence or even adulthood (4). According to the Global Burden of Disease 2019, asthma accounted for approximately 0.85% of the total disability-adjusted life years among the global

population, but 2.29% of children aged 5–14 years had asthma (5); it is also becoming more common in children in China (6). According to the results of the Third Nationwide Survey of Childhood Asthma in urban areas of China, the total incidence of asthma among children aged 0–14 years in Chinese cities was 3.02% in 2010, which has significantly increased over the past decade (7).

The Global Initiative for Asthma (GINA) considers two levels of asthma control assessment: (1) evaluation of the current therapeutic effect and (2) evaluation of the prognosis (8). Lung function-related factors are considered good prognostic indicators, and GINA recommends the annual measurement of lung function indicators in patients with asthma (8,9). The commonly used lung function evaluation indicators are forced expiratory volume at 1 s (FEV₁), forced vital

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capacity (FVC), and FEV₁/FVC (ratio of FEV₁ to FVC) (10). Berhane et al. (4) hypothesized that gender differences in the effects of asthma on lung function, commonly observed in school-age children and adolescents, may reflect differences in the duration and age of onset of asthma. Another study showed that the overall mean FVC level difference between adolescents with and without asthma remained not significant after gender stratification (11). In addition, different studies have also mentioned the influence of gestational age and birth weight (12) and body adiposity/body mass index (BMI) (10) on lung dysfunction in school-age children. Most studies have conducted a comparative analysis of patients with asthma and healthy populations or assessed lung function factors in healthy populations.

However, the factors that affect lung function in children with asthma remain unclear. Therefore, this study aimed to analyze the possible factors of lung function in children with asthma based on clinical data to provide advice on clinical practice.

Methods

Data sources

The study was approved by the Ethics Committee of Chengdu Women's and Children's Central Hospital. Newly diagnosed asthma patients aged 3–18 years admitted to the Respiratory Department of Chengdu Women's and Children's Central Hospital in Sichuan from July 2020 to June 2021 were enrolled. The exclusion criteria were (1) history of asthma; (2) history of pneumonia, bronchial pneumonia, or respiratory diseases; and (3) lack of lung function detection data. Finally, data from 195 patients were included in the final analysis (Figure 1). The data used in the study were extracted from hospital information system (HIS), radiology information system, picture archiving and communication systems, laboratory information system (LIS), clinical information system (CIS), and electronic medical records systems at Chengdu Women's and Children's Central Hospital.

The collected data could be categorized as (1) demographic data, including age, sex, BMI for age Z score, mode of delivery, and birth weight; (2) disease features including asthma type, complications, and onset season; and (3) lung function indices, including FVC/FVC_{predicted}, FEV₁/FEV_{1predicted}, FEV₁%/FEV₁%_{predicted} (FEV₁% = FEV₁/FVC × 100%), and abnormal lung function.

Lung function test and quality control methods for lung function

Spirometry is commonly performed in adults and school-age children, as well as preschoolers, but quality control methods for adults are not suitable for preschoolers (13). The 2007 American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines set specific requirements for quality control of lung ventilation function in preschoolers (13).

Evaluation instruments and equipment

A spirometer (Yeager Company, Germany) was used in this study and calibrated by a volume scaler at each startup, with an error ≤3% indicating normal condition. Temperature (37°C), standard atmospheric pressure (101.08 kPa), and gas state of saturated water vapor (BTPS) were used for calibration at the beginning of each session.

Patients' height and weight were measured while barefoot. A skilled technician performed the tests in accordance with the ATS standards. The patients were asked to sit with their feet on the ground and their head at a normal level. The upper nose was clamped, and a mouthpiece was provided. The patients were instructed to hold the mouthpiece tightly with their lips and not block it with their tongue, ensuring that the mouth and nose did not leak air. Tight belts and clothing were not worn. The patients were allowed to practice one to two times before the test. The optimal value was considered as the parameter record, and the FEV₁, FVC, peak expiratory flow (PEF), forced expiratory flow (FEF)_{25%}, FEF_{50%}, FEF_{75%} were calculated as the percentages of the predicted value.

The quality control methods of lung function measurement for 3- to 6-year-old preschoolers were as follows: quickly achieved PEF, smooth expiratory descending branch, no cough, and glottis closure. The test was performed again if the back-extrapolated volume (VBE) was >80 mL, or 12.5% of FVC. If there was no error in the testing process, then the data were retained. Otherwise, the data were excluded. If the cessation of flow occurred at >10% of the peak flow, this maneuver was classified as premature termination. The starting point of FEV_t was determined by VBE. The optimal expiratory flow-volume curve shows the maximum sum of FEV_t + FVC. Ideally, the tested child should complete at least two acceptable tests, and the difference between FVC and FEV_t should be <0.1 L or 10%. If there is only one satisfactory maneuver, the data from this test should still be included.

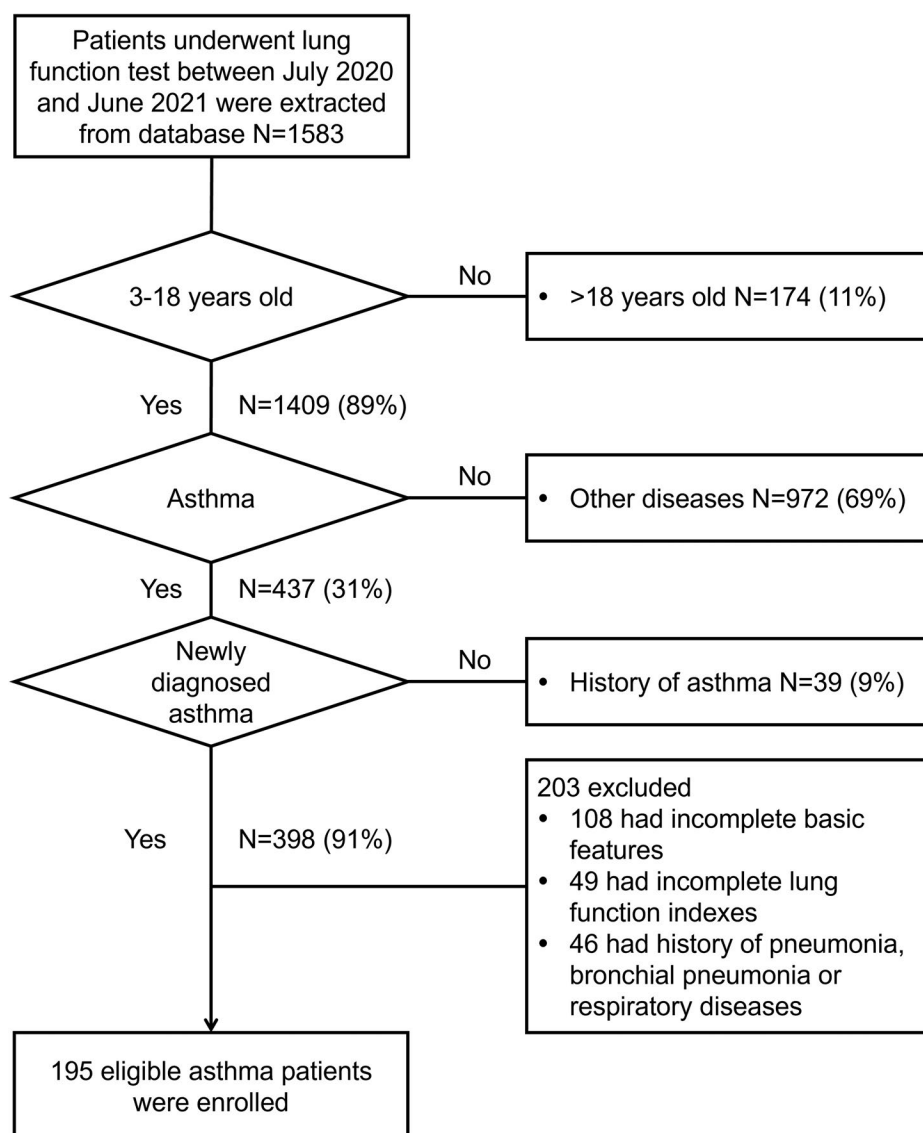


Figure 1. Overview of patients included in the study and number of patients for analysis.

The quality control methods of lung function measurement for children ≥ 6 years old are as follows. Measurements were taken at least three times during the measurement process, and the error between the two best times should be $<5\%$, no abnormality in the flow rate volume curve was seen, and the time volume curve indicated the plateau of the expiratory phase.

Definition of the variables

BMI for age Z score

BMI was calculated as weight (kg)/height (m) (2). Age-specific BMI Z-scores are defined as the difference between the measured BMI of children and the median BMI of a reference population with the same

age and gender, divided by the reference population BMI standard deviation. The BMI for age Z score can be divided into three groups [Z score < -2 is too low, -2 to 2 is normal, and >2 is too high (14)].

Asthma types

Asthma types were divided according to the doctor's diagnosis of cough variant asthma (CVA) and common asthma.

Lung function indexes

Lung function was evaluated by four indexes: FVC/FVC_{predicted} (ratio of FVC measured value to predicted value), FEV₁/FEV_{1predicted} (ratio of FEV₁ measured

value to predicted value), $FEV_1\%/FEV_{1\%predicted}$ (defined $FEV_1\%$ as the ratio of the FEV_1 to the FVC, " $FEV_1\%/FEV_{1\%predicted}$ " means the ratio of $FEV_1\%$ measured value to predicted value); abnormal lung function.

Abnormal lung function

In addition to these three indicators ($FVC/FVC_{predicted}$, $FEV_1/FEV_{1predicted}$, $FEV_1\%/FEV_{1\%predicted}$), six other lung function indicators were measured (Supplementary Table S1). When the indicator value was $\geq 80\%$, the indicator was normal. A doctor determined whether the lung function was abnormal using nine measurement indexes. If one of the measured indicators was abnormal ($<80\%$), then the patient was defined as having abnormal lung function.

Statistical analysis

Statistical analyses were conducted using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA). Figures were plotted using GraphPad Prism version 7.01 (GraphPad Software Inc., San Diego, California, USA). Variables were expressed as the mean with standard deviation or count (percentage) according to their distribution. Factors associated with $FVC/FVC_{predicted}$, $FEV_1/FEV_{1predicted}$ and $FEV_1\%/FEV_{1\%predicted}$ were analyzed using univariate linear regression. All factors in the univariate linear regression were included in the multivariate linear regression using forward stepwise method to screen the independent predictors of $FVC/FVC_{predicted}$, $FEV_1/FEV_{1predicted}$ and $FEV_1\%/FEV_{1\%predicted}$. The accuracy of the multivariate linear regression was assessed using a standardized residual. Factors affecting lung function were analyzed using univariate and multivariate logistic regression. All tests were two-sided. Statistical significance was set at $p < 0.05$.

Results

Baseline characteristics of the children with asthma

The results showed that the average age of patients in this study was 6.7 years, the proportion of female patients was 48.7% ($n=95$), the mean BMI for age Z score was 0.29, and the mean birth weight was 3.2 kg. Among these children, 87 (44.6%) and 94 (48.2%) patients were delivered via spontaneous vaginal delivery and cesarean section, respectively. Of the 175 patients with asthma, 89.7% had common asthma. A total of 79.5% of the patients did not develop related

complications. In terms of time, a higher proportion of patients became ill during winter. Combined with the relevant lung function indicators, 60% of the patients (117) had normal lung function. The detailed results are presented in Table 1. The proportion of asthmatic children that had normal $FVC/FVC_{predicted}$, $FEV_1/FEV_{1predicted}$ and $FEV_1\%/FEV_{1\%predicted}$ is listed in Supplementary Table S2.

Univariate and multivariate linear regression results of the factors affecting lung function in children with asthma

Results of $FVC/FVC_{predicted}$ value

Univariate linear regression analysis showed that age ($B = -1.326$, $p < 0.001$), BMI for age Z score ($B = 1.637$, $p = 0.039$), cesarean delivery ($B = 3.609$, $p = 0.047$), and autumn onset ($B = -4.997$, $p = 0.030$) were significantly correlated with $FVC/FVC_{predicted}$. Multivariate linear

Table 1. Baseline characteristics of asthmatic children.

Parameters	Asthmatic children (N=195)
Demographics	
Age (years), mean $\pm$ SD	6.7 $\pm$ 2.5
Gender, no. (%)	
Female	95 (48.7)
Male	100 (51.3)
Height (cm), mean $\pm$ SD	121.1 $\pm$ 14.9
Weight (kg), mean $\pm$ SD	25.8 $\pm$ 16.0
BMI (kg/m ²)	
Mean $\pm$ SD	16.4 $\pm$ 2.3
Range	12.3–25.5
BMI for age Z score, mean $\pm$ SD	0.29 $\pm$ 1.12
Mode of delivery, No. (%)	
Natural childbirth	87 (44.6)
Cesarean delivery	94 (48.2)
Unknown	14 (7.2)
Birth weight (kg), mean $\pm$ SD	3.2 $\pm$ 0.5
Disease features	
Diagnosis, No. (%)	
CVA	20 (10.3)
Common Asthma	175 (89.7)
Complication, No. (%)	
No	155 (79.5)
Yes	40 (20.5)
Rhinitis	18 (9.2)
Bronchitis	14 (7.2)
URI	5 (2.6)
Others	5 (2.6)
Onset season, No. (%)	
Spring	53 (27.2)
Summer	46 (23.6)
Autumn	35 (17.9)
Winter	61 (31.3)
Lung function indexes	
$FVC/FVC_{predicted}$ (%), mean $\pm$ SD	105.8 $\pm$ 12.4
$FEV_1/FEV_{1predicted}$ (%), mean $\pm$ SD	105.9 $\pm$ 14.7
$FEV_1\%/FEV_{1\%predicted}$ (%), mean $\pm$ SD	100.2 $\pm$ 8.1
Abnormal lung function, no. (%)	
Yes	78 (40.0)
No	117 (60.0)

SD, standard deviation; BMI, body mass index; CVA, cough variant asthma; URI, upper respiratory infection; FVC, forced vital capacity; FEV_1 , forced expiratory volume at one second; $FEV_1\% = FEV_1/FVC \times 100\%$, ratio of the FEV_1 to the FVC.

regression analysis found that age ($B = -1.385$, $p = 0.001$), BMI for age Z score ($B = 1.661$, $p = 0.045$), and cesarean delivery ($B = 4.471$, $p = 0.013$) were significantly correlated with $FVC/FVC_{\text{predicted}}$. The $FVC/FVC_{\text{predicted}}$ value was lower in asthmatic children with increasing age or with a lower BMI for age Z score. Children with asthma had lower $FVC/FVC_{\text{predicted}}$ values if they were delivered by natural childbirth. The detailed results are presented in Table 2.

Results of $FEV_1/FEV_{1\text{predicted}}$ value

The univariate linear regression analysis showed that age ($B = -2.054$, $p < 0.001$), birth weight ($B = 4.980$, $p = 0.022$), and autumn onset ($B = -5.367$, $p = 0.049$) were significantly correlated with $FEV_1/FEV_{1\text{predicted}}$. The multivariate linear regression analysis found that age ($B = -2.092$, $p < 0.001$) and birth weight ($B = 4.593$, $p = 0.027$) were significantly correlated with $FEV_1/FEV_{1\text{predicted}}$. In children with asthma, the $FEV_1/FEV_{1\text{predicted}}$ value was lower

with increasing age or lower birth weight. The detailed results are presented in Table 3.

Results of $FEV_1\%/FEV_{1\text{predicted}}\%$ value

Univariate linear regression analysis showed that age ($B = -0.762$, $p = 0.001$) was significantly correlated with $FEV_1\%/FEV_{1\text{predicted}}\%$. The results of the multivariate analysis were the same ($B = -0.834$, $p = 0.001$). The detailed results are presented in Table 4.

Multivariate logistic regression results of the risk factors for abnormal lung function in children with asthma

The multivariate logistic regression analysis of lung function results showed that age ≥ 6 years and CVA were risk factors for abnormal lung function. The detailed results are presented in Table 5.

Table 2. Factors associated with $FVC/FVC_{\text{predicted}}$

Variables	B	SE	t	p value	95% CI	
					Lower	Higher
Univariate linear regression						
Age	-1.326	0.342	-3.877	<0.001	-2.001	-0.651
Male	-0.770	1.777	-0.433	0.665	-4.275	2.735
BMI Z score	1.637	0.786	2.081	0.039	0.086	3.188
Cesarean delivery vs. natural childbirth	3.609	1.802	2.003	0.047	0.053	7.165
Birth weight	2.989	1.839	1.625	0.106	-0.640	6.617
Common Asthma vs. CVA	0.409	2.929	0.140	0.889	-5.368	6.186
Complication	2.334	2.194	1.064	0.289	-1.994	6.663
Spring vs. other seasons	1.795	1.993	0.900	0.369	-2.137	5.726
Summer vs. other seasons	1.427	2.091	0.682	0.496	-2.697	5.550
Autumn vs. other seasons	-4.997	2.288	-2.184	0.030	-9.509	-0.485
Winter vs. other seasons	0.575	1.916	0.300	0.765	-3.205	4.354
Multivariate linear regression (forward)						
Age	-1.385	0.391	-3.544	0.001	-2.156	-0.613
Cesarean delivery vs. natural childbirth	4.471	1.781	2.511	0.013	0.956	7.986
BMI Z score	1.661	0.823	2.018	0.045	0.036	3.286

Boldface represents $p < 0.05$. FVC, forced vital capacity; SE, standard error; CI, confidence interval; BMI, body mass index; CVA, cough variant asthma.

Table 3. Factors associated with $FEV_1/FEV_{1\text{predicted}}$

Variables	B	SE	t	p value	95% CI	
					Lower	Higher
Univariate linear regression						
Age	-2.054	0.395	-5.206	<0.001	-2.833	-1.276
Male	0.148	2.110	0.070	0.944	-4.013	4.309
BMI Z score	1.515	0.937	1.617	0.108	-0.333	3.364
Cesarean delivery vs. natural childbirth	2.930	2.185	1.341	0.182	-1.381	7.241
Birth weight	4.980	2.148	2.319	0.022	0.742	9.219
Common asthma vs. CVA	-1.922	3.473	-0.553	0.581	-8.773	4.928
Complication	0.529	2.611	0.202	0.840	-4.622	5.679
Spring vs. other seasons	3.640	2.356	1.545	0.124	-1.007	8.286
Summer vs. other seasons	1.241	2.482	0.500	0.618	-3.655	6.138
Autumn vs. other seasons	-5.367	2.721	-1.972	0.04	-10.733	0.000
Winter vs. other seasons	-0.715	2.274	-0.315	0.753	-5.200	3.770
Multivariate linear regression (forward)						
Age	-2.092	0.453	-4.618	<0.001	-2.986	-1.198
Birth weight	4.593	2.052	2.238	0.027	0.542	8.644

Boldface represents $p < 0.05$. FEV_1 , forced expiratory volume at one second; SE, standard error; CI, confidence interval; BMI, body mass index; CVA, cough variant asthma.

Table 4. Factors associated with $FEV_1\%/FEV_{1\%predicted}$.

Variables	<i>B</i>	SE	<i>t</i>	<i>p</i> value	95% CI	
					Lower	Higher
Univariate linear regression						
Age	−0.762	0.225	−3.388	0.001	−1.206	−0.319
Male	−1.789	1.152	−1.553	0.122	−4.061	0.484
BMI Z score	−0.253	0.518	−0.488	0.626	−1.275	0.769
Cesarean delivery vs. natural childbirth	−0.372	1.195	−0.311	0.756	−2.730	1.986
Birth weight	−0.372	1.195	−0.311	0.756	−2.730	1.986
Common Asthma vs. CVA	−2.569	1.901	−1.352	0.178	−6.318	1.180
Complication	−1.814	1.429	−1.269	0.206	−4.632	1.005
Spring vs. other seasons	1.609	1.297	1.240	0.216	−0.950	4.168
Summer vs. other seasons	0.272	1.365	0.199	0.842	−2.420	2.963
Autumn vs. other seasons	−0.672	1.509	−0.445	0.657	−3.649	2.304
Winter vs. other seasons	−1.249	1.246	−1.002	0.318	−3.707	1.209
Multivariate linear regression (forward)						
Age	−0.834	0.256	−3.260	0.001	−1.338	−0.329

Boldface represents $p < 0.05$. FEV₁% = FEV₁/FVC × 100%; SE, standard error; CI, confidence interval; BMI, body mass index; CVA, cough variant asthma.

Boldface represents $p < 0.05$. $FEV_1\% = FEV_1/FVC \times 100\%$; SE, standard error; CI, confidence interval; BMI, body mass index; CVA, cough variant asthma.

Table 5. Factors associated with abnormal lung ventilation function.

Items	Univariate logistic regression	Multivariate logistic regression		
	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)
Age (≥ 6 vs. < 6 years)	0.001	2.761 (1.489–5.121)	0.004	2.759 (1.391–5.472)
Male	1.000	1.000 (0.564–1.774)	0.618	1.187 (0.606–2.326)
BMI Z score (> 2 vs. ≤ 2)	0.492	0.717 (0.277–1.853)	0.976	0.982 (0.301–3.205)
Cesarean delivery vs. natural childbirth	0.672	0.879 (0.485–1.595)	0.591	0.834 (0.431–1.616)
Birth weight (≥ 2.5 vs. < 2.5 kg)	0.170	2.786 (0.644–12.052)	0.097	4.726 (0.755–29.584)
Common asthma vs. CVA	0.156	2.147 (0.747–6.171)	0.036	4.704 (1.104–20.047)
Complication	1.000	1.000 (0.492–2.033)	0.417	1.440 (0.597–3.471)
Onset season				
Spring	Reference	–	Reference	–
Summer	0.112	1.941 (0.858–4.394)	0.225	1.787 (0.700–4.560)
Autumn	0.624	1.251 (0.511–3.065)	0.871	1.091 (0.382–3.118)
Winter	0.248	1.573 (0.730–3.392)	0.569	1.291 (0.536–3.113)

Boldface represents $p < 0.05$. OR, odds ratio; CI, confidence interval; BMI, body mass index; CVA, cough variant asthma.

Discussion

In children, asthma may affect airway development and impair lung function, and lung dysfunction may persist to a large extent in adulthood (15). However, childhood asthma is a heterogeneous disease, and patients may have a varied clinical course (16). The possible factors that affect lung function in children with asthma still need to be further explored.

The National Heart Lung Institute asthma guidelines defined mild asthma as a measured FEV_1 value exceeding 80% of the predicted value. However, based on the frequency of symptoms and medication usage, asthma severity in children was not correlated with the FEV_1 category defined in the National Asthma Education and Prevention Project Guidelines (17). Several studies have found that many children with persistent asthma, even those with severe persistent asthma, have normal lung function (18). In addition, FEV_1 values of at least 100% of the predicted value may be a manifestation of persistent asthma in children (16). This was consistent with the results of this study, which showed that the lung function index of

patients with asthma was greater than the predicted value of 100%. However, this also indicates that those asthmatic children with normal lung function are more likely to be overlooked. Therefore, more attention should be given to these patients.

Asthma is more common in children than in adults (15). A retrospective cross-sectional analysis of 2,728 children conducted by the National Jewish Medical and Research Centre found that FEV_1 declined rapidly in children aged 5–11 years (19). These results are similar to those reported by Melbourne (20) and Martinez et al. (21). In this study, the univariate and multivariate analysis results showed that those who are not diagnosed until they are older have worse lung function. The sooner interventions are made, the better the patient's late-stage lung function recovery.

Obesity increases the risk of adverse health outcomes, including childhood asthma (22). Overweight and obese individuals were 1.64 times and 1.92 times more likely to develop asthma than those who were underweight/normal weight (14). Another study also reported an association between asthma and obesity

(10). Overweight or obesity further affects asthma by affecting lung function (22). However, the effect of obesity on lung function in children with asthma has not yet been determined. One study suggested that being overweight or obese was a significant risk factor for impaired lung function in early childhood after wheezing (23). Higher BMI is associated with lung dysfunction (24). However, Bekkers et al. (25) suggest that after adjusting for height, age, and other potential confounding factors, high BMI in 8-year-olds was not associated with FEV₁ or FVC. This may be related to the fact that this association may change from childhood to adulthood (25). Another study showed that the mean FVC and FEV₁ increased with BMI (11), which is similar to the results of our study, in which people with lower BMI have lower lung function than those with higher BMI. This may be because malnutrition may be associated with deteriorating lung function in adults living in low- and middle-income countries (26). In this study, the mean BMI of children with asthma was within the normal range and was close to that of the low group. In this study, children with higher BMI had better nutrition and higher lung function index. This also reiterates the nonlinear relationship between BMI and lung function, and that further exploration is needed.

A meta-analysis results showed children who had been delivered by cesarean section had a 20% increased risk of asthma (27). In non-industrialized countries, children born by cesarean section have an increased risk of developing asthma (28). A Norwegian Mother and Child Cohort Study found that children born by cesarean section were more likely to develop asthma at 36 months of age (relative risk = 1.17, 95% confidence interval: 1.03, 1.32) (29). This may be related to the microbiome in the gastrointestinal tract (30). For example, a reduction in *Bifidobacteria* and an increase in *Clostridium* in the intestine are associated with asthma in early life (31). Infants delivered by cesarean section have fewer *Bifidobacteria* and *Bacteroides* but more *Clostridium difficile* in their intestines than those delivered by natural childbirth (32). However, the causal relationship between cesarean section and asthma is arguably controversial (33). A prospective birth cohort study showed that there was no association between the mode of delivery and childhood asthma (34), which may be because of the mode of delivery of the child with asthma or the wheezing risk varies over time (i.e. age). Therefore, age-based selection of subjects may influence the findings of previous results with a shorter follow-up period (35). Whether cesarean section is a risk factor for asthma development remains unclear, but the fact

that asthma is one of the many consequences of cesarean sections cannot be overlooked (36). The link cannot be completely ruled out by available evidence. Furthermore, studies have found that the link between cesarean sections and childhood wheezing disorders may be influenced by environmental changes and may not be biologically mediated (37). In this study, patients delivered by cesarean section were found to have better lung function, which was inconsistent with past clinical experience. It can be speculated that environmental impact may be reason. In addition, although more studies currently suggest that the incidence of asthma is higher in patients who undergo cesarean section, there is no conclusive evidence that patients with cesarean section have poorer lung function than patients who are delivered by natural childbirth. At the same time, the difference in lung function parameters between adolescents born by cesarean section and those born by natural childbirth is not statistically significant (38). Therefore, further studies should be conducted on whether cesarean section is a risk factor for worse lung function in children with asthma.

Deterioration of asthma may be significantly associated with modulations in the environment (39). Viral infections, especially rhinoviruses, may cause this seasonality (40), and peak asthma incidence is consistent with seasonal patterns of related allergens and respiratory virus infection prevalence (41). The worsening of asthma in school-age children, which peaks in autumn, may also be associated with children returning to school after the summer holidays (40). This may be due to the higher probability of children being exposed to the source of infection upon return to school and the increased probability of acting as an intermediary for infection (40). It is speculated that peak viral density in autumn may also be the reason why lung function in children with asthma is worse than in other seasons. In addition, CVA was found to be a risk factor for abnormal lung function. In clinical practice, more attention should be given to lung function in patients with CVA, and treatment given as early as possible to prevent more serious consequences.

This study has some limitations. First, the small sample size may have affected the results of our analysis. Second, this study was a retrospective study based on HIS, LIS, and CIS. Therefore, some data was unavailable, and only a limited number of variables could be included in the analysis. Third, this study was a single-center study, and the extrapolation of the results needs to be further verified. Fourth, it appears that it is late to standardize the diagnosis of asthma.

In conclusion, age, BMI for age Z score, mode of delivery, and birth weight all affect the lung function of patients with asthma. Our results could help guide the management of patients with asthma in clinical practice.

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Declaration of interest

The authors declared that there was no conflict of interest associated with the manuscript.

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References

- Cevhertas L, Ogulur I, Maurer DJ, Burla D, Ding M, Jansen K, Koch J, Liu C, Ma S, Mitamura Y, et al. Advances and recent developments in asthma in 2020. *Allergy* 2020;75(12):3124–3146. doi:10.1111/all.14607.
- Stern J, Pier J, Litonjua AA. Asthma epidemiology and risk factors. *Semin Immunopathol* 2020;42(1):5–15. doi:10.1007/s00281-020-00785-1.
- Bateson TF, Schwartz J. Children's response to air pollutants. *J Toxicol Environ Health A* 2008;71(3):238–243. doi:10.1080/15287390701598234.
- Berhane K, McConnell R, Gilliland F, Islam T, Gauderman WJ, Avol E, London SJ, Rappaport E, Margolis HG, Peters JM, et al. Sex-specific effects of asthma on pulmonary function in children. *Am J Respir Crit Care Med* 2000;162(5):1723–1730. doi:10.1164/ajrccm.162.5.2001116.
- Institute-for-Health-Metrics-and-Evaluation. GDB compare. 2019. Available from: <https://vizhub.healthdata.org/gbd-compare>.
- Li X, Song P, Zhu Y, Lei H, Chan KY, Campbell H, Theodoratou E, Rudan I, Global Health Epidemiology Research Group (GHERG). The disease burden of childhood asthma in China: a systematic review and meta-analysis. *J Glob Health* 2020;10(1):010801. doi:10.7189/jogh.10.01081.
- Sha L, Shao M, Liu C, Li S, Li Z, Luo Y, Wang Q, Xu C, Zhao J, Ma Y, et al. The prevalence of asthma in children: a comparison between the year of 2010 and 2000 in urban China. *Zhonghua Jie He He Hu Xi Za Zhi* 2015;38:664–668.
- Global-Initiative-for-Asthma. Global Strategy for Asthma Management and Prevention (2021 update). Available from: <https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf>.
- Gerzon F, Jöbbsis Q, Bannier M, Winkens B, Dompeling E. Discrepancy between lung function measurements at home and in the hospital in children with asthma and CF. *J Clin Med* 2020;9(6):1617. doi:10.3390/jcm9061617.
- Wang R, Custovic A, Simpson A, Belgrave DC, Lowe LA, Murray CS. Differing associations of BMI and body fat with asthma and lung function in children. *Pediatr Pulmonol* 2014;49(11):1049–1057. doi:10.1002/ppul.22927.
- Chen YC, Huang YL, Ho WC, Wang YC, Yu YH. Gender differences in effects of obesity and asthma on adolescent lung function: results from a population-based study. *J Asthma* 2017;54(3):279–285. doi:10.1080/02770903.2016.1212367.
- Kennedy JD, Edward LJ, Bates DJ, Martin AJ, Dip SN, Haslam RR, McPhee AJ, Staugas RE, Baghurst P. Effects of birthweight and oxygen supplementation on lung function in late childhood in children of very low birth weight. *Pediatr Pulmonol* 2000;30(1):32–40. doi:10.1002/1099-0496(200007)30:1<32::aid-ppul6>3.0.co;2-9.
- Beydon N, Davis SD, Lombardi E, Allen JL, Arets HGM, Aurora P, Bisgaard H, Davis GM, Ducharme FM, Eigen H, et al.; American Thoracic Society/European Respiratory Society Working Group on Infant and Young Children Pulmonary Function Testing. An official American Thoracic Society/European Respiratory Society statement: pulmonary function testing in pre-school children. *Am J Respir Crit Care Med* 2007;175(12):1304–1345. doi:10.1164/rccm.200605-642ST.
- Azizpour Y, Delpisheh A, Montazeri Z, Sayehmiri K, Darabi B. Effect of childhood BMI on asthma: a systematic review and meta-analysis of case-control studies. *BMC Pediatr* 2018;18(1):143. doi:10.1186/s12887-018-1093-z.
- Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr* 2019;7:246. doi:10.3389/fped.2019.00246.
- Comberiati P, Spahn JD, Paull K, Faino A, Cherniack R, Covar RA. Lung mechanical properties distinguish children with asthma with normal and diminished lung function. *Clin Exp Allergy* 2020;50(4):453–462. doi:10.1111/cea.13573.
- Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF, Sorkness CA. Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. *Am J Respir Crit Care Med* 2004;170(4):426–432. doi:10.1164/rccm.200308-1178OC.
- Comberiati P, McCormack K, Malka-Rais J, Spahn JD. Proportion of severe asthma patients eligible for mepolizumab therapy by age and age of onset of asthma. *J Allergy Clin Immunol Pract* 2019;7(8):2689–2696.e2. doi:10.1016/j.jaip.2019.05.053.

19. Paull K, Covar R, Jain N, Gelfand EW, Spahn JD. Do NHLBI lung function criteria apply to children? A cross-sectional evaluation of childhood asthma at National Jewish Medical and Research Center, 1999-2002. *Pediatr Pulmonol* 2005;39(4):311-317. doi:[10.1002/ppul.20161](https://doi.org/10.1002/ppul.20161).
20. Oswald H, Phelan PD, Lanigan A, Hibbert M, Carlin JB, Bowes G, Olinsky A. Childhood asthma and lung function in mid-adult life. *Pediatr Pulmonol* 1997;23(1):14-20. doi:[10.1002/\(sici\)1099-0496\(199701\)23:1<14::aid-ppul2>3.0.co;2-p](https://doi.org/10.1002/(sici)1099-0496(199701)23:1<14::aid-ppul2>3.0.co;2-p).
21. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med* 1995;332(3):133-138. doi:[10.1056/NEJM199501193320301](https://doi.org/10.1056/NEJM199501193320301).
22. Ekström S, Magnusson J, Kull I, Andersson N, Bottai M, Besharat Pour M, Melén E, Bergström A. Body mass index development and asthma throughout childhood. *Am J Epidemiol* 2017;186(2):255-263. doi:[10.1093/aje/kwx081](https://doi.org/10.1093/aje/kwx081).
23. Sidoroff V, Hyvärinen M, Piippo-Savolainen E, Korppi M. Lung function and overweight in school aged children after early childhood wheezing. *Pediatr Pulmonol* 2011;46(5):435-441. doi:[10.1002/ppul.21386](https://doi.org/10.1002/ppul.21386).
24. Jensen ME, Gibson PG, Collins CE, Wood LG. Lean mass, not fat mass, is associated with lung function in male and female children with asthma. *Pediatr Res* 2014;75(1):93-98. doi:[10.1038/pr.2013.181](https://doi.org/10.1038/pr.2013.181).
25. Bekkers MB, Wijga AH, de Jongste JC, Kerkhof M, Postma D, Gehring U, Smit HA, Brunekreef B. Waist circumference, BMI, and lung function in 8-year-old children: the PIAMA birth cohort study. *Pediatr Pulmonol* 2013;48(7):674-682. doi:[10.1002/ppul.22722](https://doi.org/10.1002/ppul.22722).
26. Grigsby MR, Siddharthan T, Pollard SL, Chowdhury M, Rubinstein A, Miranda JJ, Bernabe-Ortiz A, Alam D, Kirenga B, Jones R, et al. Low body mass index is associated with higher odds of COPD and lower lung function in low- and middle-income countries. *COPD* 2019;16(1):58-65. doi:[10.1080/15412555.2019.1589443](https://doi.org/10.1080/15412555.2019.1589443).
27. Thavagnanam S, Fleming J, Bromley A, Shields MD, Cardwell CR. A meta-analysis of the association between caesarean section and childhood asthma. *Clin Exp Allergy* 2008;38(4):629-633. doi:[10.1111/j.1365-2222.2007.02780.x](https://doi.org/10.1111/j.1365-2222.2007.02780.x).
28. Gorris A, Bustamante G, Mayer KA, Kinaciyan T, Zlabinger GJ. Cesarean section and risk of allergies in Ecuadorian children: a cross-sectional study. *Immun Inflamm Dis* 2020;8(4):763-773. doi:[10.1002/iid3.368](https://doi.org/10.1002/iid3.368).
29. Magnus MC, Håberg SE, Stigum H, Nafstad P, London SJ, Vangen S, Nystad W. Delivery by Cesarean section and early childhood respiratory symptoms and disorders: the Norwegian mother and child cohort study. *Am J Epidemiol* 2011;174(11):1275-1285. doi:[10.1093/aje/kwr242](https://doi.org/10.1093/aje/kwr242).
30. Johnson CC, Ownby DR. The infant gut bacterial microbiota and risk of pediatric asthma and allergic diseases. *Transl Res* 2017;179:60-70. doi:[10.1016/j.trsl.2016.06.010](https://doi.org/10.1016/j.trsl.2016.06.010).
31. Kalliomäki M, Kirjavainen P, Eerola E, Kero P, Salminen S, Isolauri E. Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing. *J Allergy Clin Immunol* 2001;107(1):129-134. doi:[10.1067/mai.2001.111237](https://doi.org/10.1067/mai.2001.111237).
32. Mikami K, Takahashi H, Kimura M, Isozaki M, Izuchi K, Shibata R, Sudo N, Matsumoto H, Koga Y. Influence of maternal bifidobacteria on the establishment of bifidobacteria colonizing the gut in infants. *Pediatr Res* 2009;65(6):669-674. doi:[10.1203/PDR.0b013e31819ed7a8](https://doi.org/10.1203/PDR.0b013e31819ed7a8).
33. Bager P. Birth by caesarean section and wheezing, asthma, allergy, and intestinal disease. *Clin Exp Allergy* 2011;41(2):147-148. doi:[10.1111/j.1365-2222.2010.03635.x](https://doi.org/10.1111/j.1365-2222.2010.03635.x).
34. Salem Y, Oestreich MA, Fuchs O, Usemann J, Frey U, Surbek D, Amylidi-Mohr S, Latzin P, Ramsey K, Yamine S; Bern Basel Infant Lung Development Study Group. Are children born by cesarean section at higher risk for respiratory sequelae? *Am J Obstet Gynecol* 2022; 226(2):e1-e11. doi:[10.1016/j.ajog.2021.07.027](https://doi.org/10.1016/j.ajog.2021.07.027).
35. Juhn YJ, Weaver A, Katusic S, Yunginger J. Mode of delivery at birth and development of asthma: a population-based cohort study. *J Allergy Clin Immunol* 2005;116(3):510-516. doi:[10.1016/j.jaci.2005.05.043](https://doi.org/10.1016/j.jaci.2005.05.043). (2005).
36. Nielsen L, Nielsen MK, Heltoft KN, Schlünssen V. [It is uncertain if caesarean section is a risk factor to the development of asthma]. *Ugeskr Laeger* 2011;173:2407-2412.
37. Leung JY, Li AM, Leung GM, Schooling CM. Mode of delivery and childhood hospitalizations for asthma and other wheezing disorders. *Clin Exp Allergy* 2015;45(6):1109-1117. doi:[10.1111/cea.12548](https://doi.org/10.1111/cea.12548).
38. Brüske I, Pei Z, Thiering E, Flexeder C, Berdel D, von Berg A, Koletzko S, Bauer C-P, Hoffmann B, Heinrich J, et al.; GINIplus Study Group. Caesarean section has no impact on lung function at the age of 15 years. *Pediatr Pulmonol* 2015;50(12):1262-1269. doi:[10.1002/ppul.23196](https://doi.org/10.1002/ppul.23196).
39. Tosca MA, Ruffoni S, Canonica GW, Ciprandi G. Asthma exacerbation in children: relationship among pollens, weather, and air pollution. *Allergol Immunopathol (Madr)* 2014;42(4):362-368. doi:[10.1016/j.aller.2013.02.006](https://doi.org/10.1016/j.aller.2013.02.006).
40. Pike KC, Akhbari M, Kneale D, Harris KM. Interventions for autumn exacerbations of asthma in children. *Cochrane Database Syst Rev* 2018;3:CD012393. doi:[10.1002/14651858.CD012393.pub2](https://doi.org/10.1002/14651858.CD012393.pub2).
41. Staton TL, Arron JR, Olsson J, Holweg CTJ, Matthews JG, Choy DF. Seasonal variability of severe asthma exacerbations and clinical benefit from lebrikizumab. *J Allergy Clin Immunol* 2017;139(5):1682-1684.e1683. doi:[10.1016/j.jaci.2017.01.028](https://doi.org/10.1016/j.jaci.2017.01.028). (2017).