

Original Article

Risk factor for impaired lung function in asthmatic children: predictive value of 25-OH-D, BMI and inflammatory markers

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Abstract: Objective: This cross-sectional study investigated the associations between modifiable metabolic risk factors (vitamin D status and obesity) and pulmonary function decline in children with asthma, independent of disease duration and airway inflammation. Methods: Medical records of 430 asthmatic children (aged ≤ 14 years) were retrospectively analyzed. Using FEV1%pred $< 80\%$ as the cutoff, 171 children with pulmonary function impairment were compared with 259 children with normal pulmonary function. Clinical characteristics, pulmonary function parameters, and laboratory indices (25-(OH)-D, BMI, CRP, IL-6, TNF- α) were collected. Multivariate logistic regression and receiver operating characteristic (ROC) analyses were performed. Results: Among the 430 enrolled children, 171 (39.75%) presented with pulmonary function impairment, predominantly of mild-to-moderate severity. Compared with children with normal pulmonary function, those with impaired pulmonary function had longer disease duration, lower ACT scores, decreased 25-(OH)-D levels, and elevated BMI, CRP, IL-6, and TNF- α levels (all $P < 0.05$). 25-(OH)-D levels were positively correlated with FEV1%pred and FEV1/FVC, and negatively correlated with BMI, CRP, IL-6, and TNF- α (all $P < 0.001$). Multivariate logistic regression analysis identified prolonged disease duration (OR=1.789, 95% CI: 1.333-2.401), elevated BMI (OR=1.205, 95% CI: 1.035-1.403), increased IL-6 (OR=1.193, 95% CI: 1.086-1.312), elevated CRP (OR=1.362, 95% CI: 1.118-1.658), and secondhand smoke exposure (OR=3.336, 95% CI: 1.567-7.102) as independent risk factors for pulmonary function impairment (all $P < 0.05$). Conversely, higher ACT scores (OR=0.763, 95% CI: 0.675-0.861) and 25-(OH)-D levels (OR=0.818, 95% CI: 0.730-0.916) were associated with a lower likelihood of pulmonary function impairment (all $P < 0.01$). Ten-fold cross-validated ROC analysis demonstrated that the mean AUC values of 25-(OH)-D, BMI, IL-6, CRP, and TNF- α were 0.883, 0.806, 0.862, 0.845, and 0.827, respectively. Conclusion: Vitamin D status and secondhand smoke exposure were significantly associated with pulmonary function impairment in children with asthma. Our findings suggest a metabolic component in childhood asthma, although causal inference is limited by the cross-sectional design. Prospective studies are warranted to validate these associations and further clarify underlying mechanisms.

Keywords: Pediatric asthma, lung function impairment, 25-hydroxyvitamin D (25(OH)D), body mass index (BMI), inflammatory markers (IL-6, TNF- α , CRP), environmental tobacco smoke, ACT score, prospective analysis

Introduction

The most recent statistics indicate that inhaled corticosteroids and biologic therapies have revolutionized asthma control. Unfortunately, the global prevalence continues to rise, with approximately 10% children being affected in the industrialized countries [1]. Epidemiological data report a median incidence of 1,380.3 per 100,000 population in children under 10 years

of age. The increasing proportion of severe cases imposes a significant medical and socio-economic burden on patients and caregivers [2].

Many parents do not recognize asthma attack until the onset of persistent coughing. Early loss of lung function may impair ventilatory capacity and reduce exercise tolerance. It has also been linked to a higher risk of acute exac-

erbatation and unfavorable long-term outcomes. However, it remains unclear which children experience accelerated pulmonary function decline and whether this process is driven primarily by metabolic or environmental factors. Importantly, early impairment can have lifelong respiratory consequences [3].

The vitamin D hypothesis in asthma, suggesting that supplementation may reduce exacerbations, has prompted numerous clinical trials, yet its relevance to longitudinal lung function trajectories remains unclear [4]. Experimental studies have shown that vitamin D stabilizes epithelial tight junctions and reduces IL-6 release in vitro, potentially protecting lung function [5]. Population-based studies have demonstrated an association between asthma and vitamin D deficiency, with FEV1 approximately 100 ml lower for every 10 ng/ml decrease in 25(OH)D [6]. Nevertheless, whether this association reflects a causal effect or residual confounding (e.g., obesity and reduced sun exposure) remains controversial. Importantly, no prospective study, to our knowledge, has evaluated whether vitamin D status predicts FEV1 decline in children.

The association between BMI and lung function appears to be the strongest in children with severe obesity (BMI >95th percentile) and the weakest in children who are mildly overweight, suggesting a possible non-linear or threshold effect. Earlier studies may have overlooked this pattern by modelling adiposity as linear variable [7, 8].

Systemic inflammation (as measured by CRP, IL-6, or TNF- α) has been correlated with asthma severity; however, whether these markers accurately reflect airway inflammation or primarily reflect systemic metabolic status remains unknown. In this study, CRP, IL-6, and TNF- α were not measured as direct airway biomarkers, which would require invasive bronchoscopy, but rather as accessible systemic proxies potentially reflecting the inflammatory burden contributing to functional decline. The predictive value of CRP for FEV1 decline differs across cohorts, most likely depending on whether analyses adjust for key confounders such as BMI and vitamin D status [9].

Most existing studies have focused on a single risk factor in relation to asthma severity. To

date, no study has comprehensively assessed pediatric lung function impairment using simultaneous adjustment for vitamin D status, adiposity, and systemic inflammation, leaving it uncertain whether these factors act independently or via overlapping associations.

Although individual associations between vitamin D, obesity, and asthma outcomes have been reported, no previous study, to our knowledge, has directly compared their independent and combined predictive value for pulmonary function impairment within a single pediatric cohort, with mutual adjustment and inclusion of inflammatory markers. This study aimed to address this gap by evaluating the independent and comparative associations of these metabolic and inflammatory factors with pulmonary function impairment in children with asthma.

Methods

Study subjects

Medical records of 430 children with asthma treated at Xianyang Children's Hospital and Baoji Maternal and Child Health Care Hospital between May 2021 and October 2023 were retrospectively reviewed. All patients had physician-confirmed asthma according to the Global Initiative for Asthma (GINA) 2020 criteria [10]. Spirometry was performed within 30 days of the first visit. Diagnostic and management practices were relatively standardized during this period following the GINA 2020 update. This study was approved by the Ethics Review Committee of Xianyang Children's Hospital. Due to the retrospective design, the requirement for informed consent was waived. All patient data were anonymized prior to analysis.

Inclusion and exclusion criteria

Inclusion criteria: 1. Age ≤ 14 years; 2. Diagnosis of childhood bronchial asthma according to GINA 2020 criteria; 3. Completion of pulmonary function testing and serological tests; 4. Availability of complete clinical data.

Exclusion criteria: 1. Complicated with congenital heart disease, chronic structural lung abnormalities, or other severe respiratory diseases; 2. Coexisting immune system diseases, autoimmune diseases, or malignancies; 3. Use of

vitamin D supplementation or immunomodulatory drugs within the past 3 months; 4. Severe hepatic or renal insufficiency or endocrine/metabolic diseases.

Grouping criteria

Participants were stratified according to forced expiratory volume in one second as a percentage of predicted value (FEV1% pred). Patients with FEV1%pred <80% were assigned to the impaired pulmonary function group (n=171), while those with FEV1%pred ≥80% were assigned to the normal pulmonary function group (n=259). The impaired pulmonary function group was further classified into: mild (60%≤ FEV1%pred <80%), moderate (40%≤ FEV1%pred <60%), and severe (FEV1%pred <40%).

Collection of baseline data

Data were collected by uniformly trained medical personnel using a semi-structured questionnaire along with electronic medical record review.

Demographic and clinical characteristics: Demographic variables included age (month), sex (male/female), and ethnicity (Han/other); Disease-related variables included age at asthma onset, disease duration (the time from diagnosis to enrollment, accurate to years), disease severity; and history of hospitalization owing to asthma or related respiratory conditions within the 12 months prior to enrolment. Exposure and lifestyle factors included history of allergic disease (documented by skin prick testing or serum-specific IgE), family history of asthma (first-degree relatives), passive smoke exposure (to tobacco smoke ≥1 time per week and ≥1 hour per exposure), and regular physical activity (moderate-intensity physical exercise ≥3 times per week, ≥30 minutes per session).

Pulmonary function testing: Pulmonary function was assessed during clinical stability, defined as absence of asthma exacerbations within the preceding 4 weeks, using a Jaeger MasterScreen spirometer (CareFusion, Germany), calibrated on a daily basis. Children made at least three attempts, and the best value was recorded for analysis. Forced vital capacity (FVC% predicted) and peak expiratory flow (PEF% predicted) were recorded as secondary pulmonary function indices. Pulmonary

function testing and blood sampling were performed during clinically stable periods, defined as no asthma exacerbations, no respiratory tract infections, and no systemic glucocorticoid use within the preceding 4 weeks.

Laboratory measurements: Venous blood (5 ml) was collected from the antecubital vein in the morning after overnight fasting. Samples were centrifuged at 3,000 rpm for 10 minutes, and serum was aliquoted and stored at -80°C until analysis. Serum 25(OH)D was measured using chemiluminescent immunoassay. Serum levels of IL-6 and TNF-α were measured using high-sensitivity enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, USA), following manufacturer instructions.

Height and weight were measured with participants barefoot and wearing light clothing. Weight was measured to the nearest 0.1 kg using a calibrated digital scale, and height was measured to the nearest 0.1 cm using a stadiometer. Body mass index (BMI) was calculated as weight (kg)/height (m²). Age- and sex-specific BMI references based on World Health Organization (WHO) growth standards were used for interpretation rather than adult cutoff values.

Statistical analysis

Statistical analyses were performed using SPSS 26.0. All tests were two-tailed, and a *P* value <0.05 was considered statistically significant. Effect estimates were reported with 95% confidence intervals (CIs), with emphasis on effect sizes and precision of estimates rather than sole on statistical significance.

Continuous variables were expressed as mean ± standard deviation (SD) and compared using independent-samples *t*-tests. Categorical variables were expressed as counts and percentages (n, %) and compared using the chi-square test. Results were presented as mean differences or proportions with corresponding 95% CIs.

Associations between continuous variables were assessed using Pearson correlation analysis. Given the cross-sectional design of the study, correlation analyses were interpreted as measures of statistical association rather than causal relationships.

Table 1. Incidence of pulmonary function impairment

	Cases	Percentage (%)
Normal lung function	259	60.25
Impaired lung function	171	39.75
Mild	82	19.07
Moderate	63	14.65
Severe	26	6.05

Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminative ability of selected biomarkers for pulmonary function impairment. Area under the curve (AUC) values were compared against the null value of 0.5. When appropriate, pairwise comparisons of AUCs were conducted. ROC analysis was internally validated using 1,000 bootstrap resamples to obtain bias-corrected AUC estimates and corresponding 95% CIs.

Results

Incidence of pulmonary function impairment

Pulmonary function impairment was observed in 171 children (171/430, 39.75%). Among these, 82 cases (19.07%) were classified as mild, 63 (14.65%) as moderate, and 26 (6.05%) as severe (**Table 1**).

Baseline characteristics

Compared with children with normal lung function, those with impaired pulmonary function had significantly longer disease duration and higher prevalence of allergic history, family history of asthma, and exposure to environmental tobacco smoke (all $P < 0.001$). ACT scores were significantly lower in the impaired group. Pulmonary function parameters also differed significantly between groups. No significant differences were observed in age or sex distribution between the two groups. Detailed information is summarized in **Table 2**.

Serum 25-(OH)-D, BMI, and inflammatory markers

Serum 25-(OH)-D levels were significantly lower in children with impaired pulmonary function than in those with normal function ($P < 0.05$). In contrast, BMI and inflammatory markers (IL-6, TNF- α , and CRP) were significantly higher in the impaired group ($P < 0.05$), as shown in **Figure 1**.

Correlations between metabolic/inflammatory markers and pulmonary function

In children with impaired lung function, serum 25-(OH)-D levels were positively associated with FEV1%pred and FEV1/FVC. In contrast, BMI, IL-6, TNF- α , and CRP were negatively associated with these pulmonary function parameters (**Figure 2**).

Associations of 25-(OH)-D with inflammatory markers and BMI

In the overall cohort, serum 25-(OH)-D was inversely correlated with CRP ($r = -0.412$), IL-6 ($r = -0.387$), TNF- α ($r = -0.301$), and BMI ($r = -0.358$) (all $P < 0.001$). In subgroup analyses, similar inverse correlations were observed in both groups. The correlation coefficients in children with impaired pulmonary function -0.523 for CRP, -0.529 for IL-6, -0.488 for TNF- α , and -0.457 for BMI, which were higher than those observed in children with normal lung function (-0.288, -0.259, -0.223 and -0.186). Detailed statistics are presented in **Table 3**.

Stratified analysis by vitamin D status

Participants were categorized into three strata based on serum 25-(OH)-D levels: deficiency (< 20 ng/mL), insufficiency (20-30 ng/mL), and sufficiency (≥ 30 ng/mL). As 25-(OH)-D levels increased, CRP, IL-6, TNF- α , and BMI progressively decreased. Group comparisons are shown in **Table 4**.

Multivariate logistic regression analysis of impaired lung function

Multivariate logistic regression analysis identified several factors independently associated with impaired pulmonary function in children with asthma (**Table 5**). Longer disease duration (OR=1.789, 95% CI: 1.333-2.401, $P < 0.001$), higher BMI (OR=1.205, 95% CI: 1.035-1.403, $P = 0.017$), elevated IL-6 levels (OR=1.193, 95% CI: 1.086-1.312, $P < 0.001$), elevated CRP levels (OR=1.362, 95% CI: 1.118-1.658, $P = 0.002$), and passive smoking exposure (OR=3.336, 95% CI: 1.567-7.102, $P = 0.002$) were independently associated with higher odds of pulmonary function impairment. In contrast, higher ACT scores (OR=0.763, 95% CI: 0.675-0.861, $P < 0.001$) and higher serum 25-(OH)-D levels

Table 2. Comparison of baseline characteristics between the normal and impaired lung function groups

	Impaired lung function group (n=171)	Normal lung function group (n=259)	t/ χ^2	P
Age (years)	8.82±2.35	8.46±2.31	1.583	0.112
Sex (male/female)	101/70	147/112	0.225	0.636
Disease course (years)	3.24±1.48	2.38±1.21	6.593	<0.001
Allergic history (yes/no)	114/57	123/136	15.310	<0.001
Family history of asthma (yes/no)	68/103	59/200	14.280	<0.001
Passive smoke exposure (yes/no)	92/79	85/174	18.720	<0.001
ACT score	17.13±3.51	20.00±3.09	8.943	<0.001
FEV1%pred	70.96±8.46	91.74±7.73	26.280	<0.001
FEV1/FVC	74.92±6.11	84.36±5.27	18.570	<0.001

Note: ACT, Asthma Control Test; FEV1%pred, Forced Expiratory Volume in one second percent predicted; FEV1/FVC, Forced Expiratory Volume in one second/Forced Vital Capacity.

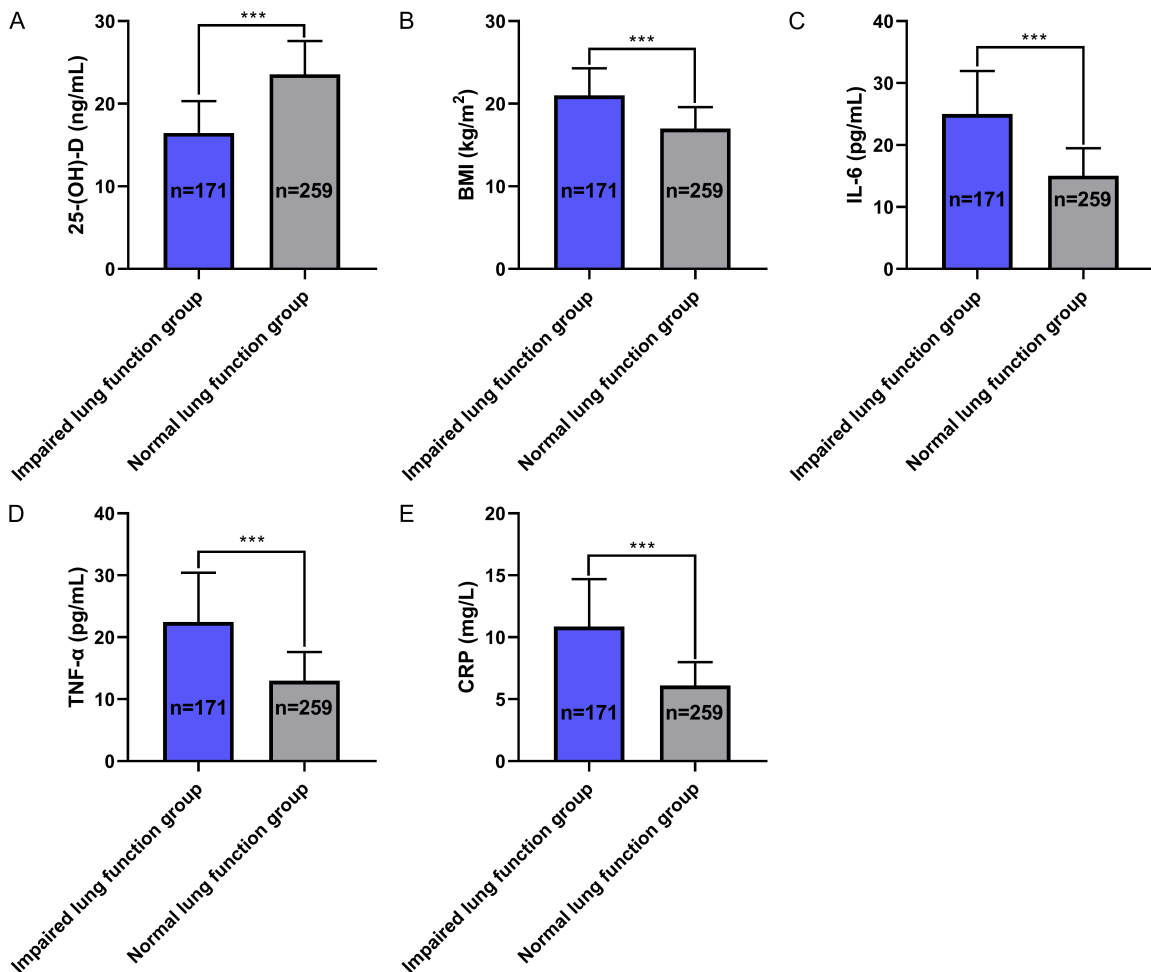


Figure 1. Comparison of serum levels of 25-(OH)-D, BMI, and inflammatory markers between children with and without pulmonary function impairment. A. 25-(OH)-D. B. BMI. C. IL-6. D. TNF- α . E. CRP. Note: 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein. ***P<0.001.

Vitamin D and lung function in pediatric asthma

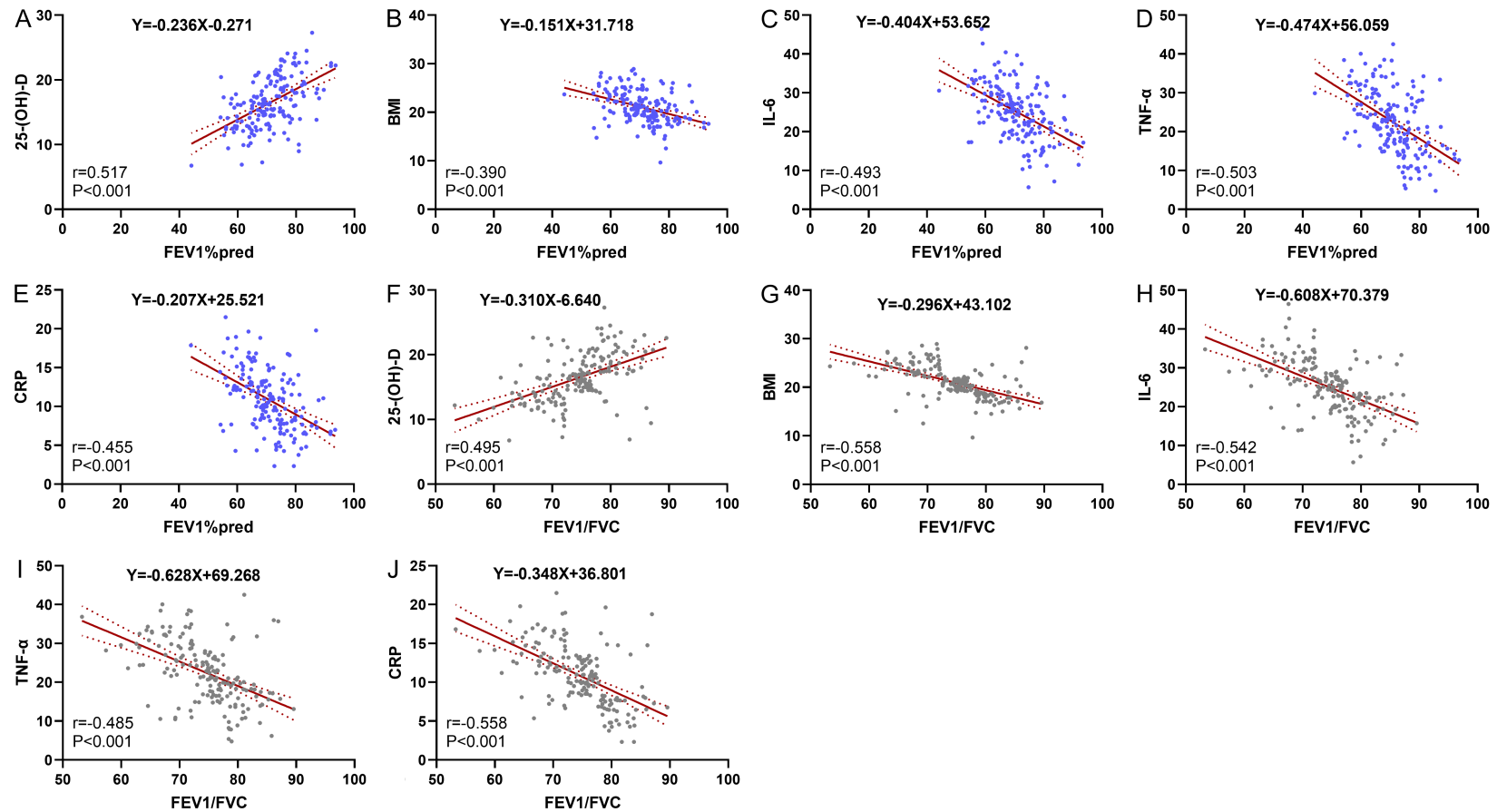


Figure 2. Associations between 25-(OH)-D, BMI, and inflammatory markers with pulmonary function in children with impaired lung function. A. Correlation analysis between 25-(OH)-D and FEV1%pred in the pulmonary function impairment group. B. Correlation analysis between BMI and FEV1%pred in the pulmonary function impairment group. C. Correlation analysis between IL-6 and FEV1%pred in the pulmonary function impairment group. D. Correlation analysis between TNF- α and FEV1%pred in the pulmonary function impairment group. E. Correlation analysis between CRP and FEV1%pred in the pulmonary function impairment group. F. Correlation analysis between 25-(OH)-D and FEV1/FVC in the pulmonary function impairment group. G. Correlation analysis between BMI and FEV1/FVC in the pulmonary function impairment group. H. Correlation analysis between IL-6 and FEV1/FVC in the pulmonary function impairment group. I. Correlation analysis between TNF- α and FEV1/FVC in the pulmonary function impairment group. J. Correlation analysis between CRP and FEV1/FVC in the pulmonary function impairment group. Note: 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein; FEV1%pred, Forced Expiratory Volume in one second percent predicted; FEV1/FVC, Forced Expiratory Volume in one second/Forced Vital Capacity.

Vitamin D and lung function in pediatric asthma

Table 3. Correlations between 25-(OH)-D and inflammatory markers as well as BMI

	All Children (n=430)		Impaired lung function group (n=171)		Normal lung function group (n=259)	
	r	P	r	P	r	P
CRP (mg/L)	-0.412	<0.001	-0.523	<0.001	-0.288	<0.001
IL-6 (pg/mL)	-0.387	<0.001	-0.529	<0.001	-0.259	<0.001
TNF- α (pg/mL)	-0.301	<0.001	-0.488	<0.001	-0.223	<0.001
BMI (kg/m ²)	-0.358	<0.001	-0.457	<0.001	-0.186	<0.001

Note: 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein.

Table 4. Comparison of inflammatory markers and BMI among different 25-(OH)-D status groups

	25-(OH)-D Deficiency Group (<20 ng/mL, n=146)	25-(OH)-D Insufficiency Group (20-30 ng/mL, n=186)	25-(OH)-D Sufficiency Group ($\geq$ 30 ng/mL, n=98)	F	P
CRP (mg/L)	8.42 $\pm$ 3.56	5.68 $\pm$ 2.48	3.24 $\pm$ 1.86	68.42	<0.001
IL-6 (pg/mL)	28.56 $\pm$ 12.48	18.92 $\pm$ 8.56	12.24 $\pm$ 6.42	52.18	<0.001
TNF- α (pg/mL)	45.68 $\pm$ 18.92	32.48 $\pm$ 14.26	22.56 $\pm$ 10.48	38.56	<0.001
BMI (kg/m ²)	22.48 $\pm$ 4.56	19.86 $\pm$ 3.68	17.42 $\pm$ 3.24	28.42	<0.001

Note: 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein.

Table 5. Multivariate logistic analysis of independent predictors for impaired lung function

	B	SE	Wald	Sig	Exp (B)	95% CI for Exp (B)	
						Lower	Upper
Disease course	0.582	0.150	15.033	<0.001	1.789	1.333	2.401
ACT score	-0.271	0.062	19.034	<0.001	0.763	0.675	0.861
25-(OH)-D	-0.201	0.058	12.056	0.001	0.818	0.730	0.916
BMI	0.186	0.078	5.748	0.017	1.205	1.035	1.403
IL-6	0.177	0.048	13.467	<0.001	1.193	1.086	1.312
TNF- α	0.070	0.044	2.484	0.115	1.072	0.983	1.170
CRP	0.309	0.101	9.423	0.002	1.362	1.118	1.658
Allergic history	0.463	0.382	1.469	0.225	1.589	0.751	3.361
Family history of asthma	0.787	0.403	3.811	0.053	2.197	0.997	4.842
Passive smoking exposure	1.205	0.385	9.771	0.002	3.336	1.567	7.102

Note: ACT, Asthma Control Test; 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein.

(OR=0.818, 95% CI: 0.730-0.916, P=0.001) were independently associated with lower odds of pulmonary function impairment. TNF- α , allergic history, and family history of asthma were not significantly associated with pulmonary function impairment after adjustment for potential confounders (all P>0.05), although family history of asthma showed a borderline association (P=0.053). Collinearity was assessed using the variance inflation factor (VIF), and all VIF values were <2, indicating no significant multicollinearity among the independent variables.

ROC curve analysis of 25-(OH)-D, BMI and inflammatory markers

ROC analysis was employed to assess the discriminatory performance of 25-(OH)-D, BMI, and selected inflammatory markers (IL-6, TNF- α , CRP) for identifying pulmonary function impairment (**Figure 3**).

After 10-fold cross-validation, the mean AUC values were 0.883 (95% CI: 0.852-0.913) for 25(OH)D, 0.806 (95% CI: 0.767-0.841) for BMI,

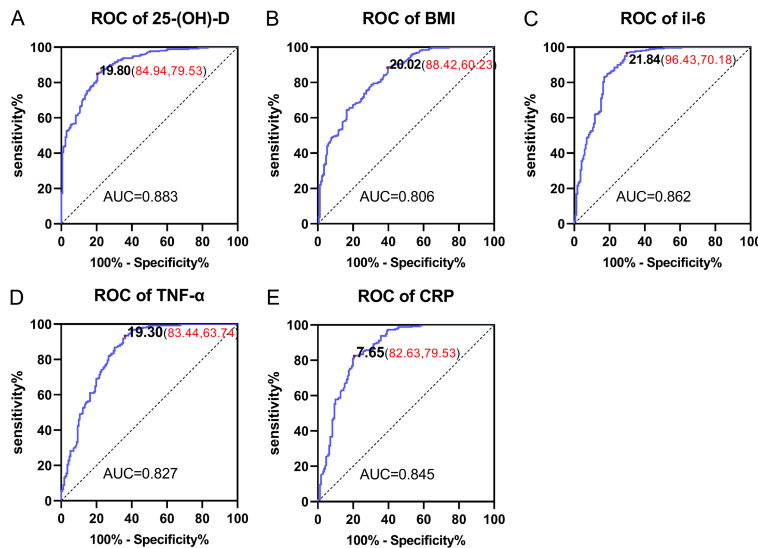


Figure 3. ROC curves for 25-(OH)-D, BMI and inflammatory markers in predicting lung function impairment. Note: ACT, Asthma Control Test; 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein.

0.862 (95% CI: 0.820-0.902) for IL-6, 0.845 (95% CI: 0.804-0.887) for CRP, and 0.827 (95% CI: 0.783-0.866) for TNF- α . The optimal cutoff value, sensitivity, specificity, and Youden index for each indicator are presented in **Table 6**.

Discussion

This study investigated the clinical characteristics and influencing factors of impaired pulmonary function in children with asthma using multi-dimensional clinical, metabolic, and inflammatory indicators. The findings showed that a substantial proportion of children with asthma exhibited impaired lung function, predominantly of mild to moderate severity. The results of the study suggest that varying degrees of airway dysfunction are common in pediatric asthma. In children, such impairment is closely associated with ongoing airway inflammation, developmental characteristics of the airway structure, and susceptibility to airway remodeling [11].

Disease duration was identified as an independent predictor for reduced lung function [12]. Longer disease duration may reflect prolonged exposure of the airways to chronic inflammation, which is characterized by persistent inflammatory cell infiltration and release of cytokines and mediators, leading to irreversible structural airway alterations, including smooth muscle hypertrophy and subepithelial fibrosis

[13]. These changes may be associated with increased airway resistance and reduced elastic recoil, ultimately contributing to progressive decline in pulmonary function. Early identification of children at risk of accelerated decline may therefore be important for timely intervention and prevention of long-term functional impairment [14].

ACT scores were also independently associated with pulmonary function status. Lower ACT scores, indicating poorer symptom control, may reflect persistent airway inflammation and inadequate disease control. Ongoing inflammatory activity, particularly eosinophilic inflammation, may contrib-

ute to airway hyperresponsiveness and sustained functional impairment. In contrast, better symptom control may be associated with reduced inflammatory activity and improved preservation of lung function [15]. These findings suggest that disease control and lung function decline are closely linked and may reflect overlapping underlying pathophysiological processes rather than independent clinical outcomes. Although inhaled corticosteroids remain a cornerstone of asthma therapy, our findings emphasize that continuous assessment of disease control may be important for preventing progressive functional decline [16].

FEV1%pred <80% and FEV1/FVC <0.85 were used to distinguish children with impaired pulmonary function from those with normal function. FEV1%pred reflects ventilatory capacity and expiratory reserve, whereas the FEV1/FVC ratio is a key indicator of airflow limitation and small airway obstruction, which is particularly relevant in pediatric asthma [17, 18]. Small airway dysfunction may occur early in the disease course. Therefore, spirometric assessment may facilitate the identification of subclinical pulmonary function decline before symptom recognition.

Pulmonary function impairment appeared to be independently associated with both metabolic factors and vitamin D status. Serum 25(OH)D

Table 6. ROC curve parameters

Variable	AUC	Optimal Cut-off Value	Sensitivity (%)	Specificity (%)	Youden Index
25-(OH)-D	0.883 (0.852-0.913)	19.80	84.94	79.53	64.47
BMI	0.806 (0.767-0.841)	20.02	88.42	60.23	48.65
IL-6	0.862 (0.820-0.902)	21.84	96.43	70.18	66.61
TNF- α	0.827 (0.783-0.866)	19.30	83.44	63.74	47.18
CRP	0.845 (0.804-0.887)	7.65	82.63	79.53	62.16

Note: 25-(OH)-D, 25-hydroxyvitamin D; BMI, body mass index; IL-6, Interleukin-6; TNF- α , tumor necrosis factor-alpha; CRP, c-reactive protein.

level <20 ng/mL were associated with a higher likelihood of pulmonary function impairment, with approximately a 2.3-fold increase in odds. This finding supports a potential role of vitamin D in immune regulation beyond its classical function in calcium homeostasis [19]. However, the underlying mechanisms remain incompletely understood. Vitamin D deficiency may be associated with persistent airway inflammation and increased airway hyperresponsiveness, particularly in the context of environmental triggers [20].

The effects of BMI are separated from vitamin D status, as mechanical squeeze and leptin-driven inflammation likely run through separate routes. Whether metabolic treatments can reverse decline remains untested. These links may benefit obese asthmatics who ignore normal inhalers [21].

Regarding inflammatory markers, CRP showed a consistent association with pulmonary function impairment, whereas IL-6 and TNF- α demonstrated less stable associations. This may suggest that CRP reflects a more integrated systemic inflammatory state, whereas single cytokine measurements may be influenced by temporal variability and biological fluctuations [22]. Elevated CRP levels (>3 mg/L) despite ongoing controller therapy may indicate persistent systemic inflammation that is not fully reflected by clinical symptom control. This dissociation may partially explain the observed discrepancy between apparent asthma control and ongoing functional decline.

Passive smoke exposure was associated with approximately a two-fold increase in the risk of pulmonary function impairment after adjustment for socioeconomic status. Oxidants from smoke may disrupt epithelial tight junction integrity and impair airway barrier function.

However, the relative contribution of impaired mucociliary clearance versus allergen sensitization-related priming remains unclear, and both mechanisms are likely involved [23]. Early and prolonged exposure, particularly in household environments, may contribute to earlier onset of lung function decline, especially in children with sustained exposure over time [24].

This study has several limitations. First, the cross-sectional design precludes causal inference and does not allow assessment of temporal relationships between exposures and lung function decline. Second, although the sample size was relatively large, data were derived from a single tertiary center, which may introduce selection bias. In addition, inflammatory markers such as CRP may exhibit biological variability, including diurnal and seasonal fluctuations. Single-time-point measurements may therefore not fully reflect chronic inflammatory status and may lead to potential misclassification. Furthermore, although high-resolution computed tomography (HRCT) can provide structural information, its use for research purposes in children is limited by ethical concerns related to radiation exposure and cannot reliably distinguish between reversible inflammation and established airway remodeling. Finally, due to the retrospective nature of the study, adjustment for several potential confounders was not possible, including detailed medication adherence, severity of allergic sensitization, and comprehensive nutritional status, all of which may influence pulmonary function and systemic inflammation.

Conclusion

Lower vitamin D levels, higher BMI, elevated CRP, and secondhand smoke exposure are independently associated with an increased risk of pulmonary function impairment in chil-

dren with asthma. The diagnostic accuracy of these markers was comparable within this derivation cohort. Nevertheless, these findings should be interpreted cautiously and require validation in larger, multicenter, prospective studies before clinical application can be recommended.

Disclosure of conflict of interest

None.

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