

Article / Original paper

## Bronchial Asthma in Adolescents with Undifferentiated Connective Tissue Dysplasia: Role of Th17 Cytokines, Vitamin D and Microelement Imbalance

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Received: 20 January 2026  
Revised: 18 February 2026  
Accepted: 21 April 2026  
Published: 29 April 2026

Funding source for publication:  
Andijan state medical institute.

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### Abstract.

**Introduction.** Bronchial asthma is a chronic inflammatory disease of the airways characterized by bronchial hyperreactivity and airway remodeling. In recent years, increasing attention has been paid to the role of undifferentiated connective tissue dysplasia (UCTD) in the development and progression of bronchial asthma in adolescents. Structural abnormalities of connective tissue may contribute to changes in the architecture of the bronchial wall, enhancement of inflammatory processes, and worsening of the clinical course of the disease. **Aim of the study.** To evaluate the role of Th17 cytokines (IL-17), transforming growth factor- $\beta$  (TGF- $\beta$ ), vitamin D status, and the balance of trace elements (zinc and magnesium) in adolescents with bronchial asthma associated with undifferentiated connective tissue dysplasia. **Material and methods.** The study included 182 adolescents aged 12–17 years. The main group consisted of patients with bronchial asthma combined with UCTD (n=92), the comparison group included patients with bronchial asthma without UCTD (n=60), and the control group consisted of practically healthy adolescents (n=30). Clinical, laboratory, immunological and biochemical methods of investigation were used. The levels of IL-17, TGF- $\beta$ , IgE, vitamin D, zinc, and magnesium were assessed. **Results and discussion.** Adolescents with bronchial asthma associated with UCTD demonstrated significantly higher levels of IL-17, TGF- $\beta$  and IgE, as well as significantly lower levels of vitamin D, zinc and magnesium compared with the control group (p<0.05). Multivariate regression analysis revealed that elevated IL-17 levels and vitamin D deficiency were independent predictors of severe bronchial asthma. These findings indicate the involvement of immune dysregulation and connective tissue abnormalities in the processes of airway remodeling and disease progression. **Conclusion.** The obtained results suggest that adolescents with bronchial asthma associated with UCTD have pronounced immune and metabolic disturbances, which may contribute to the severity of the disease and its progression. Assessment of cytokine profile, vitamin D status, and trace element balance may be important for improving the diagnosis and management of bronchial asthma in this group of patients.

**Key words:** bronchial asthma, undifferentiated connective tissue dysplasia, IL-17, vitamin D deficiency, adolescents.

**Introduction.** Bronchial asthma is one of the most common chronic diseases worldwide, affecting more than 300 million individuals and representing a major public health problem [1]. In children and adolescents, asthma is characterized by chronic airway inflammation, bronchial hyperresponsiveness, and reversible airflow obstruction. Recent studies have demonstrated that asthma is a heterogeneous disease involving multiple inflammatory pathways. In addition to the classical Th2-mediated response, the Th17 immune pathway has been increasingly recognized as an important contributor to severe and steroid-resistant asthma [3]. Interleukin-17 (IL-17) plays a key role in neutrophilic airway inflammation by stimulating epithelial cells and fibroblasts to produce pro-inflammatory cytokines and chemokines [4]. Elevated IL-17 levels have been associated with airway remodeling and increased disease severity [5]. Another important mediator involved in airway remodeling is transforming growth factor- $\beta$  (TGF- $\beta$ ). This cytokine promotes fibroblast activation, collagen synthesis, and extracellular matrix deposition in the bronchial wall [6]. Vitamin D has been identified as an important immunomodulatory factor that regulates both innate and adaptive immune responses. Several studies have shown that vitamin D deficiency is associated with increased asthma severity and reduced lung function [7,8].

In addition, micronutrients such as zinc and magnesium play an important role in antioxidant defense and immune regulation. Deficiencies of these elements have been linked to increased airway inflammation and poor asthma control [9]. Undifferentiated connective tissue dysplasia is characterized by abnormalities in collagen synthesis and extracellular matrix organization. These structural defects may contribute to increased airway

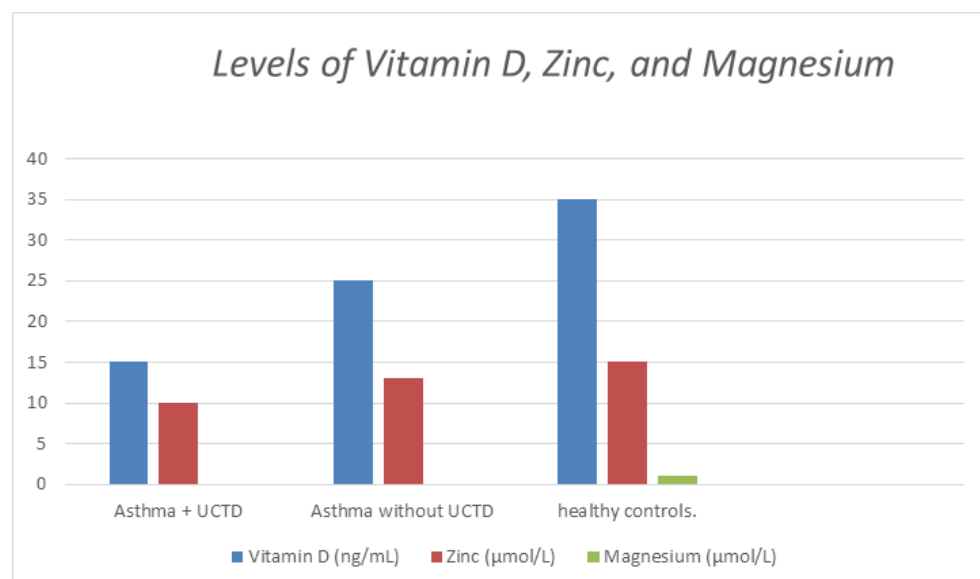
collapsibility and chronic inflammation in patients with bronchial asthma [10]. However, the combined influence of cytokine imbalance, micronutrient deficiency and connective tissue abnormalities in asthma remains insufficiently investigated.

**Aim of the study.** This study aimed to investigate the interrelationship between Th17 cytokines (particularly IL-17), TGF- $\beta$ , vitamin D levels, and micronutrient balance (zinc and magnesium) in adolescents with bronchial asthma associated with UCTD and to assess their contribution to disease severity and progression.

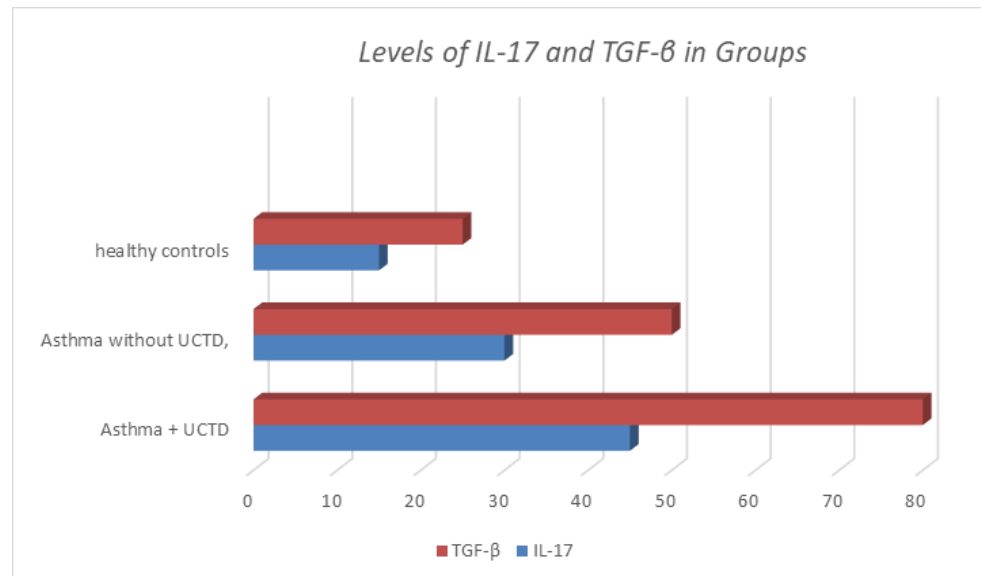
**Materials and Methods.** A total of 182 adolescents aged 12–17 years participated in the study. The main group included 92 adolescents with bronchial asthma and UCTD, the comparison group consisted of 60 adolescents with asthma without connective tissue abnormalities, and 30 healthy adolescents served as controls. The children were selected from School No. 280 of the Chilanzar District, Tashkent. Blood samples were collected and sent to the Institute of Human Immunology and Genomics for analysis. Asthma was diagnosed according to the Global Initiative for Asthma (GINA) criteria, including clinical symptoms, spirometric assessment, and bronchodilator responsiveness. UCTD was diagnosed based on phenotypic features such as joint hypermobility, scoliosis, chest wall deformities, skin hyperelasticity, mitral valve prolapse, and flat feet. Laboratory evaluations included measurement of serum IL-17, TGF- $\beta$ , IL-6, TNF- $\alpha$ , IgE, IgA, IgG, zinc, magnesium, and 25-hydroxyvitamin D levels. All assays were performed using enzyme-linked immunosorbent assay (ELISA) kits following manufacturer protocols. Statistical analyses included comparative group assessments and multivariate regression analysis to determine independent predictors of severe asthma.

**Results and Discussion.** Patients with bronchial asthma and connective tissue dysplasia demonstrated significantly higher concentrations of IL-17 and TGF- $\beta$  compared with patients without UCTD and the control group ( $p < 0.01$ ), indicating enhanced Th17-driven inflammation and profibrotic activity in this population.

**Graph-1.** Levels of Vitamin D, Zinc, and Magnesium.



In addition, vitamin D levels were significantly reduced in patients with BA+UCTD, confirming previous observations that vitamin D deficiency is associated with more severe asthma phenotypes [7,11] and suggesting a potential role of impaired immunomodulation in disease progression. A significant decrease in serum zinc and magnesium levels was also observed in the main group, consistent with studies showing that micronutrient imbalance contributes to oxidative stress and immune dysfunction in asthma [9], which may further exacerbate airway inflammation and clinical severity.

**Graph-2.** Levels of IL-17 and TGF- $\beta$  in Groups.

Multivariate regression analysis identified several independent predictors of severe asthma: IL-17 elevation (OR=2.8,  $p < 0.001$ ), vitamin D deficiency (OR=2.1,  $p = 0.002$ ), presence of UCTD (OR=3.2,  $p < 0.001$ ), and low zinc levels (OR=1.7,  $p = 0.01$ ), highlighting the multifactorial nature of asthma severity in adolescents with connective tissue abnormalities.

**Table-1.** Independent Predictors of Severe Asthma (Multivariate Regression).

Factor	$\beta$ / OR
IL-17 $\uparrow$	2.5
Vitamin D $\downarrow$	2.0
Presence of UCTD	1.8
Zinc $\downarrow$	1.5

**Conclusions.** Undifferentiated connective tissue dysplasia is frequently observed in adolescents with bronchial asthma and may significantly influence disease course. Asthma associated with UCTD is characterized by elevated IL-17 and TGF- $\beta$  levels, reflecting active inflammatory and profibrotic processes. Vitamin D deficiency and reduced zinc and magnesium levels further contribute to disease severity. IL-17 elevation and vitamin D deficiency were confirmed as independent predictors of severe asthma. These findings underscore the importance of evaluating immunological, nutritional, and structural factors in adolescents with bronchial asthma and support the development of personalized diagnostic and therapeutic strategies tailored to this patient population.

**Transparency Statement.** All procedures of the study were approved by the institutional ethics committee. Written informed consent was obtained from all parents or legal guardians of the participants. The study was funded by the grant «Bolalarda differentsiallashmagan biriktiruvchi to'qima displaziyasini tashxislash uchun innovatsion texnologiyani ishlab chiqish», and the authors declare no conflicts of interest. All study materials and data were carefully verified by the authors and are available upon request from the corresponding author. All methods are reported in sufficient detail to allow replication of the study.

**Financial Disclosure.** This study was funded by the government grant «Bolalarda differentsiallashmagan biriktiruvchi to'qima displaziyasini tashxislash uchun innovatsion texnologiyani ishlab chiqish». The authors declare no conflicts of interest.

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