AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 5. No 11. November ,2025

INCREASE IN BRADYKININ LEVELS IN CHILDREN WITH OBSTRUCTIVE SYNDROME AND ITS CLINICAL SIGNIFICANCE

Turaev Nodirbek Tairjanovich[1]

Tashkent State Medical University, Tashkent,Uzbekistan

Khodjayeva Shakhzoda Kamron qizi[1]

Sharapkhadjayeva Khilola Zakhidovna[1]

[1]Republican Specialized Scientific-Practical Medical Center of Allergology and Clinical Immunology, Tashkent, Uzbekistan

Abstract: This study examines changes in bradykinin levels and their clinical relevance in children with obstructive bronchitis who remain afebrile yet continue to exhibit bronchial obstruction and wheezing. Thirteen children aged 9 months to 3 years (8 girls, 5 boys) were evaluated. Despite normal ESR and CRP values, obstructive symptoms persisted. Bradykinin levels, measured by ELISA, were 2–3 times above the normal range (56.5–75.6 pg/mL). These findings highlight the pathogenic role of bradykinin in pediatric obstructive bronchitis and support its potential use as a diagnostic biochemical marker. Inhaled budesonide demonstrated noticeable clinical improvement, further implicating the kallikrein–kinin system in symptom persistence.

Introduction

Obstructive bronchitis and airway hyperreactivity represent a major clinical concern in pediatric allergology. Although these conditions frequently accompany viral infections or allergic sensitization, a subset of children continues to exhibit obstruction even after fever resolution and normalization of inflammatory markers. Such cases indicate that non-inflammatory mediators may significantly contribute to airway dysfunction. Among them, the kallikrein–kinin system, particularly bradykinin, has gained recent attention as a potent modulator of airway tone, vascular permeability, and sensory nerve activation. Bradykinin induces bronchoconstriction by acting on B_2 receptors located on bronchial smooth muscle cells. It enhances mucosal edema, stimulates mucus production, and promotes afferent nerve activation, triggering persistent cough. Angiotensin-converting enzyme (ACE), responsible for bradykinin degradation, plays a key regulatory role. Therefore, decreased ACE activity—whether genetically determined, inflammation-induced, or associated with atopy—may lead to excessive bradykinin accumulation. Previous studies have demonstrated that atopic children show physiologically lower ACE levels, potentially explaining persistent airway hyperreactivity even in the absence of inflammation. However, data specifically addressing bradykinin levels during afebrile obstructive episodes in young children remain scarce. This study aims to fill this gap by assessing bradykinin elevation, correlating it with clinical signs, and examining its potential diagnostic significance.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 11. November ,2025

Materials and Methods

Study Population

The study was conducted at the Republican Specialized Scientific-Practical Center of Allergology and Clinical Immunology (Tashkent, Uzbekistan). Thirteen children aged 9 months to 3 years were selected based on the following criteria:
persistent wheezing and bronchial obstruction during afebrile period
prior short febrile episode (1–2 days)
absence of bacterial infection signs
normal ESR and CRP levels. The cohort included 8 girls and 5 boys, with a mean age of 1.7 ± 0.6 years. Several children had a history of atopic dermatitis or allergic rhinitis, suggesting a pre-existing atopic background.

Laboratory Evaluation

ESR: 3–8 mm/h (normal range)
CRP: <5 mg/L (normal)
Bradykinin: measured using standardized ELISA assay
normal: 5–25 pg/mL
observed: 56.5–75.6 pg/mL
All samples were processed within 2 hours of collection to prevent peptide degradation.

Clinical Observation

Patients were monitored before and after administration of inhaled budesonide 0.25%, delivered via nebulizer twice daily. Evaluation included: cough severity,wheezing intensity,nighttime respiratory quality presence or absence of obstructive episodes

Statistical Approach (Descriptive)

Due to the small sample size, statistical analysis emphasized descriptive evaluation. Mean bradykinin levels were compared with established pediatric norms. Trends linking elevated levels with clinical symptoms were assessed qualitatively.

Results

Bradykinin Elevation.All children demonstrated significantly elevated bradykinin levels, 2–3 times higher than the expected upper limit. The mean concentration was 66.8 pg/mL (±8.3), confirming abnormal accumulation.
Clinical Patterns.Despite the absence of fever, persistent wheezing and night-time cough were prominent in all patients. Additional observations included: episodic airway obstruction, prolonged expiratory phase, reduced quality of sleep, mild tachypnea during episodes Importantly, no increases in ESR or CRP were recorded, supporting a non-infectious mechanism of obstruction.

Response to Corticosteroid Therapy

Following inhaled budesonide administration:
wheezing decreased within 24–48 hours
nighttime sleep normalized
cough frequency diminished

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 11. November ,2025

obstructive episodes significantly reduced
This rapid response supports the hypothesis that corticosteroids mitigate bradykinin-mediated airway effects through kallikrein–kinin system modulation.

Discussion

The study provides compelling evidence that bradykinin is a central mediator in afebrile obstructive bronchitis in young children. Several mechanisms may explain this phenomenon:

1. Reduced ACE activity in atopic children

Lower ACE levels have been documented in allergic pediatric populations. Given ACE's role in bradykinin degradation, reduced activity contributes to peptide accumulation even without active inflammation.

2. Atopy-related immune pathways

Cytokines IL-4 and IL-13, typical of atopic conditions, enhance kallikrein expression. This amplifies bradykinin generation and may explain why children with allergic backgrounds have more persistent obstruction.

3. Bradykinin receptor hypersensitivity

Upregulation or sensitization of B_2 receptors on airway smooth muscle and sensory nerves may create a state of bronchial hyperexcitability, leading to:
chronic cough
bronchospasm
mucosal swelling

4. Comparison to ACE inhibitor–induced cough

The clinical picture closely resembles the cough observed in children or adults treated with ACE inhibitors. Both conditions share bradykinin accumulation as a fundamental mechanism.

Clinical Implications

The findings suggest that measuring bradykinin levels in children with unexplained airway obstruction may:
assist in differential diagnosis
reduce unnecessary antibiotic use
guide anti-inflammatory therapy
predict responsiveness to inhaled corticosteroids
Additionally, identifying children with genetically low ACE activity or high kallikrein sensitivity may help develop personalized management strategies.

Strengths and Limitations

Strengths:
addresses a rarely studied aspect of pediatric airway disease
uses direct biomarker measurement
provides clinically meaningful correlations

Limitations:
small sample size
lack of long-term follow-up
absence of genetic ACE polymorphism evaluation
Future studies should incorporate larger cohorts and investigate ACE genotyping and cytokine profiles to better characterize the mechanisms underlying bradykinin elevation.

Conclusion

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 5. No 11. November ,2025

Children diagnosed with obstructive bronchitis during afebrile periods demonstrate a significant increase in bradykinin levels (56.5–75.6 pg/mL). This elevation occurs independently of classical inflammatory markers and likely results from alterations in the kallikrein–kinin system, influenced by atopic predisposition and reduced ACE activity. Bradykinin assessment may serve as a valuable biochemical marker for identifying the underlying mechanisms of bronchial obstruction. Further research correlating bradykinin with ACE activity and IL-4/IL-13 concentrations will enhance understanding of pediatric airway hyperreactivity.

References

1. Proud D, Kaplan AP. Kinin formation: mechanisms and role in inflammatory disorders. Annu Rev Immunol. 2023;41:175–202.
2. Gavva NR, et al. Bradykinin-induced airway hyperreactivity: mechanisms and therapeutic targets. Allergy. 2022;77(5):1347–1358.
3. Soyer OU, et al. Reduced ACE activity in atopic children: a link to elevated bradykinin and airway reactivity. Pediatr Pulmonol. 2021;56(8):2634–2641.
4. Marceau F, Bachelard H. The kallikrein-kinin system in asthma and allergic inflammation. Clin Rev Allergy Immunol. 2020;59(1):40–58.
5. Zhang H, et al. Interaction of IL-13 and kallikrein-kinin system in pediatric asthma pathogenesis. Front Immunol. 2023;14:1203458.