Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

CLINICAL IMMUNOBIOCHEMICAL MARKERS IN OPTIMIZING THE DIAGNOSTICS OF BRONCHIAL ASTHMA IN COMORBIDITY WITH TYPE 2 DIABETES MELLITUS

Faizullaeva N. Ya.,
Mukhtorov Sh. M.,
Raufov A. A.
Institute of Human Immunology and Genomics of the Academy of Sciences of the Republic of Uzbekistan

Abstract

The relevance of the study is due to the high frequency of bronchial asthma (BA) and type 2 diabetes mellitus (T2DM), which mutually aggravate each other. The aim of the study was to investigate clinical and immunobiochemical markers to optimize the diagnosis and assess the severity of BA combined with T2DM. Forty-two patients were examined, divided into two groups: patients with isolated BA and patients with BA and T2DM. Clinical laboratory, biochemical, and immunological studies were conducted. It was established that the IL-4 level in patients with BA was 24.7 ± 1.2 pg/ml, and in BA + T2DM - 30.1 ± 1.4 pg/ml ($p < 0.05$), while the IFN-γ level decreased to 12.3 ± 0.8 pg/ml compared to the control (18.3 ± 1.0 pg/ml; $p < 0.05$). The concentration of endothelin-1 increased from 0.81 ± 0.07 pg/ml in the control to 2.41 ± 0.12 pg/ml in comorbid pathology ($p < 0.05$), which was accompanied by an increase in HbA1c to 8.44 ± 0.91%. Thus, the comorbid course of asthma and type 2 diabetes is characterized by increased Th2-dependent inflammation, endothelial dysfunction and severe metabolic disorders, which requires comprehensive laboratory monitoring to improve the effectiveness of diagnosis and therapy.

Keywords: Bronchial asthma, type 2 diabetes mellitus, cytokines, endothelin-1, glycated hemoglobin, comorbidity, immunobiochemical markers.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

Introduction

Bronchial asthma (BA) and type 2 diabetes mellitus (T2DM) are among the most common chronic noncommunicable diseases, significantly impacting quality of life and overall morbidity in the population. According to the World Health Organization (WHO, 2024), more than 340 million people suffer from asthma, and the prevalence of T2DM exceeds 460 million cases. In recent years, an increase in the incidence of comorbidity between these conditions has been observed, due to common metabolic and inflammatory mechanisms. The presence of comorbidity significantly worsens the course of each disease, increasing the risk of exacerbations, hospitalizations, and mortality. These data emphasize the need for early detection and optimization of diagnostics of such comorbidities [2, 6, 12, 15].

The pathogenesis of combined asthma and type 2 diabetes is complex and multifaceted, involving disturbances in carbohydrate and lipid metabolism, endothelial function, and systemic inflammation. Hyperglycemia and insulin resistance promote the activation of proinflammatory cytokines and oxidative stress, leading to airway remodeling and decreased effectiveness of standard asthma therapy. At the same time, chronic inflammation in asthma contributes to pancreatic β-cell dysfunction and impaired glucose tolerance. This creates a vicious circle, where each pathology exacerbates the manifestations of the other. The clinical course in these patients is characterized by a higher frequency of exacerbations and a reduced response to standard treatment [1, 7, 10, 13].

One of the key pathogenetic links in the comorbid course of asthma and type 2 diabetes is systemic inflammation with activation of the cytokine network. Increased expression of proinflammatory cytokines such as IL-6, TNF-α, and IL-1β contributes to the development of insulin resistance, activation of endothelial cells, and increased bronchial hyperreactivity. Of particular importance is endothelin-1 (ET-1), a vasoactive peptide that is a marker of endothelial dysfunction and vascular wall remodeling [3, 8, 11, 14]. Studying the balance between cytokine and endothelial factors allows for a deeper understanding of the mechanisms of inflammation and microcirculatory disorders in this comorbidity.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

Purpose of the study: To study clinical and immunobiochemical markers in patients with bronchial asthma combined with type 2 diabetes mellitus in a comparative aspect in order to optimize early diagnosis and determine prognostic criteria for disease severity.

Materials and methods of research:
The clinical study was conducted at the Aram Private Clinic (Tashkent). It included 42 patients aged 24 to 65 years, who were being monitored for bronchial asthma (BA). Of these, 15 patients with combined BA and type 2 diabetes mellitus (T2DM) constituted the study group, while 27 patients with isolated BA constituted the comparison group. A control group of 20 relatively healthy individuals, age-matched to those in the study groups, was also formed for immunological studies. The diagnosis of BA was confirmed according to the GINA criteria (Global Initiative for Asthma, 2024), and the diagnosis of T2DM was established in accordance with WHO recommendations (2023).
For clinical evaluation, anamnesis, physical examination, and laboratory and instrumental studies were performed, including general and biochemical blood tests, coagulogram, spirometry with bronchodilator test, chest X-ray, and other standard methods.
As part of the biochemical analysis, the levels of glucose and glycated hemoglobin (HbA1c) were determined.
Immunobiochemical studies included determination of serum concentrations of endothelin-1, IL-4, and INFy cytokines. These were determined by enzyme-linked immunosorbent assay (ELISA) using certified Protein Contour and Cytokine kits (St. Petersburg, Russia).
Statistical data processing was performed using IBM SPSS Statistics, version 26.0. Results are presented as mean ± standard deviation (M ± SD). Student's t-test was used to assess intergroup differences; statistical significance was considered at $p < 0.05$.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

Research results:

An analysis of the mean age of the examined patients revealed that this indicator was significantly higher in patients with combined asthma and type 2 diabetes mellitus (45.7 ± 1.9 years) compared to patients with isolated asthma (36.1 ± 1.4 years; $p < 0.05$). This difference was approximately 1.27 times, reflecting the older age of disease onset and progression in the presence of metabolic disorders.

A comparative analysis of the gender distribution of the patients examined revealed that women predominated among those with bronchial asthma (66.7%), while men accounted for 33.3%. In the group with comorbid asthma and type 2 diabetes mellitus, the proportion of men increased to 40.0%, while that of women decreased to 60.0%. The obtained data indicate that the comorbid course of asthma and type 2 diabetes mellitus occurs in men approximately 1.2 times more often, which is likely due to more pronounced metabolic disorders and hormonal profile characteristics that contribute to the development of combined pathology.

An analysis of disease duration showed that the average duration of bronchial asthma in patients without concomitant type 2 diabetes mellitus was 16.7 ± 1.3 years, while in those with comorbid asthma and type 2 diabetes mellitus, it was 7.52 ± 0.9 years ($p < 0.05$). The disease duration in patients with comorbid pathology was 2.2 times shorter than in patients with isolated asthma.

A comparative analysis of clinical symptoms showed that patients with combined asthma and type 2 diabetes mellitus had more pronounced clinical symptoms compared to patients with isolated asthma. The frequency of dyspnea in patients with comorbid pathology was 60.0%, which was higher than the same indicator in patients with asthma without diabetes (22.2%; $p < 0.01$). Pale skin and weakness were recorded in 66.7% of cases with asthma + type 2 diabetes mellitus versus 44.4% with isolated asthma ($p < 0.05$*). Cyanosis of the nasolabial triangle and chest pain were more common in the combined form - 13.3% and 20.0%, respectively, which also indicates a more severe course of the disease. The data obtained indicate more pronounced hypoxia and vascular disorders in patients with asthma against the background of metabolic disorders.

Of particular note is the sweating indicator, whose prevalence in patients with combined asthma and type 2 diabetes reached 86.7%, compared with only 7.41%

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

($p < 0.001$*) in patients with isolated asthma. This indicates significant autonomic dysfunction and metabolic imbalance. Conversely, decreased appetite was more common in patients with isolated asthma (48.1%) compared with those with the comorbid form (40.0%), likely related to differences in glycemia and insulin resistance (Fig. 1).

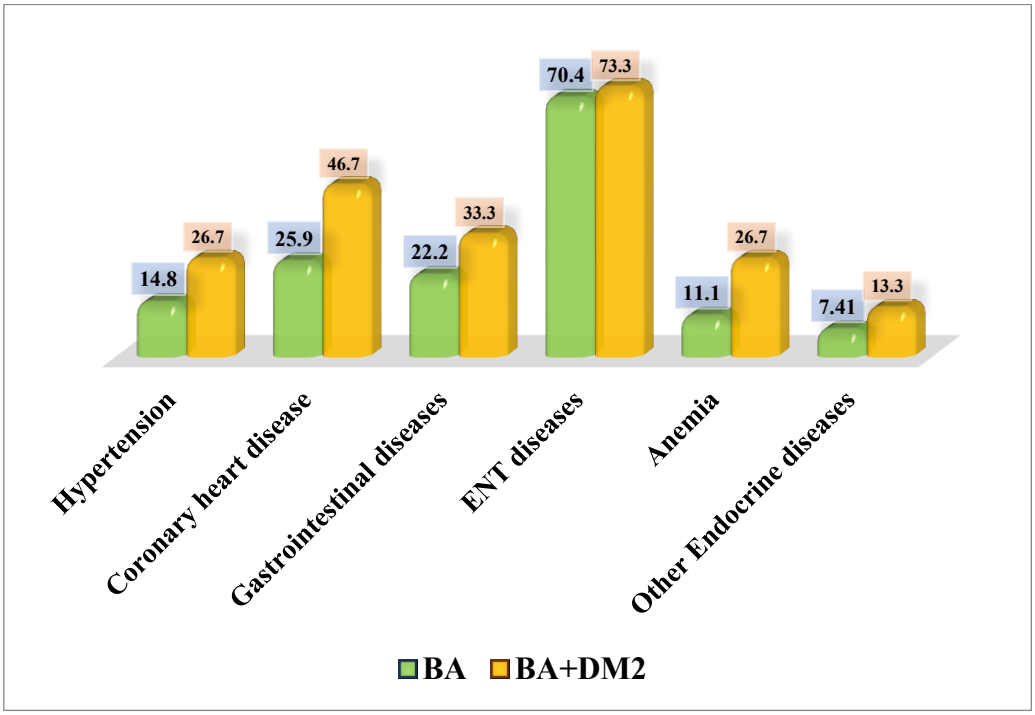

Fig. 1. Concomitant pathology in the examined groups

A comparative analysis of complications revealed that patients with comorbid asthma and type 2 diabetes mellitus had a significantly higher incidence of respiratory failure—53.3% versus 37.0% in those with isolated asthma. A similar trend was observed for pulmonary hypertension (26.7% versus 14.8%, $p < 0.05$), indicating significant damage to the vascular endothelium and impaired microcirculation in the comorbid form of the disease.

The incidence of emphysema in patients with asthma and type 2 diabetes was 13.3%, slightly higher than that in patients with isolated asthma (11.1%). Chronic heart failure was observed almost 1.8 times more often in patients with this combined pathology (46.7%) compared to patients with asthma without diabetes

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

(25.9%, $p < 0.05$), reflecting the aggravating impact of metabolic disorders on the cardiopulmonary system (Fig. 2).

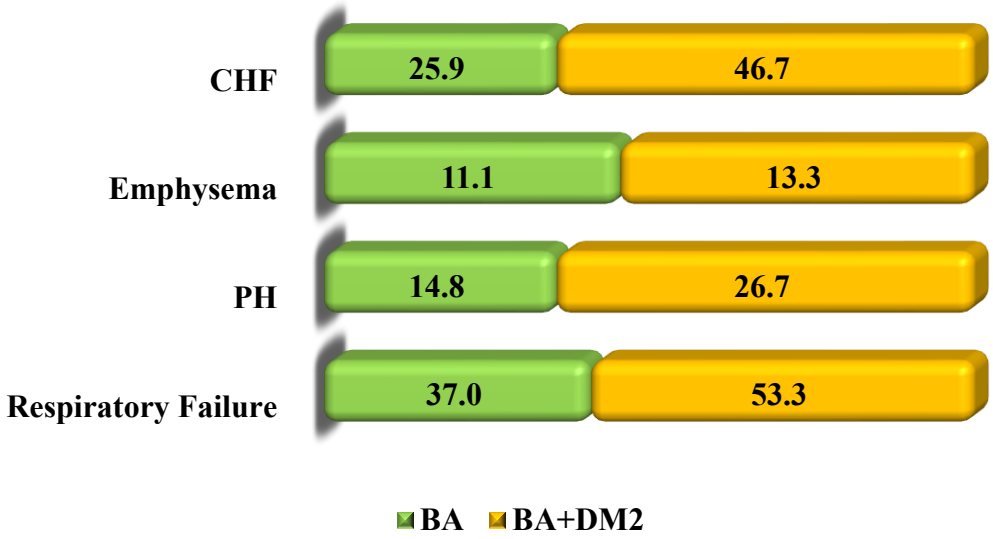

Fig. 2. Analysis of complications in the examined groups, %

A comparative analysis of carbohydrate metabolism parameters revealed significant differences between the study groups. The level of glycated hemoglobin (HbA1c) in patients with bronchial asthma was 5.94 ± 0.6%, which was slightly higher compared to the control group (5.31 ± 0.4%). The most pronounced increase was noted in patients with a combined course of bronchial asthma and type 2 diabetes: 8.44 ± 0.91%, which exceeded the control values by almost 1.6 times ($p < 0.05$). This indicates chronic hyperglycemia and impaired protein glycosylation, typical for patients with metabolic disorders. An elevated level of HbA1c reflects not only the degree of compensation of carbohydrate metabolism, but also an increase in oxidative stress, which contributes to the progression of the inflammatory process in bronchial asthma (Fig. 3).

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

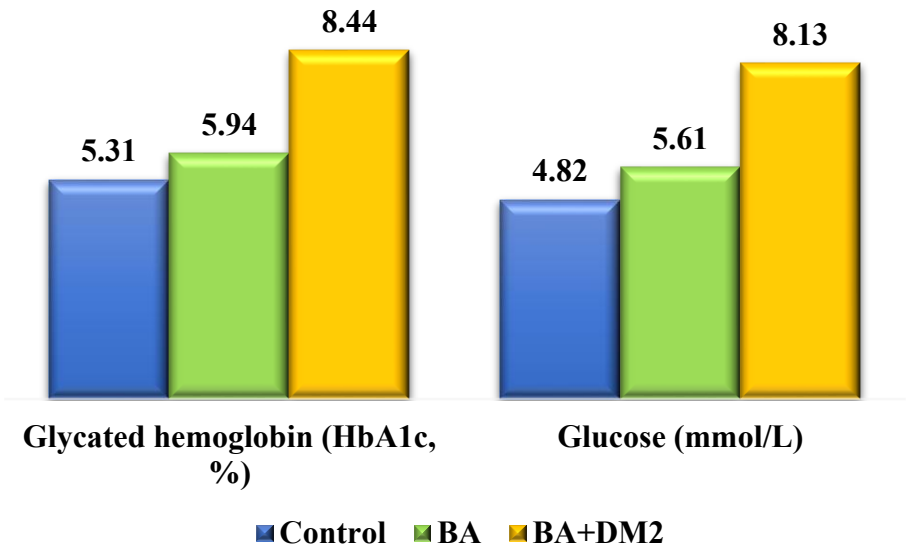

Fig. 3. Parameters of carbohydrate metabolism in the examined groups

Blood glucose levels also showed a statistically significant increase in the patient groups compared to the control group. In isolated asthma, this indicator was 5.61 ± 0.7 mmol/L, which was moderately higher than the control values (4.82 ± 0.5 mmol/L). In patients with combined pathology, glucose levels reached 8.13 ± 1.27 mmol/L, exceeding the norm by almost 1.7 times ($p < 0.05$). These data confirm a significant impairment of carbohydrate metabolism in patients with asthma and type 2 diabetes, which increases the metabolic load and promotes the activation of proinflammatory mechanisms.

Thus, the combination of bronchial asthma with type 2 diabetes mellitus is accompanied by a significant deterioration in the metabolic profile, reflecting the systemic nature of the pathological process.

Given the identified carbohydrate metabolism disturbances and their relationship with the severity of the inflammatory process, a useful step in the study was to examine immunological and biochemical markers. Particular attention was paid to indicators reflecting endothelial function and the cytokine profile. These parameters provide a deeper understanding of the mechanisms underlying the interaction between chronic inflammation and metabolic dysfunction in patients with asthma and type 2 diabetes. Analysis of cytokine levels, including

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

endothelin-1, allows for an objective assessment of the degree of systemic inflammation.

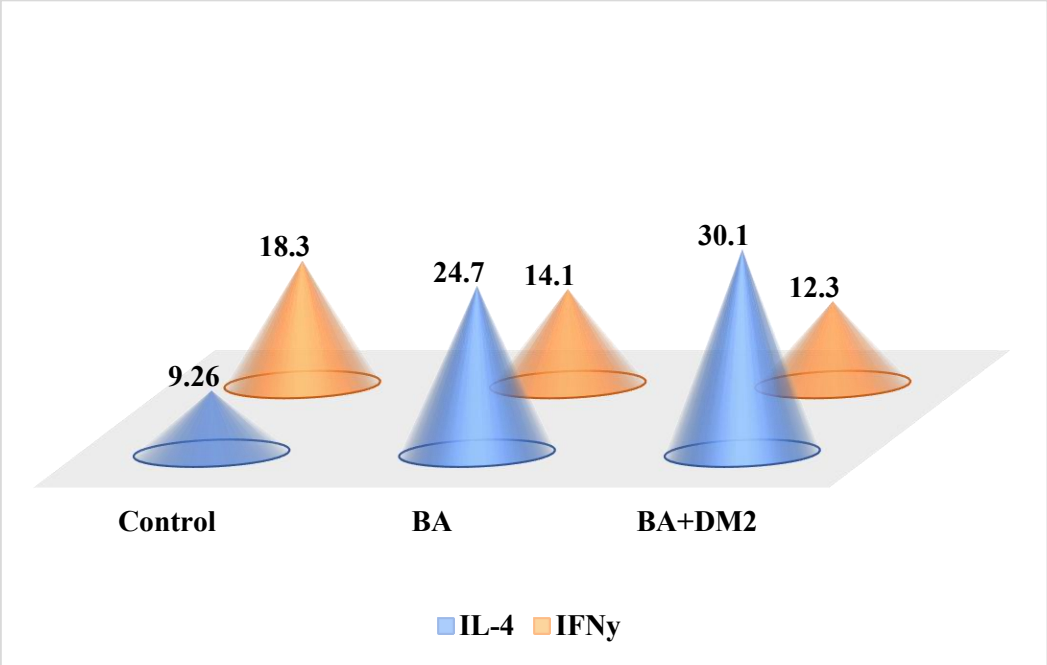

Fig. 4. Cytokine levels in the examined groups (pg/ml)

Interleukin-4 (IL-4) is a key Th2-type cytokine that regulates IgE synthesis, eosinophil activation, and the development of allergic inflammation in bronchial asthma [4]. In patients with type 2 diabetes mellitus, increased IL-4 is associated with chronic low-grade inflammation and impaired glucose metabolism through its effect on adipokine balance and insulin resistance. In our study, IL-4 levels were 9.26 ± 0.8 pg/ml in the control group, 24.7 ± 1.2 pg/ml in asthma, and 30.1 ± 1.4 pg/ml in patients with combined asthma and type 2 diabetes. IL-4 concentrations in patients with asthma were 2.7 times higher than control values ($p < 0.01$), and 3.2 times higher ($p < 0.001$) in those comorbid with type 2 diabetes. These data reflect increased Th2-dependent inflammation and IL-4 hyperproduction against the background of metabolic disturbances, which contribute to the chronic course of the disease and increased airway sensitivity.

Interferon-γ (IFN-γ), on the contrary, is the main Th1-type cytokine, providing anti-inflammatory and immunoregulatory effects, limiting the Th2 response [9]. In our study, its level was 18.3 ± 1.0 pg/ml in the control, 14.1 ± 0.9 pg/ml in BA

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

and 12.3 ± 0.8 pg/ml in patients with BA + T2DM, which is 1.3 times ($p < 0.05$) and 1.5 times ($p < 0.01$) lower than the control values, respectively (Fig. 4). A decrease in IFN-γ in patients with comorbid pathology reflects the suppression of the Th1 response caused by chronic hyperglycemia and elevated levels of proinflammatory mediators inducing a shift towards a Th2-dominant immune profile. The probable mechanism involves metabolic depletion of T lymphocytes and disruption of the JAK/STAT signaling pathways during hyperinsulinemia, which reduces IFN-γ production and exacerbates allergic airway inflammation. This cytokine imbalance can be considered one of the key immunobiochemical markers of the comorbid course of bronchial asthma and type 2 diabetes.

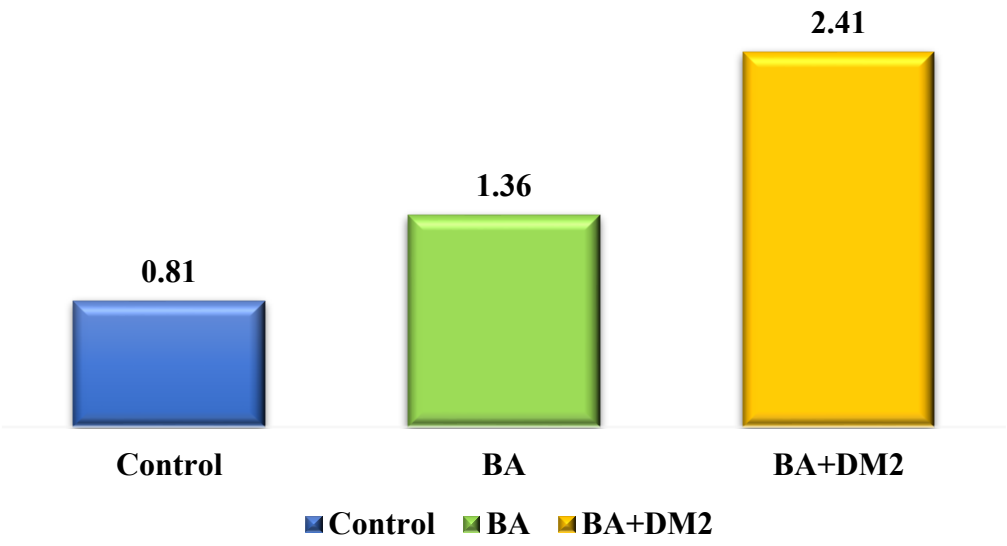

Fig. 5. Endetolin 1 level in the examined groups (pg/ml)

Endothelin-1 (EN-1) is a potent vasoconstrictor peptide synthesized by endothelial cells and involved in the regulation of vascular tone, smooth muscle cell proliferation, and inflammatory responses. In bronchial asthma, increased EN-1 levels are associated with endothelial dysfunction and airway vascular wall remodeling [5]. In patients with type 2 diabetes mellitus, hyperglycemia and oxidative stress increase EDN1 gene expression, contributing to vasoconstriction and microcirculation impairment. In our study, EN-1 concentrations were 0.81 ±

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

0.07 pg/ml in the control group, 1.36 ± 0.09 pg/ml in patients with asthma, and 2.41 ± 0.12 pg/ml in patients with a combination of asthma and type 2 diabetes. The level of EN-1 in patients with BA exceeded the control values by 1.7 times ($p < 0.01$), and in the case of comorbidity – by 3.0 times ($p < 0.001$) (Fig. 5).

The identified differences reflect a progressive impairment of endothelial function as metabolic disorders worsen. Elevated EN-1 levels in patients with asthma and type 2 diabetes are likely due to the activation of NF-κB signaling pathways and increased production of reactive oxygen species, which induce endothelin expression in the vascular endothelium. Dysregulation of the NO/EN-1 system leads to vasospasm, tissue hypoxia, and bronchial vascular remodeling, which increases bronchial obstruction and reduces the effectiveness of standard therapy. Thus, elevated EN-1 levels can be considered a marker of endothelial dysfunction and chronic inflammation in patients with the combined course of bronchial asthma and type 2 diabetes.

Discussion of the obtained results

The conducted analysis revealed that the average age of patients with comorbid bronchial asthma (BA) and type 2 diabetes mellitus (T2DM) was statistically significantly higher compared to patients with isolated bronchial asthma, which is consistent with literature data indicating an age-dependent nature of metabolic disorders and a later onset of comorbidity (Pan et al., 2025). An analysis of the gender composition revealed a relative increase in the proportion of men among patients with BA and T2DM, which is consistent with epidemiological studies demonstrating a higher predisposition of males to metabolic stress and vascular disorders (Fuseini et al., 2017). The average duration of the disease in patients with comorbid BA was 2.2 times shorter than in those with isolated asthma, which may reflect a more rapid progression of the pathological process in the context of impaired metabolism. Clinical symptoms in this group of patients were more severe: shortness of breath, weakness, sweating, and signs of tissue hypoxia were more frequently observed, indicating a systemic nature of inflammatory and metabolic disorders. The incidence of complications, such as respiratory failure, pulmonary hypertension, and chronic heart failure, was significantly higher in

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

patients with a combination of asthma and type 2 diabetes, consistent with current understanding of the synergistic effects of inflammation and endothelial dysfunction on the cardiopulmonary system (Howell et al., 2023).

Laboratory analysis revealed significant disturbances in carbohydrate metabolism: significantly higher levels of glycated hemoglobin (HbA1c) and blood glucose in patients with asthma and type 2 diabetes, indicating decompensation of metabolic processes and activation of proinflammatory cascades. Cytokine profile changes were characterized by a significant increase in IL-4 and a decrease in IFN-γ, reflecting a shift in the immune response toward Th2-dominant inflammation; similar results were obtained in studies by Lama et al. (2017). Furthermore, increased endothelin-1 (EN-1) levels in patients with combined pathology confirm the presence of severe endothelial dysfunction induced by hyperglycemia and oxidative stress. The combination of these changes reflects the integrative interaction of immune, metabolic, and vascular factors that contribute to the severe course of the disease in the comorbidity of asthma and type 2 diabetes.

Conclusion:

Thus, patients with comorbid asthma and type 2 diabetes mellitus exhibited a more severe clinical and laboratory course of the disease, accompanied by significant carbohydrate metabolism disorders, endothelial dysfunction, and immune imbalance. These data confirm that metabolic disturbances exacerbate chronic airway inflammation and contribute to the development of vascular complications. Increased IL-4 and endothelin-1 levels, coupled with decreased IFN-γ, reflect Th2 activation and weakened anti-inflammatory control. These relationships highlight the need for a comprehensive approach to the diagnosis and treatment of comorbid conditions, taking into account metabolic and immunological characteristics. Incorporating these markers into monitoring patients with asthma and type 2 diabetes mellitus will optimize risk stratification and improve the effectiveness of personalized therapy.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

References

1. Ai M, Shalaby A, Seleem MS, Rezk A, et al. Impact of Type 2 Diabetes Mellitus on Bronchial Asthma: Does Diabetes Mellitus Make Asthma Worse? Respiratory Medicine. 2020:-P.173:.
2. Al-Beltagi M. Diabetes-inducing effects of bronchial asthma. Medicine Hypotheses.2025:-P.63-94https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11718464/
3. Banecki, K.M.R.M., et al. (2023). Endothelin-1 in Health and Disease. International Journal of Molecular Sciences, 24(14),:-P.11295.https://www.mdpi.com/1422-0067/24/14/11295
4. Christen S, et al. Oxidative stress precedes systemic inflammatory response after cardiopulmonary bypass in children. Crit Care Med. 2020;33(5):-P.1125–1130.
5. Howell KA, et al. Vascular dysfunction in asthma and metabolic comorbidities. J Exp Med. 2023;220(7): :-P. 2022-2030.
6. Lama VN, et al. Cytokine profiles in asthma: Th1 vs Th2 dominance. J Invest Allergol Clin Immunol. 2011;21(5) :-P. 10-17https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7817304/
7. Lee B, et al. Antidiabetic Medication and Asthma Attacks. JAMA Intern Med. 2025:-P.1125-1132:. https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2826086
8. Lee KH, et al. Hypertension and Diabetes Mellitus as Risk Factors for Asthma Development. BMC Pulmonary Medicine. 2019;19(1):-P.910-917.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7322203/
9. Narendra DK, et al. Asthma and Hyperglycemia: Exploring the Interconnected Pathophysiology. Diagnostics. 2024;14(17):-P.1869.https://doi.org/10.3390/diagnostics14171869
10. Pan H, et al. Age-related comorbid progression in respiratory and metabolic diseases. Respiratory Research. 2025;26(1):-P.736-741 https://www.jacionline.org/article/S0091-6749(19)32357-7/pdf

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 08, November, 2025
Website: usajournals.org

11. Torres RM, et al. Association between Asthma and Type 2 Diabetes Mellitus: A Review. Frontiers in Immunology. 2021:-P.211-224https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7817304/
12. Uppal P, Zhang Y, Williams R, Singh A. Type 2 Diabetes Mellitus and Asthma: Pathomechanisms, Clinical Outcomes, and Therapeutic Opportunities. Int J Mol Sci. 2023;24:-P.324-365.https://doi.org/10.3390/ijms240xxxxx
13. Wen J, Wang C, Zhuang R, Guo S, Chi J, et al. Blood Glucose Levels, Inflammation, and Mortality in Asthmatic Populations. J Epidemiol Glob Health. 2025;15:-P.80..https://doi.org/10.1007/s44197-025-00425-7
14. Wu TD, et al. Diabetes and Glycemic Dysfunction in Asthma. J Allergy Clin Immunol Pract. 2020:-P.625-632..https://www.jaci-inpractice.org/article/S2213-2198(20)30719-4/fulltext
15. Yeryomenko G, et al. Endothelial Dysfunction in Patients Having Asthma. J Allergy Clin Immunol. 2020;146(5):-P.472-781https://www.jacionline.org/article/S0091-6749(19)32357-7/pdf