

Immunological Profile Features in Patients with Bronchial Asthma Comorbid with Type 2 Diabetes Mellitus

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Abstract Aim. To assess the characteristics of the cytokine profile (interleukin-6 [IL-6], interleukin-10 [IL-10]) in patients with bronchial asthma (BA), type 2 diabetes mellitus (T2DM), and their comorbidity, and to determine the associations of cytokine levels with parameters of carbohydrate and lipid metabolism, leptin, inflammatory markers, and pulmonary function. **Materials and methods.** A total of 90 inpatients were examined and allocated to three sex- and age-matched groups (n=30 each): BA+T2DM, isolated BA, and isolated T2DM. Clinical and laboratory assessments included fasting glucose, glycated hemoglobin (HbA1c), insulin, leptin, lipid profile, immunoglobulin E (IgE), C-reactive protein (CRP), and spirometry. Serum IL-6 and IL-10 concentrations were measured by enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed using Statistica 8.0; differences were considered significant at $p < 0.05$. **Results.** All groups demonstrated elevated IL-6 levels relative to reference values. The highest IL-6 concentrations were observed in the BA+T2DM group (37.8 ± 25.7 pg/mL), which was significantly higher than in isolated BA (19.9 ± 23.0 pg/mL; $p = 0.02$) and isolated T2DM (25.6 ± 40.7 pg/mL; $p = 0.04$). IL-10 levels were also maximal in the BA+T2DM group (26.8 ± 12.3 pg/mL) and significantly exceeded those in isolated BA (10.8 ± 4.7 pg/mL; $p = 0.0001$) and isolated T2DM (17.7 ± 9.3 pg/mL; $p = 0.002$). In patients with BA+T2DM, IL-6 was higher at glucose ≥ 10.5 mmol/L compared with glucose < 10.5 mmol/L (median 45.9 vs 22.05 pg/mL; $p < 0.05$). Leptin showed positive correlations with IL-6 ($r = 0.703$) and IL-10 ($r = 0.434$), correlated positively with atherogenic lipid parameters, and correlated negatively with high-density lipoprotein cholesterol (HDL-C) ($r = -0.581$). IL-6 was strongly correlated with CRP ($r = 0.843$) and IgE ($r = 0.673$). A strong inverse correlation was identified between IL-6 and forced vital capacity (FVC) ($\rho = -0.77$; $p < 0.001$); no significant associations were found between IL-10 and spirometric indices. **Conclusion.** Comorbid BA and T2DM is characterized by more pronounced pro-inflammatory activity (elevated IL-6), activation of a compensatory anti-inflammatory response (elevated IL-10), and close immunometabolic interactions (leptin–cytokines–lipids). Heightened systemic inflammation is associated with poorer pulmonary function, while increasing glycemia is associated with higher IL-6 levels.

Keywords Bronchial asthma, Type 2 diabetes mellitus, IL-6, IL-10, Leptin, Systemic inflammation, IgE, C-reactive protein, Spirometry

1. Relevance

Bronchial asthma (BA) and type 2 diabetes mellitus (T2DM) are among the most prevalent chronic non-communicable diseases and constitute a substantial medical and societal burden. According to the World Health Organization, approximately 262 million people were living with asthma in 2019, and the condition is associated with considerable disability and mortality [1]. According to the International Diabetes Federation (IDF; Diabetes Atlas, 11th edition), in 2024 there were about 589 million adults aged 20–79 years living with diabetes worldwide ($\approx 11.1\%$ of the adult population); the proportion of undiagnosed cases remains

high, and prevalence is expected to continue to rise [2].

The comorbidity of BA and T2DM is of particular clinical importance in the context of increasing obesity and metabolic disturbances, which may contribute to the development of a “systemic” inflammatory phenotype in a subset of patients with BA. Current evidence indicates a bidirectional association between BA and T2DM (an increased risk of T2DM among patients with BA and vice versa), and suggests that this comorbidity is linked to poorer clinical outcomes and greater difficulty achieving disease control [3,4]. Contemporary asthma management strategies emphasize the need for proactive identification and correction of comorbidities and risk factors (including metabolic abnormalities and obesity) as an integral component of improving asthma control [5].

The pathogenetic basis of an unfavorable course in comorbid BA and T2DM is considered to be chronic low-grade

inflammation involving pro-inflammatory cytokines and adipokines. Interleukin-6 (IL-6) is implicated in the mechanisms of insulin resistance and hyperglycemia and is regarded as one of the key markers of the inflammatory component in T2DM; systematic reviews have demonstrated an association between elevated IL-6 levels and the risk of developing T2DM [6–8]. At the same time, obesity-associated BA is characterized by alterations in systemic and airway inflammation, and leptin—an adipokine—has been shown to correlate with inflammatory and clinical manifestations of BA, potentially serving as a link in immunometabolic interactions [9]. Nevertheless, data on the balance between pro-inflammatory (IL-6) and anti-inflammatory (IL-10) cytokines, their relationships with glycemic control parameters, as well as with markers of allergic inflammation and pulmonary function in the setting of comorbid BA and T2DM remain limited. This underscores the need for studies examining the immunological profile in patients with this comorbidity.

Study aim. This article examines peripheral blood plasma cytokine levels in patients with bronchial asthma, type 2 diabetes mellitus, and their comorbidity, with the aim of identifying associations between inflammatory markers and hormonal–metabolic parameters that may influence the clinical course of asthma in patients with T2DM.

2. Materials and Methods

The study included 90 patients who were hospitalized in the Endocrinology and Pulmonology departments of City Clinical Hospital No. 1 and Republican specialized scientific-practical medical center of endocrinology named after academic Yo.Kh. Turakulov (Tashkent, Uzbekistan). Patients were allocated to three sex- and age-matched groups ($n=30$ each): comorbid BA and T2DM, isolated BA, and isolated T2DM.

All participants underwent a comprehensive clinical and laboratory evaluation, including hormonal and metabolic assessments with measurement of glycated hemoglobin (HbA1c), blood glucose, insulin, and leptin, as well as pulmonary function testing. BA was diagnosed according to the classification and criteria of the international consensus on asthma diagnosis and management (Global Initiative for Asthma—GINA, 2016). T2DM was diagnosed by an endocrinologist in accordance with established standards [10].

Plasma IL-6 and IL-10 concentrations were determined by ELISA using standard protocols and commercial kits (Vector-Best; DRG, Germany) on a Mindray MR-96A microplate reader at 450–620 nm, with point-to-point calibration curve construction.

Statistical analyses were performed using Microsoft Statistica 8.0. Depending on data distribution, parametric and non-parametric methods were applied; differences were considered statistically significant at $p < 0.05$.

3. Results

We performed a comparative analysis of plasma IL-6 and IL-10 levels in patients with bronchial asthma, patients with comorbid bronchial asthma and type 2 diabetes mellitus, and patients with type 2 diabetes mellitus (Table 1).

As shown in Table 1, patients in all study groups exhibited elevated levels of the pro-inflammatory cytokine IL-6 relative to reference values, which may indicate the presence of a subclinical inflammatory process.

In patients with comorbid bronchial asthma and type 2 diabetes mellitus, IL-6 levels (37.8 ± 25.7 pg/mL) were significantly higher than in those with isolated bronchial asthma (19.9 ± 23.0 pg/mL), i.e., nearly twofold ($p_{1-2}=0.02$), and 1.5-fold higher than in the isolated T2DM group (25.6 ± 40.7 pg/mL).

Table 1. Peripheral blood plasma IL-6 and IL-10 levels in female patients with type 2 diabetes mellitus, bronchial asthma, and their comorbidity (presented as mean $\pm$ SD)

Parameter	Reference range	Groups			P
		BA + T2DM (1)	BA (2)	T2DM (3)	
IL-6 (pg/mL)	0–10	37.8 ± 25.7	19.9 ± 23.0	25.6 ± 40.7	$P_{1-2}=0,02$ $P_{1-3}=0,04$ $P_{2-3}=0,05$
IL-10 (pg/mL)	4.89–36.15	26.8 ± 12.3	10.8 ± 4.7	17.7 ± 9.3	$P_{1-2}=0,0001$ $P_{1-3}=0,002$ $P_{2-3}=0,001$

Table 2. IL-6 levels (pg/mL) according to blood glucose in patients with comorbid bronchial asthma and type 2 diabetes mellitus

Subgroup	IL-6 (pg/mL), median (Q1; Q3)	Significance
Glucose < 10.5 mmol/L (1), $n=14$	22.05 (13.45; 37.9)*	$p_{1-2} < 0,05^{**}$
Glucose ≥ 10.5 mmol/L (2), $n=16$	45.9 (16.8; 61.2)*	

* Median (Q0.25–Q0.75).

** Mann–Whitney U test (difference statistically significant).

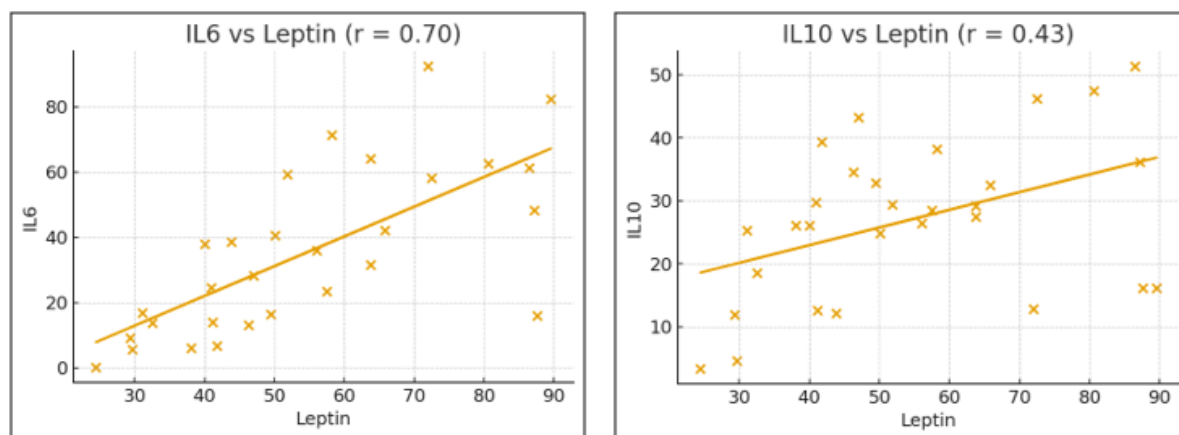


Figure 1. Correlations between leptin and IL-6/IL-10 levels in patients with comorbid bronchial asthma and type 2 diabetes mellitus

IL-10 concentrations were highest in the BA+T2DM group (26.8 ± 12.3 pg/mL), significantly exceeding the values observed in isolated bronchial asthma (10.8 ± 4.7 pg/mL) ($p_{1-2}=0.0001$) and in isolated T2DM (17.7 ± 9.3 pg/mL) ($p_{1-3}=0.002$). Differences between the isolated BA and isolated T2DM groups were also significant ($p_{2-3}=0.001$), suggesting different degrees of involvement of anti-inflammatory mechanisms in the pathogenesis of each disease.

In the BA+T2DM group, we further analyzed the relationship between IL-6 levels and the degree of glycation; the results are presented in Table 2.

Elevated glycemia was associated with a more pronounced activation of pro-inflammatory pathways. In patients with fasting glucose <10.5 mmol/L, the median IL-6 level was 22.05 pg/mL, whereas at glycemia ≥ 10.5 mmol/L it was almost twofold higher (45.9 pg/mL); the difference was statistically significant ($p < 0.05$). This finding indicates a link between poorer glycemic control and усилением the pro-inflammatory cytokine response.

Correlation analysis of metabolic parameters in patients with comorbid BA and T2DM revealed a network of associations among lipid metabolism indices, leptin, and the interleukins IL-6 and IL-10. Leptin occupied a central position in these immunometabolic interactions: its level correlated positively with IL-6 ($r=0.703$) and IL-10 ($r=0.434$) (Fig. 1), low-density lipoprotein cholesterol (LDL-C) ($r=0.446$), and triglycerides ($r=0.299$), and correlated negatively with high-density lipoprotein cholesterol (HDL-C) ($r=-0.581$). These results support the pro-inflammatory role of leptin and its association with an adverse lipid profile.

IL-6 levels showed a direct correlation with triglycerides ($r=0.579$) and leptin ($r=0.703$), reflecting its involvement in inflammation associated with dysfunctional adipose tissue. Despite its anti-inflammatory role, IL-10 also correlated positively with leptin ($r=0.434$) and IL-6 ($r=0.310$), underscoring the compensatory nature of IL-10 secretion in chronic, metabolically driven inflammation. Taken together, these findings support the presence of pronounced immunometabolic remodeling in patients with comorbid BA and T2DM, manifested by adipokine activation, deterioration of the lipid

profile, and усилением systemic inflammation.

The results of the correlation analysis between inflammatory markers and IL-6/IL-10 levels in patients with comorbid BA and T2DM are presented in Table 3.

Table 3. Correlations between inflammatory markers and IL-6/IL-10 levels in patients with comorbid BA and T2DM

Parameter	IgE	CRP	IL-6	IL-10
IgE	1,000	0,689	0,673	0,295
CRP	0,689	1,000	0,843	0,528
IL-6	0,673	0,843	1,000	0,324
IL-10	0,295	0,528	0,324	1,000

Note: Statistically significant correlations are highlighted in red in the original table.

The analysis revealed significant correlations that underscore the central role of IL-6 and IL-10 in the immunoinflammatory profile of patients with comorbid BA and T2DM. IL-6 concentrations were closely associated with C-reactive protein (CRP) and IgE levels, reflecting the combined impact of metabolic and allergic inflammation. The strong positive correlation between IL-6 and CRP ($r=0.843$) indicates high activity of low-grade systemic inflammation characteristic of T2DM, whereas the association with IgE ($r=0.673$) suggests усиление of the allergic component and increased airway hyperresponsiveness, which may compromise the effectiveness of asthma control.

IL-10, which exerts anti-inflammatory activity, also correlated with inflammatory markers, albeit substantially more weakly than IL-6. The moderate associations between IL-10 and CRP ($r=0.528$), as well as between IL-10 and IL-6 ($r=0.324$), reflect a compensatory anti-inflammatory response aimed at restraining excessive inflammation; however, the relatively low strength of these correlations suggests that this mechanism may be insufficient in the setting of comorbid BA and T2DM.

The correlation between IgE and CRP ($r=0.689$) highlights reciprocal amplification of allergic and metabolic inflammation, resulting in a more severe and persistent inflammatory milieu. Under BA–T2DM comorbidity, activated

adipose tissue may potentiate systemic inflammation, while chronic airway inflammation can further stimulate cytokine production.

Correlation analysis demonstrated a statistically significant strong inverse association between IL-6 levels and forced vital capacity (FVC) ($\rho = -0.77$; $p < 0.001$) across all examined patients, indicating lower FVC with increasing systemic inflammation. For peak expiratory flow (PEF) and forced expiratory volume in 1 second (FEV₁), a trend toward a weak positive correlation with IL-6 was observed, but it did not reach statistical significance ($p > 0.05$). No associations were identified between IL-10 levels and spirometric indices.

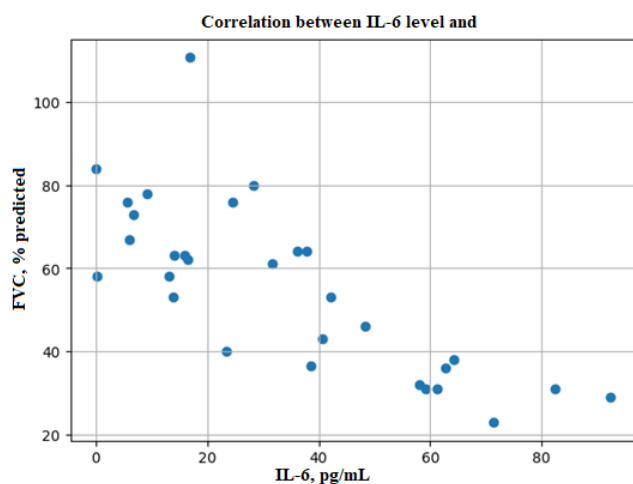


Figure 2. Correlation between forced vital capacity (FVC) and IL-6 levels in patients with isolated bronchial asthma

A pronounced inverse correlation was identified between IL-6 levels and forced vital capacity (FVC), indicating a reduction in FVC as systemic inflammation increases.

4. Discussion

The present findings confirm that both BA and T2DM are accompanied by a systemic inflammatory background; however, in the setting of comorbidity the inflammatory response appears more pronounced and complex. This allows BA–T2DM comorbidity to be viewed as a state of mutual potentiation of inflammatory mechanisms: metabolic dysregulation in T2DM enhances systemic inflammation and endothelial dysfunction, whereas chronic airway inflammation in BA sustains persistent activation of pro-inflammatory cascades. Consequently, a more stable inflammatory phenotype may develop, potentially associated with poorer symptom control and a higher frequency of exacerbations.

Of particular relevance is the observed association between IL-6 levels and glycemia. This suggests that inadequate glycemic control is accompanied by an intensified pro-inflammatory response. Pathogenetically, this relationship is plausible: hyperglycemia promotes oxidative stress, the formation of advanced glycation end products, and усиление cytokine-mediated inflammation, which may aggravate BA by increasing airway hyperresponsiveness and maintaining a

systemic inflammatory milieu.

IL-10, an anti-inflammatory cytokine, also reached its highest levels in the BA+T2DM group. At first glance, this may appear paradoxical; however, such a pattern is most plausibly interpreted as compensatory activation of anti-inflammatory pathways in response to an excessive pro-inflammatory burden. Concurrently, the significant correlations of IL-10 with IL-6 and CRP indicate that elevated IL-10 does not “switch off” inflammation, but rather reflects an attempt to limit its magnitude in the context of a chronic process.

Particular attention should be paid to the identified immunometabolic interactions. Leptin occupied a central position within the correlation network: its positive associations with IL-6 and IL-10, as well as with atherogenic lipid fractions, support the role of dysfunctional adipose tissue as a source of adipokines and inflammatory mediators. Thus, in BA–T2DM comorbidity a “vicious circle” emerges: adipokine-driven inflammation enhances cytokine activity, while systemic inflammation exacerbates metabolic disturbances, thereby sustaining the chronic course of both diseases.

Correlations between IL-6 and IgE point to a clinically important interplay between allergic and metabolic inflammation. The association of IL-6 with IgE suggests that, in the setting of comorbidity, not only systemic inflammation but also immunological activity related to the allergic component of BA is amplified, which may compromise the effectiveness of disease control. The functional relevance of this inflammatory burden is further supported by the inverse correlation between IL-6 levels and FVC: greater systemic inflammation is associated with reduced ventilatory capacity. Taken together, these findings indicate that IL-6 may be considered a marker reflecting not only laboratory evidence of inflammatory activity but also a potentially adverse impact on respiratory functional parameters.

Additional considerations

Recent studies have emphasized the potential role of anti-aging genes, particularly **Sirtuin-1 (SIRT1)**, in the regulation of inflammatory and metabolic processes associated with chronic diseases such as bronchial asthma and type 2 diabetes mellitus. SIRT1 is a NAD⁺-dependent deacetylase involved in the control of cellular metabolism, oxidative stress, and inflammatory signaling pathways.

Decreased activity of SIRT1 has been associated with the development of hyperglycemia, insulin resistance, and excessive inflammatory responses. In patients with type 2 diabetes mellitus, reduced SIRT1 expression may contribute to increased production of pro-inflammatory cytokines, including **interleukin-6**, which plays an important role in systemic inflammation. In bronchial asthma, impaired SIRT1 signaling may also enhance airway inflammation and worsen disease severity.

Therefore, assessment of **Sirtuin-1 as a potential biomarker** may be useful in patients with bronchial asthma combined with type 2 diabetes mellitus. Monitoring SIRT1 levels may help identify patients at higher risk of inflammatory

and metabolic complications and may contribute to the development of more targeted therapeutic approaches.

5. Conclusions

Elevated IL-6 levels relative to reference values were identified in patients with BA, T2DM, and their comorbidity, with the most pronounced increase observed in the BA+T2DM group, reflecting усиление of systemic inflammation in the setting of comorbidity.

In BA+T2DM, pro-inflammatory activity was associated with metabolic disturbances: IL-6 levels were significantly higher at glucose ≥ 10.5 mmol/L; leptin correlated with IL-6/IL-10 and with atherogenic lipid profile parameters (with an inverse association with HDL-C), supporting the contribution of immunometabolic mechanisms.

IL-6 was associated with markers of systemic and allergic inflammation (CRP and IgE) and showed an inverse correlation with forced vital capacity (FVC), indicating that greater inflammatory activity is linked to poorer pulmonary function.

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