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CLINICAL AND IMMUNOBIOCHEMICAL MARKERS IN THE DIAGNOSIS OF BRONCHIAL ASTHMA COMBINED WITH TYPE 2 DIABETES MELLITUS

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

Abstract
The aim of the study was to investigate clinical, laboratory and immunobiochemical markers in patients with bronchial asthma (BA) combined with type 2 diabetes mellitus (T2DM). A comparative analysis of clinical manifestations, carbohydrate metabolism parameters, fibrinolysis and the antioxidant system was performed. In patients with combined pathology, a significant increase in the level of tissue plasminogen activator (tPA) to 6.78 ± 0.42 ng/ml versus 2.21 ± 0.31 ng/ml in the control ($p < 0.001$) and a decrease in plasminogen activator inhibitor-1 (PAI-1) to 14.5 ± 0.9 μg/ml compared to 24.6 ± 1.2 μg/ml ($p < 0.01$) were observed. Superoxide dismutase (SOD) activity in patients with asthma and type 2 diabetes was reduced to 1001.7 ± 75.4 pg/ml, which is 1.5 times lower than in the asthma group (1201.8 ± 68.2 pg/ml) ($p < 0.05$). These changes were accompanied by signs of increased oxidative stress and impaired antioxidant defense. The obtained data confirm the involvement of metabolic and immunobiochemical shifts in the pathogenesis of the comorbid course of asthma and type 2 diabetes and can be used to optimize early diagnosis and prognosis of the disease.

Keywords: Bronchial asthma, type 2 diabetes mellitus, immunobiochemical markers, superoxide dismutase, tPA, PAI-1, diagnostics.

Introduction

According to the World Health Organization, bronchial asthma (BA) and type 2 diabetes mellitus (T2DM) are among the most common chronic diseases, significantly impacting quality of life and mortality. The global prevalence of asthma reaches 4–8%, while T2DM accounts for over 10% of the adult population, with both diseases demonstrating a steady upward trend. Comorbidity between asthma and T2DM is becoming increasingly common, driven by shared risk factors, including obesity, physical inactivity, and chronic systemic inflammation. This combination significantly worsens the clinical course, increases the frequency of

hospitalizations, and reduces the effectiveness of standard therapy. Epidemiological data indicate the need to identify new diagnostic criteria and pathogenetic links in the interactions between these diseases [2, 7, 9, 15].

Current research indicates that asthma and type 2 diabetes share common pathogenesis, based on chronic inflammation and metabolic disturbances. Hyperglycemia promotes oxidative stress, the production of proinflammatory cytokines, and microcirculatory impairment, which exacerbates bronchial hyperreactivity. In turn, long-term inflammation in the airways can increase insulin resistance, creating a vicious cycle of metabolic-inflammatory changes. These processes lead to altered endothelial function and an imbalance in the antioxidant defense system. Thus, understanding these common pathogenetic mechanisms is crucial for early diagnosis and treatment optimization [1, 3, 8, 14].

The immunological mechanisms of the comorbid course of asthma and type 2 diabetes remain poorly understood. Of particular interest are changes in the levels of cytokines, immunoglobulins, and systemic inflammatory markers, reflecting the degree of immune imbalance. Little data exists on the relationship between the activation of cellular and humoral immunity and the severity of clinical manifestations in these patients. Insufficient study of immunobiochemical markers complicates differential diagnosis and prognosis of the disease [4, 6, 10, 12]. This necessitates a comprehensive analysis of clinical and immunobiochemical parameters in the coexistence of asthma and type 2 diabetes.

Purpose of the study:

To study the role of clinical and immunobiochemical markers in the development of comorbidity of bronchial asthma in combination with type 2 diabetes mellitus.

Materials and methods of research:

Clinical material was collected at the Aram private clinic in Tashkent. The study included 42 patients aged 24 to 65 years, including 15 patients with combined asthma and type 2 diabetes (the study group), and 27 patients with isolated asthma (the comparison group). Asthma was diagnosed according to the GINA criteria (Global Initiative for Asthma, 2024), and T2DM was diagnosed based on WHO recommendations (2023).

To assess the clinical condition, the following were performed: anamnesis, physical, laboratory, and instrumental examination (blood chemistry, coagulogram, spirometry, bronchodilator test, chest X-ray, etc.). Biochemical studies included determination of glucose levels, glycosylated hemoglobin (HbA1c), and superoxide dismutase (COD).

Immunological studies were carried out to determine the content of tPA, PAI, as well as the activity of superoxide dismutase (SOD) in the blood serum using the Protein Contour test systems and the ElisaKid kit (China).

Statistical processing of data was performed using the SPSS 26.0 package; differences were considered significant at $p < 0.05$.

Research results:

An analysis of the average age of the examined groups showed that patients with bronchial asthma had an average age of 36.1 ± 1.8 years, while in the case of a combination of bronchial asthma and type 2 diabetes mellitus, this figure was 45.7 ± 2.3 years (Fig. 1).

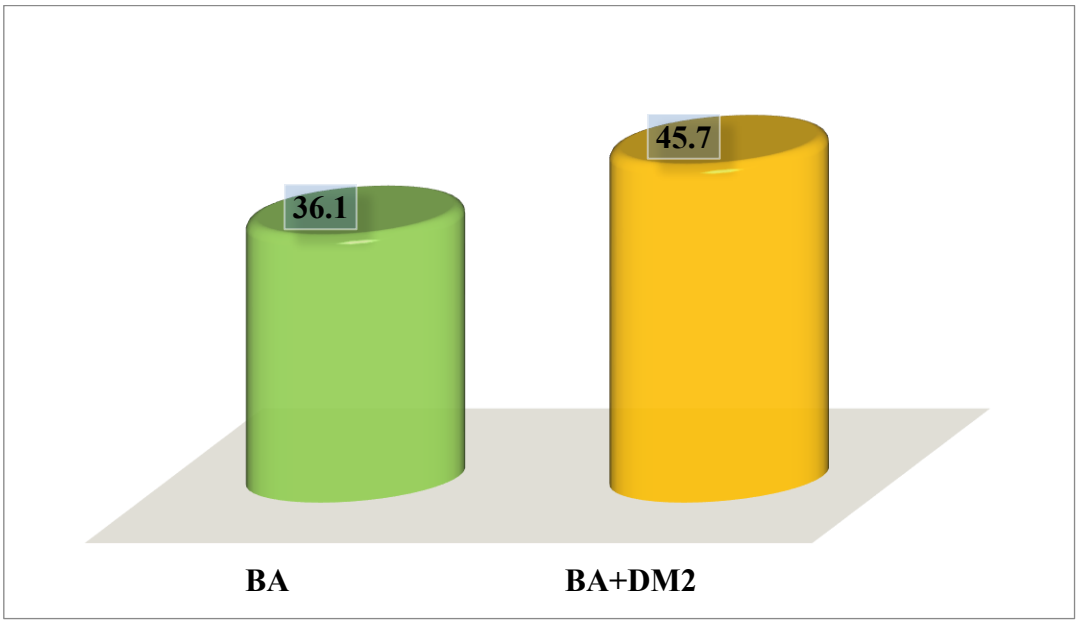

Fig. 1. Average age of the examined patients, (M±m)

The distribution of patients by gender showed that among patients with isolated bronchial asthma, men constituted 33.3% and women 66.7%. However, when bronchial asthma was combined with type 2 diabetes mellitus, the proportion of men increased to 40.0% and women decreased to 60.0%. Women predominated in both groups; however, in the presence of concomitant diabetes mellitus, a tendency toward an increase in the proportion of men was noted (Fig. 2).

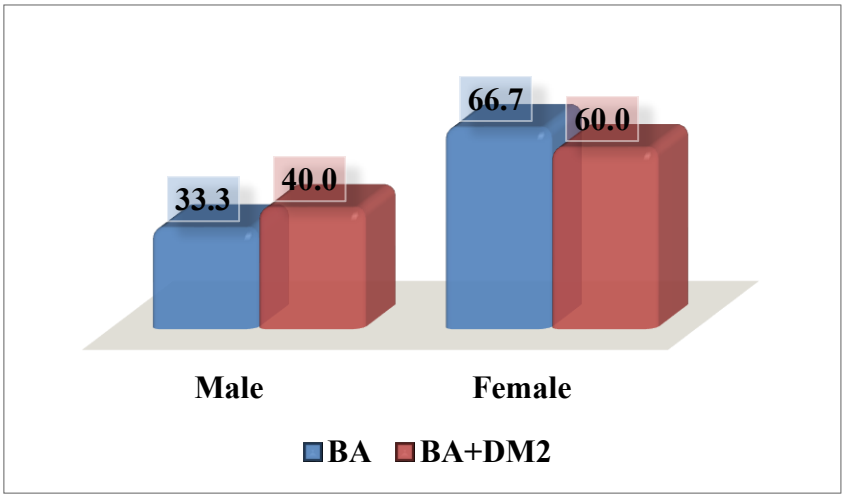

Fig. 2. Gender distribution of the surveyed groups, (%)

An analysis of disease duration indicators revealed that in patients with isolated bronchial asthma, the average disease duration was 16.7 ± 1.9 years, while in those with combined asthma and type 2 diabetes mellitus, it was 7.5 ± 1.3 years. The disease duration in patients in the first group was approximately 2.2 times longer than in patients with comorbid pathology, which is confirmed by the statistical significance of the difference ($p < 0.05$). The difference in indicators reflects the later development of comorbid pathology in patients with bronchial asthma (Fig. 3).

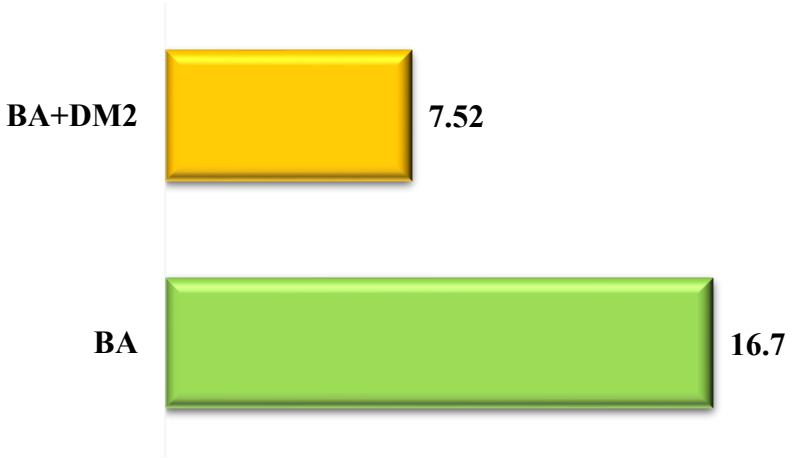

Fig. 3. Duration of illness in the examined groups, (M±m), (P ≤0.05)

A comparative analysis of the frequency of the main complaints in the examined patients revealed significant differences between the groups with isolated bronchial asthma and with a combination of bronchial asthma and type 2 diabetes mellitus. Patients in the comorbid group more often experienced shortness of breath (60.0% versus 22.2%), pale skin (66.7% versus 44.4%), weakness (66.7% versus 44.4%) and especially sweating (86.7% versus 7.4%), which indicates more pronounced manifestations of systemic disorders and autonomic dysfunction ($p < 0.05$). The frequency of cyanosis of the nasolabial triangle and chest pain was slightly higher in patients with combined pathology (13.3% and 20.0%, respectively), but the differences did not reach statistical significance ($p > 0.05$). The rate of appetite loss was somewhat higher in patients with isolated asthma (48.1% versus 40.0%), which may be related to the specific course of the inflammatory process and the therapeutic effects of the medications used (Fig. 4). The data obtained indicate that when asthma is combined with type 2 diabetes, clinical symptoms are characterized by greater severity of systemic manifestations, reflecting the metabolic and autonomic aggravation of the disease.

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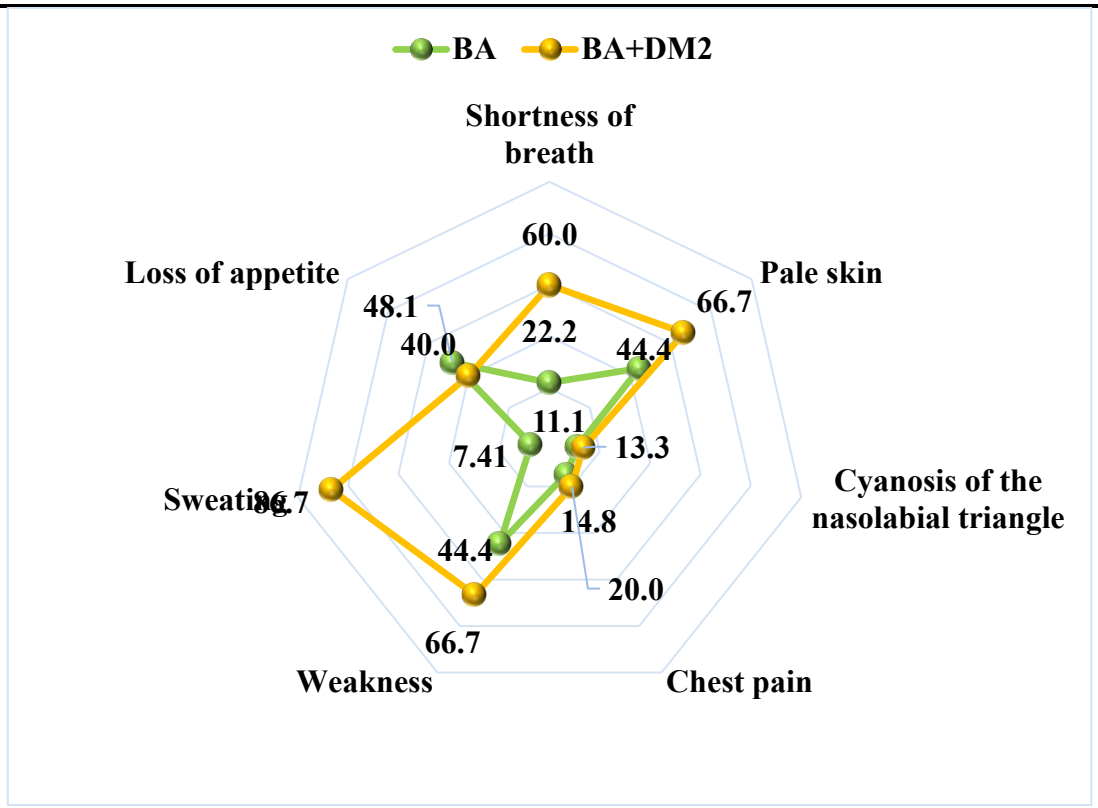

Fig. 4. Clinical symptoms and complaints of the examined groups, (%), (P ≤0.05)

An analysis of the comorbidity structure showed that patients with combined asthma and type 2 diabetes mellitus had a higher incidence of chronic diseases compared to the isolated asthma group. The most pronounced differences were observed in coronary heart disease (46.7% versus 25.9%) and hypertension (26.7% versus 14.8%), reflecting a close relationship between metabolic disorders and cardiovascular disease. The incidence of gastrointestinal diseases and anemia was also higher in the comorbid group (33.3% and 26.7%, respectively) compared to patients without diabetes mellitus (22.2% and 11.1%), indicating more pronounced metabolic and hemodynamic disorders. ENT pathology was common in both groups (73.3% in asthma + type 2 diabetes mellitus and 70.4% in asthma alone), without demonstrating significant differences. Other endocrine diseases (endemic, diffuse, and toxic goiter) were observed in a small number of patients, somewhat more frequently in those with comorbid conditions (13.3% vs. 7.4%). The combined data confirm that the coexistence of type 2 diabetes mellitus and bronchial asthma is accompanied by an increased frequency and severity of associated somatic diseases, particularly cardiovascular diseases.

A comparative analysis of the complication rate showed that respiratory failure (RF) was recorded in 53.3% of patients in the comorbid group versus 37.0% with bronchial asthma, which is approximately 1.4 times higher. The incidence of pulmonary hypertension (PH) in combined pathology was 26.7%, which was 1.8 times higher than in the group with isolated bronchial asthma (14.8%, $p < 0.05$). Pulmonary emphysema was slightly more common in patients with bronchial asthma and type 2 diabetes (13.3% versus 11.1%), but the difference

was not statistically significant. The incidence of chronic heart failure (CHF) was significantly higher in patients with comorbidity (46.7% versus 25.9%), which corresponds to a 1.8-fold increase in the complication rate ($p < 0.05$). The obtained results reflect a more severe and systemic course of the disease in patients with a combination of bronchial asthma and type 2 diabetes mellitus, which is due to the complex impact of metabolic and inflammatory factors on the respiratory and cardiovascular systems.

Table 1 Carbohydrate metabolism indicators in the examined groups

Indicator	Control (n=20)	BA (n=27)	BA + T2DM (n=15)
Glycated hemoglobin (HbA1c, %)	5.31 ± 0.4	5.94 ± 0.6	8.44 ± 0.91
Glucose (mmol/l)	4.82 ± 0.5	5.61 ± 0.7	8.13 ± 1.27

Comparative analysis of carbohydrate metabolism parameters showed that the level of glycated hemoglobin (HbA1c) in the BA+DM2 group was 8.44 ± 0.91% and exceeded the value in the control group (5.31 ± 0.4%) by approximately 1.6 times and the group with isolated BA (5.94 ± 0.6%) by 1.4 times ($p < 0.001$). The blood glucose concentration in patients with combined pathology reached 8.13 ± 1.27 mmol/l, which is 1.7 times higher than the control values (4.82 ± 0.5 mmol/l) and 1.45 times higher than the level in isolated bronchial asthma (5.61 ± 0.7 mmol/l) ($p < 0.001$) (Table 1). The obtained data reflect a significant decompensation of carbohydrate metabolism in patients with a combination of bronchial asthma and type 2 diabetes mellitus, which confirms the leading role of metabolic disorders in the aggravation of the clinical course of the disease.

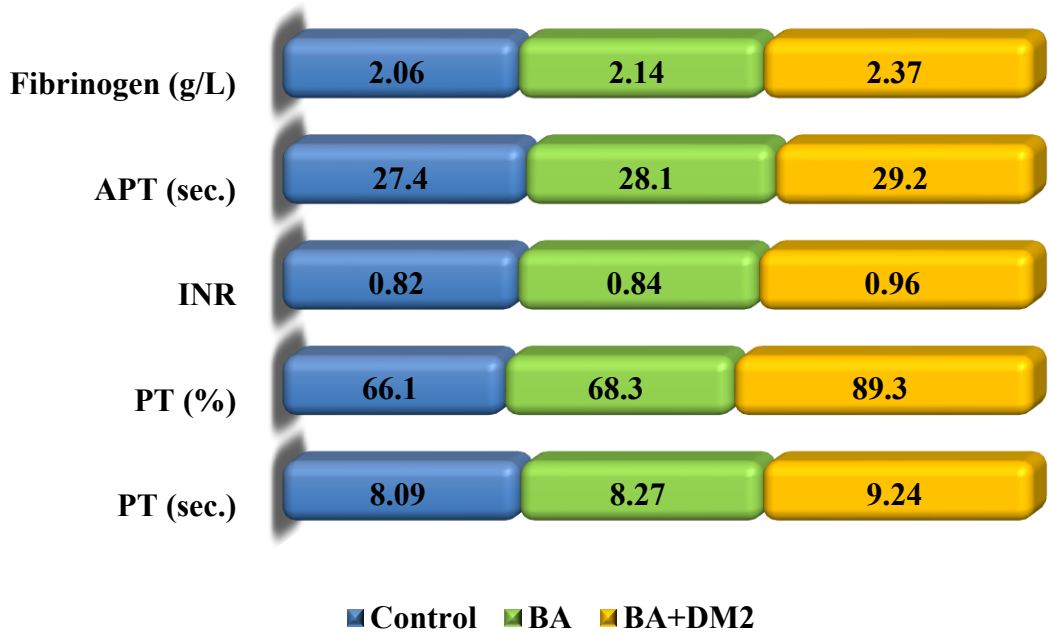

Fig. 5. Analysis of the coagulogram in the examined groups

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A comparative analysis of hemostasis parameters revealed that the prothrombin time (PT) in patients with bronchial asthma and type 2 diabetes was 9.24 sec, which exceeded the value in the control group (8.09 sec) by approximately 1.14 times and the group with isolated bronchial asthma (8.27 sec) by 1.12 times ($p < 0.05$). The prothrombin index (PTI) in patients with combined pathology was significantly higher (89.3%) compared to the control group (66.1%) — by 1.35 times and the bronchial asthma group (68.3%) — by 1.31 times ($p < 0.01$), indicating activation of the prothrombin component of hemostasis. The international normalized ratio (INR) values in patients with BA+DM2 were 0.96, exceeding the control values (0.82) by 1.17 times and the BA group values (0.84) by 1.14 times ($p < 0.05$). The activated partial thromboplastin time (APTT) also tended to increase (29.2 s versus 27.4 s in the control and 28.1 s in BA), but the differences did not reach statistical significance. The fibrinogen concentration in BA+DM2 was 2.37 g/L, which was 1.15 times higher than the control values (2.06 g/L) and 1.11 times higher than the BA value (2.14 g/L) ($p < 0.05$) (Fig. 5). The data collected indicate increased activity of the coagulation component of hemostasis in the combination of bronchial asthma and type 2 diabetes mellitus, which may reflect increased inflammatory-thrombotic processes and an increased risk of vascular complications.

To better understand the pathogenesis of bronchial asthma, both in isolation and in combination with type 2 diabetes mellitus, an analysis of immunobiochemical parameters was conducted. Both diseases are known to be accompanied by chronic inflammation and metabolic disorders; however, the nature and extent of immune shifts associated with these conditions remain poorly understood. Assessing the activity of immunobiochemical factors allows us to identify the relationship between the metabolic and inflammatory components of the pathological process [5, 11]. Of particular interest is the identification of markers reflecting disturbances in the hemostatic system and oxidative stress, which is important for assessing the severity and prognosis of the disease. Analysis of the obtained data allows us to identify key differences in immunobiochemical reactions in patients with different asthma courses.

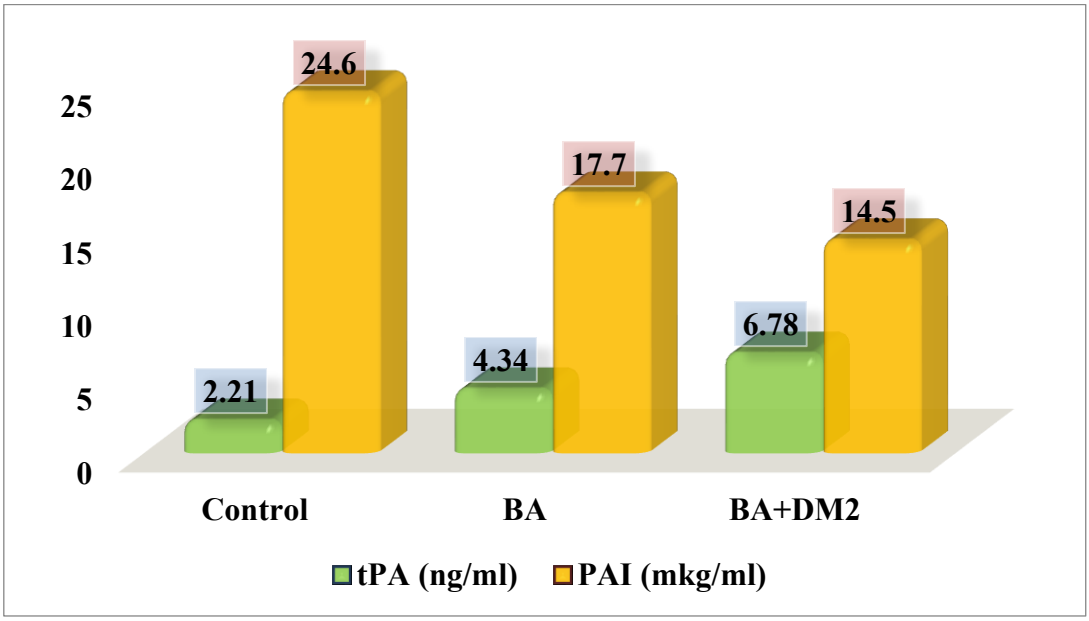

Fig. 6. Level of hemostasis markers in the examined groups, (P ≤0.05)

Tissue plasminogen activator (tPA) is a key enzyme initiating the conversion of plasminogen to plasmin and ensuring fibrinolysis [13]. An increase in its level reflects compensatory activation of the fibrinolytic component with increased intravascular coagulation and inflammation. In the present study, the tPA concentration in patients with isolated bronchial asthma was 4.34 ± 0.52 ng/ml, which was approximately 1.96 times higher than the control group (2.21 ± 0.36 ng/ml) ($p < 0.01$). In patients with a combination of bronchial asthma and type 2 diabetes mellitus, the tPA level reached 6.78 ± 0.71 ng/ml, which is 3.1 times higher than the control values and exceeded the BA group indicator by 1.56 times ($p < 0.001$).

Plasminogen activator inhibitor (PAI-1) is the main regulator of fibrinolysis, suppressing the activity of tPA and preventing the dissolution of fibrin clots [8]. In patients of the control group, the average level of PAI-1 was 24.6 ± 2.1 μg/ml, in isolated BA it decreased to 17.7 ± 1.8 μg/ml, which is 1.4 times lower than the norm, and in the combined course of BA + T2DM it decreased to 14.5 ± 1.6 μg/ml, which is 1.7 times lower than the control values and 1.2 times lower than the BA group ($p < 0.05$) (Fig. 6).

The identified changes indicate an imbalance in the fibrinolytic system in patients with asthma and type 2 diabetes. Increased tPA levels in the presence of decreased PAI-1 levels may reflect a compensatory response to chronic inflammation and tissue hypoxia, leading to endothelial cell activation. At the same time, excessive fibrinolytic activity may be accompanied by microvascular damage and worsening inflammation, which collectively increases the clinical severity of the disease in patients with comorbidities.

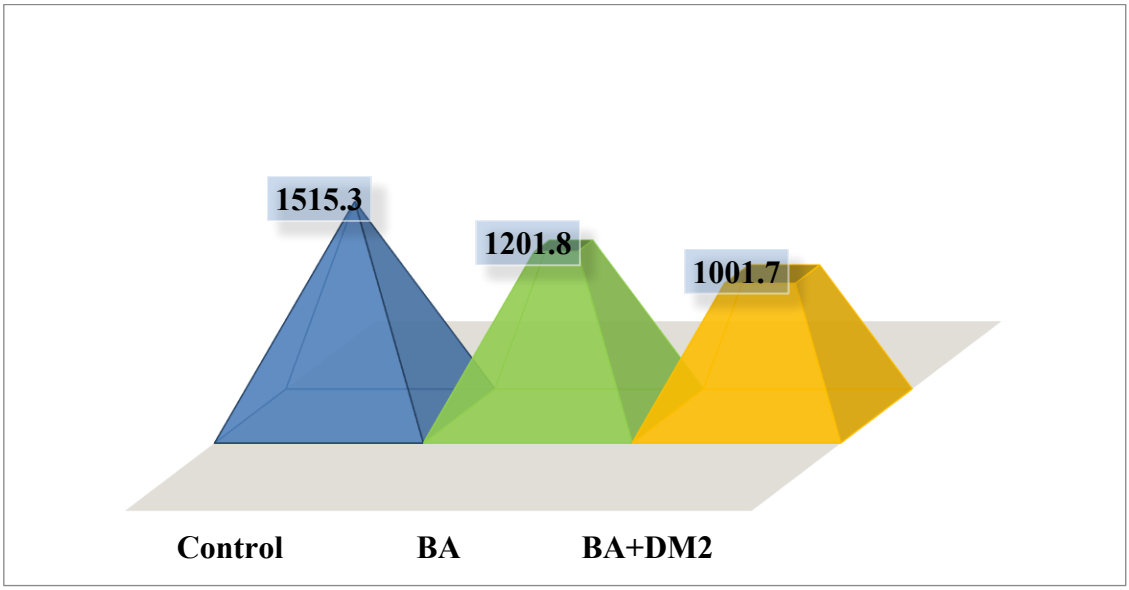

Fig. 7. Superoxide dismutase level in examined patients (pg/ml)

Superoxide dismutase (SOD) is a key enzyme in the first line of antioxidant defense, catalyzing the dismutation of superoxide anion radical into hydrogen peroxide and molecular oxygen. A decrease in its activity reflects depletion of the antioxidant system and increased oxidative stress, which is important in chronic inflammatory diseases such as asthma and type 2 diabetes. In patients with asthma, this indicator decreased to 1201.8 ± 115.6 conventional units, which

is approximately 1.26 times lower than the control value, indicating the development of moderate oxidative stress due to chronic airway inflammation. In patients with both asthma and type 2 diabetes, the enzyme activity was even lower—1001.7 ± 108.9 conventional units. units, which is 1.51 times lower than the control level and 1.2 times lower than the isolated asthma indicator ($p < 0.05$) (Fig. 7).

The data obtained indicate a significant suppression of antioxidant defense in comorbid conditions, which can be explained by the combined effects of hyperglycemia, activation of lipid peroxidation, and chronic systemic inflammation. These factors lead to an overload of antioxidant enzyme systems and, consequently, a decrease in SOD activity, which increases damage to cellular structures and worsens the course of the disease.

Discussion of the obtained results

The study confirmed the presence of significant clinical, laboratory, and immunobiochemical differences between patients with isolated bronchial asthma (BA) and patients with a combination of bronchial asthma and type 2 diabetes mellitus (BA + T2DM). The obtained data are consistent with the observation that patients with BA have increased systemic oxidative stress and decreased antioxidant defense (Sahiner, Birben, Erzurum et al., 2011). A higher frequency of shortness of breath, weakness, sweating, and signs of respiratory failure in the BA + T2DM group confirms the data that diabetes and carbohydrate metabolism disorders aggravate the course of BA through metabolic and vascular mechanisms (Al-Beltagi, 2025). The increased incidence of complications, including pulmonary hypertension and chronic heart failure, reflects the relationship between endothelial dysfunction, hyperglycemia, and inflammation, as also noted in the literature (Badran, 2022). Laboratory parameters demonstrated a significant disruption of carbohydrate metabolism in patients with asthma and type 2 diabetes—an increase in HbA1c and blood glucose, consistent with data on the impact of chronic inflammation and diabetes on the course of asthma (Fernando, 2020). Concurrently, an increase in fibrinogen and activation of hemostasis were noted, which are part of the complex metabolic changes in diabetes and metabolic syndrome (Al-Hamodi, 2011).

Immunobiochemical analysis revealed a significant decrease in superoxide dismutase (SOD) activity in patients, especially in the comorbid group, consistent with data on weak antioxidant defenses in asthma (Bazan-Socha et al., 2022). Changes in the fibrinolytic system were also recorded—increased tPA levels and decreased PAI-1—indicating a hemostatic imbalance and supported by data on diabetes (Altalhi, 2021).

Conclusion:

Thus, patients with comorbid asthma and type 2 diabetes mellitus exhibit significantly more pronounced clinical manifestations, hyperglycemia, hypercoagulability shifts, and decreased antioxidant enzyme activity compared to patients with isolated asthma. A comparison with literature data confirms the key role of chronic systemic inflammation and oxidative stress in the development of this comorbidity. The established patterns suggest that antioxidant and

hemostatic markers can be considered promising diagnostic criteria for assessing disease severity and monitoring treatment effectiveness.

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