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CLINICAL AND IMMUNOBIOCHEMICAL PREDICTORS IN THE DIAGNOSIS OF BRONCHIAL ASTHMA IN COMORBIDITY WITH TYPE 2 DIABETES MELLITUS

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Abstract

The aim of this study was to perform a comprehensive evaluation of 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, hemostatic system indices, and antioxidant defense was carried out. It was found that superoxide dismutase (SOD) activity in patients with comorbid pathology decreased to 1001.7 ± 75.4 pg/mL, which was 1.5 times lower than in the group with isolated bronchial asthma (1201.8 ± 68.2 pg/mL) ($p < 0.05$), indicating pronounced oxidative stress. At the same time, a significant increase in MMP-9 levels was observed: in BA patients it was 120.7 ± 2.25 ng/mL, while in patients with BA combined with T2DM it increased to 175.3 ± 3.23 ng/mL, exceeding control values (31.5 ± 1.23 ng/mL) by more than 5 times and those of isolated asthma by 1.45 times ($p < 0.05$). These findings indicate an important role of inflammatory and tissue remodeling processes in the pathogenesis of comorbid conditions. The obtained data confirm that metabolic and immunobiochemical alterations significantly contribute to the development of combined BA and T2DM and may be useful for improving early diagnosis and prognostic assessment.

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Keywords: bronchial asthma, type 2 diabetes mellitus, MMP-9, immunobiochemical markers, superoxide dismutase, oxidative stress, diagnostics.

КЛИНИЧЕСКИЕ И ИММУНОБИОХИМИЧЕСКИЕ ПРЕДИКТОРЫ В ДИАГНОСТИКЕ БРОНХИАЛЬНОЙ АСТМЫ ПРИ СОПУТСТВИИ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

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Резюме:

Целью настоящего исследования явилась комплексная оценка клинико-лабораторных и иммунобиохимических показателей у пациентов с бронхиальной астмой при её сочетании с сахарным диабетом 2 типа. Проведён сравнительный анализ клинической симптоматики, параметров углеводного обмена, системы гемостаза и антиоксидантной защиты. Установлено, что активность супероксиддисмутазы у больных с коморбидной патологией снижалась до 1001,7 ± 75,4 пг/мл, что в 1,5 раза ниже по сравнению с группой изолированной бронхиальной астмы (1201,8 ± 68,2 пг/мл) ($p < 0,05$), отражая выраженное усиление окислительного стресса. Одновременно выявлено достоверное повышение уровня MMP-9: при БА он составлял 120,7 ± 2,25 ng/mL, тогда как при сочетании БА с СД2 увеличивался до 175,3 ± 3,23 ng/mL, превышая контрольные значения (31,5 ± 1,23 ng/mL) более чем в 5 раз и показатели изолированной астмы — в 1,45 раза ($p < 0,05$). Полученные результаты свидетельствуют о значимой роли воспалительно-деструктивных процессов и ремоделирования тканей в формировании коморбидной патологии. Совокупность выявленных изменений подтверждает участие метаболических и иммунобиохимических

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нарушений в патогенезе сочетанного течения бронхиальной астмы и сахарного диабета 2 типа и может быть использована для совершенствования ранней диагностики и прогностической оценки заболевания.

Ключевые слова: бронхиальная астма, сахарный диабет 2 типа, MMP-9, иммунобиохимические маркеры, супероксиддисмутаза, оксидативный стресс, диагностика.

According to analytical data from the World Health Organization, bronchial asthma and type 2 diabetes mellitus are among the most significant chronic noncommunicable diseases, significantly impacting morbidity, disability, and mortality. Both conditions are widespread worldwide and are characterized by a steady upward trend, making them highly medical and socially significant. In recent years, an increase in the frequency of their comorbidity has been observed, which is associated with the presence of common risk factors, including obesity, physical inactivity, and chronic systemic inflammation. The comorbidity of these pathologies is accompanied by a more severe clinical course, increased exacerbations, and decreased effectiveness of standard therapy. Therefore, there is a growing need for a more in-depth study of the mechanisms of their interactions and the search for new diagnostic approaches [2, 7, 9, 15].

Modern research confirms that asthma and type 2 diabetes share common pathogenesis, rooted in chronic inflammation and metabolic disturbances. Impaired carbohydrate metabolism is accompanied by increased oxidative stress, activation of proinflammatory cytokines, and microcirculatory changes, all of which contribute to increased bronchial hyperreactivity. In turn, prolonged inflammation in the airways can contribute to the progression of insulin resistance, creating a mutually aggravating pathological process. These changes are accompanied by the development of endothelial dysfunction and an

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imbalance in the antioxidant system. Overall, a unified pathogenetic platform is emerging, uniting metabolic and inflammatory mechanisms [1, 3, 8, 14].

The immunological characteristics of the comorbidity of bronchial asthma and type 2 diabetes mellitus remain poorly understood and require further analysis. Of particular interest are changes in the levels of cytokines, immunoglobulins, and systemic inflammatory markers, reflecting the degree of immune imbalance. The scientific literature provides limited data characterizing the relationship between the activation of cellular and humoral immunity and the severity of clinical manifestations of the disease. Insufficient knowledge of immunobiochemical parameters complicates differential diagnosis and prognosis assessment in this patient population. This necessitates further research aimed at clarifying the immunopathogenetic mechanisms underlying the comorbid process [4, 6, 10, 12].

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 83 patients aged 24 to 65 years, including 36 patients with combined asthma and type 2 diabetes (the study group), and 47 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

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studies included determination of glucose levels, glycosylated hemoglobin (HbA1c), and superoxide dismutase (COD).

Immunological studies were conducted to determine the content of MMP-9, as well as the activity of superoxide dismutase (SOD) in the blood serum using the ElisaKid test systems (China).

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

Research Results

A comparative analysis of the age characteristics of the examined patients revealed significant differences between the study groups. Among those with bronchial asthma, the average age was 36.1 ± 1.8 years, reflecting a predominantly younger patient population. In the group with combined asthma and type 2 diabetes mellitus, this figure was significantly higher, reaching 45.7 ± 2.3 years. This difference may indicate a later onset of comorbid pathology due to metabolic disorders (Fig. 1).

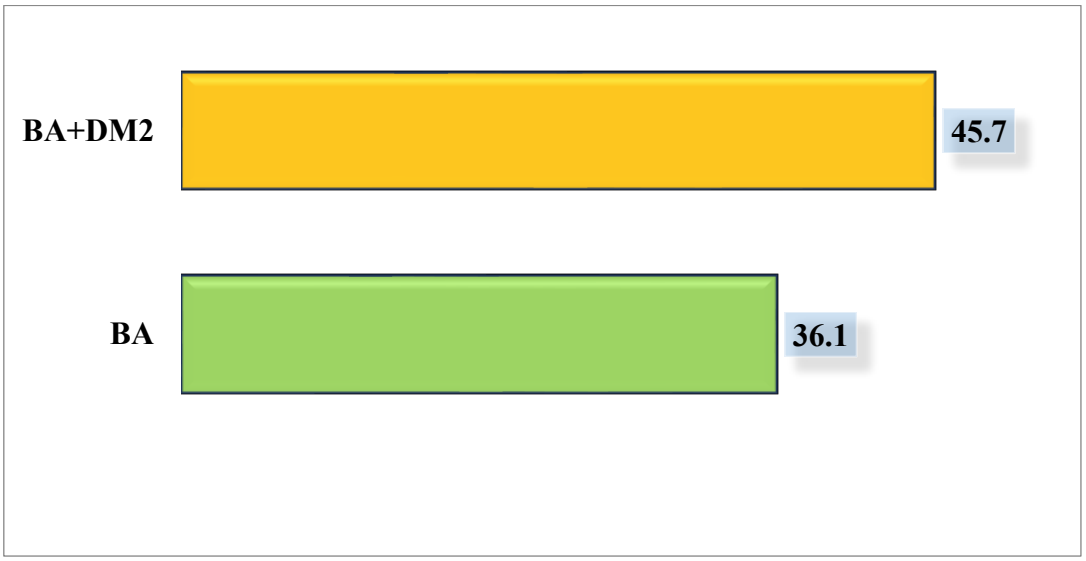

Fig. 1. Average age of the examined patients, (M±m)

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An analysis of the gender distribution of the patients examined revealed differences in gender distribution between the study groups. In the group with isolated asthma, women predominated, accounting for 61.7%, while men were represented in smaller numbers—38.3%. When asthma was combined with type 2 diabetes, this proportion shifted: the proportion of men increased to 42.3%, while the proportion of women decreased to 57.7%. Despite the continued female predominance in both groups, a trend toward a relative increase in the number of men was observed in the presence of comorbid pathology (Fig. 2).

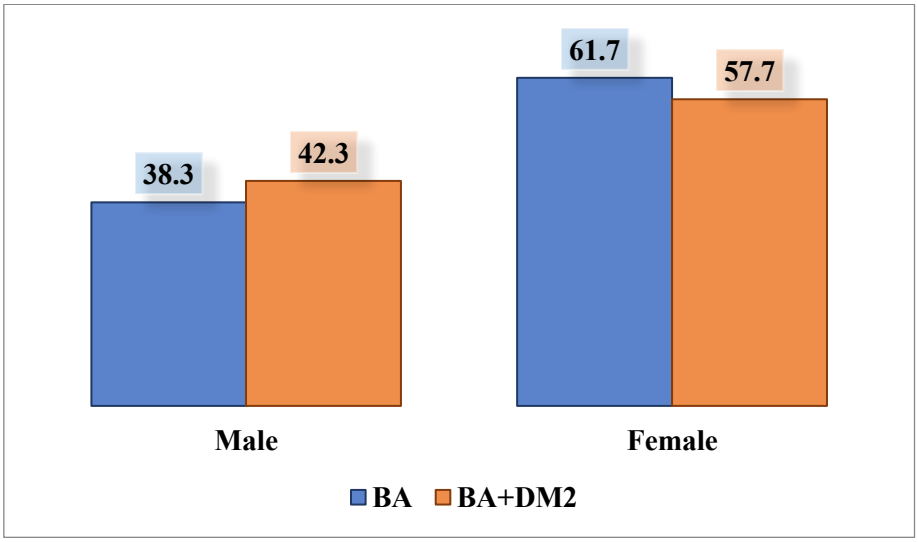

Fig. 2. Gender distribution of the surveyed groups, (%)

An assessment of disease duration revealed significant differences between the study groups. In patients with isolated asthma, the average disease duration was 16.7 ± 1.9 years, indicating a long-term chronic course of the pathology. In the group with a combination of bronchial asthma and type 2 diabetes mellitus, this indicator was significantly lower and equaled 7.5 ± 1.3 years. It was found that the disease duration in the first group was more than twice as long as in patients with comorbid pathology, and the differences were statistically significant ($p < 0.05$). These identified differences may indicate a later onset of type 2 diabetes

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mellitus in patients with bronchial asthma and the development of a comorbid condition at a certain stage of the disease. (Fig. 3).

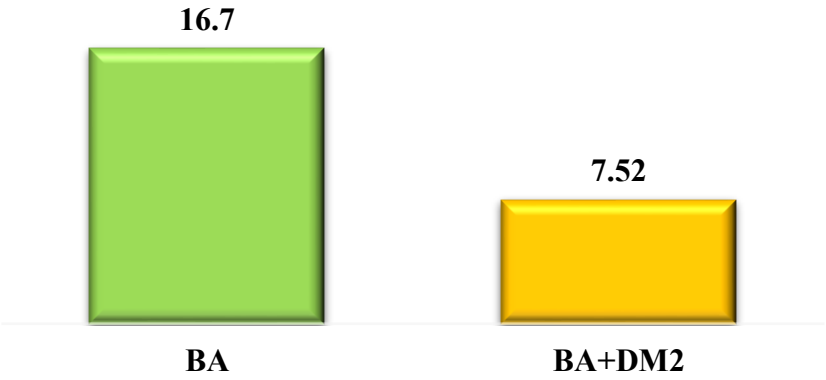

Fig. 3. Duration of illness in the examined groups, (M±m), (P ≤0.05)

A comparative assessment of the frequency of the main clinical complaints in the examined patients demonstrated significant differences between the groups with isolated asthma and its combination with type 2 diabetes mellitus. Patients with comorbid pathology significantly more often reported symptoms such as shortness of breath, pale skin, general weakness, and, in particular, increased sweating, indicating more pronounced systemic disorders and involvement of the autonomic nervous system ($p < 0.05$). The incidence of cyanosis of the nasolabial triangle and chest pain was also somewhat higher in the comorbidity group. At the same time, decreased appetite was slightly more often observed in patients with isolated bronchial asthma, which may be due to the characteristics of the inflammatory process and the impact of the therapy (Fig. 4). The obtained results indicate a more severe and systemically burdened nature of the clinical picture in the combination of bronchial asthma with type 2 diabetes mellitus, reflecting the complex metabolic and neurovegetative effects of the disease.

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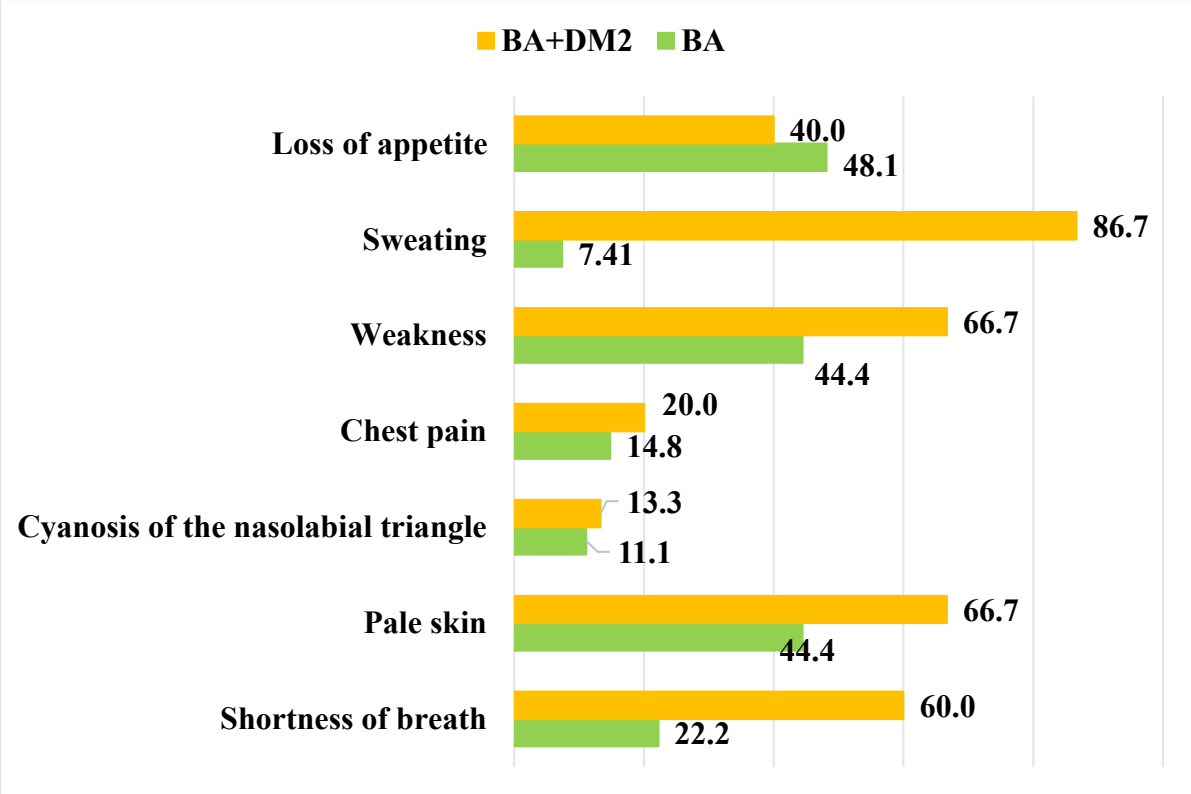

Fig. 4. Clinical symptoms and complaints of the examined groups, (%), (P ≤0.05)

An analysis of the comorbidity profile revealed that patients with both asthma and type 2 diabetes mellitus had a higher prevalence of chronic diseases compared to those with isolated asthma. The most significant differences were found in the incidence of coronary heart disease (46.7% versus 25.9%) and arterial hypertension (26.7% versus 14.8%), indicating a close relationship between metabolic disorders and cardiovascular disease. The incidence of gastrointestinal diseases and anemia was also higher in the comorbidity group (33.3% versus 26.7%) compared to patients without diabetes mellitus (22.2% versus 11.1%), reflecting more pronounced metabolic and hemodynamic

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disturbances. ENT pathologies were recorded with a high frequency in both groups (73.3% in patients with asthma and type 2 diabetes mellitus and 70.4% in patients with asthma alone), without demonstrating significant differences. Other endocrine disorders, including various forms of goiter, were relatively rare but were detected somewhat more frequently in patients with combined pathology (13.3% versus 7.4%). Overall, the obtained data confirm that the addition of type 2 diabetes mellitus to asthma is accompanied by an increased frequency and severity of associated somatic diseases, primarily cardiovascular ones.

A comparative assessment of the complication rate demonstrated a more severe course of the disease in patients with comorbid pathology. Thus, respiratory failure was detected in 53.3% of patients with a combination of bronchial asthma and type 2 diabetes, while with isolated bronchial asthma - in 37.0%, which is approximately 1.4 times higher. The frequency of pulmonary hypertension in the comorbid course was 26.7%, which is 1.8 times higher compared to the bronchial asthma group (14.8%, $p < 0.05$). Pulmonary emphysema was registered somewhat more often in patients with combined pathology (13.3% versus 11.1%), but the differences did not reach statistical significance. A significantly higher prevalence was noted for chronic heart failure - 46.7% versus 25.9%, which also corresponds to an increase of almost 1.8 times ($p < 0.05$). The obtained results indicate a more pronounced systemic nature of the pathological process in the combination of bronchial asthma and type 2 diabetes mellitus, caused by the combined influence of metabolic and inflammatory mechanisms on the respiratory and cardiovascular systems.

Table 1 Carbohydrate metabolism indicators in the examined groups

Indicator	Control (n=20)	BA (n=47)	BA + T2DM (n=36)
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

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A comparative assessment of carbohydrate metabolism parameters revealed significant differences between the study groups. In patients with a combination of bronchial asthma and type 2 diabetes mellitus, the glycated hemoglobin (HbA1c) level was 8.44±0.91%, which was approximately 1.6 times higher than the control group (5.31±0.4%) and 1.4 times higher than the values in patients with isolated bronchial asthma (5.94±0.6%) ($p<0.001$). A similar trend was observed in the blood glucose level analysis: in patients with comorbid pathology, it reached 8.13 ± 1.27 mmol/L, which was 1.7 times higher than the control values (4.82 ± 0.5 mmol/L) and 1.45 times higher than the values in the group with bronchial asthma (5.61 ± 0.7 mmol/L) ($p < 0.001$) (Table 1). The identified differences indicate significant carbohydrate metabolism disorders in patients with comorbid pathology. The obtained results confirm the significant role of metabolic decompensation in the development of a more severe clinical course of the disease.

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 disturbances; 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]. Analysis of the obtained data allows us to identify key differences in immunobiochemical reactions in patients with different asthma patterns.

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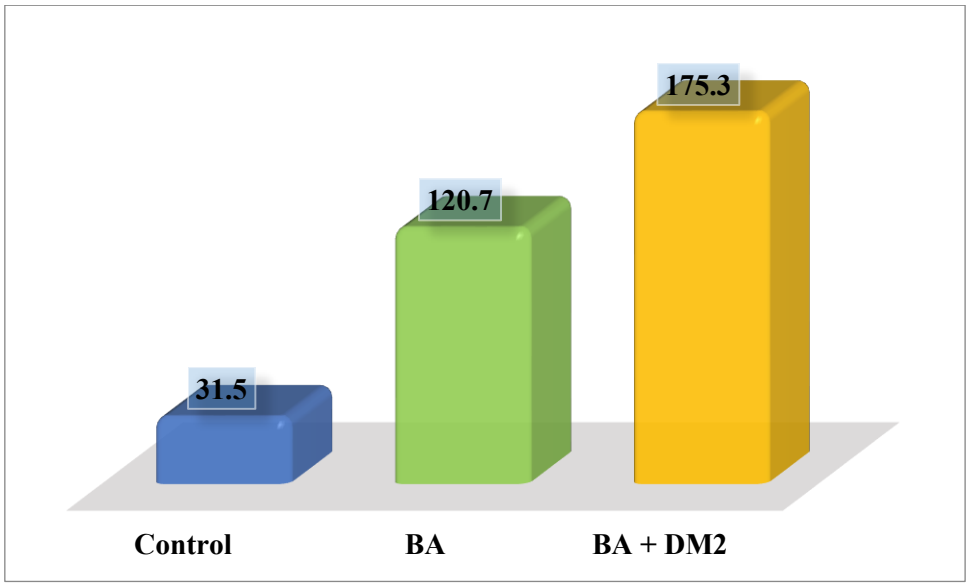

Fig. 6. Metalloproteinase level 9 at examined groups, (ng/mL)

A comparative analysis of MMP-9 levels revealed significant intergroup differences. In the control group, this indicator was 31.5 ± 1.23 ng/mL, while in patients with bronchial asthma, it increased to 120.7 ± 2.25 ng/mL, which is more than 3.8 times higher than the control value. In patients with bronchial asthma and type 2 diabetes mellitus, the MMP-9 level reached 175.3 ± 3.23 ng/mL, which is approximately 5.6 times higher than the control value and 1.45 times higher than the BA group. The obtained data indicate significant activation of matrix remodeling and inflammation processes in patients with asthma. Moreover, maximum marker values are observed in comorbid pathology, indicating an intensification of the pathological process.

The observed increase in MMP-9 levels in patients with asthma and type 2 diabetes mellitus reflects the synergistic effects of chronic inflammation and metabolic disturbances. MMP-9 is known to be involved in extracellular matrix degradation, contributing to airway remodeling and the progression of airflow obstruction. An additional increase in its concentration in the presence of diabetes

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mellitus may be associated with activation of the AGE-RAGE signaling pathway and increased oxidative stress, leading to more severe tissue damage and the maintenance of chronic inflammation. Overall, MMP-9 can be considered an important pathogenetic marker reflecting the severity and systemic nature of the disease in comorbid conditions (Fig. 6).

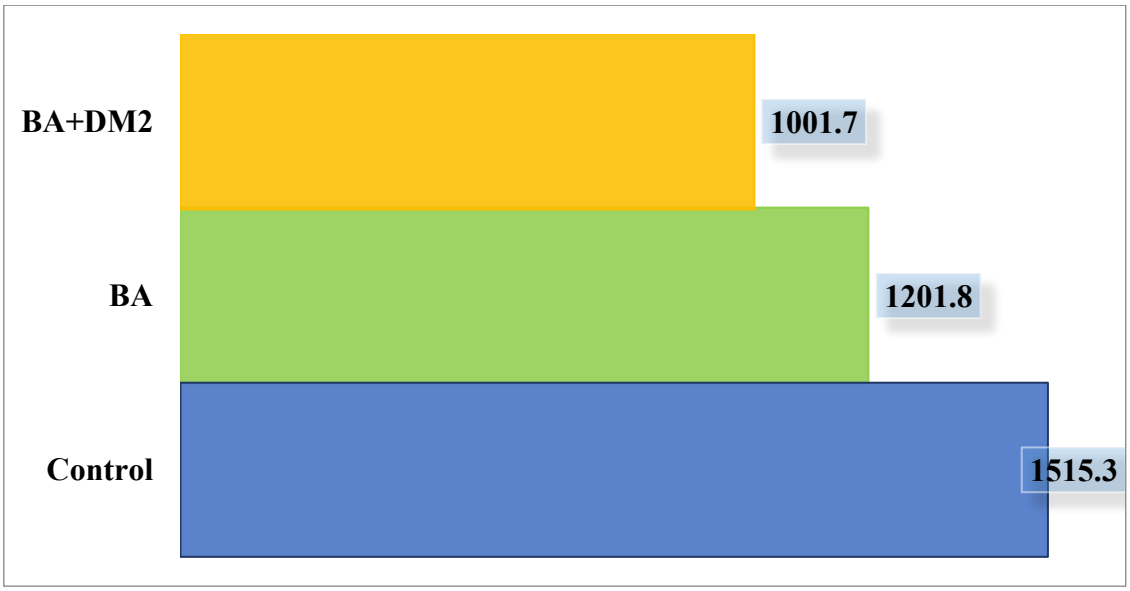

Fig. 7. Superoxide dismutase level in examined patients (pg/ml)

Superoxide dismutase (SOD) is considered a key enzyme in the primary antioxidant defense, neutralizing the superoxide anion radical by converting it into hydrogen peroxide and molecular oxygen. Decreased activity of this enzyme reflects an imbalance between prooxidant and antioxidant mechanisms and indicates increased oxidative stress, which is particularly important in chronic inflammatory and metabolic diseases, including bronchial asthma and type 2 diabetes. In patients with bronchial asthma, SOD levels decreased to 1201.8 ± 115.6 conventional units, which is approximately 1.26 times lower than control values, indicating the development of moderate oxidative stress against the background of chronic airway inflammation. In the group with a combination of bronchial asthma and type 2 diabetes mellitus, enzyme activity decreased even

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more significantly—to 1001.7 ± 108.9 conventional units, which is 1.51 times lower than the control level and 1.2 times lower than the values for isolated asthma ($p < 0.05$). These results indicate progressive depletion of the antioxidant system in comorbid conditions and increased oxidative tissue damage (Fig. 7).

The obtained data indicate a pronounced suppression of antioxidant protection in combined pathology, which can be explained by the combined effect of hyperglycemia, activation of lipid peroxidation and chronic systemic inflammation.

Discussion of the Obtained Results

The study revealed significant clinical, laboratory, and immunobiochemical differences between patients with isolated asthma and those with type 2 diabetes mellitus. The findings confirm that asthma is associated with significant systemic oxidative stress, accompanied by a decrease in the body's antioxidant capacity, consistent with data from several authors (Sahiner, Birben, Erzurum et al., 2021). Patients with comorbid conditions had a higher incidence of clinical manifestations, including shortness of breath, general weakness, increased sweating, and signs of respiratory failure, indicating a more severe course of the disease. These observations are consistent with current understanding that carbohydrate metabolism disorders in diabetes mellitus contribute to the progression of asthma through metabolic and vascular mechanisms (Al-Beltagi, 2025). The increased incidence of complications such as pulmonary hypertension and chronic heart failure reflects the influence of hyperglycemia, endothelial dysfunction and chronic inflammation, which is also supported by literature (Badran, 2022).

Laboratory analysis revealed significant carbohydrate metabolism disturbances in patients with bronchial asthma and type 2 diabetes mellitus, manifested by elevated HbA1c and blood glucose levels, consistent with the results of other studies (Fernando, 2020). Additionally, increased fibrinogen levels and activation

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of the hemostatic system were noted, which are characteristic components of metabolic changes in diabetes and metabolic syndrome (Al-Hamodi, 2021). Immunobiochemical analysis revealed a significant decrease in superoxide dismutase activity, especially in the comorbidity group, indicating depletion of antioxidant defense and consistent with data on its decline in asthma (Bazan-Socha et al., 2022). A significant increase in matrix metalloproteinase-9 (MMP-9) levels was also observed, most pronounced in patients with bronchial asthma and type 2 diabetes, reflecting increased inflammation and tissue remodeling. The obtained results are consistent with literature data, where MMP-9 is considered a key mediator of extracellular matrix destruction and the progression of bronchial obstruction in asthma (Vignola et al., 2021; Cataldo et al., 2022).

Conclusion

Thus, patients with comorbid asthma and type 2 diabetes mellitus exhibit more pronounced clinical manifestations of the disease, accompanied by significant carbohydrate metabolism disturbances and decreased antioxidant system activity, compared to patients with isolated asthma. The observed hyperglycemia, combined with suppression of the enzymatic antioxidant defense system, indicates the development of a pronounced metabolic-inflammatory imbalance, which exacerbates the pathological process. Against this background, increased MMP-9 levels reflect the activation of extracellular matrix degradation and tissue remodeling, indicating the progression of structural changes in the airways. The identified changes confirm the involvement of this marker in the pathogenesis of comorbid pathology and its association with disease severity.

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