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ASTHMA–CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP: IMMUNOBIOCHEMICAL MARKERS, OXIDATIVE STRESS, KLOTHO PROTEIN AND THEIR ROLE IN OPTIMIZING PULMONARY HYPERTENSION DIAGNOSTICS

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Summary.

The overlap of bronchial asthma and Chronic obstructive pulmonary disease (COPD) is associated with more severe disease progression and earlier onset of pulmonary hypertension (PH), necessitating novel diagnostic approaches.

Objective. *To optimize the diagnosis of pulmonary hypertension in patients with asthma–COPD overlap (ACO) using immunobiochemical markers, oxidative stress parameters, and Klotho protein measurement.*

Materials and Methods. *A total of 120 patients were examined (asthma, n = 45, COPD, n = 50, ACO, n = 25) using clinical, instrumental, and immunobiochemical assessment (IL-4, IL-18, TNFα, VEGF-A, Klotho, SOD).*

Compliance with ethical standards. *Written informed consent was obtained from all patients prior to their participation in the study. All procedures were approved by the Ethics Committee of the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan (Protocol № . 2025-0003) and were conducted in accordance with the principles of the Declaration of Helsinki adopted in October 2024 at the 75th General Assembly of the World Medical Association.*

Statistical analyses were performed using SPSS 26.0. Data are presented as arithmetic mean (M) ± standard deviation (SD) or standard error of the mean (m). Differences were evaluated using Student's t-test and the Mann–Whitney U-test. A p-value < 0.05 was considered statistically significant.

Funding: *This work was carried out within the framework of the research plan of the Bukhara State Medical Institute (05.2022 DSc.135) entitled «Development of new approaches to early diagnosis, treatment, and prevention of pathological conditions affecting the health of the population of the Bukhara region after COVID-19 (2022-2026)», as well as on the basis of baseline funding of the research project of the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan «Immunobiochemical and molecular-genetic diagnostics of the cardiorespiratory system in patients with overlapping bronchial asthma and chronic obstructive pulmonary disease in the experimental setting» (Protocol No. 2, 2024).*

Results. *In ACO patients, mean pulmonary artery pressure was 1.8-fold higher compared with asthma patients (24.0 ± 2.1 vs 13.3 ± 1.7 mmHg, p<0.01). IL-18 levels were 3.4-fold higher than in controls (252.6 ± 12.3 vs 73.8 ± 6.4 pg/mL, p<0.001). Klotho protein concentration in ACO with PH exceeded control values by 6.4-fold (42.3 ± 3.1 vs 6.54 ± 0.72 pg/mL, p<0.001), indicating a compensatory response.*

Conclusion. *The combined clinical and immunobiochemical data confirm the hypothesis that the overlap of bronchial asthma and COPD is associated with the most severe course and rapid development of pulmonary hypertension. Immunobiochemical markers, including cytokine profiles, oxidative stress indicators, and Klotho levels, provide valuable tools for improving the accuracy of diagnosis and prognosis in asthma–COPD overlap patients.*

Keywords: *Asthma; Chronic Obstructive Pulmonary Disease; Overlap; Pulmonary Hypertension; Cytokines; Klotho Protein; Oxidative Stress; Diagnostics.*

Introduction

The overlap of bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD) represents a significant challenge in modern pulmonology. This clinical phenotype combines the features of both conditions and is associated with a more severe course and poorer prognosis. Patients with BA/COPD overlap experience frequent exacerbations, accelerated decline in lung function, and an increased risk of disability [1-4]. Diagnostics is complicated by overlapping clinical and functional characteristics of the diseases. These factors highlight the need for novel biomarkers and methods to assess pathogenesis in order to optimize diagnostics and therapy [5, 6].

Immunobiochemical studies have demonstrated that systemic inflammation, characterized by activation of proinflammatory cytokines, increased oxidative stress, and disruption of the antioxidant system plays a central role in the development of BA/COPD overlap. Oxidative stress contributes to the progression of broncho-obstruction, endothelial injury, and the development of pulmonary hypertension. Recently, the Klotho protein has attracted considerable attention due to its antioxidant, anti-inflammatory, and cytoprotective properties [7-10]. Reduced Klotho levels are associated with impaired lung function, vascular dysfunction, and an increased risk of pulmonary hypertension. Consequently, Klotho measurement may serve as a novel diagnostic and prognostic tool for BA/COPD overlap [11-14].

Pulmonary hypertension in BA/COPD overlap patients arises from chronic inflammation, hypoxia, and endothelial dysfunction. Evaluation of immunobiochemical markers in this context enables early diagnosis and guides the selection of optimal therapy [15-18]. Assessment of cytokine profiles, oxidative stress levels, and Klotho concentration can support risk stratification and facilitate a personalized approach. This strategy can reduce the

incidence of complications and improve the effectiveness of pharmacotherapy [19, 20]. Consequently, investigating the pathogenetic mechanisms of BA/COPD overlap remains a critical task in contemporary medicine.

Objective of the study: To optimize the diagnosis of pulmonary hypertension in patients with bronchial asthma–COPD overlap based on analysis of immunobiochemical markers, assessment of oxidative stress, and Klotho measurement.

Materials and methods of the study

The study included 120 patients treated in the pulmonology and allergology departments of the Bukhara Regional Multidisciplinary Medical Center between 2021 and 2024, divided into three groups: Group I (n = 45) – patients with bronchial asthma (BA); Group II (n = 50) – patients with COPD; Group III (n = 25) – patients with BA/COPD overlap. Inclusion criteria were age 18-70 years and a clinically and instrumentally confirmed diagnosis. Exclusion criteria included oncological diseases, decompensated cardiovascular conditions, and acute infections.

Clinical and functional diagnostics were performed according to GINA and GOLD 2022 recommendations, including spirometry, bronchodilator testing, and echocardiography for pulmonary hypertension assessment. Pulmonary hypertension (PH) severity was classified according to Rybakov M. K., 2008: mean pulmonary artery pressure (MPAP) of 20-40 mmHg indicated moderate PH, 40-60 mmHg – significant PH, and >60 mmHg – severe PH.

Immunobiochemical analyses included measurement of IL-4, IL-18, TNF-α, VEGF-A, Klotho, and superoxide dismutase (SOD) levels.

Cytokines and Klotho protein in blood serum were measured using a three-stage «sandwich» ELISA method with Vector-Best reagents (Novosibirsk, Russian Federation).

Statistical analyses were performed using SPSS 26.0. Data are presented as arithmetic mean (M) ± standard deviation (SD) or standard error of the mean (m). Differences were evaluated using Student's t-test and the Mann–Whitney U-test. A p-value < 0.05 was considered statistically significant.

Compliance with ethical standards. Written informed consent was obtained from all patients prior to their participation in the study. All procedures were approved by the Ethics Committee of the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan (Protocol №. 2025-0003) and were conducted in accordance with the principles of the Declaration of Helsinki adopted in October 2024 at the 75th General Assembly of the World Medical Association.

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Results of the study

The mean age of patients with bronchial asthma was 41.2 ± 2.4 years, which was significantly lower by a factor of 1.17 compared with patients with COPD (48.3 ± 2.1 years). Comparison between the BA group and the BA/COPD overlap group, where the mean age was 53.4 ± 2.6 years, showed that patients with overlap were 1.30 times older than those with BA and, on average, 1.11 times older than those in the COPD group.

Analysis of gender distribution revealed a predominance of females in the BA and overlap groups, whereas a higher proportion of males was observed in the COPD group. This pattern may be associated with higher smoking prevalence among men (Fig. 1).

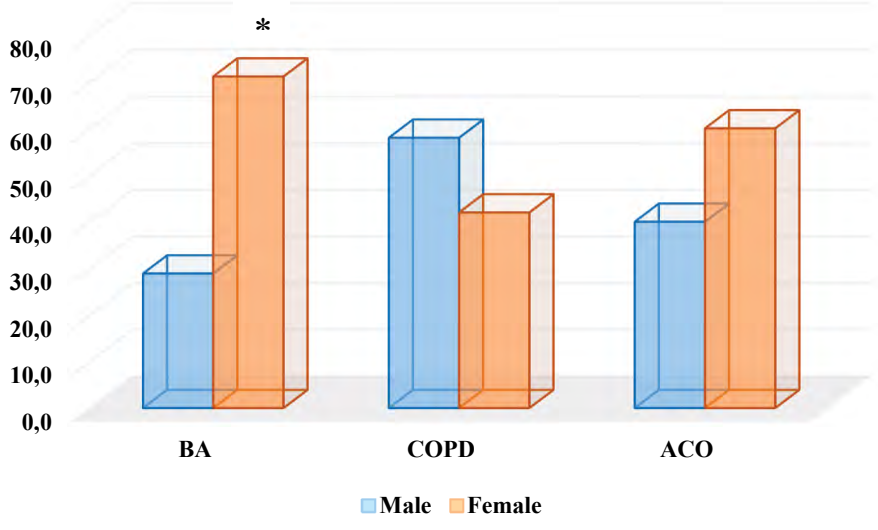

Fig. 1. Gender distribution of patient groups (%), (*P≤0.05)

The duration of the disease in BA patients was 15.2 ± 1.4 years, which was 1.74 times higher ($p < 0.05$) than in the COPD group (8.71 ± 0.9 years) and 2.08 times ($p<0.001$) higher in the BA /COPD overlap group (7.32 ± 0.8 years), indicating a longer course of asthma compared with other phenotypes.

Analysis of complaints revealed that in patients with BA/COPD overlap, the frequency of dyspnea was 72.0%, 1.70 times higher than in BA (42.2%, $p<0.05$) and slightly higher than in COPD (68.0%, 1.06 times). Skin pallor in the ACO group was observed in 64.0%, exceededing BA by 1.20 times (53.3%) but not significantly different from COPD (62.0%). Cyanosis of the nasolabial triangle was 2.05 times more frequent than in BA (64.0% versus 31.1%, $p<0.05$), and 1.14 times more frequent than in COPD (56.0%). Chest pain in patients with decussation was observed in 52.0%, 3.33 times more frequent than in BA (15.6%, $p<0.001$) and 1.37 times more frequent than in COPD (38.0%). Complaints of weakness were noted in 68.0% of ACO patients, 2.79 times higher than in BA (24.4%, $p<0.001$) and 1.09 times higher than in COPD (62.0%). Sweating was observed 4.95 times more often than in BA (44.0% versus 8.89%, $p<0.001$) and 1.47 times more often than in COPD (30.0%). Appetite decrease was most pronounced in ACO (80.0%), 2.25 times higher than in BA (35.6%, $p<0.001$) and 1.60 times higher than in COPD (50.0%, $p<0.05$).

Analysis of concomitant pathology in patients with overlapping asthma and COPD revealed that the frequency of concomitant hypertension (HT) reached 68.0%, 4.36 times higher than in BA (15.6%, $p<0.001$) and 1.31 times higher than in COPD (52.0%). Coronary heart disease (CHD) was also observed predominantly in BA (68.0%), 2.04 times more common than in asthma (33.3%, $p<0.01$) and 1.48 times more common than in COPD (46.0%). Gastrointestinal diseases were identified in 44.0% of ACO patients, exceeding BA by 1.98 times (22.2%, $p<0.05$) and COPD by 1.16 times (38.0%). ENT pathology was more common in BA (66.7%) and ACO (60.0%), whereas in COPD it was significantly less frequent (46.0%). Anemia in overlap patients was detected 2.31 times more often than in BA (36.0% versus 15.6%, $p<0.01$), and 1.20 times more often than in COPD (30.0%). Among endocrine disorders, prevalence was highest in COPD (38.0%), 2.44 times higher than in BA (15.6%), while ACO patients had an intermediate rate (28.0%). The smoking factor was of particular importance: it was present in the majority of ACO and COPD patients (84.0%), 12.6 times higher than in BA (6.67%, $p < 0.001$), confirming its key role in the pathogenesis of COPD and bronchial asthma overlap.

In patients with BA/COPD overlap, complications were detected significantly more often than in isolated forms of the diseases. Thus, respiratory failure in BA/COPD overlap occurred in 80.0%, 2.00 times more frequently than in BA (40.0%, $p<0.001$), and 1.54 times more frequently than in COPD (52.0%, $p<0.05$).

Cardiovascular pathology deserves particular attention: pulmonary heart disease was most pronounced in ACO (68.0%), 4.36 times higher than in BA (15.6%, $p<0.001$), and 1.36 times higher than in COPD (50.0%). Chronic heart failure (CHF) was recorded in 76.0% of COPD patients, 2.44 times higher than in BA (31.1%, $p<0.001$), while in ACO its frequency was 56.0%, occupying an intermediate position relative to BA. It is noteworthy that radiographic signs of emphysema were more often recorded in COPD (68.0%), minimal in BA (13.3%, 5.11 times less, $p<0.001$), and 52.0% in ACO, indicating pronounced remodeling of lung tissue. These results demonstrate that in BA/COPD overlap, complications develop more frequently than in isolated BA, with cardiovascular pathology (pulmonary heart disease and CHF) acting as the leading component in the clinical picture.

Next, we analyzed echocardiographic data of the right heart in the examined patient groups. Mean pulmonary artery pressure was lowest in the control group (10.0 ± 0.61 mm Hg) and patients with BA (13.3 ± 0.72 mm Hg), whereas in COPD (26.0 ± 1.21 mm Hg) and ACO (24.0 ± 1.13 mm Hg) it increased by 1.95 and 1.80 times compared with BA ($p < 0.05$), reflecting the development of pulmonary hypertension. Pulmonary artery diameter in COPD patients (26.0 ± 0.81 mm) was 1.32 times higher than in the control group (20.0 ± 0.52 mm) and 1.17 times higher than in BA (22.2 ± 0.63 mm). In ACO (24.0 ± 0.72 mm), expansion was also observed compared to the control (1.21 times). Right atrial dimensions showed similar changes: height in COPD and ACO (44.0 ± 1.22 mm) exceeded the control (40.0 ± 1.00 mm) by 1.12 times. The transverse dimension was highest in COPD (34.0 ± 1.01 mm), 1.17 times greater than in BA (28.9 ± 0.62 mm) and 1.13 times greater than in the control (30.0 ± 0.71 mm). The parasternal dimension of the right ventricle in COPD (30.0 ± 1.0 mm) was 1.2 times larger than in the control (25.0 ± 0.62 mm), and the apical dimension increased to 38.0 ± 1.17 mm versus 35.0 ± 0.94 mm in the control (1.09 times). Interestingly, right ventricular wall thickness decreased: in COPD and ACO (4.01 ± 0.24 mm), it was 1.25 times lower than the control (5.02 ± 0.34 mm), indicating dystrophic myocardial changes due to chronic overload (Fig. 2).

Thus, the most pronounced structural and functional changes in the right heart and signs of pulmonary hypertension were detected in COPD (46%, n=23) and ACO (56%, n=14), whereas in BA (28.9% n=13) these changes were minimal.

The next stage of our research was to conduct an immunological examination of the patient groups.

Cytokine profile analysis showed that the IL-4 levels in the BA group (25.3 ± 1.21 pg/mL) were significantly higher than in the control values (9.36 ± 0.62 pg/mL) by 2.7 times ($p<0.001$), and in BA complicated by pulmonary hypertension (29.3 ± 1.43 pg/mL); they further increased by 1.16 times compared to BA without complications. This reflects the activation of the Th2 component of immunity, contributing to the maintenance of chronic inflammation and remodeling of the airways.

IFN-γ showed opposite dynamics: in BA (13.5 ± 0.84 pg/mL), levels decreased relative to the control (17.5 ± 0.92 pg/mL) by 1.30 times, and in BA with PH (11.3 ± 0.71 pg/mL) by 1.55 times ($p < 0.05$). A decrease in IFN-γ indicates weakening of the Th1 response, shifting the balance toward Th2-mediated reactions.

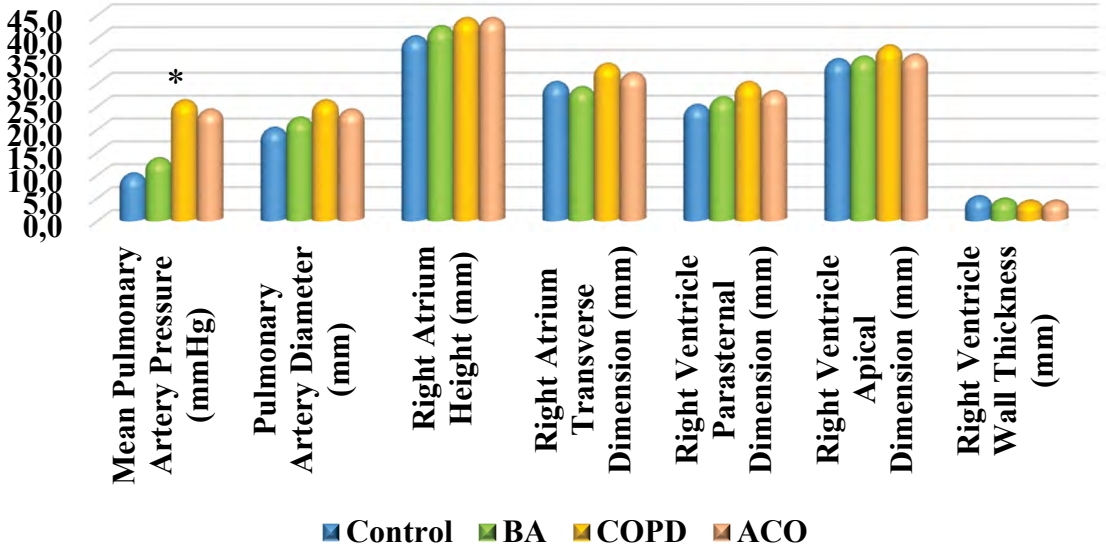

Fig. 2. Analysis of echocardiography data in the examined subjects, (*P≤0.05)

IL-18 increased significantly: in the BA group (193.2 ± 9.4 pg/mL), it exceeded the control (73.8 ± 5.11 pg/mL) by 2.62 times ($p<0.001$), and in BA with PH (237.5 ± 11.2 pg/mL) by 3.21 times ($p<0.001$), confirming the role of IL-18 in activating inflammatory cascades and endothelial dysfunction.

TNF-α showed a significant increase: in BA (36.8 ± 1.8 pg/mL), levels were 2.02 times higher than in the control (18.3 ± 1.1 pg/mL) ($p<0.001$), and in BA with PH (48.8 ± 2.3 pg/mL), 2.71 times higher ($p<0.001$). This cytokine promotes chronic inflammation, apoptosis activation, and lung tissue remodeling.

The angiogenesis factor VEGF-A in BA (170.3 ± 8.22 pg/mL) exceeded the control (154.8 ± 7.91 pg/mL) by 1.12 times, whereas in PH (195.6 ± 9.1 pg/mL), its concentration was 1.26 times higher, indicating activation of angiogenic mechanisms as a compensatory response to hypoxia.

The endothelial marker EN1 in BA (1.53 ± 0.08 pg/mL) was 1.92 times higher than in the control (0.82 ± 0.05 pg/mL) ($p<0.001$), and in BA with PH (2.53 ± 0.12 pg/mL) it was 3.11 times higher ($p<0.001$), indicating pronounced endothelial dysfunction.

Of particular interest is the Klotho protein, the concentration of which in BA (17.6 ± 0.92 pg/mL) exceeded the control (6.54 ± 0.41 pg/mL) by 2.72 times ($p<0.001$), and in BA with PH (21.3 ± 1.13 pg/mL) by 3.31 times ($p<0.001$). Its increase can be interpreted as an adaptive protective mechanism aimed at reducing oxidative stress and slowing vascular remodeling.

Superoxide dismutase (SOD) activity in the BA group (1203.7 ± 45.6 pg/mL) and BA with PH (1002.5 ± 41.8 pg/mL) was reduced compared with the control (1503.7 ± 52.4 pg/mL) by 1.25 and 1.5 times, respectively ($p<0.05$), reflecting depletion of antioxidant protection and increased oxidative stress processes (Fig. 3).

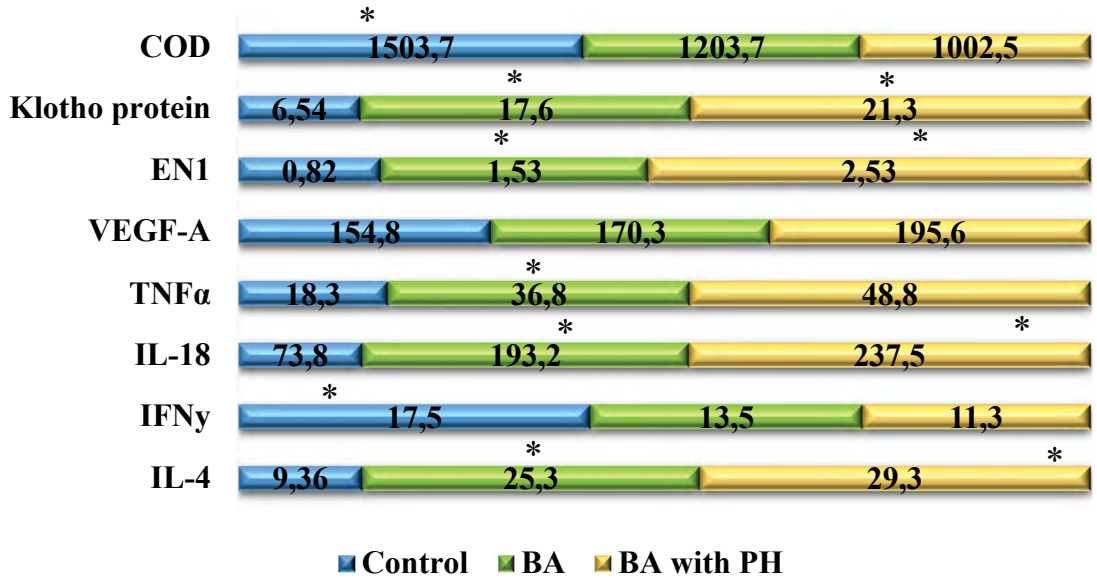

Fig. 3. Immunobiochemical markers in the examined groups with BA (pg/mL, P≤0.05)

Thus, BA, especially when complicated by pulmonary hypertension, is accompanied by a shift in the immune response towards anti-inflammatory reactions, activation of angiogenesis, endothelial dysfunction, and decreased antioxidant potential. An increase in the Klotho levels can be considered a compensatory mechanism aimed at limiting the damaging effects of inflammation and hypoxia.

Immunological studies were then conducted by dividing each group into subgroups with or without pulmonary hypertension.

Analysis of the cytokine profile revealed that the IL-4 concentration in patients with COPD was 15.5 ± 0.92 pg/mL, 1.66 times higher than in the control group (9.36 ± 0.61 pg/mL) ($p<0.05$). In the COPD subgroup with pulmonary hypertension, it increased to to 18.6 ± 1.12 pg/mL, 1.99 times higher than the control ($p<0.001$).

Conversely, IFN-γ levels tended to decrease: in COPD (12.2 ± 0.72 pg/mL), they were 1.43 times lower than in the control (17.5 ± 0.91 pg/mL), and in COPD with PH (10.6 ± 0.62 pg/mL) 1.65 times lower ($p<0.05$).

IL-18 increased significantly: in the COPD group, levels were 215.6 ± 10.4 pg/mL, 2.9 times higher than in the control (73.8 ± 5.15 pg/mL, $p<0.001$), and in PH 272.3 ± 12.2 pg/mL, 3.71 times higher than the norm ($p<0.001$).

A significant increase was also noted for TNF-α: in COPD (42.3 ± 2.12 pg/mL), levels exceeded the control (18.3 ± 1.11 pg/mL) by 2.31 times ($p<0.001$), and in COPD with PH (64.7 ± 3.21 pg/mL) by 3.52 times ($p<0.001$), confirming the role of TNF-α in maintaining inflammation, cellular damage, and vascular wall remodeling.

VEGF-A, a key angiogenesis factor, increased moderately: in COPD 201.4 ± 9.32 pg/mL, 1.31 times higher than the control (154.8 ± 7.93 pg/mL), and in PH 257.6 ± 11.5 pg/mL, 1.67 times higher than the control values ($p<0.05$).

The endothelial activation marker EN1 in COPD patients was 2.12 ± 0.12 pg/mL, 2.62 times higher than the control (0.82 ± 0.04 pg/mL, $p<0.001$). In COPD with PH, it reached 3.42 ± 0.17 pg/mL, 4.24 times higher than the norm ($p<0.001$), reflecting progression of endothelial dysfunction.

Klotho protein levels in COPD were 30.5 ± 1.62 pg/mL, 4.71 times higher than the control (6.54 ± 0.42 pg/mL, $p<0.001$). In COPD with PH, levels increased to 37.6 ± 1.92 pg/mL, 5.73 times higher than the control level ($p<0.001$).

Superoxide dismutase (SOD) activity in COPD patients (951.6 ± 42.1 pg/mL) and in those with COPD and PH (910.7 ± 39.8 pg/mL) was lower than in the control group (1503.7 ± 52.4 pg/mL) by 1.58 and 1.65 times, respectively ($p < 0.05$) (Fig. 4).

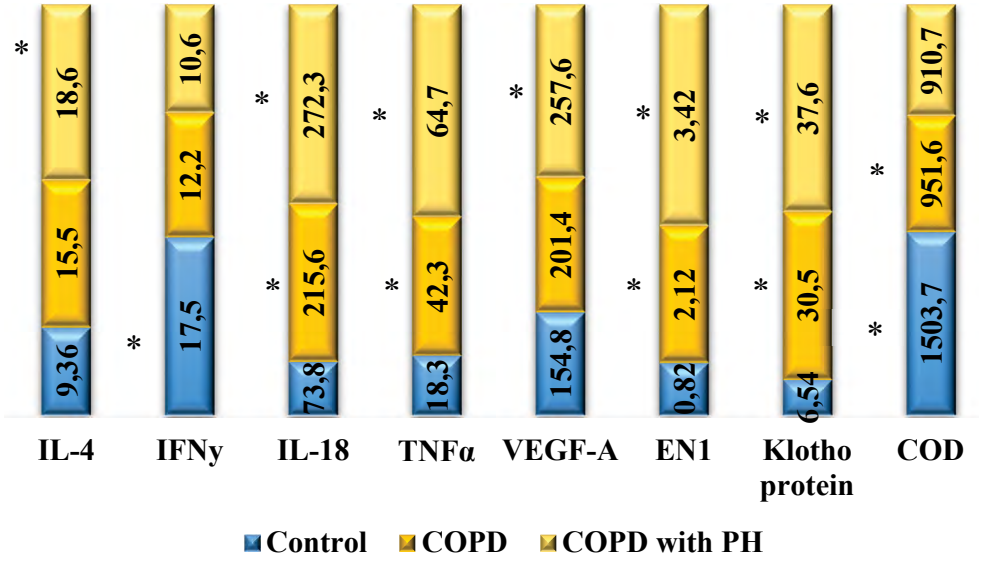

Fig. 4. Immunobiochemical markers in the examined groups with COPD (pg/mL, *P≤0.05)

Overall, these results demonstrate that COPD, particularly when complicated by pulmonary hypertension, is associated with pronounced inflammatory shifts, activation of angiogenesis, and endothelial dysfunction, accompanied by decreased antioxidant potential. Increased Klotho protein reflects an adaptive response of the organism.

In patients with overlapping asthma and COPD (ACO), IL-4 levels were 32.3 ± 1.62 pg/mL, 3.45 times higher than in the control (9.36 ± 0.61 pg/mL, $p<0.001$). In ACO with PH, levels increased to 37.5 ± 1.92 pg/mL, 4.01 times higher than the norm ($p<0.001$).

IFN-γ concentration decreased: in ACO, levels were 11.8 ± 0.72 pg/mL, 1.48 times lower than the control (17.5 ± 0.91 pg/mL), and in ACO with PH, 9.34 ± 0.62 pg/mL, 1.87 times lower than the norm ($p<0.05$).

IL-18 increased significantly: in ACO, levels were 252.6 ± 12.8 pg/mL, 3.44 times higher than the control (73.8 ± 5.13 pg/mL, $p<0.001$). In ACO with PH, concentration reached 312.1 ± 14.5 pg/mL, 4.22 times higher than the norm ($p<0.001$).

TNF-α also showed a significant increase: in ACO, levels were 56.5 ± 2.62 pg/mL, 3.11 times higher than the control (18.3 ± 1.13 pg/mL) ($p<0.001$), and in ACO with PH, 72.2 ± 3.31 pg/mL, 3.94 times higher than the norm ($p<0.001$).

VEGF-A concentrations in ACO were 244.4 ± 10.2 pg/mL, 1.58 times higher than the control ($p<0.05$), and in PH 301.7 ± 12.7 pg/mL, 1.95 times higher than the norm ($p<0.05$), indicating active stimulation of angiogenesis and remodeling of pulmonary vessels characteristic of pulmonary hypertension.

The endothelial dysfunction marker EN1 in ACO was 3.15 ± 0.15 pg/mL, 3.82 times higher than the control ($p<0.001$), and in ACO with PH 3.81 ± 0.18 pg/mL, 4.61 times higher than the norm ($p<0.001$).

Klotho protein levels significantly increased: in ACO, 35.9 ± 1.75 pg/mL, 5.53 times higher than the control (6.54 ± 0.44 pg/mL, $p<0.001$), and in ACO with PH, 42.3 ± 2.03 pg/mL, 6.55 times higher than the norm ($p<0.001$).

The activity of the antioxidant enzyme SOD decreased: in patients with ACO it was 915.6 ± 40.1 pg/mL, 1.64 times lower in than the control group (1503.7 ± 52.4 pg/mL) ($p<0.05$). In ACO with PH, levels decreased to 901.3 ± 38.7 pg/mL, 1.67 times lower than the norm ($p<0.05$) (Fig. 5).

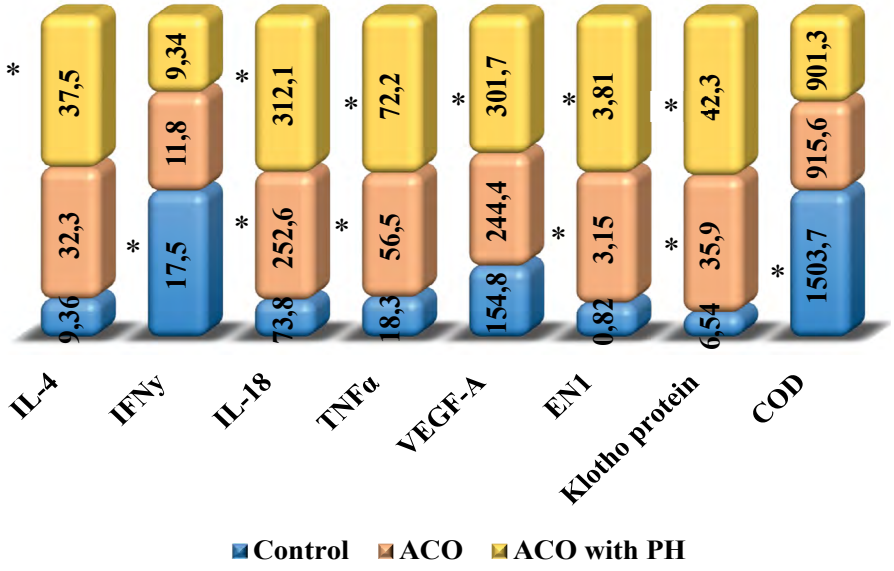

Fig. 5. Immunobiochemical markers in the examined groups with ACO (pg/mL, *P≤0.05)

Overall, the data confirm that in ACO, particularly when complicated by pulmonary hypertension, pronounced inflammatory and angiogenic changes occur, accompanied by endothelial dysfunction, reduced antioxidant protection, and compensatory increase in Klotho protein. This indicates a complex interaction of immunobiochemical mechanisms in disease pathogenesis and emphasizes the need to consider them when optimizing therapy.

Discussion of the obtained results

Analysis of clinical data revealed that in patients with bronchial asthma combined with COPD, the disease course is more severe compared with isolated forms. In the overlap group, more rapid decompensation of respiratory function and earlier development of pulmonary hypertension were observed, whereas in patients with only bronchial asthma or COPD, this process progressed more slowly. The presence of overlap was associated with a higher frequency of cardiovascular complications, including pulmonary heart disease and signs of chronic heart failure, confirming the clinical significance of the combined lesion and indicating high risks of disease progression.

Immunological studies have shown that patients with overlap and pulmonary hypertension exhibited the greatest cytokine, manifested as a sharp increase in proinflammatory markers and a decrease in anti-inflammatory factors. IL-18 and TNF-α were significantly higher than in the BA and COPD groups, reflecting active maintenance of chronic inflammation. At the same time, IFN-γ levels decreased, indicating suppression of the antiviral component of immunity. Increased VEGF-A synthesis and elevated expression of the endothelial dysfunction marker were accompanied by increased pulmonary artery pressure, directly linking immune disturbances with the development of pulmonary hypertension.

An increase in the Klotho protein levels was also detected in patients with overlap and PH, which can be considered a compensatory mechanism aimed at limiting oxidative stress. However, the magnitude of this response was insufficient, as antioxidant activity remained below control values.

Conclusion

The combined clinical and immunobiochemical data confirm the hypothesis that the overlap of bronchial asthma and COPD is associated with the most severe course and rapid development of pulmonary hypertension. Assessment of cytokine profiles, oxidative stress indicators, and Klotho levels allows optimization of diagnostics and enhances the accuracy of disease prognosis in clinical practice. These results underscore the importance of early detection of overlap phenotypes and the search for therapeutic strategies targeting immune and endothelial dysfunction.

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АСТМА – ХРОНІЧНЕ ОБСТРУКТИВНЕ ЗАХВОРЮВАННЯ ЛЕГЕНІВ: ІМУНОБІОХІМІЧНІ МАРКЕРИ, ОКСИДАТИВНИЙ СТРЕС, БІЛОК КЛОТО ТА ЇХНЯ РОЛЬ В ОПТИМІЗАЦІЇ ДІАГНОСТИКИ ЛЕГЕНЕВОЇ ГІПЕРТЕНЗІЇ

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Резюме.

Перекриття бронхіальної астми та хронічного обструктивного захворювання легень (ХОЗЛ) пов'язане з більш тяжким перебігом захворювання та більш раннім розвитком легеневої гіпертензії (ЛГ), що вимагає нових діагностичних підходів.

Мета. Оптимізувати діагностику легеневої гіпертензії у пацієнтів з перекриттям астми та ХОЗЛ за допомогою імунобіохімічних маркерів, параметрів окисного стресу та вимірювання білка Клото.

Матеріали та методи. Було обстежено 120 пацієнтів (астма, n = 45, ХОЗЛ, n = 50, АСО, n = 25) за допомогою клінічної, інструментальної та імунобіохімічної оцінки (IL-4, IL-18, TNFα, VEGF-A, Klotho, SOD).

Дотримання етичних стандартів. Письмову інформовану згоду було отримано від усіх пацієнтів перед їх участю в дослідженні. Усі процедури були схвалені Етичним комітетом Інституту імунології та геноміки людини НАН Республіки Узбекистан (протокол № 2025-0003) і виконані відповідно до принципів Гельсінської декларації, ухваленої у жовтні 2024 року на 75-й Генеральній асамблеї Всесвітньої медичної асоціації.

Статистичний аналіз проводився за допомогою SPSS 26.0. Дані представлені у вигляді середнього арифметичного (M) ± стандартне відхилення (SD) або стандартна похибка середнього (m). Різниця оцінювалася за допомогою t-критерію Стьюдента та U-критерію Манна-Уїтні. Значення $p < 0,05$ вважалося статистично значущим.

Фінансування. Дане дослідження виконано в рамках плану науково-дослідних робіт Бухарського державного медичного інституту (05.2022 DSc.135) «Розробка нових підходів до ранньої діагностики, лікування та профілактики патологічних станів організму, що впливають на здоров'я населення Бухарського регіону після COVID-19 (2022-2026)», а також на основі базового фінансування теми науково-дослідних робіт Інституту імунології та геноміки людини НАН Республіки Узбекистан «Імунобіохімічна та молекулярно-генетична діагностика кардіореспіраторної системи у хворих із поєднанням бронхіальної астми та хронічного обструктивного захворювання легень в експерименті» (протокол № 2, 2024).

Результати. У пацієнтів з АКО середній тиск у легеневій артерії був у 1,8 раза вищим порівняно з пацієнтами з астмою (24,0 ± 2,1 проти 13,3 ± 1,7 мм рт. ст., p<0,01). Рівень IL-18 був у 3,4 раза вищим, ніж у контрольної групи (252,6 ± 12,3 проти 73,8 ± 6,4 пг/мл, p<0,001). Концентрація білка Клото у пацієнтів з АКО та ЛГ перевищувала контрольні значення у 6,4 раза (42,3 ± 3,1 проти 6,54 ± 0,72 пг/мл, p<0,001), що свідчить про компенсаторну реакцію.

Висновок. Комбіновані клінічні та імунобіохімічні дані підтверджують гіпотезу, що перекриття бронхіальної астми та ХОЗЛ пов'язане з найважчим перебігом та швидким розвитком легеневої гіпертензії. Імунобіохімічні маркери, включаючи профілі цитокінів, показники окисного стресу та рівні Klotho, є цінними інструментами для підвищення точності діагностики та прогнозування у пацієнтів з перекриттям астми та ХОЗЛ.

Ключові слова: астма; хронічне обструктивне захворювання легень; перекриття; легенева гіпертензія; цитокіни; білок Клото; окиснювальний стрес; діагностика.

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