TIBBIYOT
TA'LIMI & INNOVATSIYALARI

O'ZBEKISTON RESPUBLIKASI
19 20
TOSHKENT TIBBIYOT AKADEMIYASI

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- 14.00.00 - Tibbiyot fanlari;
- 14.00.01 - Akusherlik va ginekologiya;
- 14.00.02 - Morfologiya;
- 14.00.03 - Endokrinologiya;
- 14.00.04 - Otorinolaringologiya;
- 14.00.05 - Ichki kasalliklar;
- 14.00.06 - Kardiologiya;
- 14.00.07 - Gigiena;
- 14.00.08 - Oftal'mologiya;
- 14.00.09 - Pediatriya;
- 14.00.10 - Yuqumli kasalliklar;
- 14.00.11 - Dermatologiya va venerologiya;
- 14.00.12 - Tibbiy reabilitologiya;
- 14.00.13 - Nevrologiya;
- 14.00.14 - Onkologiya;
- 14.00.15 - Patologik anatomiya;
- 14.00.16 - Normal va patologik fiziologiya;
- 14.00.17 - Farmakologiya va klinik farmakologiya;
- 14.00.18 - Psixiatriya va narkologiya;
- 14.00.19 - Klinik radiologiya;
- 14.00.20 - Tibbiy genetika;
- 14.00.21 - Stomatologiya;
- 14.00.22 - Travmatologiya va ortopediya;
- 14.00.23 - Hamshiralik ishini tashkil etish;
- 14.00.24 - Sud tibbiyoti;
- 14.00.27 - Xirurgiya;
- 14.00.28 - Neyroxirurgiya;
- 14.00.41 - Xalq tabobati;
- 14.00.35 - Bolalar xirurgiyasi;
- 14.00.34 - Yurak-qon tomir xirurgiyasi

№10-SON

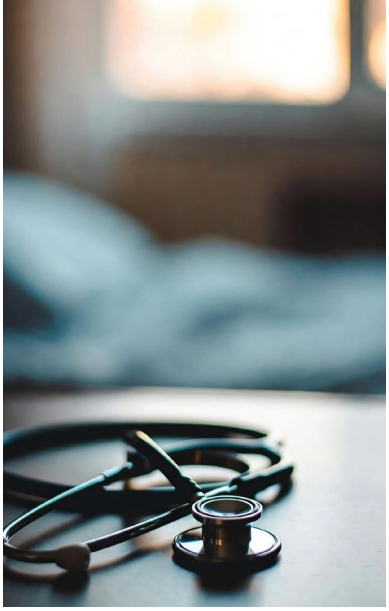
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Litsenziya raqami: №745444













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ilmiy elektron jurnali O‘zbekiston Respublikasi Axborot va ommaviy kommunikatsiyalar agentligi (AOKA) tomonidan 2024-yil 9-oktabrdan boshlab c-5669651 raqami ostida rasmiy ro‘yxatdan o‘tkazilgan.

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MUNDARIJA

KARDIORENAL SAMARADORLIK NUQTAI NAZARIDAN FINERENON VA EPLERENONNING CHAP QORINCHA OTISH FRAKSIYASI SAQLANGAN YURAK YETISHMOVCHILIGI BEMORLARIDAGI QIYOSIY BAHOLANISHI 21
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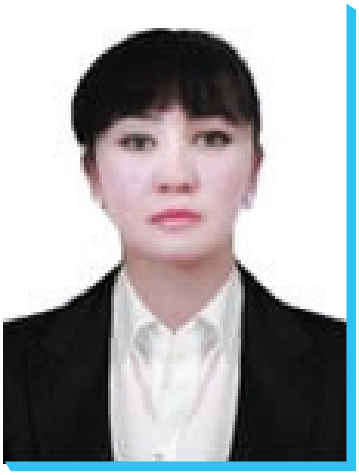
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COMPREHENSIVE ASSESSMENT OF CLINICAL, LABORATORY, AND INSTRUMENTAL CHARACTERISTICS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE



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Abstract: Currently, considerable attention is being devoted to identifying the risk factors associated with the development of chronic obstructive pulmonary disease (COPD). Smoking is a major risk factor that contributes to the development of pathological processes in the lungs, including systemic inflammatory responses, oxidative stress, the production of inflammatory cytokines, increased procoagulant activity, enhanced oncogene expression, and other systemic effects. Proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukins (ILs), play an important role in disturbances of hemostasis in patients with chronic obstructive pulmonary disease (COPD). IL-6 is identified as a principal cytokine involved in activating coagulation processes, whereas TNF-α also affects coagulation, with IL-6 exerting an indirect influence. Furthermore, IL-8 contributes to the regulation of blood coagulation through its effects on the secretion of procoagulant and anticoagulant factors and plasminogen inhibitors.

Keywords: proinflammatory cytokines, oxidative stress, interleukin, coagulation.

Annotatsiya: Hozirgi vaqtda surunkali obstruktiv o‘pka kasalligi (SO‘OK) rivojlanishining xavf omillarini o‘rganishga alohida e’tibor berilmoqda. Xavf omillari orasida chekish o‘pkada patologik jarayonlarning rivojlanishiga, ya’ni tizimli yallig‘lanish reaksiyalarining yuzaga kelishiga, oksidlovchi stressga, yallig‘lanish sitokinlari ishlab chiqarilishiga, prokoagulyant omillar faolligining oshishiga, onkogenlar ekspressiyasining kuchayishiga va boshqa tizimli ta’sirlarga sabab bo‘ladi. Yallig‘lanish oldi sitokinlari — o‘sma nekrozi omili alfa (O‘NO-α) va interleykinlar (IL) 6 va 8 SO‘OKda gemostaz buzilishida muhim rol o‘ynaydi. Koagulyatsiya jarayonlarini faollashtiradigan asosiy sitokinlardan biri IL-6 hisoblanadi. O‘NO-α ham koagulyatsiya jarayonlariga ta’sir qiladi, IL-6 esa bilvosita ta’sir ko‘rsatadi. Bundan tashqari, IL-8 prokoagulyant va antikoagulyant omillar hamda plazminogen ingibitorlari sekretsiyasiga ta’sir qilish orqali qon ivishining boshqarilishida ishtirok etadi.

Kalit so‘zlar: yallig‘lanish oldi sitokinlari, oksidlovchi stress, interleykin, koagulyatsiya.

Аннотация: В настоящее время особое внимание уделяется исследованию факторов риска развития хронической обструктивной болезни лёгких (ХОБЛ). Среди этих факторов курение способствует развитию патологических процессов в лёгких, включая системные воспалительные реакции, оксидативный стресс, выработку воспалительных цитокинов, повышение активности прокоагулянтных факторов, усиление экспрессии онкогенов и другие системные эффекты. Провоспалительные цитокины, включая фактор некроза опухоли альфа (ФНО-α) и интерлейкины (IL), играют важную роль в развитии нарушений гемостаза у пациентов с хронической обструктивной болезнью лёгких (ХОБЛ). Одним из основных цитокинов, активирующих процессы свёртывания крови, является IL-6. ФНО-α также влияет на процессы свёртывания, тогда как IL-6 оказывает опосредованное влияние. Кроме того, IL-8 участвует в регуляции свёртывания крови, воздействуя на секрецию прокоагулянтных и антикоагулянтных факторов, а также ингибиторов плазминогена.

Ключевые слова: провоспалительные цитокины, оксидативный стресс, интерлейкин, коагуляция.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disorder of the respiratory system associated with environmental exposures. It causes structural damage to the airways and lung parenchyma. The disease is characterized by persistent airflow obstruction and emphysematous changes, accompanied by the development and exacerbation of chronic respiratory failure. Interleukin-6 (IL-6) plays a substantial role in local and systemic inflammatory processes in COPD and affects pulmonary tissue elasticity. These alterations may contribute to irreversible structural changes in the bronchial airways. Such mechanisms are important in the progression of pathophysiological changes and the development of pulmonary emphysema in patients with COPD (Celli B.R., 2012).

LITERATURE REVIEW

Increased neurohormonal activity stimulates the secretion of cytokines and hormone-like proteins by lymphocytes, monocytes, and granulocytes. The inflammatory phenotype can be differentiated according to the cytokines involved. An eosinophilic phenotype is associated with IL-4 and IL-10, whereas a neutrophilic phenotype is linked to IL-6 and IL-8 (Vitkina T.I., Denisenko Yu.K., 2017). Oxidative stress further aggravates the imbalance between proteinases and antiproteinases. This process promotes antiproteinase inactivation and proteinase activation, including the activation of metalloproteinases. Oxidants also stimulate tumor necrosis factor alpha (TNF-α), which induces the expression of inflammatory genes, including those encoding IL-8 and TNF-α, thereby sustaining the inflammatory response [3, 4, 12].

RESEARCH METHODOLOGY

The study was conducted between 2021 and 2023 among patients treated in the Pulmonology Department of the Samarkand Regional Multidisciplinary Medical Center. The first group comprised 32 patients younger than 50 years, including 10 women (31.25%) and 22 men (68.75%). The second group included 28 patients aged 50 years and older, consisting of 4 women (14.3%) and 24 men (85.7%). The mean age in Group 1 was 36.8 ± 0.7 years, with an age range of 21–50 years. In Group 2, the mean age was 61.0 ± 0.6 years, and the age range was 51–76 years. The principal study cohort consisted of 60 patients with a history of smoking. Their mean age was 48 ± 5.11 years. Men predominated, accounting for 46 patients (76.7%), while women represented 14 patients (23.3%). The mean duration of smoking was 32 years. According to the reported classification, 12 patients were assigned to Grade I, 29 to Grade II, and 19 to Grade III.

Laboratory investigations in the principal and control groups were performed at the laboratory of the Samarkand Regional Multidisciplinary Medical Center. IL-6 was measured using IL-6 a-8768 reagents (Vector-Best) and a Mindray MR-96A semi-automated immunoassay analyzer.The hemostatic system was evaluated using prothrombin time, prothrombin index, international normalized ratio (INR; referred to as MNO in the original text), thrombin time, fibrinogen concentration, and activated partial thromboplastin time (APTT). Reagent kits manufactured by Technology-Standard were used to assess hemostasis. Plasma IL-6 levels in patients with smoking-associated conditions were considered a rapid and sensitive biomarker for the diagnosis of smoking-related disorders.

ANALYSIS AND RESULTS

The assessment of inflammatory markers revealed considerable changes in fibrinogen concentrations and proinflammatory cytokine levels across the study groups. These changes were more pronounced in Group 1, suggesting a more marked systemic inflammatory response. The most evident differences were observed in fibrinogen and IL-6 concentrations. The principal group also demonstrated elevated levels of anti-inflammatory cytokines. Overall cytokine activity in patients with smoking-associated conditions, referred to as chronic obstructive pulmonary disease (COPD; SOO‘K in the original text), was reported to be significantly higher than that in healthy controls. IL-6, described in the original report as having anti-inflammatory effects, was substantially elevated in the principal group compared with the control group. These findings were interpreted as evidence of an imbalance in the cytokine system.

Table 1.
Results of immunological analysis

Controle groups	Fibrinogen	CRP	IL – 6
Group-1(60)	5,48±1,4	32, 2 ±1 5,1	62,0±20,81
Group-2 (30)	2, 52 ±0,3	2,8±0,5	8,4±2,5
Normal	2-4 mg / l	0-5 mg / l	7 pg / ml

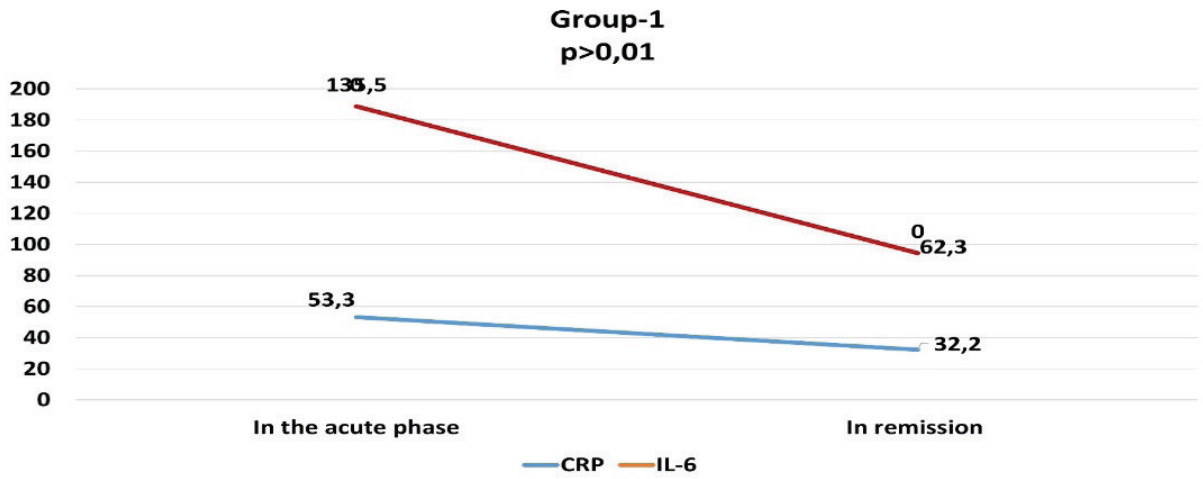


Figure 1. The connection between inflammation took cytokine-IL - 6 and inflammatory marker-CRO.

The alterations in hemostatic parameters identified during the investigation were considered indicative of a tendency toward hypercoagulation. This tendency was associated with a shortened activated partial thromboplastin time (APTT) and thrombin time. Reduced anticoagulant activity, particularly lower antithrombin III levels, and decreased fibrinolytic potential were also described in patients with COPD. Changes in fibrinolytic activity were observed across the study groups and were primarily attributed to increased kallikrein levels, which were also associated with spontaneous euglobulin lysis. Although statistically significant increases in these indices were reported in Group 1 of the control group, the assessment of other statistical parameters did not reveal additional significant changes, as presented in Table 2.

Table 2.
Results of analysis of hemostasis

Groups	Parameter				
	PT	PI	INR	TT	Fibrinogen
Group-1(60)	1 2,9 ±0,2	106,1±3,6	0,78± 0,5	8,4 ±1,3	5,48±1,4
Group-2(30)	15,0±0,3	85,9±2,0	1,05±0,0 9	18,4±0,3	2,57±0,3
Normal	14-18	80-105	0,85-1,15	10-20	2-4

Time of Prothrombin time (PT), prothrombin index (PI), INR, TT-time of trombin, fibrinogen-F. Prothrombin time (PT), prothrombin index (PI), international normalized ratio (INR; MNO in the original text), thrombin time (TT), and fibrinogen (F) were assessed. Platelet aggregation activity and the rheological characteristics of blood were also investigated. Following treatment, the remission phase was associated with a substantial reduction in hemostasis-related platelet activity and changes in platelet aggregation. Improvements in the rheological properties of blood were also reported.The results concerning changes in platelet aggregation activity and blood rheology during treatment are summarized in Table 3.

Table 3.
Aggregation activity of platelets during remission after treatment

Parameter	1 – group (60)		P_{1-2}
	Result	Δ %	
Spontaneous aggregation %	27,8±2,3	-38,2	<0,05
ADP-induced aggregation	93,8±2,2	-33,2	<0,05
Blood viscosity	5,7±0,3	-24,6	>0,05
Erythrocyte aggregation index	1,55±0,03	-9,3	<0,05
Erythrocyte deformation index	1,06±0,05	+6,5	<0,05

Beta-blockers and diuretics are known to reduce insulin sensitivity and aggravate dyslipidemia. Nevertheless, findings from studies conducted in recent years indicate that beta-blockers do not necessarily have adverse effects on the lipid profile [9, 10]. For this reason, changes in blood lipid parameters during treatment were of particular interest in the present study. At baseline, lipid abnormalities were reported in 75 (80%) patients. These abnormalities included changes in plasma cholesterol and triglyceride levels, alterations in very-low-density lipoprotein concentrations, a marked increase in low-density lipoprotein levels, and a reduction in high-density lipoprotein levels. A substantial increase in the atherogenicity index was also observed.

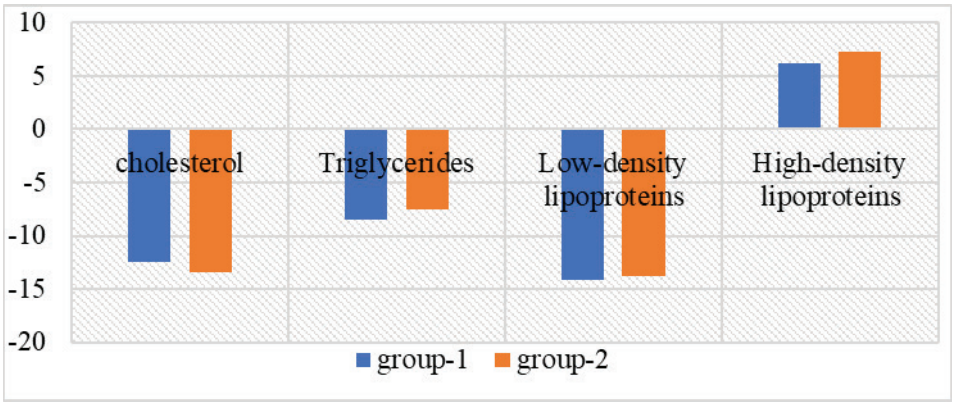


Figure 2. Lipid spectrum

The post-treatment assessment of inflammatory parameters indicated a reduction in fibrinogen concentrations and proinflammatory cytokine levels at the time of assessment. These changes were described as more pronounced in the relevant study group, as presented in Table 4. Cytokine activity was reported to decrease substantially in patients with COPD and in the healthy and comparison groups. The observed changes were interpreted as indicating a more balanced profile of proinflammatory cytokines.

Table 4.
Results of immunological analysis

Review groups	Fibrinogen	CRP	IL – 6	IL – 8
Group-1 (60)	5,48±1,4	32,2±15,1	62,0±20,81	48,0±9,2
Group-2 (30)	2,52±0,3	2,8±0,5	8,4±2,5	25,4±8,4

CONCLUSION

The findings of this study indicate that elevated proinflammatory cytokine levels may contribute to the deterioration of smoking-associated conditions in some patients. Measuring inflammation-related cytokines in patients with these conditions may support disease prediction because these biomarkers demonstrate a strong association with disease parameters. Furthermore, the findings concerning cytokine concentrations during the rehabilitation of patients with COPD were consistent with results reported in COPD-related research. The observed increase in proinflammatory cytokines was associated with a higher risk of disease exacerbations,

which, in turn, was linked to more frequent hospital visits. Overall, the results highlight the potential importance of inflammatory cytokines in assessing disease progression and predicting exacerbations in patients with smoking-associated respiratory conditions.

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