ORIGINAL ARTICLE

CONTENTS

Characteristics of pro-inflammatory markers: C-reactive protein and interleukin-6 in patients with secondary bronchiectasis in chronic obstructive pulmonary disease combined with gastroesophageal reflux disease

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ABSTRACT

Aim: To assess the nature and severity of changes in inflammatory markers—C-reactive protein (CRP) and interleukin-6 (IL-6)—in patients depending on the presence of secondary bronchiectasis in the setting of COPD and GERD

Materials and Methods: 130 patients in the remission phase of COPD GOLD-3, group E, were examined by clinical, laboratory, and instrumental methods. The levels of CRP and IL-6 were measured in the peripheral blood serum. The control group - of practically healthy individuals (PHI) 15 respondents.

Results: The frequency of exacerbations in the previous year in Group I ranged from 1.7 to 2.5 and did not differ between subgroups ($p > 0.05$). In Group II - from 2.0 to 3.4 and showed difference between: subgroups Ib and IIb, subgroups IIa – IIb ($p < 0.05$). CRP levels were higher in patients with COPD + BE, showing a 47.0% increase ($p < 0.001$) compared to COPD alone. There was increase 30.7% ($p < 0.001$) in CRP levels in patients with neutrophilic-type inflammation COPD compared to eosinophilic-type. IL-6 showed an increase, ranging from 2.5 to 7 times higher ($p < 0.05$; $p < 0.001$) compared to the PHI group. The analysis of the obtained results indicates a more pronounced increase in IL-6 levels in groups with secondary BE.

Conclusions: COPD remains one of the leading causes of disability and mortality worldwide. Correlation analysis between CRP, IL-6 levels, and exacerbation frequency revealed strong positive correlations in groups with combined pathology and the neutrophilic type of inflammation in COPD ($r = +0.96$ to $r = +0.86$).

KEY WORDS: chronic obstructive pulmonary disease, secondary bronchiectasis, gastroesophageal reflux disease, CRP, IL-6, diagnosis

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INTRODUCTION

The 21st century has been marked by the rapid and progressive development of medicine as a whole and all its branches in particular, including diagnostics, prevention, treatment, and scientific research. All these advancements are aimed at achieving the crucial goal of improving patients' quality of life. This issue is especially relevant among a significant cohort of individuals with respiratory diseases.

Respiratory system disorders rank among the leading causes of morbidity and mortality worldwide. In terms of fatality rates among nosological groups, COPD is second only to cardiovascular pathologies, particularly ischemic heart disease and stroke [1-5].

According to the concept formulated by Academician Feshchenko Yu.I. (2023), timely diagnosis is a critically important component of effective management for patients with pulmonary pathology. It ensures high-quality treatment outcomes, disease control, and complication prevention. The proposed strategies not only align with the clinical guidelines developed by the World Health Organization (WHO) but also correspond to the goals of the Global Alliance against Chronic Respiratory Diseases (GARD), aimed at reducing the prevalence and severity of respiratory diseases worldwide [6].

When assessing the severity of COPD progression, we rely on data regarding the frequency of exacerbations and the intensity of clinical symptoms. However, an analysis of the obtained results indicates that the variability in the degree of emphysema severity and bronchial lumen changes can be observed even in patients with identical forced expiratory volume in one second (FEV1) values. Since a noticeable increase in FEV1 in such patients occurs later than the regression of clinical symptoms, this may delay the detection of positive disease dynamics [7-9].

Given the above, the search for and application of more sensitive biomarkers is highly relevant for assessing disease destabilization, evaluating therapy

effectiveness, enabling early diagnosis of exacerbations, and predicting potential complications. Respiratory comorbidity, especially when it involves simultaneous damage to the same organ—such as COPD and secondary bronchiectasis—is a significant factor contributing to poor prognostic outcomes [2,10,11].

Studies indicate that secondary bronchiectasis coexists with COPD in 20–60% of cases, exacerbating symptom burden, increasing hospitalization frequency, reducing therapeutic efficacy, and leading to a worse prognosis compared to single-pathology cases [2,10]. However, it is not only monosystemic but also intersystemic polymorbidity that plays a crucial role. For instance, gastrointestinal tract involvement—such as gastroesophageal reflux disease (GERD)—can act as both a predictor of respiratory disease development and a factor that worsens existing conditions. According to international studies, GERD is one of the most prevalent disorders affecting individuals in the third millennium.

The epidemiology of GERD varies significantly across different countries, ranging from 65.0% in the United Kingdom (J.R. Bennet) to 2.3% in China (M. Chen et al.). The presence of GERD in patients with COPD leads to frequent exacerbations, a shortened remission period, and a progressive decline in pulmonary function parameters [12]. The progression of chronic diseases is accompanied and exacerbated by the activation of oxidative stress, an imbalance in redox processes, and an increase in the levels of pro-inflammatory mediators and acute-phase proteins [4,13-16]. One of the most sensitive markers of the acute phase of inflammation is CRP, the level of which is proportional to the intensity of the inflammatory process [4,14]. CRP can activate a pathological cycle of mutual induction: synthesized in the liver under the influence of inflammatory response regulators – cytokines (IL-6), as a central protein of the acute phase of inflammation, it binds to phospholipids of damaged cells, activating subsequent phagocytosis, and stimulates the production of pro-inflammatory cytokines [8,17-19].

AIM

To assess the nature and severity of changes in inflammatory markers—C-reactive protein (CRP) and interleukin-6 (IL-6)—in patients depending on the presence of secondary bronchiectasis in the setting of COPD and GERD.

MATERIALS AND METHODS

The study was conducted at the Municipal Non-Profit Enterprise «Center for Infectious Diseases of the Ivano-Frankivsk Regional Council.» A survey of 130 patients under observation in the remission phase of COPD GOLD-3, group E, was carried out. All patients were divided into groups depending on the established diagnoses and the type of inflammatory response: Group I included 68 individuals with COPD, divided as follows: subgroup Ia - 44 patients with COPD and a neutrophilic type of inflammatory response, subgroup Ib - 8 patients with COPD, a neutrophilic type of inflammatory response, and secondary bronchiectasis, subgroup Ic - 16 patients with COPD and an eosinophilic type of inflammatory response; Group II included 62 individuals with COPD combined with GERD, divided as follows: subgroup IIa - 34 patients with COPD+GERD, neutrophilic type of inflammatory response, subgroup IIb - 25 patients with COPD+GERD, neutrophilic type of inflammatory response, and secondary bronchiectasis, subgroup IIc - 3 patients with COPD+GERD and an eosinophilic type of inflammatory response. The control group consisted of 15 practically healthy individuals. Patients with COPD received basic COPD therapy: tiotropium bromide 18 mcg, 1 inhalation per day, fixed combination of budesonide/formoterol 320/9 mcg, 1 inhalation twice daily. Secondary bronchiectasis was verified during previous hospitalizations for COPD exacerbation using CT scans, applying the criteria proposed by N. Aidich et al.: direct signs (broncho-arterial ratio >1, absence of bronchial tapering, visualization of peripheral bronchi within 1 cm of the costal pleura in contact with the mediastinal pleura) and indirect signs (peribronchial thickening, mucus plugging, mosaic pattern, centrilobular nodules, atelectasis/consolidation).» [14]. In Group II, the duration of GERD anamnesis was 11±2.4 years. All patients with GERD received maintenance therapy with proton pump inhibitors. In both patient groups, the concentration of C-reactive protein in the blood serum was determined using the «CRP-latex-test» reagent kit (Ukraine), and the level of IL-6 [1] using the «ELISA KIT» reagent kit (USA).

Statistical processing was performed using the statistical function package of «Microsoft Excel» programs. The reliability of the obtained indicators was confirmed by calculating the error (±m) for relative values, and the significance of the difference in data in the comparative cohorts was proven based on the calculation of Student's t-test and the determination of the accuracy of the error-free forecast (P) using the table.

ETHICS

This work complies with the principles of the Declaration of Helsinki.

Table 1. General Characteristics of the Studied Groups

Main characteristics	Group I COPD			Group II COPD+ GERD		
Number of patients	68			62		
Sex (m, f)	41 m; 27 f			34 m; 28 f		
Age	65.3 ± 3.9			67.3± 4.2		
Frequency of exacerbations during the year in subgroups	Ia n-44	Ib n-8	Ic n-16	IIa n-34	IIb n-25	IIc n-3
	1	2	3	4	5	6
	2.2 p_{1-4}>0.05	2.5 p_{1-2}>0.05	1,7 p_{1-3}>0,05	2,7 p_{4-5} <0,05	3,4 p_{2-5} <0,01	2
Duration of history, years	COPD 18.4 ± 2.1			COPD 19.3 ± 2.9 GERD 14.5 ± 3.4		
Smoking status						
Smoker	54 (79.4%)			53 (85.5%)		
Former smoker	14 (20.6%)			9 (14.5%)		
Smoking history by sex (pack/years)	23.1±2.1 - m; 11.2 ±1.9 - f			24.1±1.8 - m; 10.1 ±2.4 - f		
Severity level for COPD	GOLD 3, Group E			GOLD 3, Group E		

Notes: n – number of patients; p - value of the difference between the data the frequency of exacerbations
Source: compiled by the authors of this study

RESULTS

The gender distribution of morbidity was characterized by a predominance of males in both patient groups: Group I consisted of 41 (60.3%) males and 27 (39.7%) females; Group II consisted of 34 (54.8%) males and 28 (41.2%) females (Table 1). The average age of patients was uniformly distributed in Groups I and II: 65.3 ± 3.9 and 67.3 ± 4.2, respectively. In Group I, the frequency of exacerbations ranged from 1.7 to 2.5 and did not significantly differ between subgroups (p > 0.05). In Group II, the fluctuations were 2.0 to 3.4 and differed significantly not only between Ib and IIb (p < 0.01) but also within the subgroup IIa – IIb (p < 0.05).

Smoking history in pack-years in each group: Group I - 23.1±2.1 males; 11.2±1.9 females; Group II - 24.1±1.8 males and 10.1±2.4.

CRP indicators is characterized by its increase in the peripheral blood serum in all groups compared to the reference values (p<0.05 - p<0.001) (Table 2). When comparing CRP levels within the COPD patient group, a statistically significant increase in this indicator was observed in patients with COPD+BE compared to COPD by 47.0% (p<0.001), and a significant increase in the indicator by 30.7% (p<0.001) between patients with COPD with eosinophilic inflammation and COPD with neutrophilic inflammation. Also, the CRP level in the COPD+GERD+BE patient group was significantly higher by 90.0% (p<0.001) compared to COPD+BE patients, and by 74.8% (p<0.001) compared to COPD+GERD patients.

The dynamics of the pro-inflammatory cytokine IL-6 (Table 2) demonstrates a significant increase of 2.5 to 7 times (p<0.05; p<0.001) compared to the control group. A significant increase in the level of the pro-inflammatory cytokine by 39.8% (p<0.05) was observed between the COPD+BE and COPD+GERD+BE subgroups, between COPD with neutrophilic inflammation and COPD+BE by 62.2% (p<0.05), and between COPD+GERD with neutrophilic inflammation and COPD+GERD+BE by 62.44% (p<0.001).

The study of the relationship between systemic immuno-inflammatory activation indicators, markers of the systemic inflammatory response of the body, and the frequency of exacerbations is important.

It was established that in patients with COPD in all subgroups, there is a strong positive correlation between the frequency of exacerbations and CRP levels (r= +0.89, p<0.001; r=+0.91, p<0.001; r=+0.78, p<0.001) (Fig. 1; Fig.2; Fig.3).

Similarly, the correlation in all subgroups of the COPD group is characterized by a similar dynamic, a strong positive correlation between the frequency of exacerbations and IL-6 levels (r= +0.86, p<0.001; r=+0.91, p<0.001; r=+0.78, p<0.001) (Fig. 4; Fig.5; Fig.6)

However, it should be noted that the lowest expression of a strong correlation was in the COPD group with eosinophilic inflammation.

The dynamics of the correlation dependence in the COPD+GERD+BE group is demonstrated in Table 3.

In the presence of COPD with neutrophilic inflammation + GERD and COPD+GERD+BE, strong positive correlations were established between the frequency of exacerbations

Table 2. Levels of CRP (mg/L) and IL-6 (pg/mL) in Peripheral Blood Serum in the Studied Groups

CRP IL-6	The Studied Groups							p1	p2	p3	p4	p5
	PHI, n=15	Group I n=68			Group II n=62							
		I a n=44	I b n=8	I c n=16	II a n=34	II b n=25	II c n=3					
		1	2	3	4	5	6					
CRP, mg/L in peripheral blood serum	1.34± 0.31	5.93±0.44 p<0.001 -Δ_{1-2} 47.0%	8.18±0.26 p<0.001 -Δ_{2-5} 90.0%	4.11±0.21 p<0.001 Δ_{1-3} 30.7%	8.89±0.33 p<0.001 -Δ_{1-4} 50.0%	15.54±0.22 p<0.001 -Δ_{4-5} 74.8%	7.87±0.17 p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
IL-6, pg/mL	3.10± 0.19	9.50± 1.97 p<0.01 -Δ_{1-2} 62.2%	15.41± 2.24 p<0.001 -Δ_{2-5} 39.8%	7.80± 2.1 p<0.05 Δ_{1-3} 17.9%	13.26± 1.96 p<0.001 -Δ_{1-4} 39.6%	21.54± 1.98 p<0.001 -Δ_{4-5} 62.44%	11.32± 2.10 p<0.01	p<0.05	p<0.05	p>0.05	p>0.05	p<0.001

Notes: Δ - absolute changes between values
p - significance of the difference between groups and PHI
p1 - significance of the difference between group I b and II b
p2 - significance of the difference between group I a and I b
p3 - significance of the difference between group I a and I c
p4 - significance of the difference between group I a and II a
p5 - significance of the difference betw
een group II a and II b
Source: compiled by the authors of this study

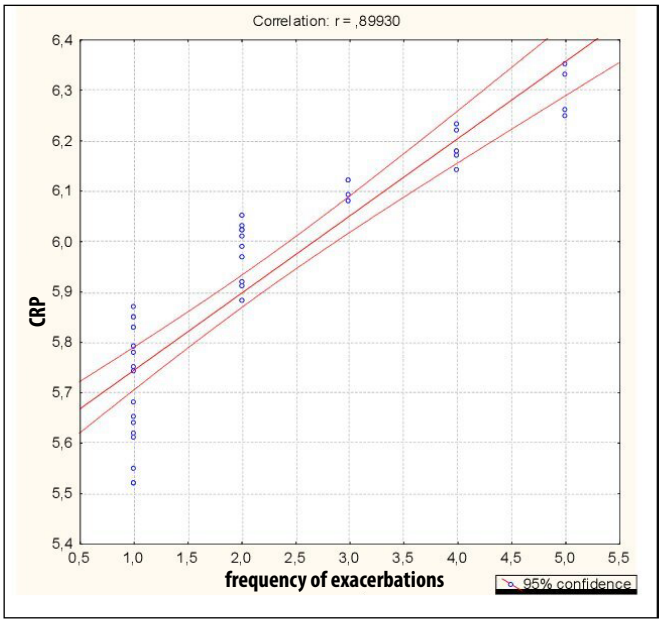

Fig. 1. Correlation between the frequency of exacerbations and CRP in patients with COPD with neutrophilic type of inflammation
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

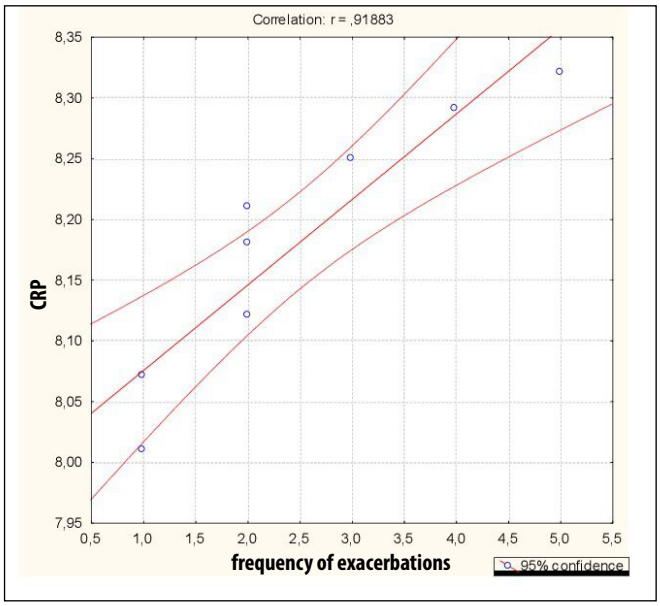

Fig. 2. Correlation between the frequency of exacerbations and CRP in patients with COPD + BE
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

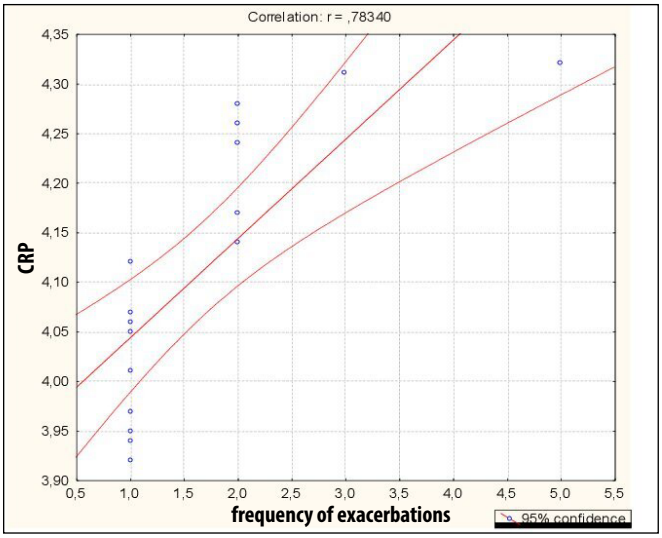

Fig. 3. Correlation between the frequency of exacerbations and CRP in patients with COPD with eosinophilc type of inflammation
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

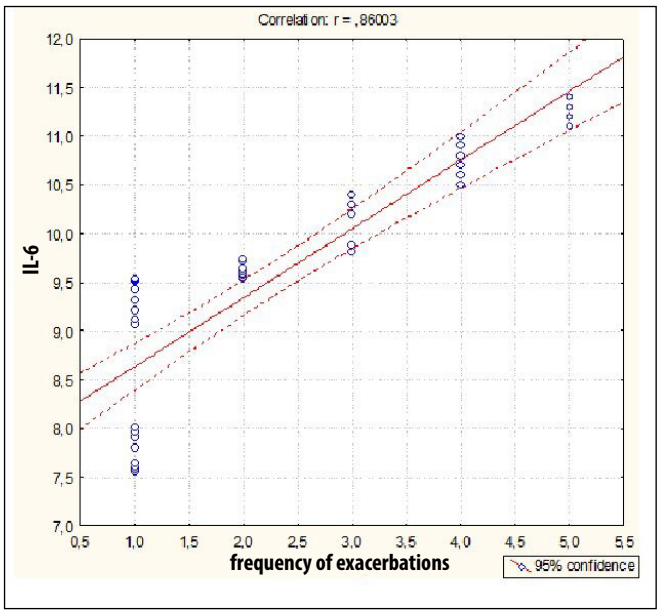

Fig. 4. Correlation between the frequency of exacerbations and IL-6 in patients with COPD with neutrophilic type of inflammation
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

and the pro-inflammatory cytokine IL-6 (r=+0.91, +0.91) and the acute-phase inflammation marker CRP (r=+0.92, +0.96) (Table 3). In the COPD group with eosinophilic inflammation + GERD, the correlation with frequency was positive, of moderate strength (r=+0.42, +0.49).

DISCUSSION

The progressive course and tendency of respiratory diseases to develop local and systemic complications are driven by multifactorial etiology, complex pathogenesis, and dependence on the cellular type of the inflammatory process, contributing to their high prevalence. A hallmark of these conditions is the worsening severity, which increases the risk of patient disability. This phenotype is associated with an increased risk of exacerbations, severe airway obstruction, and higher mortality rates [10].

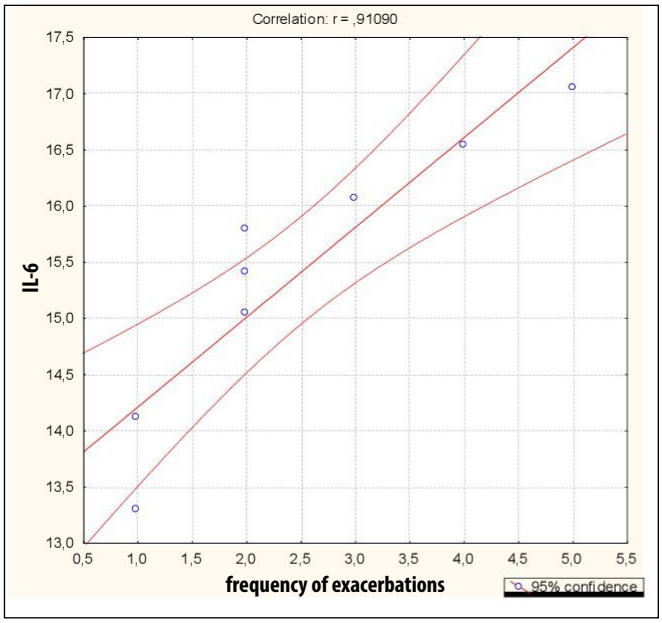

Fig. 5. Correlation between the frequency of exacerbations and IL-6 in patients with COPD+GERD+BE
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

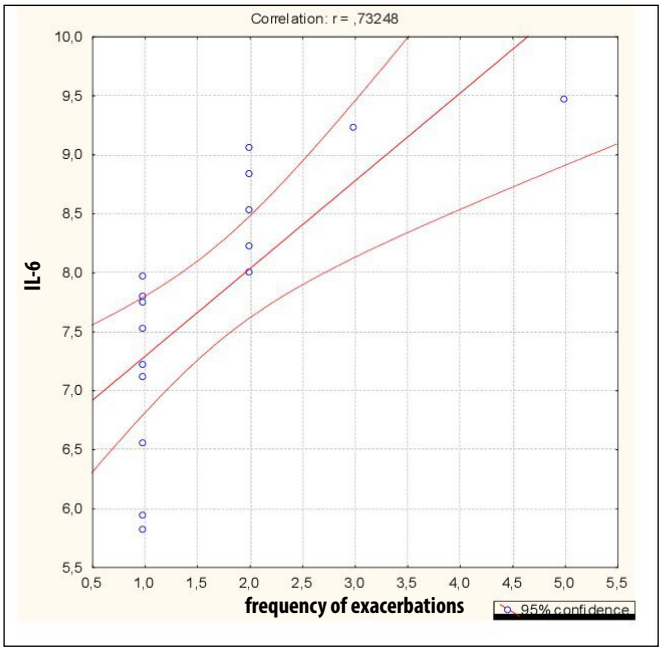

Fig. 6. Correlation between the frequency of exacerbations and IL-6 in COPD patients with eosinophilic type of inflammation + GERD
Notes: 1) r – the correlation coefficient, 2) p – value
Picture taken by the authors

Currently, chronic respiratory diseases frequently coexist with existing comorbidities, leading to a worsening of the course of each individual disease and complicating the diagnostic process, which subsequently affects the effectiveness of the dominant pathology's treatment. The combination of COPD, secondary BE and GERD is an example of interfering syntropy of diseases, in which the illnesses are not only interconnected but also contribute to the aggravation of each other's course [2,11]. The phenomenon of chronic cough is often associated with the presence of concomitant GERD. Extraesophageal manifestations of GERD are observed in 75% of patients with COPD. The presence of comorbid GERD in patients with COPD leads to a shortening of the COPD remission period, a decrease in pulmonary function indicators, which complicates the diagnostic and treatment process. Therefore, there arises a pressing need to choose an alternative comprehensive therapeutic and preventive strategy that will improve the course of diseases and enhance the quality of life of patients [11,12].

Analysis of the frequency of exacerbations during the year, before enrollment in the study, characterized the general trend described in the literature by a number of authors – an increase in morphofunctional changes from exacerbation to exacerbation, and the presence of additional factors such as obstruction, bronchiectasis, and GERD increased the number of exacerbations. The opinion regarding the role of harmful factors, particularly smoking, which is a common factor in the development and progression of both diseases and leads to more frequent and clinically severe exacerbations, remains indisputable [16]. High percentages of smoking history in pack-years in each group: Group I - 23.1±2.1 males; 11.2±1.9 females; Group II - 24.1±1.8 males and 10.1±2.4 females require careful attention and intensification of the physician's work with these patients to eliminate harmful habits. CRP indicators increased not only in compared to the reference values ($p<0.05$ - $p<0.001$), but in patients with COPD+BE compared to COPD by 47.0% ($p<0.001$), and by 30.7% ($p<0.001$) between patients with COPD with eosinophilic inflammation and COPD with neutrophilic inflammation to. Thus, we observe a more pronounced acute-phase inflammation indicator among patients with a predominant neutrophilic type of inflammation and polymorbidity.

The analysis of dynamics of the pro-inflammatory cytokine demonstrates a more pronounced increase in IL-6 in both subgroups with secondary bronchiectasis: by 39.8% ($p<0.05$) - between the COPD+BE and COPD+GERD+BE subgroups, by 62.2% ($p<0.05$) - between COPD with neutrophilic inflammation and COPD+BE, by 62.44% ($p<0.001$) - between COPD+GERD with neutrophilic inflammation and COPD+GERD+BE. Its may characterize the intensity of the inflammatory response in polymorbidity, in patients in the remission phase. Thus, we observe a strong positive correlation of systemic inflammation markers with the frequency of exacerbations in groups with combined pathology and neutrophilic inflammation IL-6 (r=+0.91, +0.91), CRP

Table 3. Correlation matrix between systemic immuno-inflammatory activity parameters, systemic inflammation marker of the body, and frequency of exacerbations in patients of Group II

Indicator	II a frequency of exacerbations	II b frequency of exacerbations	IIc frequency of exacerbations
CRP	+0.92	+0.96	+0.42
IL-6	+0.91	+0.91	+0.49

Source: compiled by the authors of this study

(r=+0.92, +0.96). In the COPD eosinophilic inflammation + GERD group, this correlation was defined as positive, of moderate strength (r=+0.42, +0.49). The obtained data suggest that polymorbidity and the predominance of neutrophilic inflammation may be predictors of a more pronounced 'smoldering inflammation' in patients in the remission phase.

Therefore, in our opinion, there is an urgent need to develop and adhere to an algorithm for managing patients with combined pathologies, which includes quality basic therapy to prevent exacerbations in general, and those leading to hospitalizations in particular.

CONCLUSIONS

1. The epidemic of respiratory and gastrointestinal diseases spreading worldwide is causing the formation of a new cluster of patients with polymorbid lesions. In this case, not only is diagnosis complicated and obstacles to treatment effectiveness arise, but there is also a need for great vigilance and caution in the patient-doctor collaboration to form a roadmap of preventive approaches to prevent exacerbations and improve the patient's quality of life. The gender distribution maintains a trend with a predominant number of males 75 (57.7%), 55 (42.3%) – females.
2. The CRP indicator is characterized by its increase in peripheral blood serum in all groups compared to the control group ($p<0.05$ - $p<0.001$). Analysis of CRP levels within the COPD patient group showed a statistically significant increase in this indicator in patients with COPD+BE compared to COPD by 47.0% ($p<0.001$), and a significant increase in the indicator by 30.7% ($p<0.001$) between patients with COPD with eosinophilic inflammation and COPD with neutrophilic inflammation. Also, the CRP level in the COPD+GERD+BE patient group was significantly higher by 90.0% ($p<0.001$) compared to COPD+BE patients, and by 74.8% ($p<0.001$) compared to COPD+GERD patients.
3. The dynamics of IL-6 are characterized by a significant increase of 2.5 to 7 times ($p<0.05$; $p<0.001$) compared to the control group. A significant increase in the level of the pro-inflammatory cytokine by 39.8% ($p<0.05$) was observed between the COPD+BE and COPD+GERD+BE groups, between COPD with neutrophilic inflammation and COPD+BE by 62.2% ($p<0.05$), and between COPD+GERD with neutrophilic inflammation and COPD+GERD+BE by 62.44% ($p<0.001$). The analysis of the obtained results demonstrates a more pronounced increase in IL-6 in both groups with secondary bronchiectasis, which may characterize the intensity of the inflammatory response in polymorbidity, in patients in the remission phase..
4. Correlation analysis between systemic immuno-inflammatory activity parameters, systemic inflammation markers of the body, and the frequency of exacerbations is characterized by strong positive correlations in groups with combined pathology and neutrophilic inflammation (r=+0.96 - r=+0.86). In the COPD group with eosinophilic inflammation + GERD, this correlation was defined as positive, of moderate strength.
5. The progression and prognostic probability of exacerbations of chronic inflammatory processes are directly related to elevated levels of CRP and IL-6, and the level significantly increases with the development of polymorbidity, for example, in COPD such as secondary BE and GERD. Thus, the determination of CRP and IL-6 can be used as a marker for predicting the probable deterioration or destabilization of COPD, as well as the development of polymorbidity.

REFERENCES

1. Adaptovana klinichna nastanova, zasnovana na dokazakh «Khronichne obstruktyvne zakhvoriuvannia lehen». [Adapted evidence-based clinical guideline "Chronic obstructive pulmonary disease"]. NAMN Ukraina, Kyiv. 2020. http://www.ifp.kiev.ua/ftp1/metoddoc/nastanova_hozl_2020.pdf?fbclid=IwAR2UE1kIKszXZfEMa9pUn2HPtZSaQo8vZtpUZr__SM-5ZdFQLvZJGpq3SBg [Accessed 14 December 2025] (Ukrainian)

2. Elhussini MSH, Asmaa MM, Hoda AE, Gharib A. Bronchiectasis as co morbidity with COPD or ILD: complex interactions and severe consequences The Egyptian Journal of Bronchology. 2023;17:19. doi:10.1186/s43168-023-00192-8. DOI
3. Global action plan for the prevention and control of noncommunicable diseases 2013-2020 https://www.who.int/publications/i/item/9789241506236 [Accessed 14 December 2025]
4. Korzh NV, Ostrovskyy MM. Dynamics of systemic inflammatory markers in case of exacerbation of COPD (III degree of bronchial obstruction) in overweight patients with the optimization of management and treatment. The Pharma Innovation Journal. 2021;10(3):09-13.
5. Leading causes of death and disability 2000-2019: A visual summary https://www.who.int/data/stories/leading-causes-of-death-and-disability-2000-2019-a-visual-summary [Accessed 14 December 2025]
6. Global Alliance against Chronic Respiratory Diseases https://www.who.int/groups/global-alliance-against-chronic-respiratory-diseases-(gard) [Accessed 14 December 2025]
7. Hassan A, Jabbar N. C-reactive Protein as a Predictor of Severity in Chronic Obstructive Pulmonary Disease: An Experience From a Tertiary Care Hospital. Cureus. 2022;14(8):e28229. doi: 10.7759/cureus.28229. DOI
8. Shevchuk–Budz UI. Kharakterystyka hostrofaznoho markera zapalennya – S-reaktyvnyy proteyin, u patsiyentiv z khronichnymy urazhennyamy bronkhiv. [Characteristics of the acute phase marker of inflammation — C-reactive protein in patients with chronic bronchial lesions]. Tuberkul'oz, zakhvoryuvannya lehen', VIL-infektsiya. 2023;4(55). doi:10.30978/TB-2023-4-5. (Ukrainian) DOI
9. Deng Z-Ch, Zhao P, Cao Ch et al. C reactive protein as a prognostic marker in chronic obstructive pulmonary disease. Exp Ther Med. 2014;7(2):443-446. doi: 10.3892/etm.2013.1441. DOI
10. Polverino E, Dimakou K, Hurst J et al. The overlap between bronchiectasis and chronic airway diseases: state of the art and future directions. Eur Respir J. 2018;52:1800328. doi:10.1183/13993003.00328-2018. DOI
11. Zhang XX, Pang LJ, Lv XD, Zhang HY. Risk factors for bronchiectasis in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Clinics (Sao Paulo). 2021;76:e2420. doi: 10.6061/clinics/2021/e2420. DOI
12. Semenova N., Oparina T. Otsinka efektyvnosti kombinovanoho likuvannya u patsiyentiv z komorbidnym perebihom KHOZL ta HERKH. [Evaluation of the effectiveness of combined treatment in patients with comorbid COPD and GERD.] Skhidnoyevropeys'kyy zhurnal vnutrishn'oyi ta simeynoyi medytsyny. 2023;2:80-83. doi: 10.15407/internalmed2023.02.080. (Ukrainian) DOI
13. Gumeniuk MI, Ignatieva VI, Matviienko YuA et al. Markery systemnoho zapalennya u khvorykh na khronichne obstruktyvne zakhvoryuvannya lehen' [Systemic inflammation markers in patients with chronic obstructive pulmonary disease.] Ukrainskiy Pul'monolohichniy Zhurnal. 2014;3:33–36. (Ukrainian)
14. Korzh NV. Diahnostyka ta prohnozuvannya rozvytku zahostren' KHOZL u khvorykh z nadmirnoyu vahoyu. [Diagnosis and prognosis of COPD exacerbations in overweight patients.] Medychni perspektivy. 2018;23(1):82-86. doi: 10.26641/2307-0404.2018.1(part1).127242. (Ukrainian) DOI
15. Ostrovskyy MM. Zapalennya yak prychyna kashlyu ta rozvytku uskladnen': mozhlyvosti suchasnykh innovatsiynykh mukolitykiv. [Inflammation as a cause of cough and complications: role of modern mucolytics.] Ukrainskiy Pul'monolohichniy Zhurnal. 2021;2:41–46. doi: 10.31215/2306-4927-2021-29-2-41-46. (Ukrainian) DOI
16. Zhang M, Wan Y, Jin Y et al. Cigarette smoking promotes inflammation in patients with COPD by affecting the polarization and survival of Th/Tregs through up-regulation of muscarinic receptor. PLoS ONE. 2014;9(11):e112350. doi: 10.1371/journal.pone.0112350. DOI
17. Vynnychenko LB, Orlovskiy VF, Zharkova AV et al. Influence of inflammatory cytokines on the course of chronic obstructive pulmonary disease. [Influence of inflammatory cytokines on the course of chronic obstructive pulmonary]. Visnyk medyko-biolohichnykh doslidzhen'. 2021;1(7):46-53. doi:10.11603/bmbr.2706-6290.2021.1.12087. (Ukrainian) DOI
18. Christopher CB, David G et al. C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations. N Engl J Med. 2019;381:111-20. doi: 10.1056/NEJMoa1803185. DOI
19. Ostrovskyy M., Savelikhina I., Korzh N et al. C-reactive protein and the type IV collagen measurementin severe COPD: Value of roflumilast. European Respiratory Journal. 2021;58(65):PA556. doi: 10.1183/13993003. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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