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# CRP levels in bronchoalveolar lavage as markers of inflammatory process intensity in patients with infiltrative tuberculosis combined with chronic bronchitis

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Despite the tendency to certain stabilization of TB morbidity and mortality rates, the epidemical situation in Ukraine is still complex. Annually the disease affects approximately 32 thousand people and over 6 thousand Ukrainians die <sup>[12]</sup>. In 2012 some positive dynamics on the decrease in TB morbidity rate to 0.5% was observed among the urban population of Ukraine as compared to 2011, though the incidence increased among the rural population to 4.8% in 2012 <sup>[18]</sup>.

The clinical-and-laboratory examination involved 120 patients, and the CRP level in bronchoalveolar lavage was determined in 59 patients. Development of infiltrative tuberculosis in patients with chronic bronchitis is accompanied by the 5.15 times ( $p < 0.05$ ) increase of CRP levels in bronchoalveolar lavage as compared to patients with exclusively infiltrative tuberculosis.

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**Keyword:** Infiltrative tuberculosis, chronic bronchitis, C-reactive protein, erythrocyte sedimentation rate (ESR).

### 1. Introduction

Tuberculosis is one of the oldest diseases, which can affect all organs and systems of the human body, and unfortunately kills millions of people every year. Over the past few decades, there have been significant changes in the epidemiology, clinical picture, structure of clinical forms, complications and comorbidities of pulmonary tuberculosis <sup>[1, 2, 3, 17]</sup>. The number of patients with serious complications and chronic bronchial pathologies has increased, predetermining the development of more severe TB types, leading to respiratory malfunction and reducing the effectiveness of treatment <sup>[3, 4, 6, 13]</sup>. The study of tuberculous process characteristics under the epidemic conditions, rapid evolution of functional and endoscopic diagnostics, and the increase in number of thoroughly examined patients in phthisiatric institutions draws doctors' attention to

concomitant endobronchial inflammatory processes and bronchoobstruction <sup>[1, 8, 13]</sup>. Highly evaluating the research findings of leading authors, it must be stressed, that not all questions dealing with the problem are resolved. Nowadays TB in Ukraine appears to be the most common contagious disease that comes first in the structure of people's mortality from infectious diseases <sup>[20, 22]</sup>. 680 671 TB patients are registered in Ukraine that makes up 1.4% of all the country's population, the number of patients with an active form of TB amounts to 144 041 cases (21.2%) <sup>[20]</sup>. This data is based on the records made on the registration of most patients when applying for consultation in healthcare facilities, that's why presumably the number of such patients is 1.5 - 2 times higher, as most cases aren't still diagnosed <sup>[11, 19]</sup>. The rate of TB morbidity in Ukraine became the most critical

after 1990 and has gone beyond exclusively medical problems at the strategic state level. Over the period of 2003–2007 the epidemiological situation of TB morbidity in Ukraine has not improved. Thus, the incidence of all TB forms has increased by 3.0% [11]. The incidence of newly diagnosed pulmonary tuberculosis in Ukraine has also increased by 4.5% - from 68.4 cases per 100 thousand people in 2003 to 71.5 cases per 100 thousand people in 2007. The incidence of destructive pulmonary tuberculosis among newly diagnosed cases in Ukraine has increased by 23.9% — from 24.7 cases to 30.6 cases per 100 thousand people. The TB mortality rate has increased by 3.7 % from 21.8 to 22.6 cases per 100 thousand people [11, 19, 21].

In 2012 the TB morbidity rate was 20% lower as compared with its rate in 2005. The morbidity rate decreased by 19.2%, and the rate of mortality decreased by one-third (31.4%) [12].

Despite the tendency to certain decrease in TB morbidity and mortality rates, the epidemiological situation in Ukraine still remains complex [12].

One of the prominent characteristics of current situation is that the aspect of TB process association with other comorbide pathologies is commonly observed. Specifically, the research findings by Raznatovska O.M. [16, 25] indicate that the signs of chronic bronchitis in patients with newly-diagnosed pulmonary TB were observed in more than half cases (the fluctuation median ranges from 54.5 to 71.2%).

According to the data provided by scientific literature [3, 16, 26], the causing factors of bronchoobstructive syndrome (BOS) in patients with pulmonary TB include meta- and post tuberculous pneumo fibrosis with damage to the architectonics and topography of bronchopulmonary system, resulting in bronchial deformation, formation of bronchiectasis, torpid course of tuberculosis, progressive inflammatory changes in bronchial mucosa with compromised local immune defense and development of mucociliary insufficiency [6].

An important role in the development of bronchoobstructive syndrome in TB patients pertains to bronchial hyper-reactivity (BHR) followed by dysfunction of effector cells as a result

of the reaction of bronchial mucosa to tuberculous intoxication [15]. Thus the intensity of inflammatory changes in the lower respiratory tract depends on the severity of exudative phase of tuberculous inflammation [14, 15]. According to Chernushenko K.F. and the co-authors the immune base of the bronchoobstructive syndrome in TB patients is represented by hyper-sensitivity and delayed bronchial hyper-reactivity [24].

It has been established that lung disorders are accompanied by systemic changes associated with inflammatory activity of pulmonary tissue cells, its hypoxia and influence on general metabolism, as well as the impact of such risk factors as cigarette smoking, industrial pollutants, genetic factors, etc. [5]. It is accompanied by the development of the so-called oxidative stress and changes in the levels of inflammatory mediators and acute-phase proteins [10]. Acute-phase proteins and C-reactive proteins are among important biomarkers reflecting the severity of inflammatory processes in the body [23].

Characteristics of CRP – mainly its non-specific character (regarding the root causes of inflammation) and high correlation of its concentration in blood with the severity of tuberculosis and COPD stage, its use as the diagnostic marker of COPD development in patients with bronchial asthma, makes CRP more convenient inflammatory marker in contrast to such markers as erythrocyte sedimentation rate (ESR), leukocyte count and differential WBC count shift. However the changes in their balance in bronchoalveolar lavage at the development of infiltrative pulmonary tuberculosis in patients with chronic bronchitis are still not investigated for now.

Therefore, little knowledge of combined course of pulmonary tuberculosis and chronic bronchitis and related diagnostic problems require further scientific investigations.

## 2. Materials and methods

In order to investigate the influence of chronic bronchitis on the course of infiltrative tuberculosis all patients were divided into three experimental groups: group I was composed of 40 patients with chronic bronchitis; group II included 40 patients

with infiltrative tuberculosis; group III included 40 patients suffering from infiltrative tuberculosis associated with chronic bronchitis. The clinical-and-laboratory examination involved 120 patients and the CRP level in bronchoalveolar lavage was determined in 59 patients. The control group included 15 apparently healthy individuals.

The diagnosis of infiltrative tuberculosis was stated and verified on the basis of the order of Ministry of Health Care of Ukraine no 1091 from November 21, 2012 – «On approval of the uniform clinical protocol for primary, secondary (specialized) and tertiary (highly specialized) medical care of tuberculosis» [12]. Chronic bronchitis was diagnosed on the basis of the International Statistical Classification of Diseases and Related Health Problems 10th Revision; clinical, physical and instrumental signs (productive cough over the couple of months within 2 years; wheezing, 2-3 exacerbation episodes a year within 2 years; retaining the signs of impaired ventilation in the remission phase; radiological signs of sclerosis) [7, 9].

**3. Results:** Complete blood cell count showed

changes in leukogram: marked leukocytosis was revealed in 29 (72,5%) patients and lymphopenia was observed in 18 (45%) patients from group I; among group II patients leukocytosis was revealed in 34 (85%) individuals and lymphopenia was observed in 30 (75%) patients, that was 1.67 times higher ( $p < 0.05$ ) as compared to patients with chronic bronchitis. As a result of combination of the investigated nosologies we have fixed further significant increase in lymphopenia incidence to 87.5% and leukocytosis incidence increased to 36 (90%) cases ( $p < 0.05$ ). It should also be mentioned that the increase in lymphopenia in group III patients correlated with ( $r = 0.78$ ;  $p < 0.05$ ) the rise of ESR to  $39.3 \pm 3.4$  mm/hr. This parameter exceeded the like data in group I and II patients, where it made up  $18.1 \pm 3.7$  mm/hr and  $28.4 \pm 2.3$  mm/hr, respectively.

While defining the CRP level in bronchoalveolar lavage our findings have revealed (chart 1) the tendency for significant 3.28 increase of C-reactive protein level in bronchoalveolar lavage of patients with chronic bronchitis in acute phase as compared to apparently healthy individuals ( $p < 0.05$ )

**Chart 1:** The indices of C-reactive protein in bronchoalveolar lavage (mg/l) in patients with infiltrative tuberculosis depending upon the occurrence of chronic bronchitis, (M±m)

Index	Groups of the investigated individuals				p1	p2
	Apparently healthy individuals, n=15	Patients with chronic bronchitis, n=18 (group I)	Patients with infiltrative tuberculosis, n=14 (group II)	Patients with infiltrative tuberculosis combined with chronic bronchitis, n=27 (group III)		
C-reactive protein	1.65±0.11	5.42±0.37	2.11±0.28	10.87±1.45	<0.05	<0.05

Notes: p1 – significance of parameter difference between the indices of the investigated groups;

p2 - significance of parameter difference between the indices of the investigated groups and control group.

In infiltrative tuberculosis the given index was 1.28 times higher than the analogic index in the control group patients, and group III patients with combined pathology were identified maximal 6.56 times increase in CRP level as compared to the group of apparently healthy individuals ( $p < 0.05$ ). Consequently, the given index in group I patients made up ( $5.42 \pm 0.37$ ) mg/l, and was 2.57 times higher than in patients with selective infiltrative pulmonary tuberculosis (see chart. 1). Though, we have identified the highest levels of C-reactive protein in bronchoalveolar lavage in patients with infiltrative pulmonary tuberculosis combined with chronic bronchitis, and the described index appeared to be 2 times higher than in group I patients and 5.15 times higher than in group II ones ( $p < 0.05$ ).

#### 4. Conclusions

The manifestation of clinical-and-functional features of the development of infiltrative tuberculosis in patients with chronic bronchitis is significantly followed by the 5.15 times' increase of CRP level in bronchoalveolar lavage ( $p < 0.05$ ), as compared to the findings in patients suffering solely from infiltrative tuberculosis.

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