MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
SUMY STATE UNIVERSITY
MEDICAL INSTITUTE

Eastern Ukrainian Medical Journal

2, Rymskogo-Korsakova st., Sumy 40007, Ukraine
e-mail: EUMJ@med.sumdu.edu.ua
eumj.med.sumdu.edu.ua
ISSN: 2663-5909 (print)

DOI: https://doi.org/10.21272/eumj.2021;9(4):362-372

Abstract

Vasyl B. Kushnir
ORCID:0000-0002-0545-6838
Department of Tuberculosis, Pulmonology and Family Medicine, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine;
Department of General and Clinical Immunology and Allergology, V. N. Karazin Kharkiv National University, Kharkiv, Ukraine

INDICATORS OF CLINICAL, RADIOLOGICAL, AND LABORATORY STATUS IN MALE PATIENTS WITH NEWLY DIAGNOSED INFILTRATIVE PULMONARY TUBERCULOSIS

Introduction. In Ukraine, despite the free medical care in the field of tuberculosis, the effectiveness of tuberculosis treatment does not meet WHO standards. With the lack of resistance of Mycobacterium tuberculosis to the first-line anti-TB agents, the desired improvement in clinical and radiological results in the first 2 months of treatment is not always possible to achieve. The causes of the poor efficiency remain unknown and require detailed study.

The objective was to study clinical, radiological, and laboratory data of male inpatients with newly diagnosed infiltrative pulmonary tuberculosis at the beginning of treatment.

Materials and Methods. 133 men with newly diagnosed infiltrative pulmonary tuberculosis sensitive to the first-line anti-TB agents were examined. The data of clinical, radiological, and laboratory parameters were studied; immunological parameters of IL-4, IL-10, IFN-γ, and data of phagocytic activity of neutrophils were additionally examined. All patients were tested for anxiety and depressive disorders using the State-Trait Anxiety Inventory and Beck Depression Inventory.

Results. It was found that at the beginning of treatment, patients with pulmonary destruction cavities had a 2.7-fold higher incidence of intensive bacterial excretion and a 1.6-fold reduction in IFN-γ levels as compared with patients without lung tissue destruction. Men with an extended infiltrative process in the lungs presented with fever and symptoms of intoxication more than 2.5 times more often, with cough – more than 4 times more often, with a history of weight loss – more than 2.9 times more often, with Mycobacterium tuberculosis detected by microscopy – more than 6.2 times more often vs. men with a limited process in the lungs.

Conclusions. Patients with newly diagnosed infiltrative pulmonary tuberculosis who had destructive changes in lung tissue and a significant extension of the pathological process were characterized by more pronounced clinical manifestations, intoxication, activation of systemic inflammatory response factors, decreased activity of the cellular immune system, and psychological disorders.

Keywords: newly diagnosed pulmonary tuberculosis, infiltrative tuberculosis, clinical data, laboratory data, symptoms, bacterial excretion.

Corresponding author:
Vasyl B. Kushnir, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine; V. N. Karazin Kharkiv National University, Kharkiv, Ukraine
e-mail: dikaryok@gmail.com

Резюме

Василь Б. Кушнір
ORCID:0000-0002-0545-6838
кафедра фтизіатрії, пульмонології та сімейної медицини Харківської медичної академії післядипломної освіти, м. Харків, Україна;
кафедра загальної та клінічної імунології та алергології медичного факультету Харківського національного університету ім. В. Н. Каразіна, м. Харків, Україна

ПОКАЗНИКИ КЛІНІКО-РЕНТГЕНОЛОГІЧНОГО ТА ЛАБОРАТОРНОГО СТАТУСУ У ХВОРИХ ЧОЛОВІЧОЇ СТАТІ З ВПЕРШЕ ВИЯВЛЕНИМ ІНФІЛЬТРАТИВНИМ ТУБЕРКУЛЬОЗОМ ЛЕГЕНЬ

Вступ. В Україні, при наявності безкоштовної медицини в сфері фтизіатрії, ефективність лікування туберкульозу не досягає поставлених ВООЗ норм. При відсутності резистентності мікобактерій туберкульозу до I ряду протитуберкульозних препаратів не завжди вдається досягти бажаної клініко-рентгенологічної динаміки за перші 2 місяці лікування. Причини низької ефективності даного процесу залишаються відкритими та потребують детального вивчення.

Метою роботи було дослідження клініко-рентгенологічних та лабораторних показників хворих на вперше діагностований інфільтративний туберкульоз легень на етапі початку лікування в умовах стаціонару.

Матеріали та методи. Було обстежено 133 чоловіки із вперше діагностованим інфільтративним туберкульозом легень зі збереженою чутливістю до I ряду протитуберкульозних препаратів. Вивчено дані клінічних, рентгенологічних та лабораторних показників, додатково проводилось обстеження імунологічних параметрів IL-4, IL-10, γ-INF та даних фагоцитарної активності нейтрофілів. Усі пацієнти пройшли тестування для визначення тривожно-депресивних розладів за допомогою опитувальників Спілбергера-Ханіна та Бека.

Результати дослідження. Встановлено, що на початку лікування пацієнти з порожнинами розпаду в легенях мали в 2,7 разів більшу частоту масивного бактеріовиділення та зниження рівня γ-INF у 1,6 разів у порівнянні з хворими без деструкції легеневої тканини. У чоловіків з поширеним інфільтративним процесом у легенях підвищення температури та симптоми інтоксикації відмічалися частіше ніж у 2,5 рази, кашель – частіше ніж у 4 рази, втрата ваги в анамнезі – частіше ніж у 2,9 рази, виявлення мікобактерій туберкульозу методом мікроскопії – частіше ніж у 6,2 рази проти чоловіків з обмеженим процесом в легенях.

Висновки. Пацієнти із вперше діагностованим інфільтративним туберкульозом легень, які мають деструктивні зміни в легеневій тканині та значну розповсюдженість патологічного процесу характеризуються більш вираженим ступенем інтоксикації, клінічним проявом, активацією факторів системної запальної відповіді, зниженням активності клітинної ланки імунітету та порушеннями психологічного стану.

Ключові слова: вперше виявлений туберкульоз легень, інфільтративний туберкульоз, клінічні дані, лабораторні дані, симптоматика, бактеріовиділення.

Автор, відповідальний за листування:
Василь Б. Кушнір, Харківська медична академія післядипломної освіти, м. Харків, Україна; Харківський національний університет ім. В. Н. Каразіна, м. Харків, Україна
e-mail: dikaryok@gmail.com

How to cite/ Як цитувати статтю: Kushnir VB. Indicators of clinical, radiological, and laboratory status in male patients with newly diagnosed infiltrative pulmonary tuberculosis. *EUMJ*. 2021;9(4):362-372
DOI: https://doi.org/10.21272/eumj. 2021;9(4):362-372

Introduction/Вступ

The global issue of tuberculosis, which has been challenging humanity for millennia, remains relevant today. In the structure of causes of infectious disease deaths, tuberculosis has ranked first for a long time [1] and is estimated to hold this position for the next few years [2, 3].

Even though patients stay at the hospital and take medications constantly, it is not always possible to achieve the 85% treatment effectiveness rate recommended by the WHO [4]. That is why improving the effectiveness of pulmonary tuberculosis treatment is a goal of paramount importance in the modern tuberculosis service.

Infiltrative pulmonary tuberculosis is more common than other clinical variants [5] and correlates with a high risk of developing destruction cavities, which are closely associated with bacterial excretion and are an indication for surgery in case of ineffective conservative therapy [6]. Due to the predominance of the exudative type of inflammatory process and the lack of reparative fibrosis in the areas of specific involvement of the lung tissue, the risk of unfavorable course of pulmonary tuberculosis increases [7].

Prolonged hospital stay, stigmatization of the disease, alcohol and drug abuse, smoking, lack of social and material support, drug-induced side effects, and intoxication play a significant role in the prolongation of the pathological process [8, 9]. In case of slow improvement in clinical and radiological study results, persisting bacterial excretion or serious adverse reactions to etiotropic therapy, the duration of the intensive phase of treatment (IP) may be extended to 90 doses by the decision of the Central Medical Advisory Committee (CMAC). Due to the prolongation of IP, the state bears additional expenses, and the patient is exposed to additional psychological pressure [10]. The need to prolong IP is usually justified and aimed at improving the effectiveness of treatment.

Due to innovations in the health care domain, changes in socio-economic standards and trends in attitude towards health, the current clinical and radiological picture of tuberculosis has undergone significant changes [11]. That is why a detailed study of these parameters at the stage of hospitalization allows us to identify modern features of the tuberculosis process.

Objective. The study of clinical, radiological, and laboratory data of male patients with newly diagnosed infiltrative pulmonary tuberculosis at the beginning of treatment.

Materials and Methods

The research was carried out in 2019–2021 at the Municipal Non-Profit Enterprise of the Kharkiv Regional Council "Regional TB Dispensary No. 1". 133 patients with newly diagnosed infiltrative pulmonary tuberculosis (ND IPTb) were selected for the study.

Inclusion criteria were: male sex, ND IPTb, bacterial excretion confirmed by sputum culture, susceptibility of Mycobacterium tuberculosis (MBT) to first-line anti-TB agents.

Exclusion criteria were: a history of drug abuse; refused treatment; other radiological forms of pulmonary tuberculosis; acute emergencies; acute inflammatory diseases of nontuberculous origin; chronic diseases, i.e. hepatitis, HIV, chronic obstructive pulmonary disease (COPD), bronchial asthma (BA), cardiovascular diseases, diabetes mellitus, cancer, autoimmune, systemic and mental diseases.

At the baseline, all patients had a chest X-ray and sputum culture analysis to determine the presence of MBT in accordance with the current order of medical care for patients with tuberculosis [12, 13]. Standard laboratory tests were also performed: complete blood count, urine analysis, and blood chemistry.

Additionally, the level of cytokines (IL-4, IL-10, IFN- γ) in blood serum was assayed by three-site solid-phase sandwich ELISA using corresponding anti-IL-4, anti-IL-10 and anti-IFN-γ monoclonal antibodies (ZAO Vector-Best, Russian Federation); ceruloplasmin (CP) level – by Ravin method, and haptoglobin level – by reaction with

rivanol using standard reagent kits (PrAT Reagent, Ukraine).

Standardized self-assessment scales (questionnaires) were used to assess patients' anxiety and depression. These questionnaires can be used by general practitioners without psychiatrist involvement and do not require special training. The anxiety reactions of the respondents were determined using the State-Trait Anxiety Inventory. The patient's distress was evaluated using Beck Depression Inventory (BDI) [14].

The study was conducted in accordance with the requirements of Good Clinical Practice, the Council of Europe Convention on Human Rights and Biomedicine, the Declaration of Helsinki of the World Medical Association and approved by the local Ethics Commission of the Kharkiv Medical Academy of Postgraduate Education (Minutes No. 3 dated 12.10.2021). All patients gave their informed consent to participate in the study.

Statistical data were analyzed using the Statistica program. Quantitative data were presented as a mean value (M) and standard deviation (SD). The Mann–Whitney U-test was used to compare the values between groups. The critical value of 0.05 referred to the significance level in a hypothesis test.

Results

The study included 133 male patients aged 18 to 55 years (mean age 39.57 ± 9.01). Among the patients included, 55.6% (n = 74) of subjects did not have a regular job, 49.6% (n = 66) were unmarried, 89.5% (n = 119) were smokers, and 78.2% (n = 104) were light drinkers.

According to the questionnaires aimed at detecting anxiety and depression conditions, the Beck Depression Inventory average score was 12.66 ± 6.27, and the number of patients with no signs of depression, with mild depression and moderate depression was 54.9% (n = 73), 35.3% (n = 47) and 9.8% (n = 13), respectively.

In the main group of patients, State-Trait Anxiety Inventory testing for state anxiety gave a mean score of 31.87 ± 9.6, and for trait anxiety, it was 26.39 ± 10.43. According to the questionnaire, no patient showed a high level of state or trait anxiety. Moderate levels of state anxiety were observed in 73.7% (n = 98), and trait anxiety – in 36% (n = 48) of men.

At the beginning of treatment, symptoms of intoxication were observed in 75.9% (n = 101) of patients, and 69.9% (n = 93) of patients had hyperthermia and lowgrade fever (37.21 ± 0.48 °C). In 41.3% (n = 55) of men, there was a decrease in body weight by more than 5 kg over the past 2 months. The mean body mass index (BMI) at admission was 21.15 ± 1.78 kg/m^2, which corresponded to normal values. During a detailed examination, complaints of cough and shortness of breath during exercise were observed in 51.2% (n = 68) of subjects, while decreased appetite was reported in 75.9% (n = 101) of patients. The average respiratory rate among patients was 19.13 ± 1.77 breaths per minute.

The results of complete blood count at the baseline were as follows: color index – 1.01 ± 0.08, RBC – 3.73 ± 0.45*10^{12}/L, HGB – 136.38 ± 15.57 g/L, WBC – 7.02 ± 1.87*10^9/L, PLT – 244.2 ± 40.25*10^9/L; ESR – 26.99 ± 12.68 mm/h, i.e. more than twice as much as the normal limits. The WBC differential was as follows: EOS averaged 3.17 ± 1.44%, STAB – 3.48 ± 1.55%, SEG – 62.23 ± 6.17%, LYM – 26.61 ± 5.96%, and MON – 4.52 ± 2.01%. Red blood cell counts and white blood cell counts were within normal limits.

Blood chemistry did not reveal significant abnormalities for the studied parameters. The total protein level equaled 65.36 ± 8.17 g/L, which was the lower limit of normal, as well as its albumin fraction – 37.6 ± 3.51 g/L; creatinine reached the upper limit of normal – 0.10 ± 0.08 mmol/L; urea – 6.00 ± 2.18 mmol/L; cholesterol – 3.95 ± 0.87 mmol/L; bilirubin – 14.34 ± 4.18 μmol/L; thymol test – 2.29 ± 1.14 IU; glucose – 4.67 ± 0.73 mmol/L. Alanine aminotransferase (ALT) was slightly higher than normal – 0.9 ± 0.49 μmol/L, which is one and a half times higher than normal, while the level of aspartate aminotransferase (AST) was 0.55 ± 0.27 μmol/L, which exceeded normal values by 1.2 times.

Acute-phase proteins were studied separately. There was an increase in the levels of haptoglobin up to 2.37 ± 0.9 g/L and ceruloplasmin up to 495.3 ± 85.6 mg/L. The level of C-reactive protein (CRP) averaged 17.33 ± 7.90 mg/L, which is almost 3 times as much as the normal values.

When studying immunological parameters, we paid attention to some cytokines, namely: the level of IL-4 at the baseline was 0.35 ± 0.46 pg/mL, IL-10 – 4.89 ± 3.35 pg/mL, and IFN-γ – 3.35 ± 2.18 pg/mL.

CD4/CD8 ratio in the majority of patients showed normal values = 2.18 ± 0.27. The level of circulating immune complexes (CIC) at admission was elevated – 138.29 ± 59.06 IU. The phagocytic number (PhN) was 3.44 ± 1.32, while the phagocytic index (PhI) equaled 79.71 ± 8.91%; the

index of phagocytosis completeness (PhCI) was 1.05 ± 0.16. Among the indicators of phagocytic activity in the main group of patients, no significant abnormalities were in general observed.

According to the results of X-ray examination, 24.8% (n = 33) of patients had limited infiltrative changes in the lungs, which did not involve more than 2 segments of one lung; in 40.6% (n = 54) of subjects, the process involved more than 2 segments within one lung, and in 34.6% (n = 46) of cases, the tuberculosis process was observed in both lungs. The destructive changes were observed in 60.1% (n = 80) of patients; among them, 70% (n = 56) had less than 2 destruction cavities visualized, and in the remaining 30% (n = 24) of cases, there were 3 or more caverns.

MBT were detected in all patients with ND IPTb at the baseline; among them, intensive bacterial excretion (M +) was detected by smear microscopy in 58.6% (n = 78) of patients; 80.8% (n = 63) of these were clinical cases with destructive changes.

Detailed distribution of clinical, radiological, and laboratory data with regard to the extension of the tuberculosis process and the presence of destructive changes in the lungs are shown in Tables 1 and 2.

The results of the study showed that destructive changes in the lungs were associated with hyperthermia and lowgrade fever; intoxication syndrome; cough; weight loss of more than 5 kg in the past 2 months; mild to moderate depression; moderate state and trait anxiety; the spread of the infiltrative process of the lungs; bacterial excretion; marked increase in ESR and decreased total protein level; suppression of the proinflammatory immune response expressed in low levels of IFN-γ against the background of normal values of IL-4 and IL-10; a significant increase in haptoglobin and ceruloplasmin levels as indicators of the inflammatory response; decreased phagocytic activity represented by the reduced PhI and PhN.

Analysis of clinical, radiological, and laboratory data with regard to the extension of the tuberculosis process demonstrated a close correlation between the spread of infiltrative changes and numerous parameters. The extension of tuberculosis was strongly associated with intensive bacterial excretion, destructive changes in the lungs, hyperthermia and lowgrade fever, cough, intoxication syndrome, anxiety and depressive disorders, increased haptoglobin, and ESR. It was also found that the group of patients with both lungs involved differed from other groups. Thus, these patients had a history of a more pronounced decrease in BMI and body weight; a greater decrease in IFN-γ, PhN, PhI, PhCI levels; and a more significant increase in ceruloplasmin level.

The results showed that patients with ND IPTb demonstrated deterioration in a number of clinical, radiological, and laboratory data that correlated with extension of the infiltrative process and the number of destruction cavities. First of all, we should pay attention to the correlation between the frequency of intensive bacterial excretion and the presence of destruction cavities, which increased the risk of microscopic detection of MBT in sputum by 2.7 times. In the case of extended radiological forms of tuberculosis (involving more than 2 segments of one or both lungs), the risk of MBT detection using this method increased by 6.2 times as compared to limited forms (involving no more than 2 segments).

Clear results were observed for the connection between destruction cavities and extended forms of the infiltrative process [15, 16]. The more extended the pathological process, the more likely the destruction.

Among the complaints, special attention was paid to cough, which was three times more common in patients with destructive changes, and ≥ 4 times more common in patients with the extended pathological process. Patients with destructive and extended forms of tuberculosis had a history of weight loss in the past 2 months more than twice as frequently. The severity of intoxication and temperature rise was 1.5 times greater in men with destruction cavities in the lungs. The same symptoms were more than twice as common in patients with the extended infiltrative process.

As for the laboratory data, ESR was 1.2 times higher in patients with destruction cavities and 1.7 times higher in patients with the extended process. A decrease by 1.6 and 1.3 times in IFN-γ and PhN levels, respectively, was observed in patients with destructive changes; by 1.2 and 1.1 times – in patients with extended tuberculosis within one lung, and by 2.6 and 1.57 times – in patients with the extended pathological process in both lungs. Haptoglobin and ceruloplasmin levels were 1.5 and 1.2 times higher in men with destructive changes. The same parameters were 1.9 and 1.3 times higher in patients with extended tuberculosis involving both lungs as compared with limited tuberculosis forms.

Table 1 – Distribution of the clinical, radiological, and laboratory parameters with regard to the destructive changes in the lungs

Parameter	No destructive changes in the lungs	Destructive changes in the lungs	p
BMI, kg/m^2	19.80 ± 1.81	19.58 ± 1.78	p = 0.810
Smoking, %	83 (n = 44)	93.7 (n = 75)	p = 0.168
Body temperature rise, %	54.7 (n = 29)	80 (n = 64)	p < 0.001
Body temperature, °C	37.03 ± 0.48	37.34 ± 0.44	p < 0.001
Intoxication, %	56.6 (n = 30)	88.75 (n = 71)	p < 0.001
Cough, %	22.64 (n = 12)	70 (n = 56)	p < 0.001
A history of weight loss, %	15.09 (n = 8)	58.75 (n = 47)	p < 0.001
Beck Depression Inventory, average score	10.17 ± 4.07	14.36 ± 6.90	p < 0.001
No depression, %	77.36 (n = 41)	40 (n = 32)	p = 0.002
Mild depression, %	22.64 (n = 12)	43.75 (n = 35)	p < 0.001
Moderate depression, %	0 (n = 0)	16.23 (n = 13)	p < 0.001
State-Trait Anxiety Inventory, average score:			
- State anxiety	27 ± 11.2	35.19 ± 6.63	p < 0.001
- Trait anxiety	21.89 ± 8.37	29.24 ± 10.67	p = 0.01
Mild state anxiety, %	52.83 (n = 28)	8.75 (n = 7)	p < 0.001
Moderate state anxiety, %	47.17 (n = 25)	91.25 (n = 73)	p < 0.001
Mild trait anxiety, %	86.8 (n = 46)	48.75 (n = 39)	p = 0.003
Moderate trait anxiety, %	13.2 (n = 7)	51.25 (n = 41)	p = 0.003
Extension of the infiltrate, %:			
- Up to 2 segments within one lung	43.4 (n = 23)	12.5 (n = 10)	p < 0.001
- More than 2 segments within one lung	35.85 (n = 19)	43.75 (n = 35)	p < 0.001
- Both lungs	20.75 (n = 11)	43.75 (n = 35)	p < 0.001
M+	28.3 (n = 15)	78.75 (n = 63)	p < 0.001
RBC, 10^{12}/L	3.62 ± 0.46	3.80 ± 0.44	p = 0.008
Hb, g/L	136.72 ± 17.45	136.15 ± 14.30	p = 0.658
ESR, mm/h	23.83 ± 12.02	29.09 ± 12.75	p = 0.047
WBC, 10^9/L	7.21 ± 1.86	6.89 ± 1.87	p = 0.071
NEU, %	66.66 ± 5.49	65.08 ± 6.57	p = 0.118
SEG, %	63.64 ± 5.75	61.29 ± 6.30	p = 0.047
LYM, %	26.26 ± 5.20	26.84 ± 6.43	p = 0.236
MON, %	4.21 ± 1.84	4.73 ± 2.10	p = 0.166
ALC	1.86 ± 0.52	1.82 ± 0.58	p = 0.391
Total protein, g/L	67.88 ± 8.09	63.69 ± 7.84	p = 0.039
ALT, μmol/L	0.82 ± 0.47	0.96 ± 0.49	p = 0.417
AST, μmol/L	0.52 ± 0.25	0.57 ± 0.28	p = 0.519
IL-4, pg/mL	0.32 ± 0.35	0.37 ± 0.52	p = 0.935
IL-10, pg/mL	4.84 ± 2.43	4.92 ± 3.86	p = 0.915
IFN-γ, pg/mL	5.12 ± 1.88	2.18 ± 1.46	p < 0.001
Haptoglobin, g/L	1.78 ± 0.68	2.73 ± 0.89	p < 0.001
Ceruloplasmin, mg/L	429.02 ± 86.22	512.79 ± 71.47	p < 0.001
CRP, mg/L	16.92 ± 7.85	17.60 ± 7.98	p = 0.725
CD4/CD8	2.1 ± 0.17	2.23 ± 0.31	p = 0.008
CIC, IU	125.25 ± 58.4	146.94 ± 58.25	p = 0.252
PhI, %	84.89 ± 6.72	76.28 ± 8.54	p < 0.001
PhN	4.25 ± 0.97	2.91 ± 1.25	p < 0.001
PhCI	1.10 ± 0.13	1.01 ± 0.16	p = 0.052

Table 2 – Distribution of the clinical, radiological, and laboratory parameters with regard to the extension of the infiltrative process in the lungs

Parameter	Up to 2 segments within one lung	More than 2 segments within one lung	Both lungs	p
BMI, kg/m^2	19.92 ± 1.52	19.95 ± 1.84	19.15 ± 1.83	p_{1-2} = 0.321 p_{1-3} = 0.067 p_{2-3} = 0.033
Smoking, %	84.84 (n = 28)	85.19 (n = 46)	97.83 (n = 45)	p_{1-2} = 1.000 p_{1-3} = 0.103 p_{2-3} = 0.018
Body temperature rise, %	27.27 (n = 9)	75.93 (n = 41)	93.48 (n = 43)	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.057
Body temperature, °C	36.80 ± 0.39	37.23 ± 0.42	37.49 ± 0.37	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} < 0.001
Intoxication, %	36.36 (n = 12)	83.33 (n = 45)	95.65 (n = 44)	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.032
Cough, %	12.12 (n = 4)	48.15 (n = 26)	82.61 (n = 38)	p_{1-2} = 0.051 p_{1-3} < 0.001 p_{2-3} < 0.001
A history of weight loss, %	12.12 (n = 4)	35.79 (n = 19)	69.57 (n = 32)	p_{1-2} = 0.083 p_{1-3} < 0.001 p_{2-3} < 0.001
Beck Depression Inventory, average score	10.42 ± 4.97	11.67 ± 5.66	15.52 ± 6.82	p_{1-2} = 0.687 p_{1-3} < 0.001 p_{2-3} = 0.001
No depression, %	69.7 (n = 23)	61.11 (n = 33)	36.96 (n = 17)	p_{1-2} < 0.001 p_{1-3} = 0.012 p_{2-3} < 0.001
Mild depression, %	30.3 (n = 10)	33.33 (n = 18)	41.3 (n = 19)	p_{1-2} = 0.003 p_{1-3} = 0.002 p_{2-3} = 0.323
Moderate depression, %	0 (n = 0)	5.56 (n = 3)	21.74 (n = 10)	p_{1-2} = 0.160 p_{1-3} = 0.002 p_{2-3} = 0.007
State-Trait Anxiety Inventory, state anxiety average score	25.52 ± 11.32	34.31 ± 8.18	33.72 ± 7.7	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.713
Mild state anxiety, %	60.6 (n = 20)	12.96 (n = 7)	17.39 (n = 8)	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.533
Moderate state anxiety, %	39.4 (n = 13)	87.04 (n = 47)	82.61 (n = 38)	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.533
State-Trait Anxiety Inventory, trait anxiety average score	19.36 ± 6.98	25.48 ± 10.23	32.26 ± 9.41	p_{1-2} = 0.251 p_{1-3} < 0.001 p_{2-3} < 0.001
Mild trait anxiety, %	96.97 (n = 32)	68.52 (n = 37)	34.78 (n = 16)	p_{1-2} = 0.103 p_{1-3} < 0.001 p_{2-3} < 0.001
Moderate trait anxiety, %	3.03 (n = 1)	31.48 (n = 17)	65.22 (n = 30)	p_{1-2} = 0.103 p_{1-3} < 0.001 p_{2-3} < 0.001
Number of cavities, % - ≤ 2 segments	27.27 (n = 9)	57.41 (n = 31)	34.78 (n = 16)	p_{1-2} < 0.001 p_{1-3} = 0.006 p_{2-3} < 0.001
- > 2 segments	3.03 (n = 1)	7.41 (n = 4)	41.3 (n = 19)	p_{1-2} = 0.083 p_{1-3} < 0.001 p_{2-3} < 0.001
M+	12.12 (n = 4)	74.07 (n = 40)	73.91 (n = 34)	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.811

Parameter	Up to 2 segments within one lung	More than 2 segments within one lung	Both lungs	p
RBC, 10^{12}/L	3.63 ± 0.41	3.70 ± 0.32	3.82 ± 0.58	p_{1-2} = 0.184 p_{1-3} = 0.054 p_{2-3} = 0.177
Hb, g/L	140.42 ± 11.28	137.06 ± 12.71	132.67 ± 20.09	p_{1-2} = 0.804 p_{1-3} = 0.116 p_{2-3} = 0.165
ESR, mm/h	17.27 ± 5.96	29.11 ± 11.59	31.48 ± 13.89	p_{1-2} < 0.001 p_{1-3} < 0.001 p_{2-3} = 0.471
WBC, 10^9/L	7.51 ± 1.93	7.20 ± 1.87	6.45 ± 1.7	p_{1-2} = 0.249 p_{1-3} < 0.001 p_{2-3} = 0.117
NEU, %	65.85 ± 5.97	65.87 ± 6.37	65.41 ± 6.25	p_{1-2} = 0.375 p_{1-3} = 0.93 p_{2-3} = 0.77
SEG, %	62.52 ± 6.14	62.44 ± 6.2	61.76 ± 6.27	p_{1-2} = 0.378 p_{1-3} = 0.965 p_{2-3} = 0.988
LYM, %	26.52 ± 5.86	26.3 ± 6.36	27.04 ± 5.63	p_{1-2} = 0.505 p_{1-3} = 0.617 p_{2-3} = 0.843
MON, %	4.58 ± 1.82	4.54 ± 1.98	4.46 ± 2.21	p_{1-2} = 0.516 p_{1-3} = 0.616 p_{2-3} = 0.814
LYM, g/L	1.95 ± 0.58	1.84 ± 0.49	1.74 ± 0.59	p_{1-2} = 0.629 p_{1-3} = 0.025 p_{2-3} = 0.274
Total protein, g/L	66.43 ± 8.65	65.12 ± 7.88	64.87 ± 8.26	p_{1-2} = 0.902 p_{1-3} = 0.58 p_{2-3} = 0.536
ALT, μmol/L	0.86 ± 0.5	0.85 ± 0.44	1.01 ± 0.52	p_{1-2} = 0.985 p_{1-3} = 0.901 p_{2-3} = 0.071
AST, μmol/L	0.54 ± 0.25	0.52 ± 0.27	0.58 ± 0.28	p_{1-2} = 0.831 p_{1-3} = 0.752 p_{2-3} = 0.422
IL-4, pg/mL	0.27 ± 0.35	0.45 ± 0.54	0.28 ± 0.40	p_{1-2} = 0.157 p_{1-3} = 0.86 p_{2-3} = 0.149
IL-10, pg/mL	4.75 ± 3.21	5.52 ± 3.47	4.25 ± 3.25	p_{1-2} = 0.08 p_{1-3} = 0.371 p_{2-3} = 0.06
IFN-γ, pg/mL	4.85 ± 1.92	3.72 ± 1.97	1.83 ± 1.62	p_{1-2} = 0.221 p_{1-3} < 0.001 p_{2-3} < 0.001
Haptoglobin, g/L	1.59 ± 0.60	2.19 ± 0.66	3.09 ± 0.88	p_{1-2} = 0.026 p_{1-3} < 0.001 p_{2-3} < 0.001
Ceruloplasmin, mg/L	419.89 ± 64.37	471.69 ± 84.35	531.16 ± 76.12	p_{1-2} = 0.057 p_{1-3} < 0.001 p_{2-3} < 0.001
CRP, mg/L	16.16 ± 8.00	17.63 ± 8.07	18.47 ± 7.49	p_{1-2} = 0.441 p_{1-3} = 0.298 p_{2-3} = 0.465
CD4/CD8	2.18 ± 0.25	2.15 ± 0.25	2.20 ± 0.30	p_{1-2} = 0.938 p_{1-3} = 0.896 p_{2-3} = 0.407
CIC, IU	133.06 ± 58.82	135.39 ± 61.21	145.46 ± 57.24	p_{1-2} = 0.852 p_{1-3} = 0.838 p_{2-3} = 0.275
PhI, %	85.52 ± 5.04	80.43 ± 8.10	74.7 ± 9.29	p_{1-2} = 0.01 p_{1-3} < 0.001 p_{2-3} = 0.002

Parameter	Up to 2 segments within one lung	More than 2 segments within one lung	Both lungs	p
PhN	4.21 ± 1.07	3.64 ± 1.18	2.67 ± 1.24	$p_{1-2} = 0.394$ $p_{1-3} < 0.001$ $p_{2-3} < 0.001$
PhCI	1.13 ± 0.14	1.08 ± 0.13	0.96 ± 0.16	$p_{1-2} = 0.68$ $p_{1-3} = 0.001$ $p_{2-3} < 0.001$

Note: $_1$, $_2$ and $_3$ indexes for the p-value correspond to group numbers

The evaluation of the psychological state of patients requires a separate analysis. It was demonstrated that depressive and anxiety disorders were twice as common in patients with destructive forms of tuberculosis. In the cases of extended tuberculosis process involving both lungs, the cases of mild and moderate depression were more frequent as compared to limited forms of tuberculosis. Moderate state anxiety was twice as prevalent in patients with extended forms of tuberculosis. Moderate trait anxiety was rare in groups with limited forms of tuberculosis, but was twice as common in patients with the pathological process involving both lungs vs. extended infiltrative changes in one lung.

Thus, in patients with ND IPTb, the presence of destructive changes in lung tissue and a great extension of tuberculosis were determinants of clinical, radiological, and laboratory status, which predetermined the features of the disease. These parameters characterized more expressed degrees of intoxication, clinical manifestations, activation of systemic inflammatory response factors, decreased activity of the cellular immune system, and psychological disorders.

Conclusions/Висновки

Working-age men with ND IPTb manifested with extended pulmonary processes and destructive changes in lung tissue in 75.2% and 60.1% of cases, respectively; intensive bacterial excretion – in 58.65% of cases; symptoms of intoxication – in 75.9% of cases; increased haptoglobin, ceruloplasmin, and C-reactive protein (CRP) with average values of 2.37 ± 0.9 g/L, 495.3 ± 85.6 mg/L and 17.33 ± 7.90 mg/L, respectively; mild or moderate anxiety in 100% of cases and symptoms of mild or moderate depression according to the Beck Depression Inventory – in 45.1% of cases.

In patients with ND IPTb, the presence of destructive changes in lung tissue and greater extension of tuberculosis were closely associated with more intensive bacterial excretion, severe intoxication and cough, the history of weight loss, more expressed activation of a systemic inflammatory response (increased ESR, haptoglobin, ceruloplasmin levels), imbalance of immune status parameters (greater decrease in IFN-γ and PhN), as well as psychological disorders represented by the most common symptoms of depression and anxiety.

Prospects for future research/Перспективи подальших досліджень

Further research suggests the study of the clinical, radiological, and laboratory parameters after the intensive phase of treatment and comparison of them with the baseline data.

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(received 26.10.2021, published online 29.12.2021)

(одержано 26.10.2021, опубліковано 29.12.2021)

Conflict of interest/Конфлікт інтересів

The authors declare no conflict of interest.

Acknowledgements/Джерела фінансування

The research is a part of the PhD thesis of Vasyl Borysovych Kushnir, a postgraduate student of the Department of Tuberculosis, Pulmonology, and Family Medicine. Financing from own resources.

Information about the authors/Відомості про авторів

Кушнір Василь Борисович – аспірант кафедри фтизіатрії, пульмонології та сімейної медицини Харківської медичної академії післядипломної освіти, вул. Амосова, 58, м. Харків; асистент кафедри загальної та клінічної імунології та алергології медичного факультету Харківського національного університету імені В. Н. Каразіна, пл. Свободи, 6, м. Харків, Україна
e-mail: dikaryok@gmail.com
тел.: +380966213989
ORCID: https://orcid.org/0000-0002-0545-6838