



STATE OF SYSTEMIC AND LOCAL IMMUNE RESPONSE IN PATIENTS WITH OSTEOARTICULAR TUBERCULOSIS IN THE PERIOPERATIVE PERIOD

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Article history:	Abstract:
Received: 8 th February 2026 Accepted: 7 th March 2026	Bone and joint tuberculosis represents one of the most severe extrapulmonary forms of tuberculosis infection, constituting, according to various data, from 3 to 5% in the structure of all registered cases of tuberculosis. The disease is characterized by steadily progressive destructive damage to bone tissue, which often leads to persistent loss of joint function, disability of patients, and a significant decrease in their quality of life.
Keywords: Osteoarticular tuberculosis, bone and joint tuberculosis, systemic immune response, local immunoreactivity, perioperative period, T-lymphocytes, cytokines, immunodeficiency, surgical treatment of tuberculosis, immunological indicators	

INTRODUCTION. Bone-joint tuberculosis (BJT) accounts for 3-5% of all forms of the disease, which is equivalent to 270-450 thousand new cases annually. The total number of patients with specific bone and joint lesions in the world reaches 300-900 thousand people. Despite the relatively low share in the structure of overall morbidity, CST is characterized by a severe clinical course and a significant burden on the healthcare system.

Diagnosis of CST remains one of the most complex problems of phthisioorthopedics, which is due to the difficulties of clinical interpretation, as well as the limited sensitivity of bacteriological and histological verification methods, which does not exceed 60%. The disease develops slowly, often proceeds latently or under the guise of nonspecific pathology of the musculoskeletal system, which leads to late detection. In most cases, the diagnosis is made at the stage of formed destructions, pronounced deformities, and complications. Even with the possibility of complete treatment by modern conservative and surgical methods, the level of disability reaches 70%.

PURPOSE OF THE RESEARCH: State of systemic and local immune response in patients with osteoarticular tuberculosis in the perioperative period

MATERIALS AND METHODS OF RESEARCH: To solve the set task, a comprehensive examination of 223 patients aged 18-87 years with bone-articular forms of tuberculosis was conducted, who were examined and treated in the period 2022-2024 at the Bukhara Regional Center for Phthisiology and Pulmonology. The dissertation work was carried out at the Bukhara State Medical Institute.

At the first stage, a retrospective-prospective analysis of clinical and laboratory data was conducted in 223 patients with the verified bone-joint form of tuberculosis.

In the second stage of the study, an in-depth immunological examination of 115 patients selected from the general cohort was conducted.

The diagnosis was made based on clinical and functional data in accordance with the international consensus on the diagnosis and treatment of phthisiatric diseases. Diagnoses were verified based on a thorough medical history, clinical, laboratory (general blood analysis), biochemical blood analysis, and instrumental (radiography of the chest organs, MSCT).

Assessment of immune status included phenotyping of lymphocyte populations using monoclonal LT series antibodies, determination of the concentration of immunoglobulins A, M, G in blood serum, levels of pro- and anti-inflammatory cytokines in blood serum and sperm plasma. Indicators of the cellular link of immunity (CD3+, CD4+, CD8+, CD4/CD8, CD16+, CD20+, CD25+, CD95+), humoral link (IgG, IgA, IgM), cytokine profile (IL-1 β , IL-6, TNF- α , IL-4, IFN- γ , IP-10), endothelial activation (sICAM-1, sVCAM-1), as well as markers of hemostasis and fibrinolysis (tPA, PAI-1) were assessed.

To determine the content of cytokines in the blood serum of the studied groups, the three-stage "sandwich" method was used - this is a variant of three-phase ELISA.

The obtained data were subjected to statistical processing using the Fisher-Student variational statistics method and Pearson's χ^2 criterion. The distribution of genotypes of the studied polymorphisms was checked for compliance with the expected at Hardy-Weinberg equilibrium using Fisher's accurate test (Weir, 1995).



RESULTS OF THE STUDY: Analysis of the incidence of tuberculosis in the Bukhara region for 2020-2023 revealed a statistically significant increase in the proportion of extrapulmonary forms ($p < 0.05$). The share of extrapulmonary localization increased from 23.8% in 2020 to 34.8% in 2022 ($p < 0.01$) and remained at 34.3% in 2023 ($p > 0.05$ compared to 2022). The maximum absolute number of cases was registered in 2022 - 207 patients, which is 66.9% higher than the level of 2020 ($p < 0.01$). In the structure of extrapulmonary forms, bone and joint tuberculosis dominated (88.9-95.0%; $p < 0.001$). The absolute number of patients with this form increased from 113 to 189 cases, the increase was 67.3% ($p < 0.01$).

Territorial analysis showed a significant decrease in the share of the city of Bukhara from 15.9% to 7.4% ($p < 0.05$). At the same time, in the Gijduvan district, the indicator increased to 13.2% ($p < 0.05$), in the Jandar district - to 12.2% ($p > 0.05$). In the Ramitansky and Peshkunsky districts, the share increased to 11.6% and 11.1%, respectively ($p < 0.05$). Fluctuations in indicators in individual territories were variable in nature and in a number of cases did not reach statistical significance ($p > 0.05$). In general, the epidemiological dynamics is characterized by a reliable mix of morbidity in rural areas ($p < 0.05$).

Hematological changes included anemia in 41.3% of patients (Hb 96.3 ± 1.18 g/l; $p < 0.001$ relative to reference values). Leukocytosis was detected in 18.4% ($12.1 \pm 0.42 \times 10^9/l$; $p < 0.01$), lymphopenia - in 29.6% ($14.8 \pm 0.59\%$; $p < 0.001$), lymphocytosis - in 12.6% ($p < 0.05$). An increase in ESR was registered in 52.9% of patients (30.7 ± 1.06 mm/h; $p < 0.001$). The combination of anemia and lymphopenia correlated with the severity of the process ($r = 0.62$; $p < 0.01$). The data confirm the presence of severe systemic inflammation.

The biochemical profile was characterized by hyperbilirubinemia in 8.1% of patients (23.6 ± 1.36 $\mu\text{mol/l}$; $p < 0.01$). An increase in ALT was detected in 30.5% (66.7 ± 4.38 IU/l; $p < 0.001$), AST - in 12.1% (64.0 ± 7.34 IU/l; $p < 0.01$). Hypoproteinemia was noted in 12.6% (58.6 ± 1.12 g/l; $p < 0.01$). An increase in urine was registered in 41.0% (11.9 ± 0.45 mmol/l; $p < 0.001$), hyperglycemia - in 32.7% (10.1 ± 0.45 mmol/l; $p < 0.001$). The identified changes reliably correlated with the CRP level ($r = 0.58$; $p < 0.01$).

Hemostasis disorders manifested as an increase in MNO in 52.0% of patients (1.21 ± 0.04 ; $p < 0.001$), a decrease in PTI in 31.4% ($66.1 \pm 1.21\%$; $p < 0.001$). An increase in fibrinogen was noted in 62.3% (6.13 ± 0.23 g/l; $p < 0.001$). ACHTV prolongation was registered in 13.5% (51.4 ± 1.23 sec; $p < 0.001$). The level of C-reactive

protein was 7.85 ± 0.65 mg/l versus 4.43 ± 0.12 mg/l in the control ($p < 0.001$), lactoferrin was reduced to 376.5 ± 4.35 ng/ml ($p < 0.001$). The data confirm the formation of inflammatory-induced coagulopathy.

In the control group, the average concentration of 25 (OH) D was 33.2 ± 1.12 ng/ml, while in patients with bone-joint tuberculosis, this indicator decreased to 21.6 ± 0.9 ng/ml. Vitamin D availability in patients with CST was 1.54 times lower compared to the control, with a high statistical significance of differences ($p < 0.001$). A similar trend was revealed in relation to osteocalcin: in the control group, its level was 31.6 ± 1.31 ng/ml, while in patients with CST - 23.7 ± 0.9 ng/ml. The decrease in the indicator by 1.33 times was statistically significant ($p < 0.001$). The obtained data indicate suppression of bone formation processes against the background of a chronic inflammatory process.

β Crosslaps, which is a biochemical marker of bone resorption and reflects the degradation of type I collagen under the action of osteoclasts, demonstrated opposite dynamics. In patients with bone-joint tuberculosis, its level reached 1.42 ± 0.05 ng/ml, while in the control group it was 0.64 ± 0.02 ng/ml. This corresponds to an increase in the indicator by 2.22 times, with statistically significant differences ($p < 0.001$). The growth of β -crosslaps indicates the predominance of catabolic processes in bone tissue. The totality of identified changes reflects a pronounced imbalance of bone remodeling in CST.

Histomorphologically, dystrophic changes were detected in 42.2% of patients, destructive - in 38.6%, deformation - in 27.4% ($p < 0.01$ between categories). Inflammatory infiltration was registered in 32.7%, granulomas - in 9.4% ($p < 0.001$). The predominance of dystrophic and destructive forms indicates a chronic course of the disease. The frequency of late changes statistically exceeded the early forms ($p < 0.01$). This reflects the late diagnosis of the process.

Intermediate stage (II-III) was diagnosed in 42.2% of patients, late (IV-V) - in 34.5%, early (I-II) - in 23.3%. The intermediate stage exceeded the early stage by 1.8 times ($p < 0.001$). The late stage was encountered 1.5 times earlier ($p < 0.01$). Differences between intermediate and late stages did not reach statistical significance ($p > 0.05$). Data confirm the predominance of chronic forms (Table 2).

Age analysis showed a decrease in the early stage from 31.2% (18-44.9 years) to 6.1% (≥ 75 years) ($p < 0.001$). The late stage increased from 22.0% to 65.6% ($p < 0.001$). In the group of 60-74.9 years, the late stage was 53.4% ($p < 0.001$ relative to young people). The intermediate stage did not have significant age



differences ($p > 0.05$). This confirms the progression of morphological changes with age.

Granulomatous changes in young people were found in 42.9%, which is 4.5 times higher than in individuals ≥ 75 years old (9.5%; $p < 0.001$). The inflammatory reaction decreased from 38.4% to 11.0% ($p < 0.001$). Destructive changes increased from 12.8% to 33.7% ($p < 0.001$). The frequency of deformations increased from 9.8% to 36.1% ($p < 0.001$). The data demonstrate a reliable age-related transformation of the morphological profile.

Gender analysis showed that the late stage was registered in 41.2% of men versus 23.9% of women ($p < 0.01$). The early stage was more often detected in women - 30.4% versus 18.6% ($p < 0.05$). Destructive changes occurred in 66.3% of cases in men versus 33.7% in women ($p < 0.05$). Dystrophic forms also prevailed in men (61.7% versus 38.3%; $p < 0.05$). The male sex is statistically associated with a more severe morphological course of bone and joint tuberculosis.

CONCLUSIONS: In patients with osteoarticular tuberculosis before surgical intervention, a significant decrease in the absolute number of CD4+ lymphocytes and the CD4+/CD8+ ratio was revealed compared to the indicators of healthy individuals, which indicates suppression of the cellular link of immunity at the systemic level. Cytokine profile imbalance. In the preoperative period, hyperproduction of pro-inflammatory cytokines (TNF- α , IL-6, IL-1 β) is noted in combination with an increase in the level of immunosuppressive IL-10, which reflects the dysregulation of the immune response, characteristic of chronic mycobacterial infection.

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