CHARACTERISTICS OF LABORATORY PARAMETERS AND CYTOKINE PROFILES IN ZOONOTIC CUTANEOUS LEISHMANIASIS

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Background. Zoonotic cutaneous leishmaniasis remains a pressing public health concern across endemic regions. While predominantly recognized by localized ulcerative skin lesions, the disease triggers systemic hematological and biochemical alterations, including leukocytosis, accelerated erythrocyte sedimentation rate, dysproteinemia, and elevated cytolysis enzymes. However, routine clinical management frequently overlooks circulating inflammatory mediators and cytokine dynamics. Deciphering specific laboratory shifts and cytokine profiles is pivotal for staging disease severity, predicting protracted clinical courses, and objectively monitoring therapeutic outcomes.

Aim of the study. To delineate the specific patterns of hematological, biochemical and cytokine alterations in patients with zoonotic cutaneous leishmaniasis and to evaluate their clinical and predictive utility in assessing disease severity and therapeutic response.

Materials and Methods. A prospective clinical investigation was performed at the Bukhara Regional Infectious Diseases Hospital involving 120 adult patients aged 18 to 65 years with confirmed ZCL. The cohort was stratified into a main group (n=60, moderate-to-severe disease) and a comparison group (n=60, mild disease). An intact cohort of 30 age- and sex-matched healthy individuals served as the control group. Diagnosis was verified using clinical-epidemiological data and direct parasitological examination of skin ulcer scrapings. Serum levels of interleukin-4 (IL-4), interleukin-13 (IL-13), and interferon-gamma (IFN-γ) were quantified alongside complete blood counts and liver function panels. Prognostic accuracy was determined via receiver operating characteristic analysis.

Results. Immunological assessment revealed that progression of disease severity is accompanied by statistically significant elevations in both Th1- and Th2-associated cytokines ($p < 0.05$). Specifically, concentrations of the prototypical Th2 mediator IL-13 increased from 3.1±0.3 pg/mL in healthy controls to 7.4±0.6 pg/mL in the comparison group, reaching 14.2±0.9 pg/mL in the main group (a 4.5-fold increase relative to controls, $p < 0.05$). A concordant trajectory was recorded for IL-4, which rose from 2.8±0.2 pg/mL in controls to 6.9±0.5 pg/mL in mild cases and 10.8±0.7 pg/mL in moderate-to-severe cases ($p < 0.05$), reflecting pronounced Th2-skewed polarization and impaired leishmanicidal macrophage activation. Concurrently, compensatory upregulation of the Th1 marker IFN-γ was documented, rising from 5.1±0.4 pg/mL in controls to 8.2±0.6 pg/mL in the comparison group and 12.4±0.8 pg/mL in the main group ($p < 0.05$). ROC curve analysis validated the superior predictive capability of Th2 markers for anticipating moderate-to-severe and protracted disease: IL-13 yielded an area under the curve (AUC) of 0.892 (95% CI: 0.824–0.960, $p < 0.001$; cut-off value >10.5 pg/mL; sensitivity 86.7%, specificity 83.3%), while IL-4 demonstrated an AUC of 0.845 (95\% CI: 0.762–0.928, $p <0.001$; cut-off value >8.2 pg/mL; sensitivity 81.7%, specificity 80.0%). By comparison, IFN-γ exhibited a moderate predictive value (AUC = 0.781, >10.0 pg/mL, sensitivity 75.0%, specificity 71.7%).

Conclusions. The clinical progression of zoonotic cutaneous leishmaniasis is driven by an imbalance in the Th1/Th2 regulatory axis, marked by progressive cytokine secretion and a marked shift toward a Th2 immune response during moderate-to-severe disease. Elevated circulating levels of IL-13 and IL-4 reflect this Th2 polarization and serve as reliable prognostic biomarkers to identify patients at risk for protracted disease and complicated clinical outcomes.

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