

The Significance of Inflammatory Cytokines in the Early Stage of Rheumatoid Arthritis

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Abstract: Today, one of the urgent problems of rheumatology remains the problem of diagnosing rheumatoid arthritis at the early stages of its development. Therefore, early diagnosis of autoimmune diseases, in particular the development of RA in patients with joint syndrome based on immunological studies, the introduction of patients at various stages of medical care in order to prevent and reduce complications, and the development of treatment methods are among the tasks that need to be addressed in medicine. Purpose: assessment of the levels of proinflammatory cytokines TNF- α and IL6 and the study of the diagnostic value of these indicators in RA and NDA. Materials and methods: 103 patients were included in the study. All the examined patients were divided into the following groups: the main group consisted of patients with RA (53 patients) and NDA (50 patients), the control group consisted of practically healthy individuals (n=20), comparable in gender and age with the group of patients with RA and NDA. Results: An analysis of the studies showed that patients with RA had an increase in TNF- α levels by 40% and IL6 by 25% compared to patients with NDA ($P < 0.01$). In group I patients, there was a significantly higher incidence of TNF- $\alpha \geq 33.9$ and IL6 ≥ 12.8 , which proves the high diagnostic accuracy and specificity of these indicators in RA and HDA. Conclusion: thus, for the early detection of RA at the NDA stage, the study of the levels of proinflammatory cytokines TNF- α and IL6 proves the high diagnostic accuracy and specificity of these indicators, which contribute to predicting the disease and reducing the incidence of complications.

Keywords: Rheumatoid arthritis, undifferentiated arthritis, pro-inflammatory cytokines.

Introduction. A number of scientific studies are being conducted worldwide aimed at studying the role of cytokines in the pathogenetic mechanisms of RA development, early and differential diagnosis of the disease, and improving treatment and prevention methods [6]. In this regard, in patients with early and advanced RA, the analysis of pro-inflammatory cytokine levels, assessing the significance of immunological factors in the formation of disease severity, and selecting optimal treatment methods are of particular importance for conducting scientific research aimed at predicting and diagnosing the disease in its early stages [3].

In the early stages of the disease, when a person does not yet have visible symptoms, the levels of various substances that cause inflammation may already be elevated in their blood. This includes pro-inflammatory cytokines, inflammation mediators, and autoantibodies. During this period, high concentrations of cytokines and chemokines can be detected, which play a key role in the development of rheumatoid arthritis [5].

One of the key cytokines is tumor necrosis factor- α (TNF- α) and interleukin 6 (IL6) [1]. A significant increase in the expression level of TNF- α in the inflammatory focus, and in some cases throughout the body, leads to the development of various autoimmune diseases, particularly RA [2].

Purpose of the study: to assess the level of pro-inflammatory cytokines TNF- α and IL6, to study the diagnostic value of these indicators in early and advanced RA.

Materials and methods of research.

All clinical studies were conducted at the 1st multidisciplinary clinic of SamSMU in the period 2022-2024. 103 patients were included in the study. All examined patients were identified in the following groups:

- Group I consisted of 53 patients aged 48.45 ± 10.46 years, 10 (18.9%) men and 43 (81.1%) women, diagnosed with RA according to the 2010 ACR/EULAR criteria.
- Group II included 50 patients, 2 (4.0%) men and 48 (96.0%) women, with an average age of 44.2 ± 12.25 . These patients were assigned to the examination group with early RA and were observed in dynamics for 12 months until a definitive diagnosis was established.
- The control group consisted of practically healthy individuals ($n=20$), comparable in gender and age to the group of RA and NDA patients.

Research results. To determine the role of cytokine status in the course of the disease, the level of pro-inflammatory cytokines TNF- α and IL6 was examined. Analysis showed that the course of advanced RA is clearly accompanied by a higher level of inflammatory and autoimmune reactions, which was confirmed by a significantly higher level of cytokines, as in patients of group I, an increase in the level of TNF- α by 40% and IL6 by 25% was observed compared to patients of group II ($P < 0.01$) [7].

To clearly express the relationship between the sensitivity and specificity of determining TNF- α , IL6, the ROC curve was constructed in patients with early and advanced RA.

To illustrate the use of ROC analysis in determining the diagnostic value of TNF- α indicators in early and advanced RA, an example of graphical and numerical representation of this statistical data is provided. In this study, the area under the AUC-ROC curve is 0.733, which indicates the high diagnostic effectiveness of this method.

When constructing the ROC curve and analyzing the coordinates of the curve, it was established that in the diagnosis of advanced RA, the diagnostic significance of the indicator is TNF- $\alpha \geq 33.9$ pg/ml, with sensitivity - 71.7% and specificity - 61.4%.

To assess the diagnostic value of IL6 indicators in early and advanced RA, ROC analysis was used, the results of which are presented both visually and numerically. During the study, the area under the ROC curve (AUC-ROC) equal to 0.814 demonstrates the high effectiveness of this method in diagnosing, confirming its high sensitivity and specificity in differentiating between these two conditions.

When constructing the ROC curve and analyzing the coordinates of the curve, it was established that in the diagnosis of advanced RA, the diagnostic significance of the indicator is IL6 ≥ 12.8 pg/ml, with sensitivity - 75.5% and specificity - 70.0%.

Analysis of the ROC curves, conducted to determine the diagnostic significance of determining cytokine profile indicators in the diagnosis of early and advanced RA, showed that determining the level of TNF- $\alpha \geq 33.9$ pg/ml, IL6 ≥ 12.8 pg/ml had high sensitivity and relatively high specificity in the diagnosis of advanced RA.

After determining the diagnostic significance of determining cytokine profile indicators in the diagnosis of early and advanced RA, a comparative study of TNF- α , IL6 indicators was conducted in patients of groups I-II. In patients with advanced RA, a significantly higher frequency of TNF- $\alpha \geq 33.9$ was observed ($\chi^2=4.24$; $P=0.039$; OR=2.34; CI 95%: 1.03-5.29) and IL6 ≥ 12.8 ($\chi^2=11.94$; $P=0.001$; OR=4.25; CI 95%: 1.83-9.85), which proves the high diagnostic accuracy and specificity of these indicators in early and advanced RA.

Thus, the established high value of the AUC area in all the above parameters proves the high diagnostic significance of determining these cytokine profile parameters in the diagnosis of early and advanced RA.

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