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CORRELATION ANALYSIS OF IMMUNOLOGICAL INDICATORS TO IDENTIFY THE INDEX OF PROGNOSIS OF THE COURSE OF JUVENILE RHEUMATOID ARTHRITIS

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Abstract
Juvenile rheumatoid arthritis (JRA) is a chronic autoimmune disease of childhood, accompanied by joint inflammation and systemic complications. The study included a correlation analysis of eight immunological parameters in children with JRA. Reliable relationships were found between IL-8, IL-17A and INFγ, based on which the disease prognosis index (DPCI) was calculated. The highest DPCI values were observed in the seropositive form of JRA, which correlated with the severity of the clinical picture. The IL-17A/INFγ ratio can serve as an important prognostic marker. The data obtained are of diagnostic and practical importance for treatment optimization.

Keywords: Juvenile rheumatoid arthritis, cytokines, IL-17A, INFγ, immunological markers, disease prognosis index, IPTZ, correlation analysis, children, autoimmune inflammation.

Introduction

According to modern concepts, juvenile rheumatoid arthritis (JRA) is a chronic autoimmune disease characterized by destructive inflammatory damage to the joints and develops in children under 16 years of age [2, 3, 8].

In this disease, such serious manifestations of the disease as carditis, interstitial lung disease and serositis often develop. In 1/2 of patients, chronic polyarthritis recurs (with or without systemic manifestations), osteochondral destruction of joints progresses and functional insufficiency develops [1, 5, 10].

The development and progression of inflammation in rheumatic diseases is caused by autoimmune mechanisms, which are based on a violation of tolerance to one's own antigens, leading to the development of an immune response against normal tissues. This process is mediated by a complex interaction of genetic, immunological factors, various infectious agents and other environmental influences, defects in hormonal and neuroendocrine regulation [4, 6, 11].

The basis of inflammation is a cascade of biochemical and immunological processes, the regulation of which is carried out by a large number of humoral mediators. Among them, a special place is occupied by acute phase proteins and cytokines - low-molecular proteins that ensure the

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process of intercellular interactions [7, 9, 12].

Currently, changes in the cytokine profile are considered as possible trigger mechanisms for the development of juvenile rheumatoid arthritis (JRA) [5, 10].

The aim of the study: to identify significant correlations between immunological parameters and calculate the disease prognosis index (DPI) in children with juvenile rheumatoid arthritis to improve diagnosis and assess the severity of the clinical condition.

Materials and methods of research:

The study included 93 children aged 7 to 16 years suffering from juvenile rheumatoid arthritis (JRA), who were divided into two clinical groups: with seropositive and seronegative forms of the disease. Clinical material was collected in the Department of Cardiorheumatology of the clinic of the Tashkent Pediatric Medical Institute in the period 2021-2023. Almost healthy children (n = 20) of the corresponding age were used as a control group. All study participants underwent laboratory determination of eight immunological indicators (ELISA method, Vector-best, RF): interleukin-8 (IL-8), interleukin-17A (IL-17A), interferon-gamma (INFγ), C-reactive protein (CRP), antistreptolysin O (ASLO), rheumatoid factor (RF), vitamin D level and lactoferrin. The correlation analysis was used to evaluate the relationships between the parameters, with values at a significance level of $p \leq 0.05$ considered reliable. The disease prognosis index (DPI) was also calculated using the formula: DPI = IL-17A / INFγ, in order to identify the prognostic significance of the ratio of these cytokines. Statistical data processing included calculating the correlation coefficients (r) to determine the degree of relationship between the parameters. The values were determined with an average (r=0.3-0.69) and high degree (r=0.7-1.0).

Research results:

Correlation analysis of 8 immunological parameters of the main group in children with juvenile rheumatoid arthritis revealed 28 relationships, of which 4 were direct and 4 were inverse relationships. No high-degree values (r=0.7-1.0) were found in this group.

Thus, among these correlation relationships, the direct relationship between IL-8 and IL-17A (r=0.51) was significant and reliable, while the inverse relationships were between IL-8 and INFy (r=-0.50), IL-17A and INFy (r=-0.62) ($P \leq 0.05$).

One significant but weak inverse relationship was also found between antistreptolysin O and vitamin D (r=-0.33) ($P \leq 0.05$). (Fig. 4.10)

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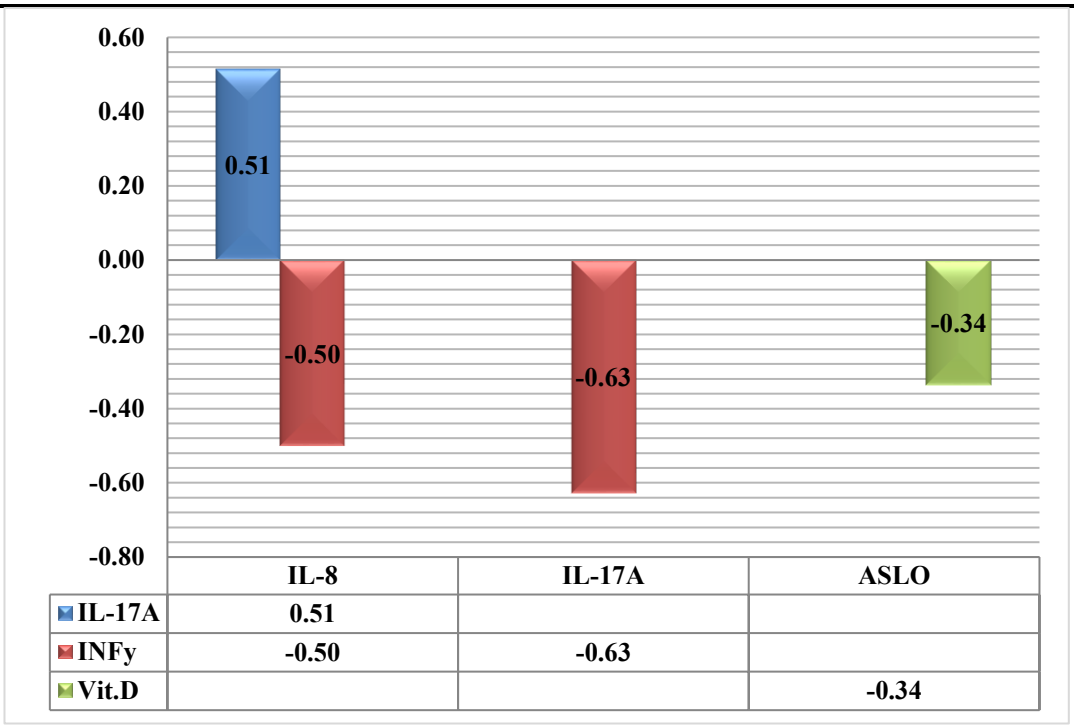

Fig. 4.10. Significant correlation relationships of immunological parameters in children with JRA (P≤0.05)

The remaining detected correlation relationships of immunological parameters had a weak insignificant relationship from r=-0.27 to r=0.41. Thus, IL-8 with CRP (r=0.16), ASLO (r=0.15), RF (r=-0.17), Vit. D (r=0.34), lactoferrin (r=-0.14); IL-17A with CRP (r=0.15), ASLO (r=0.14), RF (r=0.09), Vit. D (r=0.34), lactoferrin (r=-0.02); INFy with CRP (r=-0.27), ASLO (r=-0.22), RF (r=-0.01), Vit. D (r=-0.27), lactoferrin (r=0.04); C-reactive protein with ASLO (r=-0.04), RF (r=-0.11), Vit. D (r=-0.10), lactoferrin (r=-0.02); Antistreptolysin O with RF (r=0.04), lactoferrin (r=-0.23); Rheumatoid factor with Vit. D (r=-0.12), lactoferrin (r=0.41); Vitamin D (r=0.02) with lactoferrin (Table 1)

Table 1 Correlation relationships in patients with juvenile rheumatoid arthritis

Immunological indicators	Correlation relationships	P
IL-8 with CRP	r=0.16	0.07
IL-8 with ASLO	r=0.15	0.097
IL-8 from RF	r = -0.17	0.127
IL-8 with Vit. D	r=0.34	0.950
IL-8 with lactoferrin	r=-0.14	0.721
IL-17A with CRP	r = 0.15	0.143
IL-17A with ASLO	r=0.14	0.743
IL-17A from RF	r=0.09	0.062
IL-17A with Vit. D	r=0.34	0.382
IL-17A with lactoferrin	r=-0.02	0.08

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INFy with CRP	r = -0.27	0,077
INFy with ASLO	r=-0.22	0.106
INFy from RF	r=-0.01	0.758
INFy with Vit. D	r=-0.27	0.781
INFy with lactoferrin	r=0.04	0.153
CRP with ASLO	r=-0.04	0.643
SRB with RF	r=-0.11	0.122
CRP with Vit. D	r=-0.10	0.278
SRP with lactoferrin	r=-0.02	0.811
ASLO with RF	r=0.04	0.103
ASLO with lactoferrin	r=-0.23	0.287
RF with Vit. D	r=-0.12	0.183
RF with lactoferrin	r=0.41	0.109
Vit. D with lactoferrin	r=0.02	0.373

Our previous studies have shown that in children with JRA, the levels of cytokines - IL-17A and IFNγ - are subject to more drastic changes. In this regard, we calculated the index of the inverse ratio of these indicators using the following formula: IPTZ = IL-17A / IFNγ (IPTZ is the index of disease prognosis). To achieve this goal, we divided the sample of children with JRA (n = 93) aged 7 to 16 years into two groups with seropositive and seronegative forms.

According to the calculation data, it turned out that in practically healthy individuals (control group), the IPTS was greater than 1 and amounted to 1.71±0.15 (Table 2).

This indicator increased in patients with a seropositive form of JRA and amounted to 3.50, and in the seronegative form = 2.09.

Table 2 Content of IL-8 and IFNγ in the peripheral blood serum of examined children

Indicators	**Patients examined**		
	K.gr.	Seronegative JRA	Seropositive JRA
IL-17A	11.4	30.8	35.75
IFNγ	19.5	14.7	10.2
IPTZ	1.71	2.09	3.50

Analysis of the results of calculating the index of disease prognosis (IPTZ) showed that among those examined, an elevated index corresponded to a more severe clinical condition. For example, in patients with seropositive JRA with IPTZ equal to 3.50 and above, a higher percentage of complications, severe protracted course in combination with symptoms of intoxication were observed.

RatioIL-17A and IFNγ can serve as reliable prognostic and diagnostic criteria for the course of this disease.

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Thus, the IPTZ identified based on the ratios of IL-A and IFNγ provides the necessary information about the state of the immune system and allows predicting the course of the disease after treatment. In determining the choice and duration of the necessary therapy, the determination of the index will make a great contribution to healthcare practice.

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