

# PROGNOSTIC SIGNIFICANCE OF PROINFLAMMATORY CYTOKINES IN CHILDREN WITH SHIGELLOSIS

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**Abstract.** *The levels of tumor necrosis factors- and interleukin-1 in the blood serum in young children with Shigellosis have been investigated. The connection between the degree indexes during acute phase and type of Shigellosis course has been discovered.*

**Key words:** *children, Shigellosis, cytokines.*

Intestinal infections are one of the most frequently registered groups of children diseases [2]. According to the WHO more than 2 milliard people are suffered from enteric infection every year [3]. Nearly 1 million people death of this pathology every year [4, 7]. Among of intestinal infections the Shigellosis accounts for 60-75 % [6]. Great importance in the pathogenesis of intestinal infectious diseases, such as Shigellosis, different biologically active substances have, especially - the inflammation mediators like cytokines [1]. There are proinflammatory and anti-inflammatory interleukins. These substances regulate immune and inflammatory responses in the condition of infectious pathology. Induction of cytokine synthesis begins at the first stages of pathological process. Tumor necrosis factor- (TNF ) and interleukin-1 (IL1 ) have a special importance [5, 8].

The **aim** of the present study was to install dependency of the variant of the clinical current Shigellosis in children on the levels of proinflammatory interleukins in the blood serum.

**Methods.** The study was undertaken at the regional children's infectious hospital. We had observed 96 children from one month to three years with Shigellosis. Patients were divided into two groups according to the course of the disease. The first group included 65 patients with smooth-like course (SC) of the

disease, second group - 31 patients with wavy-like course (WC) of Shigellosis. The control group consisted of 20 healthy children of the similar age. The diagnosis was estimated using bacteriological and serological methods. We found that etiological factors of 47 children was *S. Flexneri* and in 49 - *S. S nnei*.

The patients came to the hospital for the first - the third day of the diseases. The manifestation of the disease characterized by a state of moderate in 38 children, and severe - 58 children. The main clinical manifestations of the disease were symptoms of intoxication (96 -100%), and dysfunction of the gastrointestinal tract: gastroenterocolitis (73 – 70.1%), gastroenteritis (9 - 8.6%), enterocolitis (16 - 21.3 %).

The concentration of tumor necrosis factor - and interleukins - 1 in the blood serum of the children during 1-3 days of the illness (the acute period of the disease), at 7-8 days of the illness (the period of recovery in smooth-like course of disease and period of improvement in wave-like course of Shigellosis), at 12-14 days of the disease with wave-like course of Shigellosis (the period of recovery) was evaluated.

The level of cytokines was determined by ELISA test. Statistical analysis of the results was performed using the "Exel" program. Reliability of the results was assessed by Student's criteria.

**Results.** High levels of proinflammatory cytokines (PC) in the serum in the acute phase of Shigellosis in all children were detected. The level of PC in patients significantly ( $p < 0.001$ ) higher than the level of PC in children from the control group. (Table 1, 2). This fact can be regarded as organism's reaction to penetration of pathogenic bacteria in the gastrointestinal tract and translocations of toxin from the gastrointestinal tract into the bloodstream.

Index of IL-1 of serum in the first group was  $74.2 \pm 2.3$  pg/ml and differed from that of the children of the second group -  $39.87 \pm 4.48$  pg/ml ( $p < 0.001$ ) (Table 3). The level of TNF- of patients with SC of Shigellosis amounted to  $94.83 \pm 1.9$  pg/ml and was significantly higher than the performance of children with WC of Shigellosis ( $61.39 \pm 3.48$  pg/ml) ( $p < 0.001$ ). The differences between the levels of

proinflammatory cytokines in the acute period indicate the hyporeactivity response of children with WC of Shigellosis at the onset of the disease.

On the seventh - eighth day of the disease (the period of early convalescence in a SC of Shigellosis and a period of improvement with WC) we found decrease of level of IL-1 in patients of the first group ( $48.5 \pm 1.45$  pg/ml) and the increase level of this index in children of the second group ( $57.6 \pm 13.5$  pg/ml), which meant about continuing inflammatory response in children with WC of Shigellosis. Also, in the patients of the first group we noted a decrease of concentration of TNF- ( $68,84 \pm 1,3$  pg/ml) in comparison with level of TNF- in the acute period ( $p < 0.001$ ). There were any dynamics of TNF- in patients of the second group ( $60.51 \pm 1.9$  pg/ml).

In children with WC of Shigellosis during early convalescence period (12 - 14 day after onset of the disease) were detected a slight decrease in the levels of proinflammatory cytokines in serum (IL-1 -  $37,39 \pm 4,48$  pg/ml, TNF- -  $58,43 \pm 6.1$  pg/ml) in comparison with the acute phase (IL-1  $39,87 \pm 4,48$  pg/ml TNF-  $61,39 \pm 3,48$  pg/ml) and period of improvement (IL-1  $57,6 \pm 13,5$  pg/ml TNF -  $60.51 \pm 1.9$  pg/ml). It means that process of inflammatory response in the body of patients with WC of Shigellosis is uncompleted. In our opinion, this fact is necessary to consider during rehabilitation and stage of medical follow-up.

### **Conclusion.**

1. The increased levels of tumor necrosis factor- and interleukin-1 in the blood of patients corresponds to the acute phase of systemic inflammatory response of child's body.

2. The finding of the cytokines indexes of patients in the acute stages of Shigellosis allows to predict the course of Shigellosis in young children, and to decide the therapeutic tactics of patients.

3. The rising levels of tumor necrosis factor- and interleukin-1 in serum during stages of early convalescence indicates uncompleted inflammatory response in children's organism. In our opinion, this fact is necessary to consider during rehabilitation and stage of medical follow-up.

Table 1

Content of proinflammatory cytokines in serum of patients with smooth-like current of Shigellosis (  $\pm$ m, pg/ml)

Indicators	Acute stages (n=65)	Stages of early convalescence (n=65)	Control group (n=20)
L-1	74,2 $\pm$ 2,3*' **	48,5 $\pm$ 1,45*' **	1,62 $\pm$ 0,35*
TNF-	94,83 $\pm$ 1,9*' **	68,84 $\pm$ 1,3*' **	0,87 $\pm$ 0,13*

Note. \* Reliability difference of indicators compared to the control group (p<0.001)

\*\* Reliability difference of parameters in different periods of the disease (p<0.001)

Table 2

Content of proinflammatory cytokines in serum of patients with wave-like current of Shigellosis (  $\pm$ m, pg/ml)

Indicators	Acute stages (n=31)	Stages of improvement (n=31)	Stages of early convalescence (n=31)	Control group (n=20)
L-1	39,87 $\pm$ 4,48*	57,6 $\pm$ 13,5*	37,39 $\pm$ 4,48*	1,62 $\pm$ 0,35*
TNF-	61,39 $\pm$ 3,48*	60,51 $\pm$ 1,9*	58,43 $\pm$ 6,1*	0,87 $\pm$ 0,13*

Note. \* Reliability difference of indicators compared to the control group (p<0.001)

Table 3

Content of proinflammatory cytokines in serum of patients with smooth-like current and wave-like current of Shigellosis (  $\pm$ m, pg/ml)

Indicators	Acute stages - the first group (n=65)	Acute stages - the second group (n=31)	Early convalescence stages - the first group (n=65)	Stages of improvement second group (n=31)
L-1	74,2 $\pm$ 2,3*	39,87 $\pm$ 4,48*	48,5 $\pm$ 1,45	57,6 $\pm$ 13,5
TNF-	94,83 $\pm$ 1,9*	61,39 $\pm$ 3,48*	68,84 $\pm$ 1,3**	60,51 $\pm$ 1,9**

Note. \* Reliability difference between indicators of acute period (p<0.001)

\*\* Reliability difference between indicators of early convalescence period and period of improvement ( <0,01).

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