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DYNAMICS OF SOME INFLAMMATORY MARKERS IN ACUTE INTESTINAL INFECTIONS OF VARIOUS ETIOLOGY

Agzamov Otabek Fakhrutdinovich
PhD, Republican Specialized Scientific and Practical Medical Center of Epidemiology, Microbiology, Parasitology and Infectious Diseases, Tashkent

Sadikova Nigora Majidovna
PhD, Republican Specialized Scientific and Practical Medical Center of Epidemiology, Microbiology, Parasitology and Infectious Diseases, Tashkent

Kamalov Zainitdin Sayfutdinivich
DSc, Prof., Head of Lab., Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan

Azizova Zukhra Shukhratovna
MD, PhD, Senior Researcher Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan

Abstract

Purpose of the study. To investigate inflammatory markers for determining the etiological structure of acute intestinal infections and predicting the course of the disease.

Materials and methods. A total of 103 pediatric patients hospitalized in the departments of the RSNPCMEIPD in 2023 with acute intestinal infections and an established etiological factor were examined. Bacteriological methods and PCR-based fecal screening were used for etiological diagnosis.

Results and discussion. The study analyzed the dynamics of cytokine levels (IL-1, IL-4, IL-8, IFN-α, and IFN-γ) in children with acute intestinal infections (AII) of various etiologies and severities. In moderate-severity cases, cytokine levels decreased over the course of the disease, particularly IL-4 and IFN-γ, which was statistically significant. Severe forms of infection showed a more pronounced increase in pro-inflammatory cytokines, especially in viral infections. After therapy, levels of most cytokines decreased, indicating normalization of the immune response. The results suggest that cytokines can be used as biomarkers for assessing the severity and prognosis of AII.

Keywords: Acute intestinal infections, cytokines, interleukins, inflammatory mediators

Relevance

The inflammatory process is a protective reaction of the body and can be of infectious or non-infectious etiology. Clinicians most often face the challenge of differentiating bacterial infections from other causes of fever, particularly viral infections. In cases of monoinfection, the cause of acute intestinal infection (AII) can often be suspected before laboratory confirmation based on clinical signs (e.g., pathological impurities in stool such as greenery, mucus, or blood suggest bacterial etiology, while profuse watery stool points to viral etiology). However, mixed infections (viral-bacterial or viral-viral) can significantly alter the clinical picture, complicating diagnosis and potentially leading to unjustified antibiotic therapy. As with monoinfections, the structure of mixed intestinal infections depends on age: viral agents predominate in younger children, while bacterial agents become more prominent with increasing age. Viral-viral and viral-bacterial associations are more common in younger children, whereas bacterial-bacterial associations are more frequent in older children (1,5,8).

In the early hours of inflammation, immune cells migrate to the pathological focus. For a long time, neutrophils were considered passive participants in the effector arm of the immune response (3,4,6). However, recent data indicate their involvement in the afferent response, modulating cellular and humoral immunity through the production of immunoregulatory cytokines such as IL-1, IL-6, and IL-12 (2,7). Cytokines act as intercellular messengers, regulating immune responses (4,5). They can function as synergists or antagonists, forming an interconnected system (5). Their interaction is mediated by a spectrum of mediators that depends on the type of infectious agent. Released mediators (primarily IL-1, IL-6, and IFN-γ) trigger a systemic acute-phase response, peaking on days 2–3 of inflammation (4). In some patients, an inadequate response to the infectious agent is associated with an imbalance in immune response development or the action of multiple pathogens. Therefore, simultaneous measurement of several inflammatory markers is clinically justified (7).

Purpose of the study

The above underscores the necessity and relevance of studying inflammatory markers to determine the etiological structure of acute intestinal infections and predict disease progression.

Materials and Methods

The study included 103 pediatric patients hospitalized in the RSNPCMEIPD departments in 2023 with acute intestinal infections and a confirmed etiological agent. Etiological diagnosis was performed using bacteriological methods and PCR-based fecal screening.

Cytokine levels—interleukin-1 (IL-1), interleukin-4 (IL-4), interleukin-8 (IL-8), interferon-α (IFN-α), and interferon-γ (IFN-γ)—were measured in 103 children with acute intestinal infections caused by identified pathogens. Of these, 26 (25.2%) had acute bacterial intestinal infections (S. enteritidis, Salmonella spp. + Campylobacter spp., Shigella spp. as mono- (76.9%) or mixed bacterial (23.1%) infections). Forty-five (43.7%) children were diagnosed with viral intestinal infections (rotavirus, adenovirus, norovirus, astrovirus). Thirty-two (31.1%) had mixed bacterial-viral intestinal infections.

Cytokine levels in different severities of bacterial and viral AII were compared with those in a group of conditionally healthy children (Table 1). Comparisons of cytokine status across AII groups were performed using the non-parametric Wilcoxon-Mann-Whitney test.

Results

Comparative analysis revealed a significant increase in IL-1 in both severe (9.2 ± 1.04 pg/mL) and moderate (13.1 ± 0.92 pg/mL) forms, as well as a significant increase in IL-8 in severe forms (56.2 ± 3.29 pg/mL). IFN-α and IFN-γ levels significantly exceeded control values, increasing 2.8- and 2.6-fold in moderate forms and 1.8- and 1.3-fold in severe forms, respectively.

In bacterial AII, moderate forms showed significantly higher IL-1 (1.4-fold; $P<0.05$) and IFN-γ (1.3-fold) levels compared to severe forms. In contrast, IL-8 levels were significantly higher ($P<0.05$) in severe bacterial AII compared to moderate forms (Table 1).

In viral AII, significant increases compared to controls were observed in IL-1 in severe forms (5.3 ± 1.08 vs. 12.04 ± 0.48 pg/mL), IFN-α in moderate and severe forms (55.70 ± 1.19 and 90.59 ± 2.21 pg/mL), and IFN-γ (30.46 ± 0.75 and 37.51 ± 1.09 pg/mL; $P<0.05$).

Comparative analysis of cytokine levels in viral AII by severity showed a trend of increasing IL-1, IL-4, IFN-α, and IFN-γ from moderate to severe forms. IL-1 concentration significantly increased 1.7-fold in severe viral AII compared to moderate forms. IL-4, IFN-α, and IFN-γ levels significantly increased 1.5-, 1.6-, and

1.2-fold, respectively, in severe compared to moderate viral AII. IL-8 levels showed no significant change with increasing severity.

Table 1. Cytokine levels in the serum of children with acute intestinal infections depending on etiology and severity before treatment

Indicator	Control	Bacterial (n=26)	Viral (n=45)	Viral-bacterial (n=32)
IL-1, pg/mL	5.3 ± 1.08	13.1 ± 0.92* 9.2 ± 1.04*	7.15 ± 0.14 12.04±0.48*•	8.6 ± 0.31* 10.4 ± 0.30*•
IL-4, pg/mL	2.4 ± 0.30	2.2 ± 0.20 1.8 ± 0.29*•	1.7 ± 0.11 2.6 ± 0.15•	2.5 ± 0.17 3.2 ± 0.14*•
IL-8, pg/mL	32.1 ± 3.41	34.9 ± 1.81 56.2 ± 3.29*•	38.2 ± 0.89 39.97 ± 1.40	43.8 ± 2.54* 45.2 ± 2.12*
IFN-α, pg/mL	21.5 ± 2.99	61.3 ± 2.30* 55.1 ± 3.21*•	55.70 ± 1.19* 90.59 ± 2.21*•	65.10 ± 4.06* 76.4 ± 2.38*•
IFN-γ, pg/mL	18.1 ± 1.39	32.3 ± 1.60* 24.5 ± 2.07*•	30.46 ± 0.75* 37.51 ± 1.09*•	29.26 ± 2.09* 35.2 ± 1.05*•

Note: * – P<0.05 vs. control; • – P<0.05 vs. moderate severity

Analysis of cytokine levels in mixed bacterial-viral AII before treatment showed a significant increase in all studied cytokines compared to controls (Table 1). However, in moderate mixed AII, cytokine levels (IL-1, IL-4, IL-8, IFN-α, IFN-γ) were lower than in severe forms, with significant differences only in IL-4 and IFN-γ (1.3- and 1.2-fold; P<0.05).

Cytokine dynamics were studied at disease peak and early convalescence (before hospital discharge). In moderate bacterial AII, significant decreases in IL-1, IFN-α, IFN-γ, and IL-8 (1.2-fold each; P<0.05) were observed by days 5–7 (Table 2).

In moderate viral AII, similar dynamics were noted, with significant reductions in IL-1, IFN-α, IFN-γ, IL-4, and IL-8 by days 5–7. The most pronounced decreases were in IL-4 and IL-8 (1.8- and 1.6-fold, respectively).

In moderate mixed AII, significant reductions were observed in IL-1 (1.3-fold), IL-4 (1.6-fold), IL-8 (1.3-fold), and IFN-γ (1.2-fold; P<0.05), with a non-significant decrease in IFN-α (1.1-fold; P>0.05) (Table 2).

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Table 2. Cytokine levels in the serum of children with moderate acute intestinal infections depending on etiology during disease dynamics

Indicator	Control	Bacterial (n=26)	Viral (n=45)	Viral-bacterial (n=32)
IL-1, pg/mL	5.3 ± 1.08	13.1 ± 0.92* 10.3 ± 0.74*•	7.15 ± 0.14 6.3 ± 0.13*•	8.6 ± 0.31* 6.7 ± 0.34*•
IL-4, pg/mL	2.4 ± 0.30	2.2 ± 0.20 1.8 ± 0.14*	1.7 ± 0.11 0.92 ± 0.10•	2.5 ± 0.17 1.6 ± 0.14*•
IL-8, pg/mL	32.1 ± 3.41	34.9 ± 1.81 26.2 ± 1.14*•	38.2 ± 0.89 24.4 ± 0.99•	43.8 ± 2.54* 36.4 ± 1.9*
IFN-α, pg/mL	21.5 ± 2.99	61.3 ± 2.30* 51.2 ± 2.09*•	55.70 ± 1.19* 52.3 ± 1.47*	65.10± 4.06* 55.3 ± 3.97*
IFN-γ, pg/mL	18.1 ± 1.39	32.3 ± 1.60* 26.2 ± 1.54*•	30.46 ± 0.75* 25.4 ± 0.72*•	29.26± 2.09* 21.3 ± 1.04*•

Note: * – P<0.05 vs. control; • – P<0.05 vs. moderate severity

In severe bacterial AII, only IL-4 showed a significant decrease (2-fold; P<0.05), while IL-1, IL-8, IFN-α, and IFN-γ showed a trend toward reduction (P>0.05) (Table 3).

Table 3. Cytokine levels in the serum of children with severe acute intestinal infections depending on etiology during disease dynamics

Indicator	Control	Bacterial (n=26)	Viral (n=45)	Viral-bacterial (n=32)
IL-1, pg/mL	5.3 ± 1.08	9.2 ± 1.04* 7.03 ± 10.38*	12.04 ± 0.48* 10.7 ± 0.48*	10.4 ± 0.30* 8.9 ± 0.34*•
IL-4, pg/mL	2.4 ± 0.30	1.8 ± 0.29* 0.9 ± 0.11*•	2.6 ± 0.15 1.46 ± 0.13*•	3.2 ± 0.14* 2.5 ± 0.15•
IL-8, pg/mL	32.1 ± 3.41	56.2 ± 3.29* 54.4 ± 3.16*	39.97 ± 1.40 26.5 ± 1.13•	45.2 ± 2.12* 34.4 ± 1.33•
IFN-α, pg/mL	21.5 ± 2.99	55.1 ± 3.21* 46.3 ± 3.73*	90.59 ± 2.21* 82.4 ± 2.13*•	76.4 ± 2.38* 71.3 ± 2.43*
IFN-γ, pg/mL	18.1 ± 1.39	24.5 ± 2.07* 21.3 ± 1.54	37.51 ± 1.09* 30.2 ± 1.20*•	35.2 ± 1.05 29.3 ± 1.19*•

*Note: * – P<0.05 vs. control; • – P<0.05 vs. moderate severity*

In severe viral AII, significant reductions were observed in IL-4, IL-8, IFN-α, and IFN-γ, with the most pronounced decreases in IL-4 and IL-8 (1.8- and 1.6-fold, respectively).

In severe mixed AII, reductions were similar in magnitude (1.2-, 1.3-, 1.3-, 1.1-, and 1.2-fold). Significant differences were observed in IL-1, IL-4, IL-8, and IFN-γ ($P<0.05$).

Thus, in bacterial and viral AII, IL-4 levels remained relatively low and similar between groups, suggesting minimal change in Th2 activity. IL-8 showed no significant inter-group differences, indicating similar neutrophil activation across etiologies. IFN-α was significantly elevated in viral infections, confirming an active antiviral response. IFN-γ was also higher in viral than bacterial infections. After treatment, IL-1 decreased in all groups, as did IL-4. IL-8 decreased in most groups but remained at control levels in bacterial infections. IFN-α and IFN-γ decreased but remained elevated in viral infections.

Comparative analysis revealed significant differences in cytokine levels depending on etiology and severity, both before and after treatment. Viral infections were characterized by higher pro-inflammatory cytokines (IL-1, IFN-α). Post-treatment, cytokine levels trended downward in all groups, though some remained elevated in viral infections. These data may inform the pathogenesis of AII and improve diagnostic and therapeutic strategies.

Conclusion

The study demonstrated that cytokine levels in children with acute intestinal infections vary significantly depending on etiology, disease severity, and progression. Viral infections showed more pronounced pro-inflammatory cytokine activity (IL-1, IFN-α, IFN-γ), indicating a robust antiviral response. IL-4 and IL-8 levels remained relatively low and similar across groups, suggesting limited Th2 and neutrophilic activity in AII.

With increasing severity, most cytokine levels rose, particularly in severe bacterial and viral forms. During disease progression, levels decreased by early convalescence, indicating immune response normalization post-therapy.

Notably, high IL-1 and IFN-α activity in viral infections, with post-treatment reductions, confirms therapeutic efficacy and the value of immunological monitoring. Significant inter-group differences in cytokine levels by etiology and severity support their use as potential biomarkers for diagnosis, severity assessment, and prognosis of acute intestinal infections.

REFERENCES

1. Asilova M.U., Musabaev E.I., Ubaidullaeva G.B. Viral diarrheas in the structure of acute intestinal infections in children // Journal of Infectology. – 2011. – 3(3). – P. 56–59.
2. Epifantseva N.V., Vitkovsky Yu.A., Emelyanova A.N. Polymorphism of pro-inflammatory cytokine genes in acute intestinal infections // Infection and Immunity. 2021. Vol. 11, No. 3. P. 565–569. doi: 10.15789/2220-7619-POP-1268
3. Zaitseva L.Yu., Khmelevskaya I.G., Kalutsky P.V. Clinical and immunological features of viral diarrheas in children // Bulletin of Modern Clinical Medicine. – 2017. – 10(2). – P. 30–33.
4. Kopachevskaya K.A., Molochny V.P. Dynamics of neopterin and some cytokines in the blood of young children with acute intestinal infections // Far Eastern Medical Journal. – 2016. – No. 4. – P. 42–46.
5. Murzabaeva R.T., Dubrovskaya D.N. Systemic inflammatory response in acute intestinal infections accompanied by isolation of opportunistic enterobacteria in adults // Medical Bulletin of Bashkortostan. – 2015. – Vol. 10, No. 6 (60). – P. 5–10.
6. Ryabichenko T.I., Skosyreva G.A., Obukhova O.O., Mitrofanov I.M., Timofeeva E.P., Kartseva T.V., Kurskaya O.G. Study of cytokine production in viral infections with diarrheal syndrome in children // Pediatric Infections. 2020. – 19(4). – P. 12–18. doi.org/10.22627/2072-8107-2020-19-4-12-18
7. Smirnov I.E., Mityushin I.L., Kucherenko A.G., Bakradze M.D. Cytokine profile in bacterial and viral infections in children // Russian Pediatric Journal. – 2014. – 4:14–19.
8. Tuychiev L.N., Eraliev U.E. Etiology of diarrheal syndrome in children // Medical Journal of Uzbekistan. – 2016. – No. 3. – P. 42.