

# Significance of Cytokines in Assessing the Severity of Nonspecific Ulcerative Colitis

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**Abstract** From 2021 to 2023, 80 patients with NUC who were examined and treated at the gastroenterology department of the Bukhara regional multidisciplinary medical center were included in the study. The average age of patients is  $33.2 \pm 0.8$  years. The moderate degree of NUC prevailed over the mild and severe degree. In addition to clinical, laboratory and instrumental tests, patients underwent an immunological examination, IL-6, IL-17A, TNF- $\alpha$  and fecal calprotectin were examined. It was found that the amount of cytokines increases in accordance with the increasing severity of the disease.

**Keywords** Nonspecific ulcerative colitis, Intestinal symptoms, Cytokines

## 1. Introduction

In the last decade, there has been an increase in inflammatory bowel diseases in gastroenterological patients, among which ulcerative colitis is predominant [4]. Nowadays, inflammatory bowel diseases are one of the most urgent problems of gastroenterology, and this disease is characterized by the uncertainty of its etiology, the complexity of its pathogenesis, frequent relapses, life-threatening complications, and lack of treatment [2]. Nonspecific ulcerative colitis (NUC or UC) is a chronic recurrent disease of the large intestine, which is a diffuse ulcerative inflammation of the mucous membrane of the large intestine, manifested by the development of local and systemic complications. The prevalence of UC is 26-268 among 100,000 inhabitants. The highest annual incidence of UC is found in Europe (24.3/100,000) and North America (19.2/100,000). Its frequency in these regions is 8-15 new cases per 100,000 population in 1 year, and the prevalence rate is 100,000. It corresponds to 80-120 people [3]. Currently, the following are considered the main pathogenetic causes of ulcerative colitis: genetic predisposition, disturbance of the protective function of intestines, disturbance of intestinal microflora and immune system [1]. The reasons for the change in the balance of cytokines in ulcerative colitis are still unknown, but according to assumptions, it is associated with an unusual immune response, persistence of one or more antigens, a violation of the relationship between the immune system of the intestinal mucosa and the intestinal microflora [5].

**The purpose of the study** is to improve the diagnostic methods of patients with ulcerative colitis by studying the relationship between the level of inflammatory cytokines in the serum of patients with ulcerative colitis and the severity of the inflammatory process in the colon.

## 2. Material and Methods

In the study, the survey data of 80 patients with NUC examined and treated at the department of gastroenterology and proctology of the Bukhara Regional Multidisciplinary Medical Center from 2021 to 2023 were summarized. 20 healthy individuals were included in the control group. The average age of patients is  $33.2 \pm 0.8$  years. Patients were divided into 3 age groups: 18-44 years (46 (57.5%)), 45-59 years old (24(30.0%)), 60-74 years old (10 (12.5%)). The proportion of men and women among patients with NUC, respectively 43 (53.75%), 37 (46.25%). Patients were divided into 3 groups according to severity: mild (n=16 (20%)) 1 patient, moderate (n=41 (51.2%)) patient and severe (n=23 (28.7%)) patient. Depending on the presentation of clinical symptoms, patients divided in predominantly diarrhea, tenism, abdominal bleeding, weight loss, abdominal pain form. Depending on the location of the process: distal (20%), left-sided (51%), total (29%) was divided into colitis. According to the course of the disease: acute 21 (26.2%), chronic continuous 10 (12.5%) and chronic recurrent 49 (61.2%) patients. All patients underwent a standard set of general clinical and biochemical laboratory tests: general blood analysis mainly (hemoglobin, leukocyte, erythrocyte, thrombocyte and ESR) indicators, blood biochemical analysis (urea, creatinine, ALT, AST, total protein, CRP, glucose) were checked. In addition, patients had their blood taken to check IL-6, IL-17A, TNF- $\alpha$ , and fecal calprotectin content was checked in their feces.

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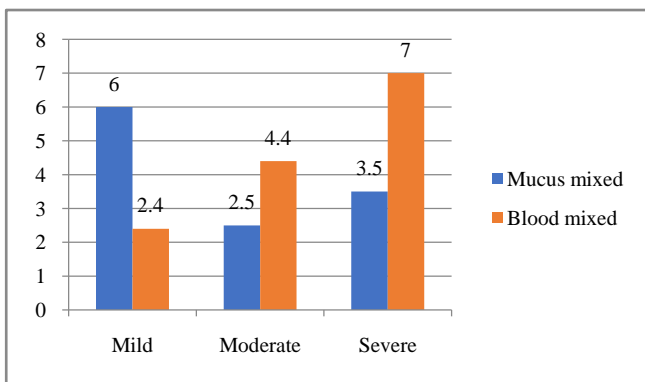
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EFGDS and colonoscopy, ultrasound examination of internal organs were performed.

### 3. Results and Analyses

When analyzing the clinical symptoms depending on the severity of the disease, it was found that abdominal pain is mainly in the moderate and severe type, and differs from the mild type in that it is higher in the moderate type, and symptoms such as nausea, vomiting and false calls are more common in the moderate and severe type. However, in the mild type, patients with constipation prevailed (table 1).

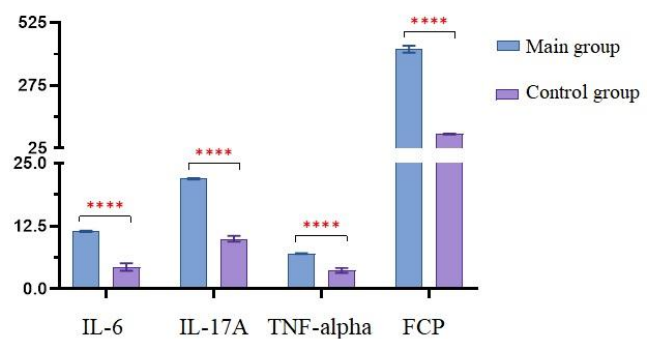
When studying the changes in stool analysis depending on the severity of the disease, blood mixed stool prevailed in the middle and severe levels of the disease. This is consistent with the data in the literature (Figure 1).



**Figure 1.** The results of litter analysis according to the level of weight of the UC

In order to study inflammatory processes in the intestines, inflammatory cytokines were analyzed in patients with UC. The amount of inflammatory markers IL-6, IL-17A, TNF- $\alpha$  and fecalcalprotectin was evaluated in patients in the main and control groups. The results of the analysis showed that the above markers increased in the main group. That is, it is possible to see a higher level of cytokines in patients with UC compared to the control group. This is consistent with the data in the literature (figure 2).

It was observed that the amount of cytokines increased in accordance with the severity of the disease, which indicates the spread and depth of the inflammatory process in the intestine (table 2).



Note: TNF- $\alpha$  – tumor necrosis factor; IL-6 – interleukin-6; IL-17A – interleukin-17A; FCP – fecalcalprotectin. Reliability level compared to the indicators of the control group: \* –  $p < 0.05$ ; \*\* –  $p < 0.01$ ; \*\*\* –  $p < 0.001$ ; \*\*\*\* –  $p < 0.0001$ .

**Figure 2.** The results of inflammatory markers

**Table 1.** The frequency of meeting clinical signs when the main group patients were distributed according to Truelove and Witts indicators

Symptoms (complaints)	Main group, n=80			Control group, n=20 (100%)
	Mild, n=17	Moderate, n=41	Severe, n=22	
Abdominal pains	1 (5.88%) <sup>^^^###</sup>	41 (100%) <sup>***</sup>	22 (100%) <sup>***</sup>	0 (0.0%)
Stomach rest	8 (47.1%) <sup>*^#</sup>	31 (75.6%) <sup>***#</sup>	8 (36.4%)	3 (15.0%)
Nausea	3 (17.6%) <sup>###</sup>	16 (39.0%) <sup>*##</sup>	17 (77.3%) <sup>**</sup>	2 (10.0%)
Constipation	13 (76.5%) <sup>***^^#</sup>	8 (19.5%)	8 (36.4%)	3 (15.0%)
False call	10 (58.8%) <sup>***###</sup>	26 (63.4%) <sup>***###</sup>	22 (100%) <sup>***</sup>	0 (0.0%)
A feeling of not emptying the bowels	14 (82.3%) <sup>***</sup>	26 (63.4%) <sup>***</sup>	10 (45.5%) <sup>***</sup>	0 (0.0%)

Note: Statistical reliability compared to the control group: \* –  $p < 0.05$ ; \*\* –  $p < 0.01$ ; \*\*\* –  $p < 0.001$ , the level of statistical reliability compared to the indicators of patients whose disease lasted for 6-10 years: ^ –  $p < 0.05$ ; ^^ –  $p < 0.01$ ; ^^ –  $p < 0.001$ ; ^^ –  $p < 0.0001$ , the level of statistical reliability compared to patients who lasted 6-10 years: # –  $p < 0.05$ ; ## –  $p < 0.01$ ; ### –  $p < 0.001$ ; ####

**Table 2.** The main group is in patients according to disease severity levels analysis of immunological markers

Disease severity	IL-6, pg/ml	IL-17A, pg/ml	TNF- $\alpha$ , pg/ml	Calprotectin, ng/ml
Mild, n=16	10.12 [9.2;10.6]	20.72 [19.5;22.1]	6.54 [5.8;7.5]	236.48 [182.3; 331.5]
Moderate, n=41	11.21 [10.2;12.5]	21.71 [19.6;23.6]	7.06 [5.9;7.8]	408.05 [311.5; 463.6]
Severe, n=23	12.87 [11.5;13.9]	23.09 [21.7;24.4]	7.39 [6.6;7.9]	566.23 [410.8;731.4]
Total, n=80	11.46 [9.2;13.9]	21.91 [19.5;24.4]	7.05 [5.8;7.9]	419.21 [182.3;731.4]

## 4. Conclusions

Based on the results of our study, patients with NUC have serum levels of pro-inflammatory TNF- $\alpha$ , IL-6, IL-17A, calprotectin was determined. The results of immunoenzyme analysis showed the highest rate in the severe level of the disease, and a relatively lower rate in the moderate and mild levels.

Therefore, as the levels of severity and activity levels of the disease increase, inflammatory markers (TNF- $\alpha$ , IL-6, IL-17A detected in blood serum and feces detected Calprotectin), the same result is the increase of inflammatory markers in the acute transitory type of the disease, and the opposite result was observed in the chronic continuous and chronic relapsing types.

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