

Characteristics of the Peri-Gastric Microflora and Degree of Gastric Dysbiosis in Patients with Rheumatoid Arthritis

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The immunity of the organism is closely related to the function of the normal microflora, which is currently considered as a peculiar organ of the immune system. This is why maintaining the ecological balance in the gastrointestinal tract is so important. It is known that the loss of normal microflora function, with the subsequent activation of opportunistic pathogens, causes disruptions in both local and systemic immune responses [3,5, 8, 12, 13, 14, 15].

The possible role of opportunistic flora as a causative or triggering factor is discussed in the context of a number of autoimmune diseases: rheumatoid arthritis [10, 11], Bechterew's disease [2], and systemic vasculitis [7]. Most authors, however, place the greatest emphasis on exogenous infections, ignoring the role of opportunistic microflora, which can serve as a source of endogenous infection and a powerful antigenic stimulus [1,4,6,9]. There are few works that address the state of gastric microflora in the context of immune disturbances in patients with rheumatoid arthritis (RA).

Therefore, identifying the role of gastric microflora in the development of immune disturbances in RA patients is a relevant task.

Objective of the study: To examine the state of the mucosal microflora of the stomach in patients with RA, taking into account the degree of disease activity.

Materials and Methods: 159 people aged 19 to 83 years were examined. Among the patients, there were 128 women and 31 men, with a female-to-male ratio of 4.13:1. The average age was 55 ± 0.86 years. The diagnosis of RA was confirmed in all cases according to the criteria of the American College of Rheumatology [1]. Of the patients, 23 (22.12%) had stage I disease activity, 63 (60.58%) had stage IX, and 14 (13.46%) had stage III. According to the course of the disease, patients were classified as follows: slow-progressing course in 94 (90.38%) patients and rapid-progressing course in 10 (9.62%) patients. **Joint Form of RA was diagnosed in 95 (100%) patients. Radiologically, stage I RA was detected in 31 (29.81%), stage II in 46 (44.23%), stage III in 26 (25.00%), and stage IV in 1 (0.96%) patient.**

The study included standard clinical and radiological examinations, microbiological analysis of stool and urine, endoscopic examination (using an "Olympus" device) of the stomach and duodenum with biopsy of the mucous membrane, and microbiological examination of the mucosal biopsy samples (MBS) of the stomach and gastric juice. Isolation and identification of microorganisms (MOs) were carried out using standard methods. Gastric and duodenal dysbiosis was characterized according to the criteria proposed by V.V. Chernin and co-authors [9].

Results of the Study:

When examining the gastric mucosal biopsies of RA patients, *peptostreptococci* were more frequently isolated in 71.4% of cases, followed by *staphylococci* and *Escherichia coli* in 50%, *Klebsiella* in 42.8%, *streptococci* in 35.7%, *enterococci* and *micrococci* in 21.4%, and more rarely *Pseudomonas* and *bacilli* in 14.2%. *Candida* yeast-like fungi were found in 8.3% of cases, with colony counts ranging from 2.77 to 10 lg CFU/g and combinations of 2 to 5 types of microorganisms.

Figure 1 shows the data on the quantitative characteristics of the peri-gastric microflora.

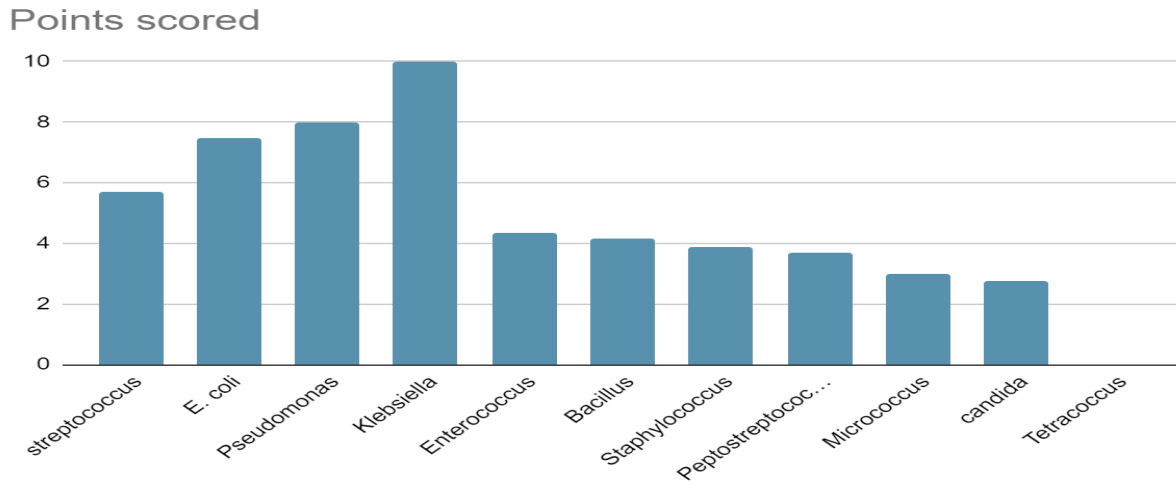


Fig. 1. Quantitative characteristics of the peri-gastric microflora of the stomach in patients with RA

When assessing the colonization of the gastric mucosa in RA patients in quantitative terms, the following results were obtained: *Klebsiella* were isolated at 10 lg CFU/g, *Pseudomonas* at 8 lg CFU/g, *Escherichia coli* at 7.47 lg CFU/g, *Streptococci* at 5.7 lg CFU/g, *Enterococci* at 4.33 lg CFU/g, *Bacilli* at 4.14 lg CFU/g, *Staphylococci* at 3.87 lg CFU/g, *Peptostreptococci* at 3.68 log CFU/g, *Micrococci* at 3 lg CFU/g, and *Candida* at 2.77 lg CFU/g.

Therefore, in all examined patients, there was a high level of both resident and opportunistic microflora, indicating the development of dysbiosis in the mucosal microflora (V.V. Chernin et al., 2011).

The results of studying the spectrum and frequency of microorganism occurrence depending on the degree of activity of the joint syndrome are shown in Figure 2.

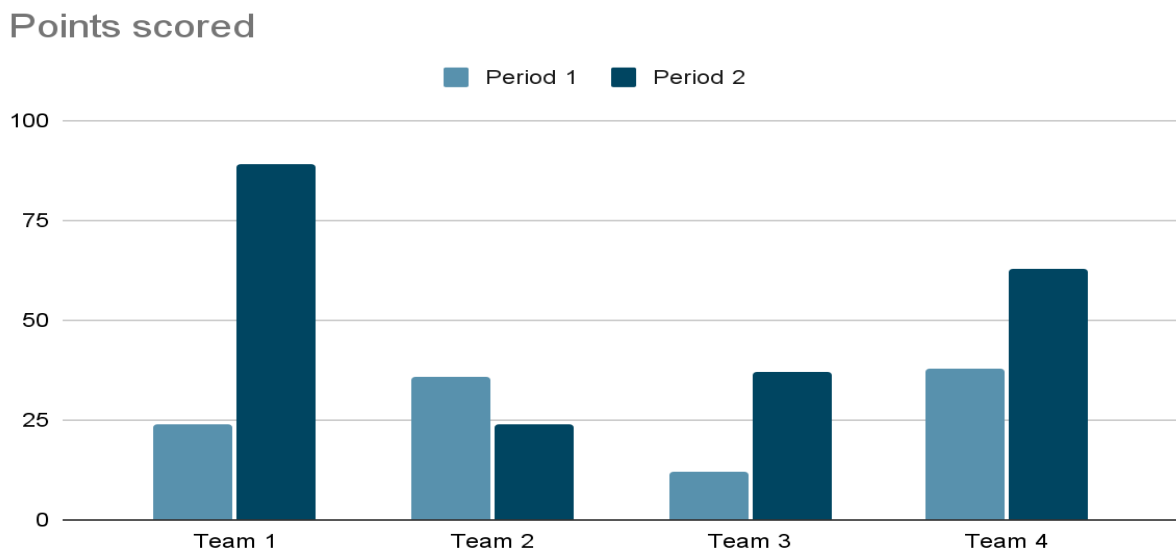


Fig. 2. Spectrum and frequency of microorganism occurrence in the mucosal layer in patients with RA depending on disease activity

In RA patients with stage I disease activity, the following frequency of microorganism occurrence was found in gastric juice: *Peptostreptococci* – 100%, *Staphylococci* – 80%, *Streptococci* and *Escherichia coli* – 40%, *Bacilli*, *Klebsiella*, *Candida*, and *Enterococci* – 20%.

In RA patients with stage II disease activity, the following frequency of microorganism occurrence was found in the gastric mucosa: approximately equal proportions of *Escherichia coli*, *Klebsiella*, and *Peptococci* – 55.5%, *Staphylococci* and *Streptococci* – 33.3%, *Enterococci* and *Pseudomonas* – 22.2%, *Bacilli* – 11.1%.

Therefore, in RA patients, the frequency of occurrence of microorganisms characteristic of the mucosal flora and opportunistic microorganisms slightly decreases as the disease activity increases.

The quantitative aspects of the mucosal microflora in RA patients were also analyzed depending on the degree of activity of the inflammatory process in the joints. The data are presented in Figure 3.

As shown in Figure 3, in RA patients with stage I disease activity, *Klebsiella* were isolated at 12 lg CFU/g, *Streptococci* at 5.03 lg CFU/g, *Staphylococci* at 4.02 lg CFU/g, *Enterococci* at 4 lg CFU/g, *Peptostreptococci* at 3.39 lg CFU/g, *Bacilli* at 3.14 lg CFU/g, *Candida* at 2.77 lg CFU/g, and *Escherichia coli* at 2.15 lg CFU/g.

In patients with stage II disease activity, *Escherichia coli* and *Klebsiella* were isolated at 9.6 lg CFU/g, *Pseudomonas* at 8 lg CFU/g, *Streptococci* at 6.15 lg CFU/g, *Bacilli* at 5.14 lg CFU/g, *Enterococci* at 4.5 lg CFU/g, *Peptostreptococci* at 3.98 lg CFU/g, and *Staphylococci* at 3.66 lg CFU/g.

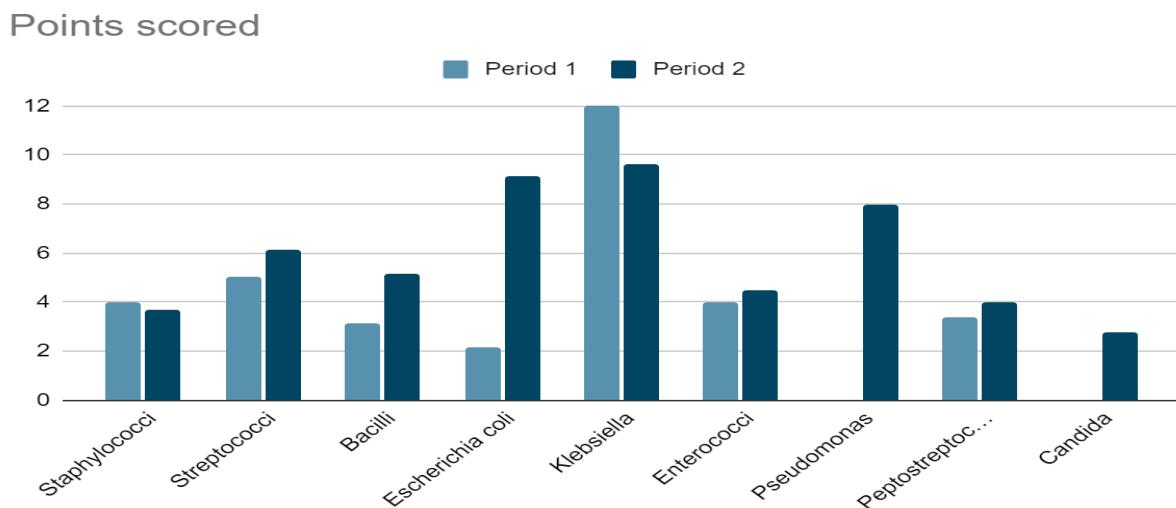


Fig. 3. Quantitative characteristics of the peri-gastric microflora of the stomach in patients with RA depending on disease activity

Therefore, in general, in RA patients, with an increase in disease activity, there was a quantitative increase in the number of cultures of both resident mucosal microflora and non-resident (anaerobic gram-positive cocci, opportunistic flora) microflora, which fits the concept of mucosal dysbiosis syndrome.

An assessment of the degree of dysbiosis of the mucosal microflora was performed, and the results are presented in Figure 4.

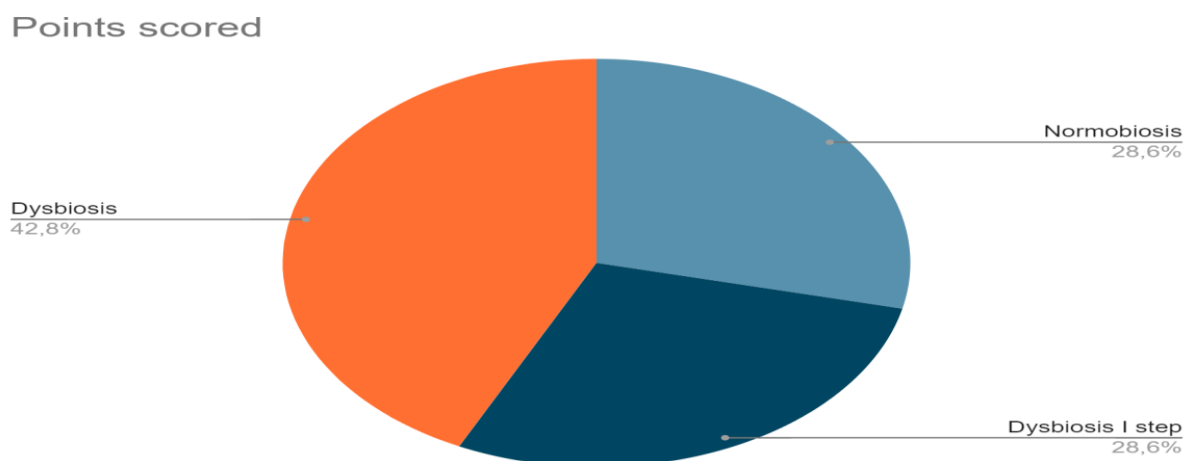


Fig. 4. Mucosal flora dysbiosis in patients with RA

As seen in the figure, 71.4% of RA patients were found to have mucosal microflora dysbiosis of varying severity (according to the classification of intra-luminal dysbiosis of the gastroduodenal zone by E.A. Beyul and I.B. Kuvaeva). The following table presents data on the severity of dysbiosis of the mucosal microflora depending on disease activity.

It was established that in RA patients, the severity of dysbiotic shifts in the peri-gastric microflora increases with the rising degree of activity of the inflammatory process in the joints. Thus, in patients with stage I RA activity, stage III dysbiosis was found in 20% of patients, while in patients with stage II RA activity, stage III dysbiosis was found in 55.5% of patients.

The development of gastric dysbiosis manifests as a change in the protective-barrier potential of this zone, as the microflora of the biotope performs a protective function – colonization resistance [4]. Another important function of normal microflora is the provision of immune defense [8]. It is likely that in the condition of dysbiosis, changes occur in the immune defense of the body, which leads to disruptions in the immune-inflammatory response. Thus, it becomes evident that the development of dysbiosis in the gastroduodenal zone should have a certain impact on the course of rheumatoid arthritis, as shown by our research. A clear relationship is observed between the severity of dysbiosis and the degree of activity of joint pathology. The higher the activity of joint pathology, the more pronounced the gastric dysbiosis, and vice versa.

Conclusions: RA patients show dysbiotic changes in the stomach. The severity of dysbiosis is directly dependent on the activity of joint pathology.

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