



Functional Disorders of the Gastrointestinal Tract During the Pandemic of a New Coronavirus Infection

Arkadiy A. Sheptulin*, Elena A. Piatenko

Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia

Aim. To analyze the literature data devoted to the study of the features of functional gastrointestinal diseases (FGID) during the pandemic of a new coronavirus infection.

Key findings. Measures taken in connection with the pandemic of COVID-19 infection (introduction of lockdown, social isolation) leads to an increase in the level of depression and anxiety and, as a consequence, to an increase in the frequency and prevalence of functional dyspepsia (FD) and irritable bowel syndrome (IBS), as well as an increase in the severity of clinical symptoms of these diseases. In turn, the overcoming of COVID-19 infection contributes to an increase in the permeability of the mucous membrane of the gastrointestinal tract and the occurrence of its inflammatory changes, which lead to the development of postinfectious (postcovid) FD and postinfectious (postcovid) IBS.

Conclusion. The problem of functional gastrointestinal diseases during the pandemic of a new coronavirus infection is very important and requires further research.

Keywords: COVID-19 infection, functional dyspepsia, irritable bowel syndrome

Conflict of interest: the authors declare no conflict of interest.

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Функциональные заболевания желудочно-кишечного тракта в период пандемии новой коронавирусной инфекции COVID-19

А.А. Шептулин*, Е.А. Пятенко

ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации, Москва, Российская Федерация

Цель обзора. Провести анализ данных литературы, посвященных изучению особенностей функциональных заболеваний желудочно-кишечного тракта (ЖКТ) в период пандемии новой коронавирусной инфекции.

Основные положения. Меры, принимаемые в связи с пандемией инфекции COVID-19 (введение локдауна, социальная изоляция), ведут к повышению уровня депрессии и тревоги и, как следствие, к увеличению частоты и распространенности функциональной диспепсии (ФД) и синдрома раздраженного кишечника (СРК), а также усилению выраженности клинических симптомов этих заболеваний. В свою очередь, перенесенная инфекция COVID-19 способствует повышению проницаемости слизистой оболочки желудочно-кишечного тракта и возникновению ее воспалительных изменений, что в дальнейшем может приводить к развитию постинфекционной (постковидной) ФД и постинфекционного (постковидного) СРК.

Заключение. Новая коронавирусная инфекция оказывает негативное влияние на течение ФД и СРК, что выражается в нарастании выраженности их клинических симптомов. Перенесенный COVID-19, особенно протекавший с гастроинтестинальными симптомами, может способствовать развитию функциональных расстройств. Особенности возникновения функциональных расстройств ЖКТ, их течения и лечения в условиях пандемии изучены недостаточно и требуют дальнейших исследований.

Ключевые слова: инфекция COVID-19, функциональная диспепсия синдром раздраженного кишечника

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The problem of functional diseases of the gastrointestinal tract (GIT) during the pandemic of the new coronavirus infection (COVID-19) has several important aspects. On the one hand, measures taken to prevent COVID-19 infection (the lockdown, social isolation, etc.) can affect the incidence of functional dyspepsia (FD) and irritable bowel syndrome (IBS), as well as their course. On the other hand, COVID-19 itself can serve as a trigger for the development of FD and IBS.

A systematic review and meta-analysis of 5 studies involving 9,074 people showed that 29.6 % of the population experiences increased stress levels during the pandemic of the new coronavirus infection. According to the analysis of 17 studies involving 63,439 people, the frequency of increased anxiety during this period was 31.9 %. According to 14 studies, which included 44,531 people, the incidence of depression during the pandemic reached 33.7 % [1]. Naturally, these psychological disorders affected the frequency of FD and IBS.

R. Nakov et al. [2] using a validated questionnaire compared the prevalence of FD and IBS in 1,896 respondents in May-August 2019 and 980 people in May-June 2020 during the lockdown. The results showed that the prevalence of IBS during this period increased from 20.0 % to 26.3 % ($p < 0.001$), and the prevalence of FD did from 12.7 % to 18.3 % ($p < 0.001$). A correlation was found between high levels of stress and the incidence of FD. A study conducted in Southeast Asian countries (Japan, China, South Korea, etc.) showed, that among patients who had been performed endoscopic examination during the pandemic, FD occurred in 44.0 % of cases, IBS did in 36.7 % [3].

The pandemic of the novel coronavirus infection also had an impact on the severity of symptoms of functional gastrointestinal diseases. T. Oshima et al. [4] noted the influence of pandemic-related factors (stress and anxiety, the need for social distancing) on the severity of FD and IBS symptoms. Patients completed a questionnaire for diagnosis of IBS and FD based according to Rome criteria III. In addition, the scales of depression and anxiety were evaluated. In a group of 5,157 people, 8.5 % of respondents were identified as had FD, 16.6 % had IBS, and 4.0 % had an overlap of IBS and FD. An increase in the severity of symptoms during the pandemic was reported by 19.6 % of patients with FD, 31.9 % of patients with IBS and 50.7 % of patients with the overlap. Poorer subjective wellness was correlated with high levels of depression and anxiety [4]. The correlation an increase in the severity of symptoms of functional diseases of the gastrointestinal tract during lockdown in patients with an increased level of anxiety was noted by other authors [5].

J.M. Sabate et al. [6] compared the effects of lockdown and stress during the COVID-19 pandemic in France in 252 patients with IBS and in 74 healthy

controls. A questionnaire was also used to assess stress levels, general condition, severity of depression and anxiety, quality of life. The levels of stress associated with fear of infection and lockdown were the same in patients with IBS and in persons of the control group, but the psychopathological disorders (depression, anxiety) and a decrease in the quality of life were more pronounced in patients with IBS. It was observed that patients with IBS compared to healthy individuals during the pandemic had a lower adherence to social distancing [7].

In Saudi Arabia, 1,255 patients with IBS were studied on the effect of stress associated with COVID-19 on the clinical manifestations of the disease and their psychological status. 63.4 % of the patients reported that they experienced stress associated with the pandemic, which included fear of the infection (43.5 %) and fear of death from it (17.2 %). 75.5 % of patients noted a decrease in daily activity due to a deterioration in wellness, 18.1 % of patients began to take sedatives [8]. Increased levels of depression and anxiety, as well as a decrease in quality of life, have been noted in patients with IBS during the COVID-19 pandemic by other authors [9].

Patients with IBS who already initially had an increased level of anxiety and depression especially hard endured the pandemic. They noted an increase in psychological distress in 92 % of cases, an increase in anxiety in 81 %, and an increase in depression in 67 %. At the same time, 48 % of these patients noted an increase in abdominal pain, 45 % of them did an increase in loose stools, 44 % had more pronounced constipation [10].

The COVID-19 pandemic also had a negative impact on the quality of medical care for patients with functional gastrointestinal diseases. The Society of Neurogastroenterology of Latin America conducted an anonymous survey of members of this society regarding the management of patients with functional gastrointestinal diseases in the pandemic. Sixty one doctors from Colombia, Mexico and Brazil took part in the survey. All respondents noted the negative impact of the pandemic on their clinical practice, resulting in a decrease in the number of face-to-face consultations and a decrease in the number of endoscopic examinations, which was due to the fears of patients, the lockdown (in Colombia) and the decision of doctors to reduce the spread of infection. At the same time, 46 % of doctors had to reduce salaries and working hours. In addition, 11.5 % of doctors were mobilized to manage patients with coronavirus infection (in Mexico and Colombia) [11].

The question of interest is how the COVID-19 infection affects the subsequent course of functional diseases of the gastrointestinal tract. J. Gubatan et al. [12] conducted retrospective study to investigate the impact of novel coronavirus infection on the severity of symptoms of IBS, FD and idiopathic

gastroparesis (IG). From March to September 2020 new coronavirus infection was detected in 83 out of tients with IG (3.07 %) and 29 out of 1,187 patients with FD (2.44 %). The severity of abdominal pain, nausea, vomiting, diarrhea, constipation increased significantly after COVID-19 infection. These patients began to use medications (proton pump inhibitors, H2-blockers and others) more often than it was before the pandemic. During the COVID-19 infection, it was not necessary to prescribe corticosteroids to these patients, which, according to the authors, indicated a mild course of the new coronavirus infection in the patients with functional gastrointestinal diseases and the absence of a cytokine “storm” in them. The frequency of detection of coronavirus RNA in patients with functional gastrointestinal disorders was similar it in the cohort of persons who did not have risk factors for COVID-19 infection (3.20 % and 3.13 %, respectively), and was lower than in the persons who had at least one these risk factor (diabetes mellitus, obesity, heart disease; 3.20 % and 5.75 %, respectively). The risk of developing COVID-19 infection in patients with functional gastrointestinal disorders increased with the presence of a diarrheal form of IBS and active smokin [12]. The authors did not confirm that taking proton pump inhibitors increases the risk of developing COVID-19 infection [13].

The extent to which COVID-19 contributes to the subsequent development of functional diseases of the gastrointestinal tract and what mechanisms involved in the realization of this influence has not been sufficiently studied. A survey of 409 children and adolescents aged 10 to 17 years in Italy showed that COVID-19 caused an increase in the incidence of functional abdominal pain and IBS [14]. However, the incidence of functional gastrointestinal disorders that developed after COVID-19 fluctuate in various works within very wide ranges.

U.C. Ghoshal et al. [15] used a questionnaire that identifies the presence of IBS, FD and their overlap in 280 patients who have had COVID-19 infection and 264 healthy individuals of the control group. IBS, FD and the overlap were diagnosed 6 months after COVID-19 in 5.3 %, 2.1 % and 1.8 % of patients, respectively. There was only 1 case IBS in the control group. The risk factors for the development of post-COVID functional gastrointestinal disorders were anosmia and ageusia during COVID-19, the presence of stomach and/or intestinal symptoms 1 and 3 months after infection, and concomitant psychopathological disorders.

A. Velez et al. [16] analyzed the frequency of functional gastrointestinal disorders (FD and IBS) that present for at least 3 months, no earlier than 6 months after COVID-19 diagnosis in 272 patients who had no symptoms of these functional diseases before COVID-19 (the authors named these disorders as “post-COVID disorders of gut–brain

interaction”). It was found that the symptoms of FD developed in 29 % of these patients, the symptoms of IBS did in 1 % of the patients, the overlap did in 9.5 % of the patients. Multivariate analysis showed that independent risk factors for post-COVID symptoms of FD and IBS were female sex and a history of depression or anxiety. Post-COVID symptoms were equally common in those patients who had COVID-19 with gastrointestinal symptoms and without them. A correlation was also found between the severity of the symptoms of FD and IBS and the presence of psychological distress.

J.W. Blackett et al. [17] revealed that the number of patients with symptoms of IBS (abdominal pain and stool disorders) increased from about 16 % to 41 % 6 months after COVID-19 ($p < 0.01$). When assessing indicators on the scale of severity of abdominal symptoms in patients whose diagnosis of IBS was established before the infection, the sum of points increased from 61 to 248 ($p < 0.01$). According to 749 post-COVID patients in Italy, 9.4 % of respondents noted abdominal pain 6 months after the COVID-19 infection and 39 % of them also had stool disorders, i.e. IBS. A positive correlation was also found between the presence of depression and anxiety in patients and the frequency of clinical symptoms of IBS [18].

Not all authors were able to confirm the increased risk of developing IBS after COVID-19 infection. D. Noviello et al. [19] assessed the frequency of symptoms of IBS in 164 patients 5 months after they had COVID-19 and in 184 persons who had not COVID-19 in past (the control group). Despite the fact that more than 50 % of patients in the main group at the time of COVID-19 infection had diarrhea, the frequency of IBS after 5 months in both groups was similar (respectively, 26.2 % and 25.1 %; $p = 0.81$).

Certain mechanisms for the formation of IBS in COVID-19 are assumed. As you know, the coronavirus enters the body using receptors for angiotensin-converting enzyme 2 (ACE2). The expression of these receptors was found not only in lungs, but also in epithelial cells of the mucous membrane of the stomach and intestines. SARS-CoV-2 interacting with ACE2 receptors on the surface of epithelial cells of the gastrointestinal mucosa can contribute to the disorders of its permeability and its inflammation [20]. Together with other factors (increased levels of serotonin in the intestinal mucosa, imbalances in the intestinal microbiota), these inflammatory changes can lead to the development of post-infectious (post-COVID) FD and post-infectious (post-COVID) IBS [21–23].

Thus, the analysis of publications on the features of functional gastrointestinal diseases during the pandemic of a new coronavirus infection shows its negative impact on the course of FD and IBS, which is expressed in increased depression and anxiety and, as a result, in an increase in the severity

of symptoms of FD and IBS. In addition, COVID-19, especially with gastrointestinal symptoms, can lead to the development of post-infectious (post-COVID) FD and post-infectious (post-COVID) IBS. At the

same time, the features of the occurrence of functional disorders of the gastrointestinal tract, their course and treatment in the pandemic have not been studied enough and require further research.

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Information about the authors

Arkadiy A. Sheptulin* — Dr. Sci. (Med.), Prof., Chair of Internal Diseases Propedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: arkalshep@gmail.com;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: <https://orcid.org/0000-0002-1395-9566>

Elena A. Piatenko — postgraduate student, Chair of Internal Diseases Propedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: piatenkoe@gmail.com;
119435, Moscow, Pogodinskaya str., 1, bld. 1.
ORCID: <https://orcid.org/0000-0001-5037-7955>

Сведения об авторах

Шептулин Аркадий Александрович* — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии ФГАОУ ВО «Первый Московский государственный университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: arkalshep@gmail.com;
119435, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: <https://orcid.org/0000-0002-1395-9566>

Пятенко Елена Александровна — аспирант кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии ФГАОУ ВО «Первый Московский государственный университет им. И.М. Сеченова» (Сеченовский Университет) Министерства здравоохранения Российской Федерации.
Контактная информация: piatenko@gmail.com;
119435, г. Москва, ул. Погодинская, д. 1, стр. 1.
ORCID: <https://orcid.org/0000-0001-5037-7955>

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* Corresponding author/Автор, ответственный за переписку