ORIGINAL ARTICLE

Irritable bowel syndrome following COVID-19: an underestimated consequence of SARS-CoV-2 infection

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KEY WORDS

COVID-19, disorders of gut–brain interaction, functional gastrointestinal disorders, gastrointestinal symptoms, irritable bowel syndrome

ABSTRACT

INTRODUCTION Gastrointestinal (GI) symptoms are a common manifestation of COVID-19.

OBJECTIVES We aimed to investigate whether GI symptoms persist in patients previously infected with SARS-CoV-2 in the form of post-infection irritable bowel syndrome (PI-IBS).

PATIENTS AND METHODS A prospective, single-center evaluation of questions regarding IBS was conducted using the Rome IV Adult Diagnostic Questionnaire among 257 patients previously hospitalized for COVID-19.

RESULTS GI symptoms (abdominal pain with diarrhea or constipation) were reported at the following time points: at discharge from the hospital, and after 3 and 6 months of follow-up. GI symptoms not meeting the full Rome IV diagnostic criteria for IBS due to too short symptom duration were reported by 28 individuals (10.6%) at hospital discharge, 58 (22.3%) after 3 months, and 70 (26.9%) after 6 months. The full Rome IV criteria for IBS were not met at discharge by any of the participants, but they were met after 3 and 6 months of follow-up in 14 (5.4%) and 15 individuals (5.8%), respectively.

CONCLUSIONS Persistent GI symptoms following COVID-19 are frequent and deserve significant and growing attention of gastroenterologists and other health care practitioners. The Rome IV criteria may be too strict to address the full spectrum of GI symptoms following COVID-19.

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INTRODUCTION SARS-CoV-2 infection is not limited to the respiratory system, but it also involves other organs, including the gastrointestinal (GI) tract. The infection of the GI tract triggers symptoms in approximately 15% of patients with COVID-19.[1] There is a growing body of evidence on the occurrence of SARS-CoV-2–related complications, including those related to the GI tract.[2] One such complication is post-infection irritable bowel syndrome (PI-IBS), which occurs in up to 10.1% of patients after a GI infection.[3,4] The main risk factors for developing PI-IBS include female sex, previous antibiotic treatment, anxiety, depression, somatization, neuroticism, and clinical indicators of intestinal inflammation.[5] Moreover, a history of *Clostridioides difficile* infection (CDI) may predispose up to 25% of patients to PI-IBS.[6] The syndrome can develop after any type of infection (viral, bacterial, fungal, or parasitic).[5,7] Interestingly, psychological conditions (anxiety or depression) are common risk factors, and the frequency of psychological disorders increased significantly during the COVID-19 pandemic, mainly due to the limited social contact and isolation.[8]

The pathogenesis of IBS following COVID-19 has been explained by the affinity of SARS-CoV-2 to intestinal cells expressing the angiotensin-converting enzyme receptor 2.[9] Zhou et al[10] hypothesized that SARS-CoV-2 can induce apoptosis

WHAT'S NEW?

To our best knowledge, the present study is the second one to reveal persistent gastrointestinal (GI) symptoms following COVID-19. Due to their frequency, post–COVID-19 GI symptoms have been drawing growing attention of gastroenterologists and other health care practitioners. The Rome IV criteria may not allow for the identification of all patients with irritable bowel syndrome after COVID-19, as they incorporate a strict symptom duration criterion. In addition to the stress associated with social isolation, a common factor during the pandemic, another possible cause of GI symptoms occurrence is alteration of the microbiota induced directly by SARS-CoV-2.

and increase intestinal permeability in the GI epithelium, which may facilitate the exposure of the enteric nervous system to harmful metabolites synthesized in the intestinal lumen. A cytokine storm is then induced by an excessive proinflammatory response and an ineffective anti-inflammatory control mechanism, which together lead to chronic inflammation and tissue damage. Hojyo et al[11] postulated that the production of various cytokines causes immune-related injuries. Therefore, effective reduction of the levels of proinflammatory cytokines in patients with severe COVID-19 is crucial for preventing deterioration of their health. Zuo et al[12] investigated changes in the gut microbiome of patients with SARS-CoV-2 infection and assessed the association of these changes with the disease severity and the presence of viral genetic material in the feces. COVID-19 patients showed an increase in opportunistic bacteria and a decrease in useful commensals. Changes in the gut microbiome were responsible for alterations in the gut–brain axis, which can induce functional changes in the GI tract. These changes may result in an elevated concentration of calprotectin in the stool and an increased release of serotonin—factors that significantly increase the permeability of the intestinal barrier and contribute to the occurrence of PI-IBS.[13-15] Patients with a history of COVID-19 have many risk factors for PI-IBS, but data on this subject are scarce. Therefore, we conducted a prospective analysis to determine the prevalence of IBS and its risk factors among patients diagnosed with COVID-19. IBS was diagnosed based on the Rome IV criteria, if a patient reported recurrent abdominal pain on average at least 1 day a week, and the pain coincided with at least 2 of the following symptoms: 1) problems with defecation, 2) change in the frequency of defecation, or 3) change in the form (appearance) of stool. The criteria needed to be met for the last 3 months, with the onset of symptoms at least 6 months prior to the diagnosis.[16]

The main aim of the study was to assess the occurrence of persistent GI symptoms using the Rome IV Diagnostic Questionnaire for Functional Gastrointestinal Disorders in Adults (R4DQ; IBS-related questions) at 3 time points: immediately after discharge from the hospital, as well as after 3 and 6 months of follow-up.

PATIENTS AND METHODS

Study design The study was a prospective, single-center evaluation of selected IBS-related questions from the R4DQ among 262 patients hospitalized for COVID-19 in the Central Clinical Hospital of the Ministry of the Interior and Administration in Warsaw, Poland from March 15 to December 15, 2020. Five patients were excluded from the analysis due to incomplete R4DQ data (response rate, 98.09%).

Statistical analysis Nominal variables are presented as numbers (percentages), and the only continuous variable (age) is presented as the median with interquartile range (IQR). The normality of distribution for the age variable was assessed with the Shapiro–Wilk test (the distribution was non-normal). The participants whose symptoms met the criteria for IBS (assessed at 3 time points) were selected and compared with the COVID-19 patients without IBS (control group). As there were no patients with IBS at the first time point (at discharge from the hospital), this group was not compared with the control group. The relationship between qualitative variables was analyzed with the χ^2 test or the Fisher exact test (depending on the number of observations in each cell). Odds ratios with 95% CIs were calculated for all 2×2 tables (but only if $n > 0$ in each cell). The age of the patients was compared between the groups using the Mann–Whitney test. The median difference was calculated with the Hodges–Lehmann estimator. All tests were 2-tailed, with a P value of 0.05 considered significant. Statistical analysis was conducted using the IBM SPSS software, Version 25.0.0.2 (IBM Corp., Armonk, New York, United States).

Ethical considerations The study protocol was approved by the Bioethics Committee of the Central Clinical Hospital of the Ministry of the Interior and Administration in Warsaw (33/2020). Anonymized data were analyzed.

RESULTS

A total of 257 patients who required hospitalization due to severe COVID-19 were included in the study. The IBS module of the R4DQ was used at 3 time points (after hospital discharge and in the third and sixth months of follow-up) to screen for the diagnosis of IBS. GI symptoms (abdominal pain with diarrhea or constipation) that did not meet the symptom duration criteria for IBS were reported in 28 (10.6%), 58 (22.3%), and 70 (26.9%) patients at discharge from hospital, and after 3 and 6 months of follow-up, respectively (TABLE 1).

The median (IQR) age in the study cohort was 68 years and most of the patients were men (141 [54.9%]). A total of 146 patients (56.8%) reported GI symptoms during COVID-19; 95 individuals (37%) experienced the symptoms before admission to the hospital and 51 (19.8%) during the hospitalization. The most prevalent GI symptoms reported were abdominal pain (25.3%), diarrhea (19.5%), nausea (3.1%), vomiting (3.5%),

TABLE 1 Frequency of gastrointestinal symptoms in the study cohort

Time point	Occurrence of GI symptoms
Discharge from the hospital	28 (10.6)
3-month follow-up	58 (22.3)
6-month follow-up	70 (26.9)

Data are presented as number (percentage) of patients.

Abbreviations: GI, gastrointestinal

TABLE 2 Characteristics of the study cohort (n = 257)

Parameter		Value
Age, y, median (IQR)		68 (53–81)
Sex	Female	116 (45.1)
	Male	141 (54.9)
Abdominal symptoms during COVID-19		146 (56.8)
Onset of abdominal symptoms prior to admission to the hospital		95 (37)
Onset of abdominal symptoms after admission to the hospital		51 (19.8)
Abdominal pain		65 (25.3)
Diarrhea		50 (19.5)
Nausea		8 (3.1)
Vomiting		9 (3.5)
Constipation		7 (2.7)
Clostridioides difficile infection		26 (10.1)
Pharmacotherapy		
Proton pump inhibitor		104 (40.5)
Antibiotic therapy		217 (84.4)
Azithromycin		154 (59.9)
Antibiotics other than azithromycin		177 (68.9)
Chloroquine		215 (83.7)
Lopinavir + ritonavir		46 (17.9)
Comorbidities		
Any comorbidity		223 (86.8)
Cardiovascular diseases		148 (57.6)
Respiratory system diseases		33 (12.8)
Diabetes		63 (24.5)
Chronic kidney disease		58 (22.6)
Nervous system diseases		68 (26.5)
Cancers		49 (19.1)

Data are presented as number (percentage) of patients unless indicated otherwise.

Abbreviations: IQR, interquartile range

TABLE 3 Number (percentage) of patients with irritable bowel syndrome at each analyzed time point

Time-point	Irritable bowel syndrome
Discharge from the hospital	0
3-month follow-up	14 (5.4)
6-month follow-up	15 (5.8)

and constipation (2.7%). The following treatments were reported: proton pump inhibitors (PPIs) in 104 patients (40.5%), antibiotic therapy in 217 (84.4%), azithromycin in 154 (59.9%), antibiotics other than azithromycin in 177 (68.9%), chloroquine in 215 (83.7%), and lopinavir + ritonavir in 46 (17.9%). Comorbidities were found in 223 patients (86.8%), including cardiovascular disease in 148 individuals (57.6%), respiratory disease in 33 (12.8%), diabetes in 63 (24.5%), chronic kidney disease in 58 (22.6%), nervous system disease in 68 (26.5%), and cancer in 49 patients (19.1%) (TABLE 2).

The IBS criteria were not met at discharge from the hospital by any of the patients, but they were met after 3 and 6 months of follow-up by 14 (5.4%) and 15 participants (5.8%), respectively (TABLE 3). None of the respondents had a positive history of IBS. The characteristics of the patients diagnosed with IBS at the second or third time point did not differ from those of the participants without IBS (P >0.05 for all analyses; TABLES 4 and 5, respectively).

DISCUSSION In our study, the IBS criteria were met after 3 months by 14 patients (5.4%) and after 6 months by 15 patients (5.8%). Surprisingly, the number of patients with GI symptoms was substantial, even though not all of them met the symptom duration criteria for IBS according to the Rome IV classification. In the third month of the follow-up, there were 57 patients (22.2%) reporting GI symptoms, and in the sixth month this number was as high as 70 (27.2%). The presence of IBS symptoms in almost one-third of the patients in the sixth month of the follow-up revealed the extent of the problem. The short follow-up duration seems to be a plausible reason for IBS being diagnosed in only 15 patients (5.8%) at month 6, despite the presence of symptoms in as many as 70 participants (27.2%). The analysis of multiple potential PI-IBS risk factors showed no significant association for any of the analyzed variables in the patients who met IBS criteria at the second and third time points.

The hypothesis of de novo IBS development following COVID-19 is still complex and not widely researched; however, in light of the frequent occurrence of GI symptoms that did not meet the IBS criteria in our study (up to one-third of the patients), it becomes highly probable. Data on the occurrence of IBS following COVID-19 are scarce. The subject was investigated by Goshal et al,[17] who were the first to report on the occurrence of functional disorders after SARS-CoV-2 infection. They confirmed that de novo functional dyspepsia (FD) and IBS were present in 2.1% and 5.3% of the patients 6 months after COVID-19,[17] which is a result similar to that observed in our study. The risk factors for functional disorders in the study by Ghoshal et al[17] included the presence of GI symptoms, anosmia, and ageusia (all of them during COVID-19), as well as psychological comorbidities. At the same time, they did not find a relationship between the treatment for COVID-19 and the development of functional disorders.

TABLE 4 Comparison of characteristics of patients with irritable bowel syndrome (IBS) at the second time point (3-month follow-up) and patients without IBS

Characteristics	IBS at 3 months		*P* value	OR/MD (95% CI)
	Yes	No		
Age, y, median (IQR)	67 (61–75)	68 (52.5–81)	0.83	–1.00 (–10.00 to 9.00)
Female sex	4 (28.6)	112 (46.1)	0.27	0.47 (0.14–1.53)
Onset of abdominal symptoms prior to admission to the hospital	4 (28.6)	91 (37.4)	0.58	0.67 (0.20–2.19)
Onset of abdominal symptoms after admission to the hospital	3 (24.1)	48 (18.8)	>0.99	1.11 (0.30–4.13)
Proton pump inhibitor	5 (35.7)	99 (40.7)	0.78	0.81 (0.26–2.48)
Antibiotic therapy	11 (78.6)	206 (84.8)	0.46	0.66 (0.18–2.47)
Azithromycin	8 (57.1)	146 (60.1)	>0.99	0.89 (0.30–2.63)
Antibiotics other than azithromycin	9 (64.3)	168 (69.1)	0.76	0.80 (0.26–2.48)
Chloroquine	12 (85.7)	203 (83.5)	>0.99	1.18 (0.26–5.49)
Lopinavir + ritonavir	5 (35.7)	41 (16.9)	0.14	2.74 (0.87–8.59)
Comorbidities	13 (92.9)	210 (86.4)	0.70[a]	2.04 (0.26–16.14)
Cardiovascular diseases	8 (57.1)	140 (57.6)	>0.99	0.98 (0.33–2.91)
Respiratory system diseases	1 (7.1)	32 (13.2)	>0.99	0.51 (0.06–4.01)
Diabetes	2 (14.3)	61 (25.1)	0.52	0.50 (0.11–2.28)
Chronic kidney disease	1 (7.1)	57 (23.5)	0.20	0.25 (0.03–1.96)
Nervous system diseases	4 (28.6)	64 (26.3)	0.76	1.12 (0.34–3.69)
Cancers	2 (14.3)	47 (19.3)	>0.99	0.70 (0.15–3.21)

Data are presented as number (percentage) of patients unless indicated otherwise.

Qualitative variables were compared using the χ^2 test or the Fisher exact test. Odds ratios (OR) with 95% CIs were calculated for all 2×2 tables that did not have a 0 in any cell. The single continuous variable (age) was reported as the median with interquartile range (IQR) and compared using the Mann–Whitney test. Median difference (MD) with 95% CI was calculated as median value for patients with IBS – median value for patients without IBS.

In our study, no correlation was found among the potential risk factors: 1) GI symptoms during COVID-19, 2) PPI administration, 3) azithromycin, 4) antibiotics other than azithromycin, 5) antibiotics in general, 6) chloroquine, lopinavir + ritonavir, and comorbidities, 7) CDI, and 8) coexisting diseases such as cardiovascular disease, chronic kidney disease, respiratory disease, nervous system disease, and cancer. Our analysis did not include the use of glucocorticosteroids, as the results of the RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial[18] were published on June 17, 2020, by the time our cohort had already been assembled. We did not find any relationship between the treatment used in COVID-19 patients, CDI, and comorbidities. Ghoshal et al[17] proved that psychological comorbidities were a risk factor for functional disorders. One of the limitations of our study is that we did not evaluate the mental state of our patients. At the same time, it seems obvious that COVID-19 contributed to deterioration of the mental state of our patients—not only the illness itself, but also the very aspect of isolation, which certainly had a negative impact on the general population.[8] Moreover, depression and anxiety caused by COVID-19 as well as hospitalization are among the proven risk factors for IBS, which makes them highly likely culprits of PI-IBS in our study.[5] Similarly, we found no relationship between PI-IBS and CDI (reported in 26 patients [10.1%]), even though there are data showing that PI-IBS may occur in 25% of patients with a history of CDI, the number of which increased during the COVID-19 pandemic.[6,19]

A study by Cooney et al[20] on the occurrence of residual GI symptoms after COVID-19, conducted at a teaching hospital in London, included 811 patients who had received a link to an online symptom survey, which they completed anonymously using unique study identifiers. Six months later, a link to the follow-up questionnaire was sent, though only 48 patients completed both questionnaires. On the basis of the second questionnaire, it was found that 21 patients (43.8%) had persistent GI symptoms, with abdominal pain and dyspepsia each affecting 14 of them (29.2%), diarrhea 9 (18.8%), constipation 5 (5.4%), and nausea 5 (5.4%). That study provides further evidence for the existence of post–COVID-19 IBS, a new disease that is yet to be described. The study had several limitations (self-reported symptoms, capture bias, small sample, and data limited to people with severe COVID-19); however, the participants reported symptoms similar to those observed in our study (eg, abdominal pain, diarrhea, constipation). Moreover, the authors of the study did not analyze their patients with the R4DQ, which makes their results difficult to refer to and compare with ours. Nevertheless, the authors

TABLE 5 Comparison of characteristics of patients with irritable bowel syndrome (IBS) at the third time point (6-month follow-up) and patients without IBS

Characteristic	IBS at 6 months		*P* value	OR/MD (95% CI)
	Yes	No		
Age, y, median (IQR)	67.5 (53–81)	71 (64.5–83.5)	0.52	–3.00 (–13.00 to 6.00)
Female sex	4 (26.7)	112 (46.3)	0.18	0.42 (0.13–1.36)
Onset of abdominal symptoms prior to admission to the hospital	5 (33.3)	90 (37.2)	0.79	0.84 (0.28–2.55)
Onset of abdominal symptoms after admission to the hospital	2 (13.3)	49 (20.2)	0.74	0.61 (0.13–2.77)
Proton pump inhibitor	3 (20.0)	101 (41.7)	0.11	0.35 (0.10–1.27)
Antibiotic therapy	13 (86.7)	204 (84.3)	>0.99	1.21 (0.26–5.58)
Azithromycin	8 (53.3)	146 (60.3)	0.78	0.75 (0.26–2.14)
Antibiotics other than azithromycin	9 (60.0)	168 (69.4)	0.56	0.66 (0.23–1.92)
Chloroquine	14 (93.3)	201 (83.1)	0.47	2.86 (0.37–22.33)
Lopinavir + ritonavir	2 (13.3)	44 (18.2)	>0.99	0.69 (0.15–3.18)
Comorbidities	13 (86.7)	210 (86.8)	>0.99	0.99 (0.21–4.60)
Cardiovascular diseases	7 (46.7)	141 (58.3)	0.42	0.63 (0.22–1.78)
Respiratory system diseases	1 (6.7)	32 (13.2)	0.70	0.47 (0.06–3.69)
Diabetes	2 (13.3)	61 (25.2)	0.37	0.46 (0.10–2.08)
Chronic kidney disease	2 (13.3)	56 (23.1)	0.53	0.51 (0.11–2.33)
Nervous system diseases	4 (26.7)	64 (26.4)	>0.99	1.01 (0.31–3.29)
Cancers	3 (20.0)	46 (19.0)	>0.99	1.07 (0.29–3.93)

Data are presented as number (percentage) of patients unless indicated otherwise.

Qualitative variables were compared using the χ^2 test or the Fisher exact test. Odds ratios (OR) with 95% CIs were calculated for all 2×2 tables that did not have a 0 in any cell. The single continuous variable (age) was reported as the median with interquartile range (IQR) and compared using the Mann–Whitney test. Median difference (MD) with 95% CI was calculated as median value for patients with IBS – median value for patients without IBS.

concluded that additional studies are urgently needed to further confirm the hypothesis of IBS after COVID-19.

There have been several scientific reports on an increased incidence of IBS during the pandemic, which is mainly related to the deterioration in mental condition, as emphasized by the authors of these studies.[5,8,17,20] Young age has been reported as an independent risk factor for IBS.[21] A study on the impact of the COVID-19 pandemic on the incidence of GI dysfunctions in Italian children and adolescents included 407 patients aged 10 to 17 years who completed a questionnaire based on the Rome III criteria, as the authors found the Rome IV criteria too strict. The incidence of IBS among children and adolescents increased from 3.8% before the pandemic to 8.8% during the pandemic.[22] The authors emphasized the need to focus on coping with stress as a factor that can limit the significant increase in IBS. Oshima et al[23] also touched upon the aspect of the 2-way gut–lung axis and the impact of stress resulting from the COVID-19 pandemic on the course of functional GI diseases. In their study, 5157 patients completed an online survey consisting of questions regarding stress, physical distance, concerns about COVID-19, and GI symptoms. FD was reported by 8.5%, IBS by 16.6%, and FD-IBS by 4% of the respondents. During the COVID-19 pandemic, 11.9% of the respondents reported an exacerbation of the existing GI symptoms, while an improvement was reported by only 2.8%. The relationship between the intensity of the GI symptoms and psychological discomfort was described, which was especially strong in the FD-IBS group. In the study by Oshima et al,[23] the definitions of FD and IBS were based on the Rome III criteria, as the Japanese version of the newer questionnaire had not been validated yet. Certainly, in the context of the Rome IV criteria, there would have been fewer cases of functional disorders, because the recent criteria are stricter than their previous version. Studies by Oshima et al[23] and Solmi et al[24] indicate that the COVID-19 pandemic negatively affected patients with functional disorders, mainly due to increased stress.[24]

Schmulson et al[2] and Ghoshal et al[17] were the first to hypothesize about the occurrence of PI-IBS after SARS-CoV-2 infection. It has been shown that respiratory sequelae of COVID-19, such as fibrosis of the alveoli, develop in the long-term follow-up.[25] This favors the hypothesis that similar degenerative changes may occur in the GI tract. There is ample evidence of the involvement of the GI tract in the course of COVID-19: the presence of SARS-CoV-2 genetic material in the stool, GI symptoms, and disturbances in the intestinal microbiota in corals. It has also been shown that changes in the GI mucosa

do not arise during the course of the disease, but sometime after recovery.[26-29]

In 2007, Marshall et al[30] published a study on patients with a history of viral gastroenteritis. After 6 months of follow-up, 12.5% of participants had symptoms of PI-IBS. In our study, the number of patients who met the IBS criteria was lower after 6 months (5.8%). Our results, as well as those reported by Ghoshal et al,[17] confirm the possibility of the occurrence of functional disorders following a viral infection, because only some of the COVID-19 patients developed GI symptoms, and this group was likely predisposed to PI-IBS.

In most of the abovementioned studies, the prevalence of GI symptoms seems to be underestimated, mainly because the follow-up is too short, which prevents the diagnosis of IBS. Functional disorders as defined in the Rome IV criteria (eg, functional diarrhea, defined as loose or watery stools without predominant abdominal pain or bothersome flatulence, occurring in more than 25% of stools, and lasting for a minimum of 6 weeks with an onset of symptoms at least 3 months prior to the diagnosis) were not considered in the previous studies; nor were organic diseases, which need to be excluded during the diagnostic process. In our study, during the 6-month follow-up, no alarm symptoms were noted (GI bleeding, unexplained iron deficiency anemia, unintentional weight loss, or family history of GI cancer).[31]

Drossman et al[32] stated that the Rome IV criteria, due to the changes made since the previous version, made the IBS diagnosis less widespread and defined the population with a more severe disease. Based on the existing and emerging discrepancies between the Rome criteria and clinical practice, by consensus of the Board of Directors of the Rome Foundation, a modification of the Rome IV diagnostic criteria was developed to enable their application in clinical practice. Four factors have been proposed that should be taken into account when formulating recommendations regarding clinical diagnosis: the nature of the symptoms, their inconvenience, frequency, and duration. The time frames regarding symptom duration seem to be the most problematic, as they limit the diagnosis of IBS in patients with short-term conditions (eg, after acute infection). Although these long time frames remain useful in the context of epidemiological studies, they are not applicable in patients who do not meet the symptom duration criterion for a diagnosis of a functional disorder. According to this commentary on the Rome IV criteria,[32] it is permissible to modify the diagnostic criteria for clinical practice, and not consider the stipulation for the symptoms to occur 6 months prior to the diagnosis a requirement. Instead, this time frame may be reduced to 8 weeks. Of note, the application of these criteria presupposes that other diagnoses have been sufficiently ruled out on the basis of the clinical picture and additional examinations, if necessary. In our model, we took into account the shortened symptom duration criterion; therefore, it is crucial to emphasize the differences in the rates of patients with IBS after its application in comparison with the rates based on the original criteria (5.4% vs 22.3% after 3 months and 5.8% vs 26.9% after 6 months, respectively, before and after modification of the criteria). After using the modified diagnostic criterion, IBS was diagnosed over 4 times more often, which underlines the limitations of the original Rome IV criteria. The proposed modifications to the criteria can serve as the basis for research to validate their application in clinical practice, and the results of such studies will certainly be included in the upcoming Rome V consensus.

Our study has some limitations, the main one being the presence of the IBS symptom duration criterion, as shown by the difference in the number of patients who met the criteria for IBS based on the R4DQ and those who did not (15 [5.8%] vs 70 [26.9%]). Even though the patients did not report any alarm symptoms, organic diseases could not be clearly ruled out; therefore, the mechanism of IBS development following COVID-19 could not be fully elucidated. No risk factors for the development of IBS as a result of COVID-19 have been identified, which made it impossible to create a predictive model. Many studies deal with the subject of mental deterioration in the context of the pandemic, which certainly has a significant impact on IBS. In our work, we did not assess the mental state of the patients. It is difficult to confirm whether deterioration of the mental state could contribute to the development of PI-IBS, so this should be confirmed in subsequent studies. Our study is the second of this kind in the world and highlights the significant problem of PI-IBS after SARS-CoV-2 infection. However, further studies with and a longer follow-up are necessary.

In conclusion, we highlighted the problem of persistent symptoms of the GI tract in the patients with a history of COVID-19. The upward trend of COVID-19 is worrying, given that over 523 million people have by now been through the disease. We also showed that the Rome IV criteria used in the diagnosis of functional disorders significantly underestimate their number. Potential causes of these disorders include disturbances in the gut microbiota and stress, which increased significantly during the pandemic.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT GR conceived the concept of the study. AZ, KL, MS, MR, MK, and WM contributed to the design of the research. AZ, KL, MS, MR, and MK were involved in data collection. AZ, KL, and MR analyzed the data. GR coordinated the funding for the project. All authors edited and approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

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