Original paper

Long-lasting dyspeptic symptoms – another consequence of the COVID-19 pandemic?

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Gastroenterology Rev 2023; 18 (2): 175–182
DOI: https://doi.org/10.5114/pg.2023.129414

Key words: functional gastrointestinal disorders, disorders of gut-brain interaction, functional dyspepsia, coronavirus disease 2019, ROME IV criteria.

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Abstract

Introduction: It is known that the virus SARS-CoV-2 can attack the gastrointestinal (GI) tract and induce gastroenteritis. This can trigger a wide variety of disorders of gut-brain interaction (DGBIs) or functional gastrointestinal disorders (FGIDs), including post-infectious dyspepsia, which remains underestimated.

Aim: To estimate the prevalence of dyspeptic symptoms following COVID-19, immediately after discharge and 3, 6, and 9 months after hospitalization.

Material and methods: A prospective, single-centre evaluation of questions regarding functional dyspepsia (FD) as assessed by the Gastroduodenal Module of ROME IV Diagnostic Questionnaire for Adult FGIDs among 320 patients who had had COVID-19.

Results: The FD ROME IV criteria were met at the respective time-points by 0.0% (0), 4.8% (12), 3.2% (8), and 3.2% (8) of cases. However, the presence of GI symptoms that suggested FD but did not meet the timeframe ROME IV criteria for FD were found in 9.6% (24), 23.5% (59), 20.7% (52), and 20.7% (52) of cases, respectively.

Conclusions: The presence and persistence of gastrointestinal dyspeptic symptoms following COVID-19 is a significant problem. The timeframe of the Rome IV criteria may underestimate the number of patients with persistent dyspeptic symptoms following COVID-19 disease.

Introduction

Disorders of gut–brain interaction (DGBIs) or functional gastrointestinal disorders (FGIDs) are the most common syndromes faced by doctors of various specializations. One such syndrome is functional dyspepsia (FD), which, based on the Rome IV Criteria, has been diagnosed in 10–20% of the general population [1–3]. FD is divided into 2 forms: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). FD is in Category B of the Rome IV Criteria: B1a – PDS and B1b – EPS [4]. The criteria for PDS include the presence, at least 3 days a week, of postprandial fullness (bothersome enough to limit daily activity) and/or early satiety that prevents patients from completing a normal-volume meal. In contrast, EPS is the occurrence, at least once a week, of upper abdominal pain (intense enough to interfere with daily activity) and/or epigastric burning. These symptoms should be present for at least 3 months, and their onset should be at least 6 months prior to diagnosis [4]. In 2022, Drossman stated that the Rome IV Criteria, which are more stringent than those of Rome III, significantly reduced the frequency of diagnoses of functional disorders and excluded

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patients with less severe forms. He also presented the limitations of the Rome Criteria in terms of practical application, mainly related to the time criterion that is necessary to make a diagnosis. Considering these discrepancies, in agreement with the board of directors of the Rome Foundation, work to modify the diagnostic criteria was undertaken. According to the agreement, the time criterion can be shortened from 6 months to 8 weeks, after other causes are excluded [5]. These far-reaching changes could contribute to more practical applicability of future Rome V criteria in clinical practice.

The aetiology of FD remains multifactorial and not fully understood; however, its causes include abnormal gastric emptying, visceral hypersensitivity, the involvement of inflammatory cells and the alterations of the mucosal barrier in the duodenum [6–11]. Some studies have shown an association between DGBIs/FGIDs and acute gastroenteritis (AGE), which may persist for a long time, even after the pathogen has been eliminated. This relationship has been confirmed for post-infectious irritable bowel syndrome (PI-IBS), which may develop regardless of the type of pathogen (viruses, bacteria, parasites, or even fungi). Several pathogens – including *Salmonella spp.*, *Escherichia coli O157*, *Campylobacter jejuni*, *Giardia lamblia*, *Helicobacter pylori*, and *Norovirus* – have also been shown to be associated with FD post-infection symptoms [12]. The pathomechanism of persistent symptoms after SARS-CoV-2 infection remains a mystery [13–15]. It has recently been shown that alterations to the duodenal microbiota were linked to gastric emptying and symptoms in functional dyspepsia [16]. SARS-CoV-2 infection has been reported to alter intestinal microbiota and trigger inflammatory and immune responses [17]. We previously documented persistent IBS symptoms among patients following COVID-19 [18].

The prevalence of post-infectious FD is not well understood, and epidemiology data are scarce. The systematic review and meta-analysis by Futagami *et al.* from 2014 found the frequency of FD after AGE to be 9.55%. Compared to the control group in the same population, it was found that the cumulative odds ratio (OR) for the development of post-infectious FD was 2.54 (95% CI: 1.76–3.65) 6 months after AGE. They also compared the cumulative OR for the development of PI-IBS 6 months after AGE, which was 3.51 (95% CI: 2.05–6.00) [12]. Choudhury *et al.* in their most recent systematic review with meta-analysis evaluated the overall frequency of GI symptoms among 296,487 patients and reported their presence in 12% after COVID-19 and 22% as part of long COVID. The frequency of dyspepsia was 0.20 (95% CI: 0.06–0.50, I^2 = 97%) [19]. However, the small number of studies and significant heterogeneity were considered as the main limitations of their systematic analysis.

Of note, during the COVID-19 pandemic, not only infectious causes increased the incidence of DGBIs/FGIDs [20]. Stress and anxiety related to isolation, fear of falling ill, or the loss of loved ones may have also been responsible for the emergence and even chronic persistence of dyspeptic ailments [21, 22].

Bearing the above in mind, we collected data regarding the upper gastrointestinal tract using the Rome IV Criteria Questionnaire at certain time-points (immediately after discharge and 3, 6, and 9 months later) in a group of patients who had had COVID-19, to investigate the frequency of FD and symptoms of FD without the Rome IV timeframe restriction.

Material and methods

Study design

In this single-centre prospective study, the Rome IV Criteria Questionnaire on the presence of FD was administered to 320 patients hospitalized for COVID-19 at the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw, Poland from 15 March 2020 to 15 January 2021. A total of 69 patients were excluded from the study: 53 because of a diagnosis of FD during hospitalization and 16 because of incomplete questionnaires. The questionnaire was administered at the following time-points: immediately after hospitalization and 3, 6, and 9 months after discharge from hospital. The Polish version of the Rome IV Criteria Questionnaire was obtained from the Rome Foundation (licensed with permission from the Rome Foundation). The primary endpoint of the study was to evaluate the incidence of FD among patients with a history of COVID-19. A secondary endpoint was an assessment of the presence of GI symptoms suggesting FD but without the timeframe criterion.

Statistical analysis

Analysis was conducted in the software program SPSS, ver. 27, using $\alpha = 0.05$. Based on the Rome IV Diagnostic Questionnaire criteria, the number of particular diagnoses among the research group was calculated at 4 time-points. Nominal variables were described as numbers and percentages; quantitative variables were described as medians with first and third quartiles (the normality of the distribution was checked with the Shapiro-Wilk test). The dependencies between diagnoses and time of measurement were analysed using McNemar's test, and the dependencies between the diagnosis of FD and selected characteristics were an-

alysed with the χ^2 test or Fisher's exact test. Quantitative variables were compared between groups with the Mann-Whitney *U* test.

Bioethical considerations

Informed consent was obtained from each patient included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) as reflected in a priori approval by the institution's human research committee – consent number 108/2020.

Results

A total of 320 patients were examined, 251 of whom completed questionnaires. Cumulatively, 69 patients were excluded: 16 due to incomplete Rome IV Criteria Questionnaires and 53 due to FD being diagnosed either before or during hospitalization.

The mean age of the patients enrolled in the study was 68 years, and the majority were men (55.4% (139)). Comorbidities were found in 219 (87.3%) patients, with the following cardiovascular diseases occurring in 143 (57.0%) of them: diseases of the digestive system (68 (27.1%)), diseases of the nervous system (66 (26.3%)), diabetes (61 (24.3%)), chronic kidney disease (56 (22.3%)), cancer (48 (19.1%)), and respiratory diseases (33 (13.1%)). During the hospital stay, the following drugs were used to treat COVID-19: antibiotics (211 (84.1%)), azithromycin (153 (61.0%)), chloroquine (211 (84.1%)), and lopinavir + ritonavir (45 (17.9%)). None of the patients were administered a proton pump inhibitor. The above data are presented in Table I.

FD (B1) was diagnosed at the following time-points: after discharge (0 (0.0%)), after 3 months (12 (4.8%)), after 6 months (8 (3.2%)), and after 9 months (8 (3.2%)). PDS (B1A) was observed at the respective time-points in the following numbers of patients: 0 (0.0%), 8 (3.2%), 5 (2.0%), and 5 (2.0%). In contrast, EPS (B1B) was found in 0 (0.0%), 7 (2.8%), 4 (1.6%), and 4 (1.6%) patients (Table II).

GI symptoms suggestive of FD (i.e. meeting the diagnostic criteria of FD apart from the Rome IV timeframe criterion) were found in the following numbers of patients: 24 (9.6%) immediately after discharge, 59 (23.5%) after 3 months, 52 (20.7%) after 6 months, and 52 (20.7%) after 9 months. GI symptoms suggesting PDS but without the time criterion were found at the respective time-points in 16 (6.4%), 43 (17.1%), 36 (14.3%), and 36 (14.3%) patients. Symptoms suggestive of EPS but without the time criterion were diagnosed at the respective time-points in 14 (5.6%), 25 (10.0%), 21 (8.4%), and 21 (8.4%) patients. There was a significant dependency between the time of measurement and diagnoses of B1 and B1A. At baseline, there was a smaller proportion of subjects with PDS (B1A) and FD (B1) than after 3, 6, or 9 months: for B1A, 6% at baseline vs. 17% 3 months afterwards and 6% at baseline vs. 14% 6/9 months afterwards; for B1, 10% at baseline vs. 24% 3 months afterwards and 10% at baseline vs. 21% 6/9 months afterwards ($p < 0.010$ for these analyses; Table III).

Among the patients with FD, there was a smaller proportion who were on antibiotic therapy (58% vs.

Table I. Characteristics of the study group

Characteristic	Value
Number of patients meeting the inclusion criteria	251
Age, median (Q1–Q3)	68.00 (52.50–81.00)
Sex, *n* (%):	
Female	112 (44.6)
Male	139 (55.4)
Antibiotic therapy, *n* (%)	211 (84.1)
Azithromycin, *n* (%)	153 (61.0)
Antibiotics other than azithromycin, *n* (%)	171 (68.1)
Chloroquine, *n* (%)	211 (84.1)
Lopinavir + ritonavir, *n* (%)	45 (17.9)
Co-existing diseases, *n* (%)	219 (87.3)
Cardiovascular diseases, *n* (%)	143 (57.0)
Respiratory system diseases, *n* (%)	33 (13.1)
Diabetes, *n* (%)	61 (24.3)
Chronic kidney disease, *n* (%)	56 (22.3)
Nervous system diseases, *n* (%)	66 (26.3)
Cancer, *n* (%)	48 (19.1)

Table II. Frequency of FD diagnoses at different time-points (meeting the timeframe criterion)

Diagnosis	Baseline	3 months afterwards	6 months afterwards	9 months afterwards
B1	0 (0.0)	12 (4.8)	8 (3.2)	8 (3.2)
B1A	0 (0.0)	8 (3.2)	5 (2.0)	5 (2.0)
B1B	0 (0.0)	7 (2.8)	4 (1.6)	4 (1.6)

All dependencies were analysed with McNemar's test. p1 – baseline vs. 3 months afterwards, p2 – baseline vs. 6 months afterwards, p3 – baseline vs. 9 months afterwards. P-values could not be calculated if there was no diagnosis at baseline or at the given time-point.

85%; OR = 0.24 95% CI: 0.07–0.80; p = 0.027) and a smaller proportion of patients who were taking antibiotics other than azithromycin (33% vs. 70%; OR = 0.22, 95% CI: 0.06–0.74; p = 0.012) compared to subjects without FD. A lower percentage of participants with co-existing diseases was observed among those with FD than among those without FD (58% vs. 89%; OR = 0.18, 95% CI: 0.05–0.60; p = 0.010). No other significant dependencies were observed after 3 months between being diagnosed with FD and any of the selected characteristics (Table IV).

There was a significant dependency between being diagnosed with FD after 6/9 months and taking antibiotics other than azithromycin (p = 0.014). Taking those antibiotics reduced the risk of having FD by 85% (95% CI for OR = 0.03; 0.74): antibiotics other than azithromycin were taken by 25% of the patients with FD and by 70% of those without it. No other dependencies were observed after 6/9 months (Table V).

Discussion

As documented by Futagami *et al.* in their systematic review and meta-analysis, the frequency of FD among adults 6 months after AGE was 9.55%, which is almost 3 times higher than in our study, where FD after 6 months was 3.2%. However, Futagami *et al.* based

Table III. Frequency of GI symptoms at different time-points (functional dyspepsia excluding the timeframe criterion)

Diagnosis	Baseline	3 months afterwards	p1	6 months afterwards	p2	9 months afterwards	p3
B1	24 (9.6)	59 (23.5)	**< 0.001**	52 (20.7)	**< 0.001**	52 (20.7)	**< 0.001**
B1A	16 (6.4)	43 (17.1)	**< 0.001**	36 (14.3)	**0.002**	36 (14.3)	**0.002**
B1B	14 (5.6)	25 (10.0)	0.061	21 (8.4)	0.248	21 (8.4)	0.248

All dependencies were analysed with McNemar's test. p1 – baseline vs. 3 months afterwards, p2 – baseline vs. 6 months afterwards, p3 – baseline vs. 9 months afterwards.

Table IV. Comparison between patients with functional dyspepsia 3 months after hospitalization and patients without functional dyspepsia

Characteristic	B1 (3 months)		*P*-value	OR/MD (95% CI)
	No	Yes		
Age, median (Q1–Q3)	68.00 (53.00–81.00)	62.00 (22.50–73.00)	0.222[2]	6.00 (–5.00–22.00)
Sex, *n* (%):				
Female	106 (44.4)	6 (50.0)	0.771	0.80 (0.25–2.54)
Male	133 (55.6)	6 (50.0)		
Antibiotic therapy, *n* (%)	204 (85.4)	7 (58.3)	0.027	0.24 (0.07–0.80)
Azithromycin, *n* (%)	147 (61.5)	6 (50.0)	0.546	0.63 (0.20–2.00)
Antibiotics other than azithromycin, *n* (%)	167 (69.9)	4 (33.3)	0.012	0.22 (0.06–0.74)
Chloroquine, *n* (%)	201 (84.1)	10 (83.3)	> 0.999	0.95 (0.20–4.49)
Lopinavir + ritonavir, *n* (%)	44 (18.4)	1 (8.3)	0.480	0.40 (0.05–3.20)
Co-existing diseases, *n* (%)	212 (88.7)	7 (58.3)	0.010	0.18 (0.05–0.60)
Cardiovascular diseases, *n* (%)	138 (57.7)	5 (41.7)	0.372	0.52 (0.16–1.69)
Respiratory system diseases, *n* (%)	32 (13.4)	1 (8.3)	0.714	0.59 (0.07–4.71)
Diabetes, *n* (%)	61 (25.5)	0 (0.0)	0.076	–
Chronic kidney disease, *n* (%)	56 (23.4)	0 (0.0)	0.074	–
Nervous system diseases, *n* (%)	65 (27.2)	1 (8.3)	0.193	0.24 (0.03–1.92)
Cancer, *n* (%)	48 (20.1)	0 (0.0)	0.130	–

Comparisons for qualitative variables were made using the χ^2 test. OR (odds ratio) with 95% confidence intervals was calculated for all 2×2 tables that did not have 0 in any cell. Medians with first and third quartiles were reported for the patients' age; these values were compared using the Mann-Whitney U test. [2]MD (median difference) with 95% confidence interval: median of patients with functional dyspepsia minus median of patients without functional dyspepsia. No p-values were calculated for being in the hospital ward because all patients were there.

Table V. Comparison between patients with functional dyspepsia 6/9 months after hospitalization and patients without functional dyspepsia

Characteristic	B1 (6/9 months)		*P*-value	OR/MD (95% CI)
	No	Yes		
Age, median (Q1–Q3)	68.00 (53.00–80.00)	68.50 (33.50–88.50)	0.927[3]	–0.50 (–17.00–22.00)
Sex, *n* (%):				
Female	107 (44.0)	5 (62.5)	0.473[2]	0.47 (0.11–2.02)
Male	136 (56.0)	3 (37.5)		
Antibiotic therapy, *n* (%)	205 (84.4)	6 (75.0)	0.617	0.56 (0.11–2.86)
Azithromycin, *n* (%)	148 (60.9)	5 (62.5)	> 0.999[2]	1.07 (0.25–4.58)
Antibiotics other than azithromycin, *n* (%)	169 (69.5)	2 (25.0)	0.014	0.15 (0.03–0.74)
Chloroquine, *n* (%)	204 (84.0)	7 (87.5)	> 0.999	1.34 (0.16–11.18)
Lopinavir + ritonavir, *n* (%)	44 (18.1)	1 (12.5)	> 0.999	0.65 (0.08–5.39)
Co-existing diseases, *n* (%)	214 (88.1)	5 (62.5)	0.068	0.23 (0.05–1.00)
Cardiovascular diseases, *n* (%)	139 (57.2)	4 (50.0)	0.728	0.75 (0.18–3.06)
Respiratory system diseases, *n* (%)	31 (12.8)	2 (25.0)	0.602	2.28 (0.44–11.80)
Diabetes, *n* (%)	61 (25.1)	0 (0.0)	0.205	–
Chronic kidney disease, *n* (%)	56 (23.0)	0 (0.0)	0.205	–
Nervous system diseases, *n* (%)	64 (26.3)	2 (25.0)	> 0.999	0.93 (0.18–4.74)
Cancer, *n* (%)	48 (19.8)	0 (0.0)	0.224	–

Comparisons for qualitative variables were made using the χ^2 test or Fisher's exact test. [2]OR (odds ratio) with 95% confidence intervals was calculated for all 2×2 tables that did not have 0 in any cell. Medians with first and third quartiles were reported for patients' age; these values were compared using the Mann-Whitney U test. [3]MD (median difference) with 95% confidence interval: median of patients with functional dyspepsia minus median of patients without functional dyspepsia. No p-values were calculated for being in the hospital ward because all patients were there.

their findings on the Rome III Criteria, which were much more lenient than the Rome IV Criteria [12, 23]. However, if we exclude the time criterion for dyspepsia, then symptoms of dyspepsia were found in many more cases at 6 months – in as many as 20.7% of individuals. The theme of the persistence of FD remains important here, which was also illustrated in our study. However, our follow-up period was longer, and after 9 months the presence of persistent FD symptoms was also observed in as many as 3.2% of the patients. On the other hand, the presence of GI symptoms suggesting FD remained constant after 9 months as compared to 6 months, which is our concern.

In the case of SARS-CoV-2 infection, a viral infection, it is necessary to look at the occurrence of DGBIs/FGIDs, which follows the infectious disease. Such a relationship was found in a study by Porter *et al.,* who reported a 1.5-fold higher frequency of FD among 1718 patients in the USA who had AGE due to the norovirus epidemic [24]. However, no analysis was conducted as to how long these symptoms may persist. The disturbing data on the maintenance of DGBIs/FGIDs in our study supports the data from other studies. Similar conclusions were drawn by Almario *et al.* in a survey among 1000 patients; they found over 75% higher incidence rates of FD and IBS compared to the pre-pandemic figures [25]. This relationship was further confirmed in the 6-month follow-up of 200 patients after COVID-19 in a study by Blackett *et al.*, who reported as many as 29% of patients with GI symptoms. The most common symptoms were diarrhoea (10%), constipation (11%), abdominal pain (9%), nausea and/or vomiting (7%), and heartburn (16%). However, they did not analyse the occurrence of FGIDs [26]. In contrast, in a study by Al-Aly *et al.*, 73,435 US veterans were analysed, with the patients reporting many dyspeptic symptoms [27]. The hypothesis that GI symptoms occur after COVID-19 was finally confirmed in a meta-analysis by Lopez *et al.*, in which as many as 12% of the patients were found to have various types of digestive disorders, which showcases the magnitude of the problem that we will have to deal with [28].

The first study published on the presence of DGBIs/FGIDs in patients who have had COVID-19 was the analysis by Ghoshal *et al.* In this prospective, multicentre, case-control study, 2 cohorts of patients were compared: 280 patients with a history of COVID-19 and 264 healthy controls. It was found that 6 months after infection, 5.3% had developed IBS, 2.1% were diagnosed with FD, and 1.8% had FD/IBS overlap syndrome. The subtype of IBS (60%) was IBS with a predominance of

diarrhoea. Therefore, we can conclude that there was a similar FD value to that of our study: 3.2% vs. 2.1% [20]. However, what remains an undoubted advantage is the 3-month-longer observation period, during which we unfortunately did not find a reduction in the occurrence of FD; on the contrary, we confirmed it was maintained at the same level of 3.2% [29]. Another study that addressed FD in patients following COVID-19 was the analysis of GI symptoms in 200 patients, published by Velez *et al.* Surprisingly, FD and IBS were found in as many as 39.5% of patients, most of whom reported dyspeptic symptoms [30]. This supports our results and emphasizes the underestimation of figures according to the Rome IV Criteria. The higher FD value compared to our study may be explained by the significant proportion of the study group in the study by Velez *et al.* being Latino (67.5%) and the fact that this population is more likely to develop FD, as demonstrated by Huerta-Franco *et al*. [29]. All the above-mentioned studies indicate a significant problem of DGBIs/FGIDs following SARS-CoV-2 infection.

Therefore, it seems important to find the relevant risk factors for DGBIs/FGIDs. Undoubtedly, one of them is SARS-CoV-2 infection. Other factors include the medicines used to treat COVID-19 patients. Among the patients with FD, there was a smaller proportion who were on antibiotic therapy (58% vs. 85%; OR = 0.24, 95% CI: 0.07–0.80; $p = 0.027$) or taking antibiotics other than azithromycin (33% vs. 70%; OR = 0.22, 95% CI: 0.06–0.74; $p = 0.012$), as well as a lower percentage of co-existing diseases (58% vs. 89%; OR = 0.18, 95% CI: 0.05–0.60; $p = 0.010$). There was also a significant dependency between being diagnosed with FD after 6/9 months and taking antibiotics other than azithromycin ($p = 0.014$). Taking those antibiotics reduced the risk of having FD by 85% (95% CI for OR = 0.03; 0.74) – those antibiotics were taken by 25% of the participants with FD and by 70% of those without it.

A doubtless limitation to our work was the failure to consider glucocorticosteroids, which was due to the treatment cohort being studied prior to the publication of the RECOVERY study [31]. There are data that glucocorticosteroids positively correlate with the occurrence of FD [32].

In contrast, Ghoshal *et al.* reported that patients with active COVID-19 and GI symptoms were at risk for DGBIs/FGIDs, which was not confirmed in our study, because our analysis excluded patients with ongoing GI symptoms to have a more precise analysis of COVID-19-related FD [20].

Interestingly, in the study by Velez *et al.*, the risk factors for the development of DGBIs/FGIDs included female gender and a history of depression and anxiety [30]. Blackett *et al.* revealed that COVID-19 patients may experience gut microbiome-mediated alterations in 5-hydroxytryptamine (5-HT) metabolism pathways, which may contribute to long-term GI and mental health symptoms [33]. In our study, no relationship was found with gender, and the presence of depression or anxiety was not investigated. However, depression and anxiety are well-known risk factors for developing DGBIs/FGIDs, and the current COVID-19 data confirm their key role as a consequence of infection [34, 35]. The drugs used to manage COVID-19 have not yet been confirmed as a risk factor for developing DGBIs/FGIDs and, surprisingly, the use of antibiotics seems to be a protective factor here, despite the fact that they are commonly known as factors that can cause disturbance to the intestinal microbiota [36]. Other protective factors against FD are yet to be found.

Taking into account the above data, it seems necessary to include DGBI-/FGID-related symptoms into the manifestations of "long COVID" or post-acute covid syndrome (PACS) [37, 38]. The presence of persistent dyspeptic symptoms that we found in our follow-up remains in line with the current definition of long COVID (post-COVID-19 syndrome or distant COVID-19). The World Health Organization (WHO) defines these symptoms as being present 3 months after SARS-CoV-2 infection, with a simultaneous duration of at least 2 months, but excluding any other diagnosis [39, 40].

Choudhury *et al*. conducted a systematic review and meta-analysis of GI manifestations in long COVID, including as many as 50 studies. This retrospective analysis included abdominal pain and FD, the incidence rates of which were assessed at 14% (95% CI: 0.04–0.38, $I^2 = 96\%$) and 20% (95% CI: 0.06–0.50, $I^2 = 97\%$). In this case, it is right to compare our results after 3 months of observation, because they meet the criteria of long COVID manifestation. Abdominal pain, which is a necessary condition for a diagnosis of EPS (B1B), was present in 14% of cases versus 10% of the patients in our study. A higher value in the meta-analysis may be related to a non-specific definition of abdominal pain, the authors not with the precision of its exact location (EPS is associated with epigastric pain). On the other hand, the highest percentage of FD in our work was in the third month of observation, though it was almost 5 times lower than the results reported by Choudhury *et al.* [41]. Golla *et al.* found that after 3 months only 1.9% had FD, which is less than half the value found in our study (4.8%). The most important conclusion from the study by Golla *et al.* is the fact that FGIDs that appeared after COVID-19 tend to persist, which is shown by the results of our work with an even longer follow-up of up to 9 months [42].

Limitations: There are some limitations in our study. First, the failure to exclude an organic disease should be mentioned (despite the fact that the patients did not report alarm symptoms). Secondly, the influence of drugs other than those used in the treatment of COVID-19 were not considered. Moreover, the failure to consider the level of anxiety and depression and the lack of dietary diaries are other limitations of our study.

Conclusions

The prevalence of FD following COVID-19 remains underestimated. It seems that healthcare personnel should pay attention to dyspeptic symptoms in patients. The risk factors for FD remain unclear, and the relationship with drugs has not been confirmed here. This makes it impossible to create predictive models for the most vulnerable patients. However, we may face another pandemic, resulting in increased DGBIs/FGIDs. The results of our study raise concern over the persistent rise in the frequency of DGBIs/FGIDs following COVID-19.

Conflict of interest

The authors declare no conflict of interest.

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Received: 24.11.2022
Accepted: 8.12.2022