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Prevalence of Irritable Bowel Syndrome, Functional Dyspepsia and their Overlap in Bulgaria: a Population-Based Study

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ABSTRACT

Aims: We aimed to evaluate the prevalence of irritable bowel syndrome (IBS), functional dyspepsia (FD), and their overlap syndrome (OS) in the Bulgarian population and to assess the risk factors associated with these disorders.

Methods: We sent an internet-based survey to Bulgarian adults. The survey collected data on socio-demographic, behavioral and lifestyle characteristics, and diagnostic questions following the Rome IV criteria to assess IBS, FD and their overlap occurrence.

Results: Data was collected from 1,896 individuals (mean age = 35.5 years, 18-65, SD=11.7), 73.1% females. The prevalence of IBS was 20% (14% were with predominant constipation, 32% with predominant diarrhea, 52% had IBS with mixed bowel habits, and 2% unclassified IBS). Gender (p=0.005), age (p<0.001), marital status (p=0.009), occupation (p=0.001), alcohol consumption (p=0.013), sexual problems (p<0.001), FD (p<0.001), and milk intolerance (p<0.001) were significantly associated with IBS. Females (p=0.032; OR: 1.50), patients with FD (p<0.001; OR: 104.98), sexual problems (p= 0.001; OR: 1.55), and milk intolerance (p<0.001; OR: 2.22) are at a higher risk of having IBS. The prevalence of FD was 12.7% (39% had postprandial distress syndrome, 33% epigastric pain syndrome, and 28% had the overlapping variant). Patients with IBS (p<0.001; OR: 127.88) and milk intolerance (p<0.001) were significantly associated with FD prevalence. The prevalence of OS was 11.7%. Gender (p=0.013), milk intolerance (p<0.001, OR: 1.65), urinary (p=0.035) and sexual problems (p<0.001, OR: 1.80) were associated with OS prevalence.

Conclusion: This is the first study to estimate the prevalence of IBS, FD, and their OS and assess the behavioral and demographic risk factors associated with these disorders in the Bulgarian population. Our results are valuable in filling in the epidemiological data gap regarding IBS, FD, and OS in Eastern Europe.

Key words: irritable bowel syndrome – functional dyspepsia – overlap syndrome – epidemiology – Bulgaria.

Abbreviations: EPS: epigastric pain syndrome; FD: functional dyspepsia FGID: functional gastrointestinal disorders; GI: gastrointestinal; IBS: irritable bowel syndrome; IBS-C: IBS predominant constipation; IBS-D: IBS predominant diarrhea, IBS-M: IBS with mixed bowel habits; IBS-U: IBS unclassified; OS: overlap syndrome; PPDS: postprandial distress syndrome (PPDS).

INTRODUCTION

Functional gastrointestinal disorders (FGID) or disorders of gut-brain interaction, are common entities characterized by chronic or recurrent abdominal symptoms, not related to structural or biochemical abnormalities [1]. Recently, in an internet-survey in 24 countries 40.7% met the diagnostic criteria for at least one FGID [2]. Such high prevalence can be defined as a public health issue, as these conditions increase healthcare costs at the state level and cause impaired quality of life in the individual [3, 4]. In the absence of any specific marker, the identification and classification of FGID are based on self-declared symptoms. Since it was published in 2016, the Rome IV diagnostic criteria classification has been considered as the gold standard in FGID identification [5]. The benefit of using the Rome criteria in clinical practice is that they allow a positive approach, avoiding redundant tests to rule out an organic cause. The definition is quite important in characterizing the prevalence of FGID; for instance from Rome III to Rome IV the prevalence of irritable bowel syndrome (IBS) has dropped from around 10% to 5% in US, Canada and the UK [6].

Among all FGID defined by the Rome Foundation, functional dyspepsia (FD) and IBS are the most frequent and the most broadly recognized [7, 8]. They appear to share similar underlying pathophysiological mechanisms, including visceral hypersensitivity [9] , abnormal gastrointestinal (GI) motility [10, 11], abnormalities of gut microbiota [12], low-grade mucosal inflammation [13], and modified central nervous system perception of pain [14]. Despite their functional characteristics, patients with IBS and/or FD represent a real health burden, being related to increased health-care usage [15], psychological disturbances [16], impaired quality of life [15, 17], and presence of overlapping FGID [18].

There have been numerous cross-sectional surveys conducted stating that IBS and FD each affect roughly 5–20% of the general population, with numbers varying considerably according to geographic regions, diagnostic criteria, and study design [19-21]. While overlap syndromes are not stated explicitly in the Rome criteria (I–IV), they may represent a distinct cohort of patients. A 2012 systematic review of 81 studies of IBS, managed in numerous countries and using many different criteria, concluded that the pooled global prevalence of the disorder was 11.2%, with prevalence reports ranging from 1.1% to 45.0% [22]. For FD, extensive population-based studies found the prevalence ranged from 10% to 30% worldwide [23]. Little can be assumed about population prevalence rates from such a comprehensive set of assessments based on multiple disorder definitions and sampling methods. Recently, a global epidemiological study of FGID reports that FD has a pooled prevalence rate of 7.2%, and IBS has a prevalence rate of 4.1% [2]. More population-based studies are needed, especially in geographical regions lacking epidemiological data on the prevalence of IBS, FD, and their overlap, such as Eastern Europe, particularly Bulgaria. Such studies will allow physicians to provide more precise estimates of the prevalence and risk factors for these disorders as well as to identify areas where further research is required.

Therefore, the aims of the current study were to evaluate the prevalence of IBS, FD, and their overlap in the Bulgarian population and to assess the risk factors associated with these disorders.

METHODS

Study design and participants

This is an observational, cross-sectional population-based study. The target population is represented by Bulgarian adults. The sample was selected from a population of social media users in Bulgaria. Understanding population health status from social media forms a new field, namely "digital epidemiology". Online content, when harnessed appropriately, can also provide useful information about diseases and health dynamics in populations [24].

The survey was conducted online, using the Medical News Survey System (Medical News Ltd,Sofia, Bulgaria). The survey was sent to all 27,276 social media followers of Medical News Ltd., the most famous Bulgarian healthcare media; 1,967 of them responded (response rate of 7.2 %). We conducted an anonymous Internet survey but considered the online response as obtained informed consent for the present study. Before data collection started, the study was reviewed by the Ethics Committee (EC) of Tsaritsa Yoanna University Hospital at the Medical University of Sofia (Sofia, Bulgaria), and deemed EC exempt because all study participants were anonymous to the investigators. The study was performed according to the STROBE statement.

The data collection extended from May 2019 to August 2019. Individuals were invited to complete an online questionnaire on general health, without mentioning that the goal of this survey was to investigate GI symptoms. The interview began with several general questions (e.g., age, gender, height, weight, marital status, ethnicity, use of medications or food supplements, diseases), and then followed with questions about drinking and smoking habits, occupation, education level, urinary problems, sexual problems, and milk intolerance. The interview continued with screening questions and questions related to IBS and FD, based on the validated Rome IV criteria [5]. Respondents with chronic illness (such as colon cancer, inflammatory bowel disease, celiac disease, peptic ulcer, diverticulitis, hemorrhoids, diabetes, liver disease, heart disease), gastrointestinal surgeries and/or physical disability were excluded.

Multiple quality assurance methods were built into the survey to minimize bias and poor quality reporting [25]. These included the software detecting missing answers for any applicable question and ensuring participants completed these before being allowed to proceed. Furthermore, taking into consideration the possibility of inconsistent responders, we excluded participants who failed two attention-test questions or were excessively inconsistent on the Rome IV diagnostic questions that were presented twice in the survey for this particular purpose.

Outcomes

The primary outcome was to identify participants who fulfilled symptom-based criteria for Rome IV IBS, FD, or overlap syndrome (OS). The Rome IV criteria define IBS as a FGID characterized by recurrent abdominal pain, on average at least one day per week over a 3-month period, associated with two or more of the following criteria: the pain is related to defecation; the pain is associated with a change in frequency of stool and/or with a change in form (appearance) of stool [5]. Moreover, we aimed to categorize IBS patients into IBS-C (predominant constipation), IBS-D (predominant diarrhea), IBS-M (IBS with mixed bowel habits), and IBS-U (unclassified). IBS-C was defined when a patient reported more than one-fourth (25%) of bowel movements with Bristol Stool Scale types 1–2 and less than one-fourth (25%) with types 6–7 only during days with abnormal bowel movements. IBS-D was diagnosed when more than one-fourth (25%) of bowel movements with Bristol Stool Scale types 6–7 and less than one-fourth (25%) with types 1–2 on days with abnormal bowel movements were reported. When more than 25% of bowel movements with Bristol Stool Scale types 1–2 and more than 25% with types 6–7 on days with abnormal bowel movements were reported, IBS-M was diagnosed. People with IBS whose bowel habits could not be accurately categorized in any of the above subtypes were considered to have IBS unclassified [5].

Functional dyspepsia was categorized into postprandial distress syndrome (PPDS), epigastric pain syndrome (EPS), or overlapping subtypes [26]. The definition of EPS was based on at least one day per week of bothersome epigastric pain, burning, or both. The definition of PPDS was based on at least 3 days per week of bothersome postprandial fullness, early satiety, or both. Those with the overlapping variant fulfilled criteria for both. The symptoms had to be present for the last 3 months with onset at least 6 months previously [26].

Patients with the overlap of IBS and FD fulfilled criteria for both disorders. All individuals in the population who did not meet Rome IV criteria for IBS or FD were used as control participants in the analyses.

The secondary outcome was to assess the risk factors associated with IBS, FD, and their overlap.

Statistical analysis

The statistical analysis was performed using SPSS for Windows, Version 25.0. (SPSS Inc., Chicago, USA). Descriptive statistic for tabular and graphical presentation of results was used. The association between IBS, FD, and OS, and demographic characteristics were evaluated by Chi-square. Logistic regression was applied to predict the independent association of demographics and behavioral factors on the odds ratios of having IBS, FD, or OS. A p-value of <0.05 was considered statistically significant.

RESULTS

The total number of questionnaires collected was 1,967, but 71 had to be discarded due to incomplete information. The final sample size was 1,896 individuals, which was 0.03% of the Bulgarian adult population [27], and consisted of 73.1% females and 26.9% males. The mean age of the participants was 35.5 years (18-65, SD: 11.7).

The prevalence of IBS in the study population was 20%. Overall, IBS-M was the most common subtype, accounting for 52% of all IBS patients in Bulgaria, with IBS-D representing 32%, IBS-C 14%, and IBS-U 2%.

The prevalence of IBS was higher among females (21.6%) compared to males (15.7%) (p=0.005). Iritable bowel syndrome prevalence was highest in participants younger than 30 compared to those between 31 and 40, individuals between 41 and 50, and those above 50 (10.6% vs. 4.9% vs. 2.6% vs. 1.9%, p <0.001). Participants in a relationship had higher IBS prevalence than the married ones and the single ones (9.1 % vs. 6.3% vs. 4.6%, p=0.009). Persons engaged in skilled or semi-skilled work had the highest prevalence of IBS, followed by students, professionals engaged in executive and administrative duties, persons engaged in work requiring manual labour or heavy machinery and unemployed (9.4% vs. 4.4% vs. 3.2% vs. 2.2% vs. 0.8%, p=0.001). Alcohol consumption was associated with IBS prevalence – non-users had a higher prevalence, compared to people with limited daily intake and those drinking more than the recommended daily drinks (10.3% vs. 8.1% vs. 1.5%, p=0.013). The prevalence of IBS was also significantly higher among those with FD than in those without FD (11.7% vs. 8.3%, p<0.001). Moreover, the prevalence of FD was significantly higher among those with IBS-D than in those with IBS-C and IBS-M and was lowest in those with IBS-U (65.3% vs. 60.4% vs. 54% vs. 42.9%, p<0.0001). Irritable bowel syndrome was more prevalent in people reporting milk intolerance than those without such an intolerance (11.1% vs. 8.9%, p<0.001). The presence of sexual problems (p<0.001) was negatively related to IBS prevalence (Table I).

The logistic regresion showed that females (p=0.032; OR: 1.50, 95%CI: 1.04-2.19), individuals with FD (p<0.001; OR: 104.98, 95%CI: 64.48-170.93), without sexual problems (p=0.001; OR: 1.55, 95%CI: 1.20-2.00) and reporting milk intolerance (p<0.001; OR: 2.22, 95%CI: 1.76-2.82) were at a higher risk of having IBS.

The prevalence of FD in the study population was 12.7%. Overall, PPDS was the most common subtype, accounting for 39% of all FD patients in Bulgaria, with EPS representing 33% and overlapping variant representing 28%.

The numerical difference in FD prevalence between men and women was found (9.9% vs. 2.8%, p=0.069), but this did not reach statistical significance. The prevalence of FD was significantly higher among those with IBS than in those without IBS (11.7% vs. 1.1%, p<0.001). Also, the prevalence of IBS was significantly higher among those with overlapping variant than in those with PPDS and was lowest in those with EPS (98.5% vs. 90.4% vs. 87.5%, p<0.0001). Furthermore, FD was more prevalent in people reporting milk intolerance than those who were not reporting milk intolerance (6.5% vs. 6.2%, p<0.001). The presence of urinary (p=0.032) and sexual problems (p<0.001) were negatively related to FD prevalence (Table II).

The logistic regression showed that individuals with IBS (p<0.001; OR: 127.88, 95%CI: 75.24-217.35) were at a higher risk of having FD.

The prevalence of OS in the study population was 11.7%. The prevalence of OS was higher among females (9.3%) compared to males (2.3%) (p= 0.013). Overlap syndrome was more prevalent in people reporting milk intolerance than those who were not reporting milk intolerance (6.5% vs. 5.4%, p<0.001). The presence of urinary (p=0.035) and sexual problems (p<0.001) were negatively related to overlap syndrome prevalence (Table III).

The logistic regression showed that individuals with milk intolerance (p=0.001; OR: 1.65, 95%CI: 1.22-2.23) and without sexual problems (p<0.001; OR: 1.80, 95%CI: 1.31-2.48) were at a higher risk of having FD.

DISCUSSION

To our knowledge, this is the first study to systematically evaluate the prevalence of IBS, FD, and their overlap in the Bulgarian population. Furthermore, the study provides a comprehensive clinical and phenotypic profile of individuals with Rome IV IBS, FD, and OS, and identifies independently associated factors. This provides a platform for understanding the current magnitude of the differences between these FGID and their overlap and prioritizing future research efforts.

The current study evaluated the prevalence of IBS among a sample population of social media users in Bulgaria as well as significant behavioral associations. The prevalence of 20% among the Bulgarian adult population was comparable to that in the Middle East [28, 29] and developed Asian countries [30].

Table I. Distribution of irritable bowel syndrome (IBS) prevalence by respondent characteristics.

	With IBS		Without IBS		Total	
Characteristics	N	%	N	%	N	p
Gender	379	20	1517	80	1896	0.005
male	80	15.7	429	84.3	509	
female	299	21.6	1088	78.4	1387	
Age						<0.001
18-30	201	10.6	611	32.2	812	
31-40	93	4.9	429	22.6	522	
41-50	49	2.6	242	12.8	291	
>50	36	1.9	235	12.4	271	
BMI category						0.105
underweight<18.5	45	2.4	142	7.5	187	
normal 18.51-24.99	220	11.6	833	43.9	1051	
overweight 25-29.99	76	4	384	20.3	460	
obese >30	37	2	159	8.4	196	
Marital status						0.009
single	87	4.6	359	18.9	446	
married	120	6.3	592	39	712	
in a relationship	172	9.1	566	29.9	738	
Education						0.104
basic education	6	0.3	12	0.6	18	
secondary education	104	5.5	360	19	464	
University degree	269	14.2	1145	60.4	1414	
Ethnicity						0.078
Bulgarian	366	19.3	1419	74.8	1785	
Turkish	9	0.5	64	3.4	73	
Roma	4	0.2	34	1.8	38	
Occupation						0.001
unemployed	15	0.8	90	4.7	105	
requiring manual labour or heavy machinery	41	2.2	122	6.4	163	
persons engaged in skilled or semi-skilled work	179	9.4	684	36.1	863	
professionals engaged in executive and administrative duties	60	3.2	366	19.3	426	
students	84	4.4	255	13.4	339	
Smoking status						0.865
non-smokers	205	10.8	798	42.1	1003	
smokers	121	6.4	504	26.6	625	
ex-smokers	53	2.8	215	11.3	268	
Alcohol Consumption						0.013
non-users	196	10.3	666	35.1	862	
limit daily intake to ≤2 standard drinks for women and ≤3 for men	154	8.1	685	36.1	839	
daily intake>2 standard drinks for women and >3 for men	29	1.5	166	8.8	195	
Sexual problems						<0.001
yes	119	6.3	313	16.5	432	
no	260	13.7	1204	79.4	1464	
Urinary problems						0.258
no	350	18.5	1425	75.2	1775	
yes	29	1.5	350	18.5	121	
Functional dyspepsia						<0.001
no	158	8.3	1497	79	1655	
yes	221	11.7	20	1.1	241	
Milk intolerance						<0.001
no	168	8.9	1011	53.3	1179	
yes	211	11.1	506	26.7	717	

In 2017 Sperber et al. [31] reported that mean IBS prevalence among individual countries ranged from 1.1% in France and Iran to 35.5% in Mexico. Recently, a large global epidemiological Internet survey reported IBS prevalence of 4.7%, ranging from 1.3% in Singapore to 7.6% in Egypt [2]. In both studies, the African continent, the Arab world, and Eastern Europe were seriously underrepresented [2, 31]. This makes the results from our study extremely important for the region, and they could serve as a comparison point for future studies.

In 2015 Rusu et al. [32] described that the prevalence of IBS in Eastern Europe varied from 14% in Romania to 28% in Croatia. Although there was no data from Bulgaria included,

Table II. Distribution of functional dyspepsia (FD) prevalence by respondent characteristics.

	With FD		Without FD		Total	
Characteristics	N	%	N	%	N	p-value
Gender	241	12.7	1655	87.3	1896	0.069
male	53	2.8	456	24.1	509	
female	188	9.9	1199	63.2	1387	
Age						0.053
18-30	123	6.5	689	36.3	812	
31-40	58	3.1	464	24.5	522	
41-50	32	1.7	259	13.7	291	
>50	28	1.5	243	12.8	271	
BMI category						0.229
underweight<18.5	28	1.5	159	8.4	187	
normal 18.51-24.99	143	7.6	908	47.9	1051	
overweight 25-29.99	51	2.7	409	21.6	460	
obese >30	19	1.0	177	9.3	196	
Marital status						0.205
single	61	3.2	385	20.3	446	
married	78	4.1	634	33.4	712	
in a relationship	102	5.4	636	33.5	7308	
Education						0.131
basic education	5	0.3	13	0.7	18	
secondary education	62	3.3	402	21.2	464	
University degree	174	9.2	1240	65.4	1414	
Ethnicity						0.455
Bulgarian	231	12.1	1554	82	1785	
Turkish	6	0.3	67	3.5	73	
Roma	4	0.2	34	1.8	38	
Occupation						0.374
unemployed	14	0.7	91	4.8	105	
requiring manual labour or heavy machinery	23	1.2	140	7.4	163	
persons engaged in skilled or semi-skilled work	111	5.9	752	39.7	863	
professionals engaged in executive and administrative duties	43	2.3	383	0.2	426	
students	50	2.6	289	15.2	339	
Smoking Status						0.890
non-smokers	124	6.5	879	46.4	1003	
smokers	82	4.3	543	28.6	625	
ex-smokers	35	1.8	233	12.3	268	
Alcohol Consumption						0.214
non-users	122	6.4	740	39.0	862	
limit daily intake to ≤2 standard drinks for women and ≤3 for men	98	5.2	741	39.1	832	
daily intake>2 standard drinks for women and >3 for men	21	1.1	174	9.2	195	
Sexual problems						< 0.001
no	159	8.4	1305	68.8	1464	
yes	82	4.3	350	18.5	432	
Urinary problems						0.032
no	218	11.5	1557	82.1	1775	
yes	23	1.2	98	5.2	121	
Irritabl Bowel Syndrome						< 0.001
no	20	1.1	1497	79	1517	
yes	221	11.7	158	8.3	379	
Milk tolerance						< 0.001
no	117	6.2	1062	56	1179	
yes	124	6.5	593	31.3	717	

the reported IBS prevalence of 20% in the current study was in this range. However, the occurrence of IBS in Bulgaria was much higher than what has been reported in many other countries [2].

Table III. Distribution of overlap syndrome (OS) prevalence by respondent characteristics.

	With OS		Without OS		Total	
Characteristics	N	%	N	%	N	p-value
Gender	221	11.7	1675	88.3	1896	0.013
male	44	2.3	465	24.5	509	
female	177	9.3	1210	63.8	1387	
Age						0.064
18-30	113	6.0	699	36.9	812	
31-40	54	2.8	468	24.7	522	
41-50	29	1.5	262	13.8	291	
>50	25	1.3	246	13.0	271	
BMI category						0.082
underweight<18.5	28	1.5	159	8.4	187	
normal 18.51-24.99	132	7.0	919	48.5	1051	
overweight 25-29.99	45	2.4	415	21.9	460	
obese >30	16	0.8	180	9.5	196	
Marital status						0.098
single	54	3.8	392	20.7	446	
married	69	3.6	643	33.9	712	
in a relationship	98	5.2	640	33.8	738	
Education						0.065
basic education	5	0.3	13	0.7	18	
secondary education	59	3.1	405	21.4	464	
University degree	157	8.3	1257	66.3	1414	
Ethnicity						0.486
Bulgarian	212	11.2	1573	83.0	1785	
Turkish	6	0.3	67	3.5	73	
Roma	3	0.2	35	1.8	38	
Occupation						0.211
unemployed	11	0.6	94	5.0	105	
requiring manual labour or heavy machinery	22	1.2	141	7.4	163	
persons engaged in skilled or semi-skilled work	100	5.3	763	40.2	863	
professionals engaged in executive and administrative duties	39	2.1	387	20.4	426	
students	49	2.6	290	15.3	339	
Smoking status						0.817
non-smokers	114	6.0	889	46.9	1003	
smokers	77	4.1	548	28.9	625	
ex-smokers	30	1.6	238	12.6	268	
Alcohol consumption						0.131
non-users	114	6.0	748	39.5	862	
limit daily intake to ≤2 standard drinks for women and ≤3 for men	89	4.7	750	39.6	839	
daily intake>2 standard drinks for women and >3 for men	18	0.9	177	9.3	195	
Sexual problems						<0.001
no	143	7.5	1321	69.7	1464	
yes	78	4.1	354	18.7	432	
Urinary problems						0.035
no	200	10.5	1575	83.1	1775	
yes	21	1.1	100	5.3	121	
Milk intolerance						<0.001
no	103	5.4	1076	56.8	1179	
yes	118	6.2	599	31.6	717	

It has already been reported that there is variance among the countries in the prevalence of IBS and other FGID [7, 9, 18]. There are several potential explanations for this variability, including genetics, cultural differences, ethnic diversity, social reporting sensitivity, levels of stress, and dietary habits. We believe that the differences found in this study are not due to a sampling bias to the methodology. However, we must point out that our sample population consisted of social media users in Bulgaria, following a healthcare website, most of them females. Probably, this is also a possible explanation for this variability. Unfortunately, this study is the first of its kind for Bulgaria and we can not compare it to previous data.

The female and younger age predominance in IBS subjects, which was found in this study, is following previous studies on IBS [22, 28, 33, 34]. However, few studies have documented a higher prevalence in male patients [35]. Several hypotheses have been suggested to describe the higher prevalence of IBS in females, i.e., higher serotonin synthesis in the brain [36], female sex hormones' impact on GI motility [37], and potential association of IBS with an anti-nociceptive mechanism decreasing pain related to pelvic events such as pregnancy and delivery [38].

Individuals who did not consume alcohol in our study were more likely to suffer from IBS compared to those who did. The relationship between alcohol consumption and IBS have been discrepant in the literature; some studies record no effect [39, 40], while others show that alcohol consumption was associated with a higher IBS prevalence [41]. Indeed, more studies are needed to reach a better perception of the relationship between alcohol and IBS.

We found that participants in a relationship and persons engaged in skilled or semi-skilled work had a higher prevalence of IBS. A few reports are supporting the premise that relationships may have an impact on the IBS prevalence, severity, and may even have an effect on response to treatment [42, 43]. However, whether being in a relationship or not leads to higher IBS prevalence, probably depends on the communication within this relationship. Therefore, support and depth would be positive attributes, while conflict would have a negative impact on IBS. Lovell and Ford [22] reported that socioeconomic status did not affect IBS prevalence; however, the studies reported that these data were scarce. Although we do not have such data, we assume that the higher prevalence of IBS among persons engaged in skilled or semi-skilled work is due to higher levels of stress and emotional problems at work.

The role of food intolerance in inciting or exacerbating IBS symptoms has been well defined [44]. The meaningful association observed in our study of IBS in patients self-reporting milk intolerance is well established and in compliance with what has been reported in the literature. There was a plethora of evidence that IBS patients commonly reported milk intolerance; however, in a recent review, Cancarevic et al. [44] did not find any conclusive evidence to suggest an objective link between IBS and lactose malabsorption. Moreover, Vernia et al. [45] concluded that there was a significant overlap between IBS and milk intolerance.

We have shown that 12.7% of the Bulgarian adult population fulfill the Rome IV criteria for FD, with PPDS representing 39% of cases, followed by EPS (33%) and the overlapping variant (28%). Our results are relatively comparable with those from a recent study in the Korean population, which reported an FD prevalence of 10.3%, and the PPDS subtype was the most common, followed by EPS and the overlapping variant [46]. In the first population-based study about FD prevalence across multiple countries, Aziz et al. [47] showed that approximately 10% of the adult population fulfill the Rome IV criteria for FD (12% in the USA, 8% in Canada and 8% in the UK), with PPDS representing the majority of cases. In a population-based endoscopic study in Italy, the prevalence of FD was 11.0% [48], while the prevalence of FD was 14.9% in a study from India [49]. Recent global epidemiological study reported that FD had a pooled prevalence rate of 7.2%, with the highest prevalence in Egypt (12.3%) and with PPDS being the most common subtype [2].

We demonstrated that the prevalence of FD was significantly higher among individuals with IBS than in those without IBS. The presence of IBS and other FGID increasing the risk of FD has also been noted previously [18, 47, 50]. Furthermore, we underscored the strength of this association, according to the FD subtype. We showed that IBS symptoms are most prevalent in the overlapping variant, then in PPDS and least prevalent in EPS, which follows previous results [47]. This might be due to the overlap variant generally endorsing more symptoms, although the difference seen between EPS and PPDS alone might suggest different pathophysiological processes or influences. A potential hypothesis is that visceral hypersensitivity could be the predominant factor driving EPS, which could explain the increased association with IBS symptoms seen in this group. In contrast, disturbed gastric accommodation and gastric emptying might drive PPDS. However, studies evaluating the role of these putative pathophysiological mechanisms among FD subtypes have shown conflicting results [51-53].

One of the strengths of our study is the described association between milk intolerance and FD. Data on the relationship between lactose intolerance and FD are scarce [54, 55]. Therefore, this potential association needs additional investigation. Lactose intolerance and FGIDs are common conditions that may coexist or even be confounded. There may be some overlap between the symptoms of lactose intolerance and FD. A few particular symptoms, such as abdominal bloating, nausea, and vomiting, may be attributed to both conditions [56, 57].

Another strength of our study is that it is the first to sample the prevalence of OS, using the Rome IV criteria for IBS and FD, across a large sample of adults from Eastern Europe. Moreover, OS was more prevalent among females and persons reporting milk intolerance. While an overlap of FD and IBS is mentioned as a possibility in the Rome IV criteria [5, 26], we found a considerable prevalence of the OS of 11.7% among the Bulgarian population. In addition, the overlap is not explained by two independent conditions that will randomly coexist in a small number of patients. This finding is consistent with population-based studies, which have revealed a substantial overlap of patients with IBS and FD [30, 58, 59].

Several limitations should be noted in this study. Selection bias is possible as we limited the study population to social

media users that might already have a better socioeconomic status and educational level compared to the general Bulgarian population. Furthermore, other factors known to be related to IBS and FD were not addressed, such as depression and anxiety. There was a female predominance in our study, which is not a significant surprise, hence in the general population, FGID were more common in females [60, 61]. In addition, the study was on adults younger than 65. Another limitation is that the diagnosis of FD was based on fulfilling symptom-based criteria and was not subsequently confirmed by clinical evaluation or endoscopy. Our study could not perform endoscopy due to its widespread dissemination and internet basis. Moreover, we did not ask participants whether they had previously experienced an endoscopy, because detailed responses, particularly for endoscopic findings, would not be reliable and could not be confirmed.

CONCLUSIONS

This is the first study to estimate the prevalence of IBS, FD, and OS and assess the risk factors associated with these disorders in the Bulgarian adult population. Our results are valuable in filling in the epidemiological data gap regarding IBS, FD, and OS in Eastern Europe. Future studies would allow an enriched understanding of the complex pathology of these disorders, and allow better management adjusted towards the risk factors related to IBS and/or FD.

Conflicts of interest: None to declare.

Authors' contributions: R. N., D.D.Y. and V.S. designed the study and wrote the manuscript. M.U., I.L., M.I., K.M.,H.V., R.H., K.I., I.K. and G.V. enrolled the patients; provided the requested patients' material and other clinical data; collected and analyzed the data; R.N. and N.N. performed statistical analyses; V.N. supervised the whole team. All the authors approved the final version of the manuscript.

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