

Risk factors of bloating and its association with common gastrointestinal disorders in a sample of Iranian adults

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ABSTRACT

Background/Aims: Bloating is an unpleasant but common gastrointestinal symptom that is experienced by many people at some stage in their lives. The current survey was conducted to investigate the epidemiology and risk factors of bloating and functional bloating (FB). In addition, we aimed to assess the association between bloating and functional gastrointestinal disorders (FGIDs).

Materials and Methods: In this cross-sectional study, the self-administered modified Rome III questionnaire was used to assess gastrointestinal symptoms and FGIDs. Severity of bloating, demographic and anthropometric measurements, physical activity level, psychological distress, and depression and anxiety were also assessed.

Results: Among the 4763 participants, 52.9% reported having experienced bloating at least occasionally in the past three months (among which 14.1% had severe or very severe symptoms); 19.7% of subjects were found to have FB. After adjusting for multiple variables, female gender, university degree, obesity, and anxiety were associated with both bloating and FB, while depression and psychological distress were only associated with bloating. The positive predictive value and negative predictive value of bloating for the diagnosis of functional bowel disorder were 92.9% and 80.1%, respectively.

Conclusion: Bloating and FB are highly prevalent in the study population. We also identified several demographic, psychological, and lifestyle-related risk factors of bloating in this population.

Keywords: Bloating, functional bloating, functional gastrointestinal disorders, Iran, epidemiology

INTRODUCTION

Bloating is an unpleasant but extremely common gastrointestinal symptom that is experienced by many people at some stage in their lives (1,2). Patients who suffer from bloating but who do not meet the criteria for the diagnosis of other functional gastrointestinal disorders (FGIDs) are categorized as having functional bloating (FB) (3). Two studies in the US (4,5), reported that bloating is seen in almost one fifth of the general population; several other studies conducted in Canada, Mexico, and Australia reported prevalences of 4.1% to 21% for FB (6-8). Previous limited studies using the Rome criteria suggest that FB has a prevalence of between 1.5% to 10% in the general population in Iran (9,10). In several Iranian studies in different selected populations, the prevalence of bloating shows a wide range of between 1.5% and 49% (11). Despite its high

prevalence, bloating remains one of the least understood symptoms related to FGIDs (2,3,5).

Although bloating is not usually the main reason patients seek health care, it is one of the most commonly reported symptoms in patients who consult physicians (12). This may be because bloating is reported to be bothersome and annoying, unlike abdominal pain, which is perceived as an alarm sign and life threatening (12). However, the direct and indirect costs of bloating approach \$260 per person per year in Iran in the general population; it imposes a greater economic burden than many other clinical conditions (13).

The pathophysiology of bloating is still largely unknown. Although a variety of etiologies have been proposed for bloating, including food intolerance, fluid

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retention, weak anterior wall muscle tone, abnormal gut microflora, inflammation, and altered bowel tonic and phasic motility, none of these has been scientifically proven (3,14). However, studies have shown both increased intestinal gas accumulation and delayed gas transit to be important causes of bloating. Distorted perception and visceral hyperalgesia may also play a role in some patients (2,3,5,14).

Physical exercise accelerates gut transit and thus reduces bloating; however, studies on healthy subjects found that physical activity accelerated gas transit but did not affect bloating. The relationship between physical activity and bloating remains unclear (5). Obesity is also an established risk factor for FGIDs; however, data regarding its effects on bloating contain discrepancies (14). Psychological therapies have also been found to be useful in improving bloating and several other FGIDs; however, it remains unclear whether an actual relationship exists between bloating and psychosocial distress (2). Studies have also evaluated the associations of bloating with smoking, marital status, age, and education level (4,5,7); however, data confirming the associations of these variables is limited.

The prevalence of bloating, as a symptom, is dramatically higher in subjects who suffer from other FGIDs, notably irritable bowel syndrome (IBS) (4). Studies have shown that more than two thirds of IBS patients may complain of bloating (4,5,15), while only about one third of subjects who did not meet the criteria for any FGIDs experienced bloating (12). Most research on bloating has considered subjects who suffer from bloating along with other gastrointestinal disorders, especially FGIDs (e.g., IBS, functional dyspepsia (FD), and functional constipation (FC) (3,16,17)); these studies do not address bloating alone.

The epidemiological features of bloating and FB have been investigated in a limited number of studies in Iran. The current survey was conducted on healthy volunteers living in Isfahan province, Iran, to investigate the epidemiology and risk factors of bloating and FB. In addition, we aimed to assess the association between bloating and several gastrointestinal disorders.

MATERIALS AND METHODS

Participants

This study is part of the Study on the Epidemiology of Psychological, Alimentary Health, and Nutrition (SEPAHAN), conducted in April to May 2010, which aimed to investigate the roles of lifestyle-related and psychosocial factors in the etiology of different FGIDs in an Iranian population. SEPAHAN is a cross-sectional study that was conducted on a group of Iranian adults working in 50 different health centers affiliated with the Isfahan University of Medical Sciences (IUMS) across Isfahan Province in the central part of Iran. The University has 20,000 non-academic employees working in hospitals, university campus, and health centers. It is noteworthy that not all these staff members are involved in health services; many of them are also involved in the administrative tasks of IUMS. The IUMS central office has direct contact with all staff in different cities and centers through its Public Relation Unit (PRU). Several months before initiation of the study, PRU staff informed participants about the contents of the questionnaires and the study aims through posters and brochures; finally, they distributed the questionnaires to the participants. To increase data accuracy and participation rates, SEPAHAN was performed in two phases. In the first phase, to collect information about demographic and lifestyle-related factors, we distributed 10,087 pretested, self-administered questionnaires; 8691 completed questionnaires were returned (response rate: 86.2%). In the second phase, data regarding common gastrointestinal symptoms and psychological profiles were collected using validated self-administered questionnaires (response rate: 64.6%). Finally, we were able to match 4763 guestionnaires from phase two with the equivalent guestionnaires in phase one using the national ID numbers of the participants. There were no differences in demographic factors between the participants in the two phases. This study was approved by the Isfahan Regional Bioethics Committee (#290363). The details of the methodological aspects of SEPA-HAN have been described previously (18).

Assessment of Gastrointestinal Symptoms

A validated modified self-administered Persian version of the Rome III questionnaire (18) was used to assess different gastrointestinal symptoms and FGIDs. We minimally modified the Rome III questionnaire with three main changes. First, instead of the seven-item rating scale used in the English version of the Rome III questionnaire to assess the frequency of each gastrointestinal symptom, we used a four-item rating scale (never or rarely, sometimes, often, always) to ensure the appropriateness of the questionnaire for administration to the participants of our study. We also omitted the question about the presence of each symptom six months prior to the evaluation; finally, we added a question about the severity of each symptom (i.e., mild or moderate and severe or very severe).

Definitions of FGIDs

Subjects who reported having experienced bloating at least occasionally in the past three months were categorized as the bloating group; participants in the bloating group who did not meet the criteria for IBS, FD, or FC were designated as having FB (19). Other disorders were defined based on their Rome III definitions (19); however, these definitions were minimally different because of the previously mentioned changes in the questionnaire. The definitions are explained in the following box.

IBS: recurrent abdominal pain or discomfort at least sometimes in the past three months accompanied by two or more of the following: 1. Improvement with defecation at least sometimes, 2. pain onset associated with a change in stool frequency, and 3. pain onset associated with a change in form (appearance) of stool at least sometimes.

Constipation-predominant IBS (IBS-C): IBS, hard or lumpy stools at least sometimes, and lack of loose, mushy, or watery stools.

Diarrhea-predominant IBS (IBS-D): IBS, lack of hard or lumpy stools, and loose, mushy, or watery stools at least sometimes.

Mixed IBS (IBS-M): IBS, hard or lumpy stools at least sometimes, and loose, mushy, or watery stools at least sometimes.

Un-subtyped IBS (IBS-U): IBS, lack of hard or lumpy stools, and lack of loose, mushy, or watery stools.

FC: 1) Two or more of the following: a) straining during defecation at least often; b) lumpy or hard stools at least often; c) sensation of incomplete evacuation at least sometimes; d) sensation of anorectal obstruction/blockage at least sometimes; e) manual maneuvers (e.g., digital evacuation, support of the pelvic floor) to facilitate defecation at least sometimes; f) fewer than three defecations per week at least often; 2) loose stools rarely present without the use of laxatives; 3) insufficient criteria for IBS.

Chronic uninvestigated dyspepsia (CUD) (equivalent to FD in this article): One or more of the following at least sometimes in the past three months: early satiation, bothersome postprandial fullness, and/or epigastric pain/burning.

Gastroesophageal reflux disease (GERD): Presence of heartburn at least sometimes during the three months prior to the study.

Functional bowel disorder (FBD): Meeting the criteria for either IBS, FB, or FC.

Assessment of Demographic and Anthropometric Variables Self-administered guestionnaires were used to assess gender, age, education level, marital status (married, unmarried [single, divorced, widowed]), and smoking history (current smoker, never smoked, or former smoker). Data on self-reported height and weight were also obtained, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants were then classified into three categories based on their BMI: normal weight (18.5 to 24.9 kg m⁻²), overweight (25.0 to 29.9 kg m⁻²), and obese (\geq 30.0 kg m⁻²). The validity of the selfreported values of weight and height was examined in a pilot study on 200 participants from the same population. We found that the self-reported values of anthropometric measures provided a reasonable data of these indices. The correlation coefficients for self-reported weight and height versus measured values were 0.95 (p<0.001) and 0.83 (p<0.001), respectively. The correlation coefficient for the computed BMIs from self-reported values and from measured values was 0.70 (p<0.001).

Assessment of Psychological Distress

The participants' psychological distress level was evaluated using a self-administered General Health Questionnaire (GHQ-12), which is a consistent and reliable instrument designed for use in general populations. The GHQ-12 consists of 12 4-item questions, each of which evaluates a particular feeling or type of behavior in the past month. A four-rating scale was used for each guestion (i.e., less than usual, no more than usual, fairly more than usual, and much more than usual). The 0-0-1-1 method was applied to score the four-item GHQ-12 questions, respectively, rather than the simple Likert scale of 0-1-2-3, as this method is believed to help eliminate any biases that may arise from respondents who tend to choose responses 1 and 4 or 2 and 3, respectively. By applying this method, each participant could score between 0 and 12 points; a threshold score of 4 or more was used to define participants with high psychological distress levels. The internal consistency of the GHQ-12, calculated with Cronbach's alpha coefficient, was found to be 0.87. Convergent validity indicated a significant negative correlation between the GHQ-12 and global guality of life score as r=-0.56, p<0.0001 in the Iranian population (20,21).

Assessment of Anxiety and Depression

The presence of anxiety and depression symptoms was evaluated using a self-administered validated Hospital Anxiety and Depression Scale (HADS) that consists of 14 items that can be divided into two 7-item subscales for anxiety (α =0.82) and depression (α =0.84). The HADS uses a four-point Likert scale ranging from 0 (not present) to 3 (considerable), resulting in a total score ranging from 0 to 21 for each subscale. A score ≥8 in either HADS subscale was considered to indicate anxiety or depression (22). The Iranian version of the HADS has good reliability for the total scale (α =0.92) and the subscales of anxiety (α =0.78) and depression (α =0.86) (23).

Assessment of Physical Activity

The General Practice Physical Activity Questionnaire was used to reflect the level of current physical activity among participants. This questionnaire is a simple validated screening tool intended for use in adults (16 to 74 years) in primary care to assess physical activity based on a four-level Physical Activity Index (Active [Sedentary job and ≥3 hours physical exercise and/ or cycling per week OR standing job and 1 to 2.9 hours physical exercise and/or cycling per week OR a physical job and some but <1 hour physical exercise and/or cycling per week OR a heavy manual job], Moderately Active [sedentary job and 1 to 2.9 hours physical exercise and/or cycling per week OR a standing job and some but <1 hour physical exercise and/or cycling per week OR a physical job and no physical exercise or cycling], Moderately Inactive [sedentary job and some but <1 hour physical exercise and/or cycling per week OR a standing job and no physical exercise or cycling], and Inactive [sedentary job and no physical exercise or cycling]) (24).

Data Entry

We used an optical mark recognition system that captures marked data in scanned pictures of the questionnaires for rapid and accurate data entry to simplify the input process and reduce the possibility of errors.

Statistical Analysis

Data were expressed as mean±standard deviation for quantitative variables and number (%) for qualitative variables. A statistical comparison between genders, patients with and without bloating or FB, and the two severity groups was performed using the χ^2 test (qualitative data) and the t-test (quantitative data). Binary logistic regression models were also used to determine independent risk factors while adjusting for potential confounders. The odds ratios (OR) and corresponding 95% confidence intervals (CI) were computed from the coefficients in the logistic regression models. Furthermore, the distribution of bloating was estimated in the IBS, IBS subtype, CUD, FC, GERD, and FBD groups. The association of bloating with each of these groups was assessed using the χ^2 test, and the OR was reported. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using conventional definitions, with bloating as the predictive test and either of the gastrointestinal disorders as the disease. Statistical analyses were performed using IBM Statistical Package for the Social Sciences version 21 (IBM Corp.; Armonk, NY, USA). A two-tailed α level of 0.05 was used to assess statistical significance in all analyses.

RESULTS

Study Population Characteristics

The general characteristics of the 4763 participants are presented in Table 1. The respondents' ages ranged from 18 to 70 years. Approximately 57% of participants were female. The population consisted mostly of married and well-educated participants. The female participants were younger and more educated than the male participants. The proportion of married individuals was higher among women than men. Women were less physically active than men.

Prevalence of Bloating and FB

Among the 4763 participants, 1734 (38.4%), 489 (10.8%), and 167 (3.7%) reported that they experienced bloating some-

Table 1. General characteristics of the 4763 participants and comparisons between the two genders

	Total	Men	Women	р
Age (mean±standard deviation, years)	36.58±8.09	38.59±8.61	35.16±7.39	<0.001
Education level				
High school diploma or less	1986 (42.8)	1124 (55.0)	862 (33.3)	< 0.001
College degree	801 (17.3)	291 (14.2)	510 (19.7)	
University degree	1849 (39.9)	630 (30.8)	1219 (47.0)	
Marital status				
Singe/divorced/widowed	874 (18.8)	245 (11.9)	629 (24.3)	<0.001
Married	3776 (81.2)	1812 (88.1)	1964 (75.7)	
Physical activity level				
Active or moderately active	2414 (51.1)	1316 (63.3)	1098 (41.4)	< 0.001
Inactive or moderately inactive	2314 (48.9)	762 (36.7)	1552 (58.6)	
Smoking status				
Current smoker	153 (3.2)	150 (7.1)	3 (0.1)	<0.001
Never or former smoker	4610 (96.8)	1956 (92.9)	2654 (99.9)	
Body mass index group				
Normal weight	2327 (52.6)	910 (46.6)	1417 (57.3)	<0.001
Overweight	1672 (37.8)	970 (44.6)	802 (32.4)	
Obese	427 (9.6)	172 (8.8)	255 (10.3)	
Anxiety				
No	4003 (86.0)	18.41 (90)	2162 (62.8)	<0.001
Yes	654 (14.0)	204 (10.0)	450 (17.2)	
Depression No	3315 (71.2)	1590 (77.8)	1725 (66.1)	<0.001
Yes	1338 (28.8)	454 (22.2)	884 (33.9)	

All data are reported as numbers (% within total population/men/women) unless expressed otherwise

Table 2. Prevalence of different population characteristics across groups with bloating and functional bloating

	Bloa	Bloating		Functiona		
	Yes	No	р	Yes	No	р
Age (years)	36.62±7.82	36.54±8.37	0.7	36.64±7.90	36.70 ±8.38	0.8
Gender						
Male	931 (39.0)	1175 (49.5)	<0.001	438 (46.6)	958 (53.0)	< 0.001
Female	1459 (61.0)	1198 (50.5)		502 (53.4)	849 (47.0)	
Education level						
High school diploma or less	932 (40.0)	1054 (45.7)	<0.001	335 (36.5)	788 (44.8)	< 0.001
College degree	412 (17.7)	389 (16.9)		168 (18.3)	304 (17.3)	
University degree	986 (42.3)	863 (37.4)		414 (45.1)	666 (37.9)	
Marital status						
Singe/divorced/widowed	420 (17.9)	454 (19.7)	0.1	164 (17.8)	358 (20.4)	0.1
Married	1924 (82.1)	1852 (80.3)		757 (82.2)	1400 (79.6)	
Physical activity level						
Active or moderately active	1163 (48.9)	1251 (53.2)	0.003	473 (50.6)	976 (54.5)	0.05
Inactive or moderately inactive	1214 (51.1)	1100 (46.8)		462 (49.4)	815 (45.5)	
Smoking status						
Current smoker	75 (3.1)	78 (3.3)	0.7	33 (3.5)	62 (3.4)	0.9
Never or former smoker	2315 (96.9)	2295 (96.7)		907 (96.5)	1745 (96.6)	
Body mass index	25.35±3.82	24.86±3.66	< 0.001	25.39±3.64	24.90±3.59	< 0.001
Anxiety score	4.62±4.04	2.46±3.00	< 0.001	3.18±3.24	1.98±2.64	< 0.001
Depression score	6.91±3.50	5.37±3.06	< 0.001	5.69±3.04	4.96±2.87	<0.001
Psychological distress score	2.61±2.95	1.53±2.38	< 0.001	1.81±2.45	1.26±2.16	< 0.001
All data are reported as numbers (% within bloating/funct	ional bloating groups) or mean-	Estandard deviation				

times, often, and always in the three months before the survey, respectively. Therefore, the overall prevalence of bloating in the study population was 52.9%. Using the Rome III diagnostic criteria for the definition of FGIDs, 19.7% of subjects were found to have FB.

General Characteristics and Prevalence of Bloating and FB

The prevalence of bloating and FB was significantly higher in women, highly educated individuals, and subjects with low physical activity levels (Table 2). In addition, increased prevalence of bloating and FB was related to higher BMI, anxiety, depression, and psychological distress (Table 2). As shown in Table 2, smoking and marital status were not related to the prevalence of bloating and FB.

Independent Risk Factors of Bloating and FB

Table 3 demonstrates the multivariate adjusted ORs of potential risk factors for bloating and FB. Female gender was related to 41% and 23% increases in odds of bloating and FB, respectively. Also, we found an independent relationship between increased educational level and the prevalence of bloating and FB. Furthermore, overweight or obese subjects

were 1.2 and 1.4 times more likely to report bloating, respectively. Although there was no relationship between obesity and FB diagnosis, obese individuals were more likely to have FB than normal weight subjects (OR: 1.45, 95% CI: 1.04-2.02). Mean while, after adjusting for potential confounders, anxiety, depression, and psychological distress were related to increased odds of bloating in the previous three months; only anxiety was independently associated with a higher likelihood of being diagnosed with FB (OR: 1.77, 95% CI: 1.17-2.66). Age, marital status, physical activity, and smoking had no association with either bloating or FB in the study population.

Severity of Bloating and its Risk Factors

Of the 2390 individuals who experienced bloating, 2033 (85.1%) experienced "mild to moderate" symptoms and 357 (14.1%) reported "severe or very severe" bloating. As indicated in Table 4, female gender was related to severity of bloating (OR: 1.5). In addition, after adjusting for multiple confounding variables, individuals with anxiety or psychological distress were 1.8 and 1.4 times more likely to experience severe or very severe bloating, respectively.

Table 3. Multivariate adjusted ORs (95% confidence interval) of potential risk factors for bloating and functional bloating

	Bloating	р	Functional Bloating	р
Age (years)	1.01 (1.00-1.02)	0.1	1.00 (0.99-1.01)	0.9
Gender				
Male	1	< 0.001	1	0.051
Female	1.41 (1.21-1.63)		1.23 (1.00-1.51)	
Education level				
High school diploma or less	1		1	
College degree	1.32 (1.08-1.61)	0.006	1.33 (1.02-1.74)	0.04
University degree	1.41 (1.20-1.64)	< 0.001	1.51 (1.23-1.87)	< 0.001
Marital status				
Singe/divorced/widowed	1	0.1	1	0.2
Married	0.88 (0.73-1.06)		0.85 (0.66-1.10)	
Physical activity level				
Active or moderately active	1	0.4	1	0.5
Inactive or moderately inactive	0.94 (0.81-1.08)		0.93 (0.77-1.13)	
Smoking status				
Never or former smoker	1	0.6	1	0.1
Current smoker	0.89 (0.58-1.36)		0.67 (0.40-1.14)	
BMI group				
Normal	1		1	
Overweight	1.20 (1.03-1.39)	0.02	1.16 (0.95-1.43)	0.1
Obese	1.38 (1.08-1.77)	0.01	1.45 (1.04-2.02)	0.03
Anxiety				
No	1	<0.001	1	0.007
Yes	2.20 (1.71-2.85)		1.77 (1.17-2.66)	
Depression				
No	1	<0.001	1	0.1
Yes	1.42 (1.18-1.71)		1.27 (0.96-1.68)	
Psychological distress				
No	1	0.003	1	0.2
Yes	1.34 (1.11-1.63)		1.21 (0.90-1.63)	

Bloating in Other Gastrointestinal Disorders

The prevalence of bloating in common gastrointestinal disorders is presented in Table 5. The prevalence of assessed FGIDs in the SEPAHAN study was as follows: IBS (21.5%), IBS-C (7.3%), IBS-D (4.3%), IBS-M (4.1%), IBS-U (5.8%), FC (15.3%), FD (15.2%), GERD (23.5%), and FBD (56.5%). The prevalence of bloating was highest (89.1%) among IBS-M cases, and lowest (59.4%) among FC cases. The PPV of bloating for the presence of FB was 39.3%. Although the PPV and specificity of bloating for diagnosis of each FGID were not high, high NPV and sensitivity were found for these gastrointestinal disorders. In addition, the PPV and NPV for the diagnosis of functional bowel disorders were approximately 93% and 80%, respectively. This diagnosis also had high sensitivity (82.4%) and specificity (91.8%) for FBDs.

DISCUSSION

Although bloating is a common symptom in the general population, few data exist regarding its prevalence, etiology, and treatment. This may be because unlike other symptoms, such as abdominal pain, people do not evaluate bloating as a warning symptom unless it becomes very severe. However, most patients rank bloating as a very bothersome symptom in comparison with other GI symptoms (25); it also accounts for a high percentage of referrals to gastroenterologists and causes increases in sick days and medication use (10). In this study, we reported a Table 4. Relationship between participants' characteristics and severity of bloating

	Mild to moderate	Severe or very severe	OR (95% CI)	р	
Age (mean±SD, years)	36.65±7.90	36.43±7.40	1.0 (0.98-1.02)	0.7	
Gender					
Male	830 (40.8)	101 (28.3)	1	0.01	
Female	1203 (59.2)	256 (71.7)	1.49 (1.08-2.05)		
Education level					
High school diploma or less	776 (39.1)	156 (45.2)	1		
College degree	348 (17.5)	64 (18.6)	0.96 (0.66-1.40)	0.8	
University degree	861 (43.4)	125 (36.2)	0.81 (0.59-1.10)	0.1	
Marital status					
Singe/divorced/widowed	349 (17.5)	71 (20.02)	1	0.4	
Married	1644 (82.5)	280 (79.8)	1.18 (0.83-1.69)		
Physical activity level					
Active or moderately active	1006 (49.8)	157 (44.2)	1	0.2	
Inactive or moderately inactive	1016 (50.2)	198 (55.8)	1.17 (0.89-1.54)		
Smoking status					
Never or former smoker	1968 (96.8)	347 (97.2)	1	0.5	
Current smoker	65 (3.2)	10 (2.8)	1.41 (0.53-3.71)		
BMI group					
Normal	958 (50.3)	157 (47.6)	1		
Overweight	746 (39.2)	131 (39.7)	1.17 (0.87-1.58)	0.3	
Obese	199 (10.5)	42 (12.7)	1.34 (0.86-2.08)	0.2	
Anxiety					
No	1643 (82.1)	222 (63.1)	1	0.001	
Yes	358 (17.9)	130 (36.9)	1.81 (1.28-2.56)		
Depression					
No	1328 (66.4)	157 (44.6)	1	0.09	
Yes	672 (33.6)	195 (55.4)	1.34 (0.96-1.87)		
Psychological distress					
No	1454 (73.1)	188 (53.6)	1	0.04	
Yes	536 (26.9)	163 (46.4)	1.38 (1.01-1.90)		

All data are reported as numbers (% within severity groups) unless expressed otherwise. OR: odds ratio; CI: confidence interval

high prevalence of bloating and FB in a sample of apparently healthy Iranian adults. We also identified some potential risk factors for bloating and FB in the studied population.

Prevalence of Bloating

According to the results of this study, bloating is a common symptom that affects almost half the population. This result is higher than the prevalences of bloating found in previous studies in the US (11% to 21%) (4,5,25,26), Canada (20.2%) (8), New Zealand (8.3%) (27), Australia (31.4%) (28), and Iran (7.6% to 25%) (9,10,29,30). This higher prevalence may be due to several factors. In our study, subjects were asked about their bloating symptoms in the last three months; the other studies investigated the presence of bloating over different time frames. Another reason for the difference between the bloating prevalences in the current study and western studies may be differences in the diet and cultural behaviors of the Iranian population. For example, the Iranian diet is higher in fiber content and lower in fat, alcohol, and coffee consumption than diets in western countries. Moreover, the perception of symptoms may be different due to factors such as social, educational, and geographic backgrounds. There is preliminary evidence that bloating as a stress-related

Table 5. Prevalence of bloating across groups with common gastrointestinal disorders

	Bloating (%)	р	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
IBS						
Yes	82.7	<0.001	35.4	92.5	82.7	58.7
No	41.3					
IBS-C						
Yes	82.5	< 0.001	12.0	97.4	82.5	52.3
No	47.6					
IBS-M						
Yes	89.1	< 0.001	7.2	99.1	89.1	51.5
No	48.5					
IBS-U						
Yes	78.6	<0.001	9.1	97.5	78.6	51.6
No	48.4					
IBS-D						
Yes	82.6	<0.001	7.2	98.5	82.6	51.3
No	48.7					
Chronic uninvestigated dyspe	epsia					
Yes	78.4	<0.001	23.7	93.4	78.4	54.9
No	45.1					
Functional constipation						
Yes	59.4	<0.001	18.1	87.5	59.4	51.5
No	48.5					
Gastroesophageal reflux dise	ase					
Yes	72.1	<0.001	33.7	86.8	72.1	56.5
No	43.5					
Functional bowel disorder						
Yes	82.4	< 0.001	92.9	80.1	82.4	91.8
No	8.2					

Sensitivity, specificity, PPV, and NPV were calculated using conventional definitions with bloating as the predictive test and either gastrointestinal disorder as the disease.

Constipation-predominant IBS (IBS-C) was classified as having IBS, hard or lumpy stools at least occasionally, and lack of loose, mushy, or watery stools.

Diarrhea-predominant IBS (IBS-D) was defined as having IBS, lack of hard or lumpy stools, and loose, mushy, or watery stools at least occasionally.

Mixed IBS (IBS-M) was defined as having IBS, hard or lumpy stools at least occasionally, and loose, mushy, or watery stools at least occasionally.

Un-subtyped IBS (IBS-U) was defined as having IBS, lack of hard or lumpy stools, and lack of loose, mushy, or watery stools.

 FBD was defined if a subject met the criteria for IBS, $\mathsf{FB},$ or $\mathsf{FC}.$

disorder may be worsened by stress and relieved by relaxation (12,15). The stress of living in an overpopulated city, namely urban stress, may also contribute to the higher prevalence of bloating in Isfahan, Iran compared to that found in other studies performed in Iran and other countries. Another reason may be selection bias. Most of the subjects we studied were educated and were all currently employed; occupational stress may be a reason for the higher prevalence of bloating in our study. The different definition criteria that were used for the presence of bloating can be considered as another explanation for the high prevalence of bloating in the current study. In our study, 14.5% of subjects suffered from bloating often or frequently in the past

three months, which is more similar to the prevalences of bloating reported in previous studies. Interestingly, in another study among US households, Sandler et al. (25) showed that 88.6% of women and 79.0% of men experienced bloating more than one day in the past month; this highlights how using different definition criteria can cause a significant change in the reported prevalence of bloating.

Prevalence of FB

The prevalence of FB was 19.7% in our study. In one study on 762 Australian adults (6), the prevalences of FB were 11.2% and 4.1% using the Rome I and II criteria, respectively. In Canada (8),

a prevalence of 13.1% has been reported based on the Rome II criteria, while Tuteja et al. (5) reported it to be 7% in US. A prevalence of 21% was also shown in a study on 324 Mexican adults based on the Rome II Modular Questionnaire (7), while another study in the same country reported a prevalence of 10.8% in 2012 (31). Two studies in Iran and Taiwan showed FB prevalences of 1.5% and 2.1% based on the Rome III criteria, respectively (30,32). The reason for the differences in the reported prevalence of FB may be the use of different criteria to determine the presence of bloating (as explained previously); also, the definition of FB is different based on the different Rome criteria. The Rome I criteria defines FB as chronic or recurrent abdominal bloating, fullness, or distension over three months (33), while Rome II defines FB as abdominal fullness or bloating for twelve weeks or more in the previous twelve months (34). However, in Rome III, FB is defined as recurrent feeling of bloating or visible distension at least three days per month for the past three months (3).

Association of Bloating with Age

In our study, after adjusting for multiple potential confounding variables, age was not correlated with bloating or FB; this is similar to findings from several studies in Iran and the US (4,10). However, in another study, Tuteja et al. (5) showed a lower prevalence of bloating in the age group above 55 years in comparison with subjects younger than 55 years after controlling for gender differences. One study in Iran (9) reported that the odds of bloating were slightly higher in the elderly (OR=1.03).

Association of Bloating and FB with Gender

In the present study, the prevalence of bloating was higher in women than in men (OR=1.41) after controlling for other potential risk factors; this is in accordance with previous studies (4,5,7-9,25,27,29,32,33). However, in one study, after controlling for age, the difference between men and women was not statistically significant (p=0.08) (5). A positive association with female gender has also been commonly reported for other FGIDs. The exact reason for this is still unclear; however, several hypotheses have been proposed. In one study, approximately 40% of female IBS patients reported that bloating is related to their menstrual cycle and is usually exacerbated perimenstrually, which is believed to be due to hormonal effects; however, bloating is not limited purely to the perimenstrual time of the cycle. Moreover, men sometimes refer to a "tight sensation" in the abdomen rather than bloating (1,25).

The prevalence of FB and its association with gender was also investigated in several previous studies. In one study performed in Mexico (7), FB was reported to be more common in women (10.7%) than in men (3.7%), which was in agreement with other studies in Mexico (31), Canada (8), and Taiwan (32) that reported a twofold higher prevalence of FB for women than for men. In Australia (6), 90.3% and 73.8% of cases with FB were women based on the Rome II and Rome I criteria, respectively.

Association of Bloating with Educational Level

We found that bloating was also associated with higher education level, even after controlling for other potential risk factors. In one study evaluating abdominal bloating in employed adults in the US, education was not associated with bloating. However, higher education was associated with a lower prevalence of bloating in patients with constipation who did not meet the criteria for IBS (5). One study in Iran showed similar results to our study, with a higher prevalence of bloating associated with higher education (9). However, in another study performed in the US, higher education level was negatively associated with bloating (4).

Association of Bloating and FB with Marital Status

In our study, bloating and FB were not associated with marital status. One study showed unmarried subjects to be more likely to report bloating, after adjusting for age and gender; however, no significant difference was reported (5). One study in the US showed a negative association between being married and bloating (4). In one study in Iran, unmarried subjects had a lower prevalence of bloating than married subjects (9).

Association with Physical Activity Level

Physical activity is believed to have a prokinetic effect on gut transit; it may also strengthen the abdominal muscle wall, which in turn can alleviate the sensation of bloating (2,35,36). In our study, a negative association was found between level of physical activity and prevalence of bloating; however, after adjusting for other potential risk factors, this association lost its significance. The results of one study in the US were also in agreement with our study (5). In one study, after air was injected in the jejenum of patients with bloating, exercise reduced the bloating sensation (37). The relationship between physical activity and bloating appears to be complex and requires further evaluation.

Association of Bloating with Smoking

In our study, no significant association was found between smoking and bloating, which is in agreement with one study in the US that reported no significant association between current smoking and bloating (4). However, in another study in the US, smoking was related to bloating even after controlling for age and gender (OR=1.74 for past smokers and 1.63 for current smokers) (5).

Association with Obesity

In our study, bloating and FB were more prevalent in subjects with higher BMI. Obesity is an established risk factor for some FGIDs (14); several limited studies have evaluated the association of this condition with bloating. In the US, New Zealand, and Australia, it was reported that subjects with BMI>30 experienced significantly more bloating after adjusting for other risk factors (27,38,39). Jiang et al. (4) also found a weak direct association between BMI and bloating. In several studies, however, no relationship was found between obesity and bloating

(40,41); a meta-analysis has also reported that there is no association between bloating and obesity, suggesting that the reported higher prevalence of bloating in obese subjects may be due to the patients' inability to differentiate actual bloating from their large abdominal body mass (42). This information shows an inconsistent relationship between obesity and bloating; further study is required.

Associations with Anxiety, Depression, and Psychological Distress

The role of psychological factors in the pathogenesis of bloating is somewhat controversial. In a study conducted by Chang et al. (15) on IBS patients, all cases who experienced bloating had normal levels of psychological symptoms, including anxiety, depression, and somatization, based on the Symptom Checklist-90-Revised. In another study conducted on IBS patients by Houghton et al. (43), no significant relationship was found between bloating and psychological distress. Heitkemper et al. (44) were also unable to demonstrate an association between bloating and psychological distress. However, in the study by Jiang et al. (4), higher scores on a somatic symptom checklist had a direct association with bloating; this suggests that bloating may partially reflect the process of somatization. In Mexico, 24% of patients with FB suffered from depression based on the Center for Epidemiological Studies Depression Scale (CES-D) (31). In our study, bloating was associated with anxiety, depression, and psychological distress, while FB was only associated with anxiety.

Severity of Bloating

In our study, almost 15% of subjects suffered from severe or very severe bloating; severe bloating was also found to be associated with female gender (OR=1.49), higher level of anxiety (OR=1.49), and psychological distress (OR=1.38). In a study on 2510 subjects in US households, more than 70% of subjects with bloating or distention complained of moderate to severe symptoms; 54% reported that these symptoms affected their daily activities. Furthermore, almost twice as many women as men rated their symptoms as severe (23.8% vs. 13.0%), which resulted in more frequent physician consultations by women (25). In another study, a marginally higher percentage of women with moderate to severe bloating had a history of depressive symptoms compared to a mild bloating group; meanwhile, this association was not significant for anxiety. However, when women were asked about the presence of anxiety or depression, both were found to have direct significant associations with the presence of bloating (45).

Bloating in Other Gastrointestinal Disorders

The prevalence of bloating is dramatically higher in subjects who suffer from other FGIDs, notably IBS (4). Studies have shown that between two thirds to 100% of IBS patients may complain of bloating in Iran and worldwide (4,5,10,15). In our study, bloating was reported by 82.7% of IBS patients. Bloating was initially considered as a diagnostic criterion for IBS (46);

it is now proposed to be a supportive symptom to discriminate IBS from organic disorders (47). Among different types of IBS, bloating has been strongly related to IBS-C in different studies (15,44,48). The higher prevalence of bloating in IBS-C subjects may be due to the possible pathophysiology of bloating, which has been explained in previous studies: increased intestinal gas accumulation, which is mostly seen in constipated subjects due to slower than normal colonic transit, is an important cause of bloating (4,14,49). However, in some other studies, the prevalence of bloating was higher in IBS-D patients than in IBS-C subjects (4,15,30,43). Some studies have also found equally high prevalences of bloating for both IBS-D and IBS-C (5). Several studies, including one recent survey, have also reported a higher prevalence of bloating in the IBS-M subtype compared to other subtypes (15,50). The results of our study show a higher prevalence of bloating among IBS-M cases. IBS-C and IBS-D patients experience less bloating; both subtypes have approximately the same prevalence.

FC has also been strongly associated with bloating; up to 50% of cases with bloating have been reported to have FC (4). However, this proportion was lower (15.7%) in one study in Iran by Sorouri et al. (30) in 2010, with a twofold increase of FC in bloating cases. Roshandel et al. (10) also reported a 73% prevalence of bloating in FC subjects in Iran; this prevalence was lower (59.4%) in our study. In our study, among different Gl disorders, bloating had the least association with FC, which was in agreement with the study by Sorouri et al. (30). Association of GERD and FD with bloating has also been shown in previous studies (4, 26). In our study, the PPV of bloating for the presence of FB was 39.3%, while in another study in Iran, 13.4% of subjects with bloating experienced FB (30).

We also found a strong association between FBD and bloating, reflecting the fact that the presence of more gastrointestinal physiological disruptions may increase risk of bloating. In the study by Sorouri et al. (30) in Iran, 77.2% of subjects with bloating had FBD (including IBS, FC, functional diarrhea, FB, and unspecified FBD); also, bloating showed a greater than 11-fold increase for FB. Previous studies evaluating the diagnostic value of bloating in other FGIDs reported high specificity (89%) but low sensitivity (38%) for bloating symptoms in the diagnosis of FGIDs. It was also shown that the absence of bloating cannot be used to rule out FGIDs (NPV=87%); however, it had a positive predictive value of 66% (5). These values were all higher in our study, in which the PPV, NPV, sensitivity, and specificity were 92.9%, 80.1%, 82.4%, and 91.8%, respectively.

Study Advantages and Limitations

The large sample size, employment of validated questionnaires, and assessment of different demographic, psychological, and lifestyle-related factors are major strong points of the present study. An advantage of our study was the simultaneous evaluation of both bloating symptoms and FB. Most previous studies present data regarding either bloating or FB. Moreover, in

contrast to previous studies, we also measured the severity of symptoms. Our study also has some limitations. Due to the cross-sectional study design, we recommend performing future prospective studies to assess causal associations. The subjects of our study were employed, educated adults living in a populated urban city; thus, generalization to the entire Iranian adult population is questionable. One other limitation of our study was that the questionnaires were self-administered; also, we did not examine the cases for potential organic disorders using history taking, physical examination, or further paraclinical evaluations.

In conclusion, this study showed high prevalences of bloating and FB in a group of Iranian adults. Female gender, higher education level, obesity, anxiety, depression, and psychological distress were the main risk factors of bloating in this study, while FB was only associated with higher education level, obesity, and anxiety. We also found that female gender, anxiety, and psychological distress were related to increased severity of bloating. To understand the pathophysiology of this common GI complaint and determine its risk factors, further prospective research is required. In addition, it should be investigated whether the incidence or severity of bloating can be decreased by targeting its modifiable risk factors (i.e., obesity, psychological disorders) in well-designed randomized clinical trials.

Ethics Committee Approval: The study was reviewed and approved by the Isfahan University of Medical Sciences Institutional Review Board.

Informed Consent: Voluntary informed consent was obtained from all subjects involved in the study prior to study inclusion.

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REFERENCES

- 1. Lea R, Whorwell PJ. Expert commentary-bloating, distension, and the irritable bowel syndrome. Med Gen Med 2005; 7: 18.
- 2. Zar S, Benson M, Kumar D. Bloating in functional bowel disorders. Aliment Pharm Therap 2002; 16: 1867-76. [CrossRef]
- Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology 2006; 130: 1480-91. [CrossRef]
- Jiang X, Locke Gr, Choung R, Zinsmeister A, Schleck C, Talley N. Prevalence and risk factors for abdominal bloating and visible distention: a population-based study. Gut 2008; 57: 756-63. [CrossRef]

- Tuteja AK, Talley NJ, Joos SK, Tolman KG, Hickam DH. Abdominal bloating in employed adults: prevalence, risk factors, and association with other bowel disorders. Am J Gastroenterol 2008; 103: 1241-8. [CrossRef]
- Boyce P, Talley N, Burke C, Koloski N. Epidemiology of the functional gastrointestinal disorders diagnosed according to Rome II criteria: an Australian population-based study. Int Med J 2006; 36: 28-36. [CrossRef]
- Schmulson M, Ortiz O, Santiago-Lomeli M, et al. Frequency of functional bowel disorders among healthy volunteers in Mexico City. Digest Dis 2006; 24: 342-7. [CrossRef]
- 8. Thompson W, Irvine E, Pare P, Ferrazzi S, Rance L. Functional gastrointestinal disorders in Canada: first population-based survey using Rome II criteria with suggestions for improving the questionnaire. Digest Dis Sci 2002; 47: 225-35. [CrossRef]
- 9. Pourhoseingholi A, Safaee A, Pourhoseingholi MA, et al. Prevalence and demographic risk factors of gastrointestinal symptoms in Tehran province. JPH 2010; 8: 42-6.
- 10. Roshandel D, Rezailashkajani M, Shafaee S, Zali MR. Symptom patterns and relative distribution of functional bowel disorders in 1,023 gastroenterology patients in Iran. Int J Col Dis 2006; 21: 814-25. [CrossRef]
- 11. Daneshpajouhnejad P, Keshteli AH, Sadeghpour S, Ardestani SK, Adibi P. Bloating in Iran: SEPAHAN systematic review no. 4. Int J Prev Med 2012; 3: S26.
- 12. Jiang X, Locke GR, Zinsmeister AR, Schleck CD, Talley NJ. Health care seeking for abdominal bloating and visible distention. Aliment Pharm Therap 2009; 30: 775-83. [CrossRef]
- 13. Roshandel D, Rezailashkajani M, Shafaee S, Zali MR. A cost analysis of functional bowel disorders in Iran. Int J Col Dis 2007; 22: 791-9. [CrossRef]
- 14. Agrawal A, Whorwell P. Review article: abdominal bloating and distension in functional gastrointestinal disorders-epidemiology and exploration of possible mechanisms. Aliment Pharmacol Ther 2008; 27: 2-10. [CrossRef]
- Chang L, Lee OY, Naliboff B, Schmulson M, Mayer EA. Sensation of bloating and visible abdominal distension in patients with irritable bowel syndrome. Am J Gastroenterol 2001; 96: 3341-7. [CrossRef]
- Fazel M, Keshteli AH, Jahangiri P, Daneshpajouhnejad P, Adibi P. Gastroesophageal reflux disease in Iran: SEPAHAN systematic review No. 2. Int J Prev Med 2012; 3: S10.
- Iraji N, Keshteli AH, Sadeghpour S, Daneshpajouhnejad P, Fazel M, Adibi P. Constipation in Iran: SEPAHAN systematic review No. 5. Int J Prev Med 2012; 3: S34.
- 18. Adibi P, Keshteli AH, Esmaillzadeh A, et al. The study on the epidemiology of psychological, alimentary health and nutrition (SEPA-HAN): overview of methodology. J Res Med Sci 2012; 17.
- Thompson W, Drossman D, Talley N, Walker L, Whitehead III W. Rome III diagnostic questionnaire for the adult functional GI disorders (including alarm questions) and scoring algorithm. Rome III: The Functional Gastrointestinal Disorders. III. McLean, VA: Degnon Associates, Inc 2006: 917-51.
- 20. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychol Med 1979; 9: 139-45. [CrossRef]
- 21. Montazeri A, Harirchi AM, Shariati M, Garmaroudi G, Ebadi M, Fateh A. The 12-item General Health Questionnaire (GHQ-12): translation and validation study of the Iranian version. Health Qual Life Outcomes 2003; 1: 66. [CrossRef]

- 22. Snaith RP. The hospital anxiety and depression scale. Health Qual Life Outcomes 2003; 1: 29. [CrossRef]
- Montazeri A, Vahdaninia M, Ebrahimi M, Jarvandi S. The Hospital Anxiety and Depression Scale (HADS): translation and validation study of the Iranian version. Health Qual Life Outcomes 2003; 1: 14. [CrossRef]
- 24. Department-of-Health. The general practice physical activity questionnaire. Department of Health, London 2006.
- 25. Sandler RS, Stewart WF, Liberman JN, Ricci JA, Zorich NL. Abdominal pain, bloating, and diarrheain the united states. Digest Dis Sci 2000; 45: 1166-71. [CrossRef]
- 26. Camilleri M, Dubois D, Coulie B, et al. Prevalence and socioeconomic impact of upper gastrointestinal disorders in the United States: results of the US Upper Gastrointestinal Study. Clin Gastroenterol Hepat 2005; 3: 543-52. [CrossRef]
- 27. Talley NJ, Howell S, Poulton R. Obesity and chronic gastrointestinal tract symptoms in young adults: a birth cohort study. Am J Gastroenterol 2004; 99: 1807-14. [CrossRef]
- 28. Talley N, Boyce P, Jones M. Identification of distinct upper and lower gastrointestinal symptom groupings in an urban population. Gut 1998; 42: 690-5. [CrossRef]
- Sohrabi S, Nouraie M, Khademi H, Baghizadeh S, Nasseri-Moghaddam S, Malekzadeh R. Epidemiology of uninvestigated gastrointestinal symptoms in adolescents: a population-based study applying the Rome II questionnaire. J Ped Gastroenterol Nutr 2010; 51: 41-5. [CrossRef]
- 30. Sorouri M, Pourhoseingholi MA, Vahedi M, et al. Functional bowel disorders in Iranian population using Rome III criteria. Saudi J Gastroenterol 2010; 16: 154-60. [CrossRef]
- López-Colombo A, Morgan D, Bravo-González D, Montiel-Jarquín A, Méndez-Martínez S, Schmulson M. The epidemiology of functional gastrointestinal disorders in Mexico: a population-based study. Gastroenterol Res Pract 2012; 2012: 606174. [CrossRef]
- 32. Chang FY, Chen PH, Wu TC, et al. Prevalence of functional gastrointestinal disorders in Taiwan: questionnaire-based survey for adults based on the Rome III criteria. Asia Pacific J Clin Nutr 2012; 21: 594-600.
- Thompson WG, Creed F, Drossman D, et al. Functional bowel disease and functional abdominal pain. Gastroenterol Int 1992; 5: 75-91.
- 34. Thompson WG, Longstreth G, Drossman D, Heaton K, Irvine E, Müller-Lissner S. Functional bowel disorders and functional abdominal pain. Gut 1999; 45: II43-II7. [CrossRef]
- 35. Sullivan SN. Functional abdominal bloating with distention. ISRN Gastroenterology 2012; 2012: 721820. [CrossRef]
- 36. Seo AY, Kim N, Oh DH. Abdominal bloating: pathophysiology and treatment. J Neurogastroenter Motil 2013; 19: 433-53. [CrossRef]

- 37. Villoria A, Serra J, Azpiroz F, Malagelada JR. Physical activity and intestinal gas clearance in patients with bloating. Am J Gastroenterol 2006; 101: 2552-7. [CrossRef]
- 38. Delgado-Aros S, Locke GR, Camilleri M, et al. Obesity is associated with increased risk of gastrointestinal symptoms: a population-based study. Am J Gastroenterol 2004; 99: 1801-6. [CrossRef]
- Talley N, Quan C, Jones M, Horowitz M. Association of upper and lower gastrointestinal tract symptoms with body mass index in an Australian cohort. Neurogastroenterol Motil 2004; 16: 413-9. [CrossRef]
- 40. Bouchoucha M, Fysekidis M, Julia C, et al. Functional gastrointestinal disorders in obese patients. The importance of the enrollment source. Obes Surg 2015; 25: 2143-52. [CrossRef]
- 41. Cremonini F, Camilleri M, Clark M, et al. Associations among binge eating behavior patterns and gastrointestinal symptoms: a population-based study. Int J Obes 2009; 33: 342-53. [CrossRef]
- 42. Eslick G. Gastrointestinal symptoms and obesity: a meta-analysis. Obes Rev 2012; 13: 469-79. [CrossRef]
- 43. Houghton LA, Lea R, Agrawal A, Reilly B, Whorwell PJ. Relationship of abdominal bloating to distention in irritable bowel syndrome and effect of bowel habit. Gastroenterology 2006; 131: 1003-10. [CrossRef]
- 44. Heitkemper MM, Cain KC, Jarrett ME, Burr RL, Crowell MD, Woods NF. Relationship of bloating to other GI and menstrual symptoms in women with irritable bowel syndrome. Dig Dis Sci 2004; 49: 88-95. [CrossRef]
- 45. Park HJ, Jarrett M, Cain K, Heitkemper M. Psychological distress and GI symptoms are related to severity of bloating in women with irritable bowel syndrome. Res Nurs Health 2008; 31: 98-107. [CrossRef]
- 46. Manning A, Thompson WG, Heaton K, Morris A. Towards positive diagnosis of the irritable bowel. BMJ 1978; 2: 653-4. [CrossRef]
- 47. Neri M, Laterza F, Howell S, et al. Symptoms discriminate irritable bowel syndrome from organic gastrointestinal diseases and food allergy. Europ J Gastroenterol Hepat 2000; 12: 981-8. [CrossRef]
- 48. Talley NJ, Dennis EH, Schettler-Duncan VA, Lacy BE, Olden KW, Crowell MD. Overlapping upper and lower gastrointestinal symptoms in irritable bowel syndrome patients with constipation or diarrhea. Am J Gastroenterol 2003; 98: 2454-9. [CrossRef]
- 49. Sadik R, Björnsson E, Simrén M. The relationship between symptoms, body mass index, gastrointestinal transit and stool frequency in patients with irritable bowel syndrome. Europ J Gastroenterol Hepat 2010; 22: 102-8. [CrossRef]
- 50. Kibune NC, Garcia MC, Silva LS, Mesquita M. Irritable bowel syndrome subtypes: Clinical and psychological features, body mass index and comorbidities. Rev Esp Enferm Dig 2016; 108: 59-64.