Trends and characteristics associated with dietary triggers and psychological distress in patients with irritable bowel syndrome: a cross-sectional study

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Abstract. – **OBJECTIVE:** Diet, visceral sensitivity, and psychological distress play an important role in Irritable Bowel Syndrome (IBS). This study focused on the relation between IBS severity, foods, visceral sensitivity, and anxiety/depression.

PATIENTS AND METHODS: Patients with IBS were investigated through (1) IBS-symptoms severity score (SSS), (2) self-reported food intolerance, (3) visceral sensitivity index (VSI), and (4) Hospital Anxiety and Depression Scale (HADS). Seventy-seven patients agreed to participate in the survey. Of them, 64 (83%) showed IBS according to Rome IV criteria and were included in the final analysis. Patients with IBS-D were 30 (47%), with IBS-C 27 (42%), and with IBS-M 7 (11%).

RESULTS: Fifty-eight patients (90%) considered at least one foodstuff as IBS trigger. Amine-rich foods represented a symptom trigger for 77% of patients, those with lectin for 70%, IACs by 48%, and capsaicin by 37%. Overweight was significantly associated with amine-rich foods (p=0.015), age >45 years (p=0.001) and non-smoking condition (p=0.033) with lectin-rich foods, male gender (p=0.005) and overweight (p=0.027) with capsaicin-containing foods. A positive VSI score was found in 59% of patients, and non-smoking condition was significantly associated (OR 10.03; p=0.009). No factors were associated with a positive HADS score, shown by 80% of patients. Severe IBS was shown by 63% of patients, being amine-rich foods (p=0.024), overweight (p=0.020), and female gender (p=0.029) independent risk factors while marriage/cohabiting a protective one (p=0.038). Amine-rich foods are an independent risk factor for severe IBS, along with overweight and female gender.

CONCLUSIONS: Clinicians should pay more attention to self-reported food intolerance in IBS patients. A personalized therapy including dietary advice as part of treatment could be of great benefit.

Key Words:
  Functional gastrointestinal disorder, Diet, Visceral sensitivity, Amine-rich foods.

Abbreviations

IBS: Irritable bowel syndrome, FGIDs: functional gastrointestinal disorders, IBS-D: IBS with predominant diarrhea, IBS-C: IBS with predominant constipation, IBS-M: IBS with mixed bowel habits, IAC: incompletely absorbable carbohydrates, IBD: inflammatory bowel disease, FODMAP: fermentable, oligo-, di-, mono-saccharides, and polyol, IBS-SSS: IBS symptom severity score, VSI: visceral sensitivity index, HADS: Hospital Anxiety and Depression Scale, OR: odds ratio, PASW: Predictive Analytics Software, SPSS: Statistical Package for Social Science statistic, SD: standard deviation, CI: confidence interval.

Introduction

Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by recurrent abdominal pain, associated with defecation or

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changes in intestinal habits, in the absence of detectable structural and biochemical abnormalities[1]. It is a common functional disease that generates a significant burden on the healthcare system and can adversely affect the quality of life of the patients[2]. IBS represents the most diagnosed gastrointestinal condition among the wide cluster of functional gastrointestinal disorders (FGIDs), although its real global prevalence and distribution are poorly documented. The recent Rome IV criteria eliminated the term non-specific "discomfort" and has considered the IBS with predominant diarrhea (IBS-D), IBS with predominant constipation (IBS-C), and IBS with mixed bowel habits (IBS-M) as a continuous disorder[3]. Perceived food intolerance is a common problem in individuals with IBS. Most of them believe that diet has a pivotal role in the disease pathogenesis and/or in the symptoms reactivation[4]. Patients with IBS believe in diet modification as a potential treatment to manage their disease. They often carry out a peculiar dietary habit likewise patients with organic disease, such as chronic inflammatory bowel disease (IBD)[5] or celiac disease[6]. Self-reported food intolerance is frequently associated with more severe symptoms. This forces the patients to initiate restrictive diets, such as a gluten-free diet or a lactose-free diet, to alleviate their symptoms[7,8]. Therefore, IBS patients' concerns represent a challenge for clinicians in setting up proper management of this condition[9]. Most patients with IBS consider certain foods as important trigger factors of their gastrointestinal symptoms. This becomes particularly true for alimentary products containing carbohydrates (highly fermentable) and fats, as well as for histamine-releasing foods and, in general, biogenic amines[10]. Patients often complain about abdominal bloating and pain, especially after the ingestion of some foods, such as milk and dairy products, wheat-derived foods, and incompletely absorbable carbohydrates (IAC)[11]. Avoiding certain foods and a self-managed diet regimen is common in IBS patients, similarly to what happens in more severe gastrointestinal disorders, such as IBD[12]. Food and dietary habit play a pivotal role in IBS, inducing patients to look for alternative medicine such as herbal products and nutraceutical compounds[13]. In this complex scenario, the current knowledge regarding the association between certain food groups and symptoms' control remains conflicting. There are insufficient data on the dietary practices of patients with IBS. Studies examining relationships between specific foods and IBS symptoms are lacking[14]. Low fermentable, oligo-, di-, mono-saccharides, and polyol (FODMAP) diet seems to have positive effects in patients with IBS, probably due to the exclusion of cereals. This supports the role of specific foods in symptoms' triggering[15]. On the other hand, self-reported food intolerance seems to be related to IBS severity, IBS subtype, but also to psychological issues such as anxiety and depression[16]. Visceral sensitivity has been recognized as a key factor in the onset and exacerbation of IBS, suggesting the use of cognitive-behavioral therapy for these patients[17].

Although a close connection has been established between dietary factors and IBS, the evidence supporting the efficacy of this approach is variable, and randomized controlled trials are few. Furthermore, restrictive diets may promote nutritional deficiencies and eating behavior disorders. Probably, the role of other aspects such as clinical and demographic characteristics of the patients should be focused to assess the benefits of implementing these various diets into routine life. The role of biogenic amines or IACs in IBS is poorly investigated compared with gluten or FODMAP[18]. With this in mind, we chose to plan a survey on specific food considered as a trigger of gastrointestinal symptoms in IBS patients but poorly investigated and evaluate potential associations with clinical and demographic characteristics, IBS severity, visceral sensitivity, and anxiety/depression status.

Patients and Methods

Patients

From July 2020 to November 2020, at Digestive Pathophysiology Unit of University Hospital in Catanzaro, in Southern Italy, a prospective study was conducted aiming to evaluate the presence of self-reported food intolerance in IBS patients and assess its impact on symptoms' severity. Patients older than 18 years, who were consecutively admitted to the outpatient clinic with a previous diagnosis of IBS, were re-evaluated for this condition according to the Roma IV criteria[19]. In the presence of features such as an onset of symptoms after 50 years of age, rectal bleeding, unexplained weight loss or iron-deficiency anemia, family history of colorectal cancer, celiac disease, or IBD), selected tests were performed

as appropriate to exclude organic diseases (e.g., complete blood cell count, fecal calprotectin, screening for celiac disease, and colonoscopy). If IBS diagnosis was confirmed, the patient was invited to answer a self-administered survey, dealing with a food questionnaire, IBS Symptom Severity Score (IBS-SSS), visceral sensitivity index (VSI) score, and Hospital Anxiety and Depression Scale[20-22]. A trained clinical team performed interviews concerning demographic characteristics, lifestyle, occupational status, level of education, relevant medical history, and the type of medications used. Exclusion criteria were the diagnosis of gastrointestinal condition other than IBS (e.g., celiac disease, IBD, and diverticular disease) when it could be considered the main disease responsible for the current symptoms, and previous gastrointestinal surgery responsible for relevant alterations in digestive functions (i.e., short bowel syndrome).

Questionnaires

The food's questionnaire was developed according to scientific literature dealing with food products mostly correlated with gastrointestinal symptoms, such as those containing biogenic amines, IAC, lectin, and capsaicin[4,10]. Foods were grouped based on their chemical composition, regarding the presence of biogenic amine, lectin, capsaicin, and IAC (Table I). Patients had to indicate which food was accompanied by any gastrointestinal symptoms after ingestion.

The IBS-SSS is a composite score of abdominal pain, number of days with abdominal pain, bloating/distension, satisfaction with bowel habits, and IBS-related quality of life[20]. Each item is rated from 0 to 100, with a total score ranging from 0 to 500 and higher scores indicating more severe symptoms. Subjects can be classified as having mild (75-175), moderate (175-300), or severe (>300) IBS symptoms.

The VSI score is used to evaluate symptoms' perception, concern caused by the intestinal disease, and the consequences on social life[21]. It consisted of 15 questions that could be answered with a number from 1 (strongly agree) to 6 (strongly disagree). Subsequently, the numbers indicated by the patient for each item were evaluated by giving a score from 0-5, and a total score was thus reached. Since the total score ranges from 0 (no gastrointestinal-specific anxiety) to 75 (severe gastrointestinal-specific anxiety), a value greater than 37.5 was chosen to indicate that the subject had an increased VSI[12,21].

The HADS questionnaire is a self-assessment mood scale specifically designed to be used in non-psychiatric settings[22]. It consists of 14 questions, seven of which are used to assess anxiety and seven for depression. Each question presents four alternatives, with a scale of values from 0 to 3, to have an optimal balance between sensitivity and specificity; the value 7 has been established as the cut-off so that test is positive for values higher than 7 for both the anxiety and depression sub-scale[22].

Table I. Food items included in the questionnaire for evaluating self-reported gastrointestinal symptoms after ingestion, grouped according to the category they belong to.

Amine-rich food	IAC food	Lectin rich food	Capsaicin-rich food
Anchovies	Apple	Beans	Cayenne/red pepper
Avocado	Apricot	Lentils	Chilli pepper
Banana	Avocado	Peas	Tabasco
Beef meat	Banana	Potato	
Beer	Beans	Wheat flour	
Cheese	Cantaloupe		
Cured meat	Cherries		
Eggplants	Cheese		
Eggs	Chocolate		
Fish	Dried fruit		
Mortadella	Milk		
Oranges	Pear		
Red wine	Peach		
Salami	Peas		
Strawberry	Plums		
Seasoned sausages Sardine	Potato		
Spinach	Wheat flour		
Tomato	Yogurt		
White meat			

Ethical Considerations

After patients received oral and written information about the study, written informed consent was obtained from each patient included in the study. All participants were informed that participation was voluntary and that consent could be withdrawn at any time without consequences. The study conforms to the ethical guidelines of the Declaration of Helsinki and was approved by the local Ethical Committee (approval No. 221/2020).

Statistical Analysis

Continuous data were expressed as a mean plus standard deviation (SD). The clinical and socio-demographic characteristics were compared with the Student *t*-test for continuous variables and with the chi-square test for categorical variables. Multivariate logistic regression analysis was performed to identify predictors of increased visceral sensitivity, anxiety/depression status, and IBS severity among patients. The odds ratio (OR) given the presence of a variable was used as a measure of association and adjusted for the effect of confounding variables. A value of $p<0.05$ was considered statistically significant. Data were analyzed using the PASW (Predictive Analytics Software) 18.0 software (IBM SPSS (Statistical Package for Social Science statistic), Chicago, IL, USA).

Results

Population Characteristics

During the study period, a total of 85 consecutive patients were admitted with a previous diagnosis of IBS. Seventy-seven (91%) of them accepted to take part in the survey, but only for 64 (83%), IBS diagnosis was confirmed according to Rome IV criteria. Of them, patients with IBS-D were 30 (47%), with IBS-C 27 (42%), and with IBS-M 7 (11%). All fulfilled the survey and were included in the final analysis. No patients had gastrointestinal cancer, neither IBD nor celiac disease, nor underwent relevant gastrointestinal surgery in the past. No other confounding factors were encountered for IBS symptoms evaluation (i.e., special diet programs such as vegetarian or vegan diet). Table II shows the demographic and clinical characteristics of the participants.

Patients' Perception of Specific Food Categories and Associated Clinical Characteristics

Of the 64 enrolled patients, 58 (90%) experienced IBS symptoms in relation to the ingestion of at least one of the food items included in our questionnaire. When patients were invited to choose which foods induced their bowel symptoms, it has been observed that amine-containing foods were indicated as a trigger by 49 patients (77%), those with lectin by 45 (70%), IACs by 31 (48%), and capsaicin by 24 (37%). Each patient made multiple choices of food (median value 7, range 2-13), and therefore the same patient was counted in more than one category. Demographic and clinical characteristics of patients, according to the specific food categories indicated as triggers of IBS symptoms, have been investigated. Compared with normal weight, the overweight condition was the only characteristic significantly associated with the choice of amine-rich foods as a symptom trigger (84% *vs.* 53%, $p=0.015$) (Figure 1A). Lectin-rich foods were indicated as the

Table II. Demographics and clinical characteristics of 64 patients with IBS according to Rome IV criteria.

Variable	Males n = 21	Females n = 43	Total
Age, years (mean ± SD)	47.3 ± 19.8	49.3 ± 18.2	47.8 ± 19.6
Employed	10 (47.6%)	18 (41.8%)	28 (43.7%)
BMI (mean ± SD)	26 ± 2.3	24.8 ± 3.2	25.2 ± 3.1
Normal weight	2 (9.5%)	13 (30.2%)	15 (23.4%)
Overweight	19 (90.5%)	30 (70%)	49 (76.5%)
Smoking	7 (33.3%)	6 (13.9%)	13 (20.3%)
Marriage/Cohabiting	15 (71.4%)	29 (67.4%)	44 (68%)
IBS-D	13 (62%)	17 (39%)	30 (47%)
IBS-C	6 (28%)	21 (48%)	27 (42%)
IBS-M	2 (10%)	5 (11%)	7 (11%)

Data are expressed as number (%) or mean; SD = standard deviation; BMI = body mass index; IBS-D = irritable bowel syndrome with predominant diarrhea; IBS-C = irritable bowel syndrome with predominant constipation; IBS-M = irritable bowel syndrome with mixed bowel habits.
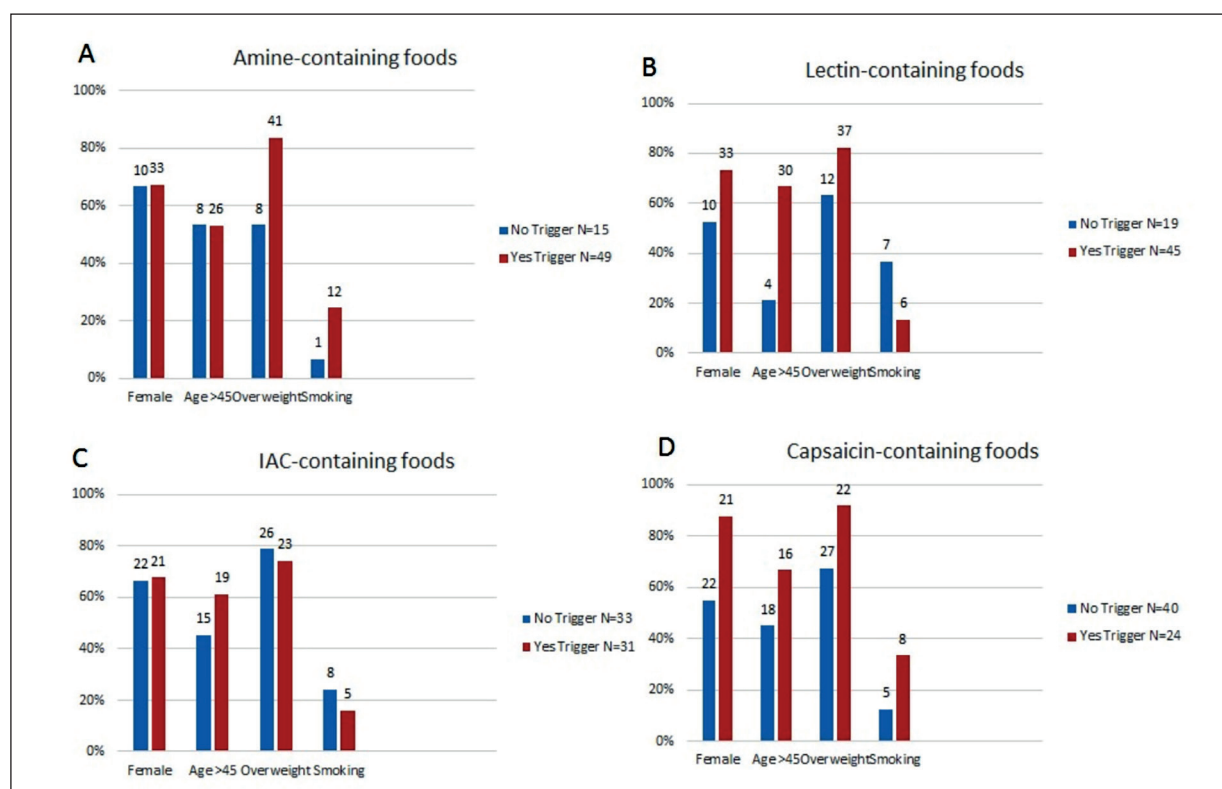
Figure 1. Triggers of symptoms as indicated by 64 patients suffering from irritable bowel syndrome according to food subgroups (amine-rich foods, Panel A; lectin-rich foods, Panel B; incompletely adsorbed carbohydrates [IACs], Panel C; and capsaicin, Panel D) and variables.

trigger of IBS symptoms mostly in older patients (67% *vs.* 21%, *p*=0.001), while smoking was negatively associated (13% vs. 37%, *p*=0.033) (Figure 1B). No variable was significantly associated with IACs (Figure 1C). Capsaicin-containing foods as IBS trigger was significantly associated with female gender (88% *vs.* 55%, *p*=0.005), overweight (92% *vs.* 68%, *p*=0.027), and smoking (33% *vs.* 13%, *p*=0.045) (Figure 1D).

Specific Food Categories, Clinical Characteristics, and IBS Symptoms Severity

Regarding IBS severity, we found a mild-moderate disease in 24 (37%) patients, while 40 (63%) showed severe symptoms. Overweight (*p*=0.020) and female gender (*p*=0.029) were the two clinical and demographic characteristics independently associated with severe IBS, while marriage/cohabiting was a protective factor (*p*=0.038). Although in patients' perception both amine-rich foods and lectin-rich foods were mostly related to symptoms' onset/worsening, only amine-rich foods were significantly associated with a severe

IBS. Neither IBS subtypes nor positive VSI and positive HADS were associated with a severe IBS (Table III). No significant association (*p*=0.86) was found with the food categories and the subtype of IBS (Table IV).

Visceral Sensitivity Index and Associated Clinical Characteristics

VSI score was positive in 38 (59%) patients. Among patients with a positive VSI score, 34 (89.5%) were non-smokers, and 4 (10.5%) were smokers, thereby non-smoker condition was an independent risk factor for increased visceral sensitivity at multivariate analysis. No differences were found for the other demographical and clinical characteristics between patients with positive and negative VSI scores (**Supplementary Table I**).

Anxiety/Depression Status and Associated Clinical Characteristics

Fifty-one (80%) patients displayed a positive score at HADS. Although at the univariate analysis being overweight significantly associated

Table III. Patients' characteristics and food triggers according to the severity of irritable bowel syndrome.

Variable	Mild-moderate IBS N = 24	Severe IBS N = 40	p (univariate analysis)	OR (CI)	p (multivariate analysis)
Age, years (mean ± SD)	45.1 ± 22.0	50.7 ± 18.3	0.273	1.023 (0.980-1.067)	0.304
Gender					**0.029**
Male	10 (41.7)	11 (27.5)	0.243	4.732 (1.255-25.754)	
Female[a]	14 (58.3)	29 (72.5)			
Smoking	6 (25)	7 (17.5)	0.470	0.167 (0.023-1.238)	0.080
Employed	7 (29.2)	21 (52.5)	0.069	4.431 (0.918-21.376)	0.064
Overweight	15 (62.5)	34 (85)	0.040	13.554 (1.510-121.644)	**0.020**
Marriage/Cohabiting	18 (75)	26 (65)	0.403	0.144 (0.022-0.935	**0.038**
Amine-rich foods	14 (58.3)	35 (87.5)	**0.008**	6.518 (1.281-33.166)	**0.024**
Lectin-rich foods	16 (66.7)	29 (72.5)	0.621	0.220 (0.034-1.414)	0.111
IAC	10 (42.7)	21 (52.5)	0.401	2.463 (0.536-11.312)	0.246
Capsaicin	11 (45.8)	13 (32.5)	0.286	0.745 (0.163-3.409)	0.705
VSI	11 (45.8)	27 (67.5)	0.088	6.392 (0.845-48.337)	0.072
HADS	14 (58.3)	37 (92.5)	**0.001**	4.906 (0.680-35.383)	0.115
IBS-D	15 (63%)	15 (37%)	**0.062**	0.401 (0.067-2.394)	0.316
IBS-C	7 (29%)	20 (50%)	**0.102**	1.143 (0.179-7.283)	0.888
IBS-M	2 (8%)	5 (13%)	**0.605**	0.875 (0.137-5.576)	0.788

Values are numbers (%), mean ±SD as indicated; IAC = incompletely absorbed carbohydrates; VSI = visceral sensitivity index; HADS = Hospital Anxiety and Depression Scale; SD = standard deviation; OR = odds ratio; CI = confidence interval; IBS-D = irritable bowel syndrome with predominant diarrhea; IBS-C = irritable bowel syndrome with predominant constipation; IBS-M = irritable bowel syndrome with mixed bowel habits. Means were compared with the use of a Student's t-test and proportions were determined with the use of a chi-square test. ORs with 95% CI in brackets are given. Bold text indicates a statistically significant difference with a p-value lower than 0.05. [a]Female gender was the reference value for multivariate analysis.

with a condition of anxiety/depression (*p*=0.03), it was no longer found under the multivariate logistic regression analysis (**Supplementary Table II**).

Discussion

With the aim to investigate perceived food intolerance in IBS patients and its association with IBS severity, visceral sensitivity, and anxiety/depression status, we found that 90% of patients enrolled in the study experienced IBS symptoms in relation to the ingestion of at least one of the food items included in the questionnaire. Consideration of recent Rome IV criteria represents a distinctive aspect of our study, as they provided a diagnostic breakthrough in the management of functional gastrointestinal disorders. Among the 77 consecutive patients who accepted to join the clinical interview, IBS diagnosis was confirmed according to Rome IV criteria for 64 (83%). According to the new criteria, this suggests that patients with IBS represent a subgroup of the patients diagnosed with the Rome III criteria[23]. Most of our patients considered amine-rich foods and lectin-rich foods as symptoms' triggers. Amine-rich foods come from the break-

Table IV. Prevalence of food categories indicated as triggers according to IBS subtype.

Variable	IBS-D N = 30*	IBS-C N = 27*	IBS-M N = 7*
Amine-rich foods	20 (66%)	22 (81%)	7 (100%)
Lectin-rich foods	21 (70%)	20 (74%)	4 (57%)
IAC	15 (50%)	13 (48%)	3 (42%)
Capsaicin	13 (43%)	10 (37%)	1 (14%)

IBS-D = irritable bowel syndrome with predominant diarrhea; IBS-C = irritable bowel syndrome with predominant constipation; IBS-M = irritable bowel syndrome with mixed bowel habits; IAC = incompletely absorbed carbohydrates. *Each patient made multiple choice, so one patient chose more than one category of food.

down or fermentation of the proteins present in cheese, chocolate, bananas, avocados, tomatoes, broad beans, wines, beer, yeast extracts, and fish products. Their bioactivity has been mainly implicated in food adverse reactions and in IBS symptoms such as bloating, nausea, vomiting, and abdominal pain[24]. Nevertheless, gastrointestinal reactions towards amine-rich foods do not manifest in the same way each time, even in the same patient with the same foods, and may have no effect on some individuals[25]. In our series, their trigger role was more pronounced in overweight patients. To now, the association between obesity and IBS remains unclear. Indeed, the prevalence of IBS in overweight persons is variable according to the population studied[26,27]. Our results highlight the need for more research into natural food chemicals and IBS, especially in patients with overweight conditions. It has been suggested that in obese persons, small bowel and colonic transit could be altered, and this may explain IBS symptoms. Alternatively, IBS symptoms may occur because of overeating in response to impaired satiation signals[28,29]. Lectins are proteins that bind carbohydrates, mainly present in legumes, grains, and dairy products, including milk, and may cause gastrointestinal disorders in some individuals[30]. Proposed pathogenic mechanisms include the interference with gut microbiota, the reduction of absorption of nutrients, a decreased acid secretion, and an increase of mucosal inflammation. However, these are proposed mechanisms from basic science research and unconfirmed in humans[31,32]. Some plant-derived lectins are not efficiently degraded by digestive enzymes; therefore, ingestion of lectins present in certain improperly cooked vegetables can result in acute gastrointestinal disorders, such as nausea, vomiting, and diarrhea[33]. In our population, lectin-rich foods were indicated as a trigger of IBS symptoms, mostly in older patients and in non-smokers, but there are no suggested explanations for these findings. The binding of lectins to epithelial cells may cause inflammation, damage to the tight junctions, and leaky gut, as well as the release of endotoxins such as lipopolysaccharides, which promotes gut permeability[31]. Currently, the lectin-free diet regimen is gaining popularity among IBS patients[34]. Food rich in IACs often causes bloating, abdominal pain, and diarrhea, and a diet with low amounts of FODMAPs has been widely investigated in the attempt to alleviate IBS symptoms[35]. Just under half of the interviewed patients indicated IACs as IBS triggers, although it has been documented that up to 70% of IBS patients report gastrointestinal symptoms after the intake of food rich in IACs[10].

All the above-mentioned associations between demographic and clinical factors and food triggers should be considered with caution, as an avoidance diet is widespread among IBS patients. Furthermore, the gastrointestinal symptoms related to several foods are amount-dependent and can be additional and cumulative. This fact makes it difficult to exclude the potential role of an overlapping mechanism[36].

The prevalence of subjects with severe IBS is widely variable, ranging from 8.4% to 55% and depending on countries and methods of evaluation[37]. Our prevalence data show a slightly higher rate, probably because patients were recruited in a University clinic, therefore selecting refractory cases already treated by general practitioners. Amine-rich foods represented an independent risk factor for a severe form of IBS, and this confirms the line of evidence that supports a role for these molecules in IBS pathogenesis[23,24]. Overweight and female gender represented the independent factors for a severe IBS, and this is coherent with available data[38,39]. Curiously, we found that the marriage and/or cohabiting status was inversely associated with severe IBS. It is recognized that IBS impacts significantly on personal relationships, and most patients reported that their partner experienced difficulties in having a relationship with them[40]. In our series, IBS severity was not associated with a specific IBS subtype, and this is according to the most recent data. Nor increased visceral sensitivity neither anxiety nor depression status were associated with a condition of severe IBS, suggesting that, although they are widely present in IBS patients, they do not impact independently on the severity of symptoms perceived by the patient[41,42]. Accordingly, recent findings raised doubt on the central role of gastrointestinal symptom-specific anxiety as a driver for symptom severity in IBS[43]. Although we did not find any significant association with the food categories and the subtype of IBS, recently, the pattern of the IBS has been associated with specific FODMAP intake[41]. Increased visceral sensitivity has been observed in more than half of the patients, confirming that it represents one of the main features in IBS[44].

Our series confirmed a high prevalence of anxiety and depression, but this was not associated with any of the examined clinical and demo-

graphic characteristics. Anxiety and depression states have been widely associated with IBS and particularly in those patients with eating disorders[45]. This suggests that anxiety and depression symptomatology should be systematically investigated in IBS patients, and their proper management should be included in IBS therapy[46].

Conclusions

Amine-rich foods are indicated as the main triggers of IBS symptoms, also representing an independent risk factor for a severe form of IBS. Increased visceral sensitivity and anxiety/depression status are frequent conditions in IBS but do not impact the severity of symptoms. Clinicians should improve their knowledge regarding the self-reported food intolerance in IBS patients and consequently request specific services from dietitians.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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