Gastroenterology Research and Practice

Irritable Bowel Syndrome

Guest Editors: Per G. Farup, Ami D. Sperber, and Magnus Simrén

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Editorial
Irritable Bowel Syndrome

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Studies of Irritable Bowel Syndrome (IBS) and other biopsychosocial disorders show a great variety of approaches to important clinical challenges. The papers in this special issue shed light on new and interesting aspects of IBS.

IBS has a surprisingly uniform worldwide distribution, from east to west and north to south, and affects males and females and all age groups [1, 2]. The prevalence rates vary from 2% to 22% and the disorder is everywhere related to a high degree of comorbidity (psychiatric distress, muscle-skeletal complaints, etc.), increased use of health care resources, and environmental factors (early life events, familial factors, infections, diet, social factors, etc.) [2, 3]. In this issue, the study by A. López-Colombo et al. "*The epdimology of functional gastrointestinal disorders in Mexico: a population-based study*" confirmed this pattern in the first population-based study on functional gastrointestinal disorders in Mexico. IBS had a prevalence rate of 16% and was associated with depression and increased use of health care resources.

A substantial proportion of patients with IBS report onset of their symptoms after acute gastroenteritis [4], and in a recent meta-analysis it was demonstrated that the risk of developing IBS following infectious gastroenteritis was increased sixfold [5]. Several risk factors for developing post-infectious IBS have been demonstrated, related to the pathogen or the infection and genetic, clinical or environmental factors [6]. However, the majority of the published studies so far have included subjects living in the industrialized world, and it is therefore not clear if the same relationship between gastrointestinal (GI) infections and the development of long-standing GI symptoms exists in the developing world. In these countries the inhabitants are exposed to acute and chronic GI infections to a larger extent, beginning already in infancy. Therefore, the contribution of Morgan et al. "*Irritable bowel syndrome and gastrointestinal parasite infection in a developing nation environment*" in this issue of Gastroenterology Research and Practice is a welcome contribution to this research area. The authors included a large group of subjects from a population-based sample in Nicaragua, and studied one group of subjects with IBS and a randomly selected group without IBS. Parasite carriage in fecal samples, which may serve as a surrogate for repeated exposures to gastrointestinal pathogens and infection, was investigated to assess the association between repeated GI infections and IBS. The main finding in this well-performed study was that no difference in parasite carriage could be demonstrated between IBS cases (16.6%) and controls (15.4%), implicating that the strong link between GI infections and development of IBS seen in investigations from the industrialized countries may not be applicable to developing countries. However, prospective studies in well-defined cohorts are needed in order to further assess this relationship, and to evaluate if post-infectious IBS is a phenomenon specific to areas where GI infections are not as common as in developing countries. It is tempting to speculate that this may be related to different immunological responses to GI infections based on the background prevalence of infections consistent with hygiene hypothesis, but this remains to be proven [7].

IBS and other functional gastrointestinal disorders are characterized by a high rate of psychosocial comorbidity as well as comorbidity with functional somatic syndromes such as fibromyalgia and chronic pelvic pain [8, 9]. These high rates have been attributed to peripheral and central hypersensitivity [10], which is modulated, in part, by stress and psychological disorders such as anxiety, depression, and

somatization [11]. Three papers in this issue relate to these subjects. The paper by M.-J. Gerson and C. Gerson "*The importance of relationships in patients with irritable bowel syndrome*" reviews the effect of a patient's relationships (family, friends, work) on the IBS illness experience. It concludes that although this is a subject that has not received sufficient attention in the medical literature and requires rigorous confirmation, relationships do have an impact on the IBS illness experience and may even have an effect on response to treatment. Doctors should inquire whether family members and intimate others are sufficiently educated about IBS, and whether they are supportive to the patient or whether there are problems that can and should be addressed. A. S. Butt et al. "*Irritable bowel syndrome and psychiatric disorders in Pakistan: a case control study*" conducted a study in Pakistan to estimate the frequency and strength of association of common mental disorders (anxiety and depression) in patients with IBS and controls. This is of particular interest because there is scant information in the medical literature on the significance of this association in Asian countries. The authors found that these disorders are more common in patients with IBS in Pakistan, as in western countries, compared to other chronic diseases including migraine and hypertension. L. B. Olafsdottir et al. "*Natural history of irritable bowelsyndrome in women and dysmenorrhea: a 10-year follow-up study*" from Iceland conducted a 10-year longitudinal study to assess associations between IBS and dysmenorrhea before and after menopause. The authors concluded that women with IBS are more likely to experience dysmenorrhea than women without IBS and that IBS symptom severity seems to increase after menopause. Although these papers focus on different specific associations between IBS and common psychosocial and comorbid conditions, taken together they add to the body of information on these relationships with IBS and do so from countries such as Pakistan and Iceland from which there is relatively little available information.

Treatment of IBS includes a general therapeutic approach, lifestyle advice with dietary recommendations, psychosocial support and pharmacotherapy, which all are effective [3]. However, since most treatments benefit only a minority, the treatment should be tailored on an individual basis. IBS is a long-lasting, often life-long, disorder with an undulating course and high placebo response rate. Despite the chronicity of the disorder, most therapeutic trials are of rather short duration, commonly 3–6 months and show a high rate of rapidly appearing relapses. S. Evangelista "*Benefits from long term treatment in irritable bowel syndrome*" gives in this issue a good overview of the benefits from long-term treatment and takes into account the natural course of the disorder, the placebo effect, and the relapse rates related to type and duration of the treatment. It is likely that prolongation of the treatment should be reserved for patients with recurrent symptoms, and that cyclic treatment might be appropriate for most patients due to the undulating natural course of the disorder.

Despite years of research, today's health care for patients with IBS still merits improvement based on better understanding of the disorder [12]. The papers included in this issue adds important new information to the IBS puzzle, but we probably still have a long way to go and many studies to perform before truly effective treatments will be available.

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References

[1] J. Y. Kang, "Systematic review: the influence of geography and ethnicity in irritable bowel syndrome," *Alimentary Pharmacology and Therapeutics*, vol. 21, no. 6, pp. 663–676, 2005.

[2] E. Rey and N. J. Talley, "Irritable bowel syndrome: novel views on the epidemiology and potential risk factors," *Digestive and Liver Disease*, vol. 41, no. 11, pp. 772–780, 2009.

[3] R. Spiller, Q. Aziz, F. Creed et al., "Guidelines on the irritable bowel syndrome: mechanisms and practical management," *Gut*, vol. 56, no. 12, pp. 1770–1798, 2007.

[4] R. Spiller and K. Garsed, "Postinfectious irritable bowel syndrome," *Gastroenterology*, vol. 136, no. 6, pp. 1979–1988, 2009.

[5] M. Thabane, D. T. Kottachchi, and J. K. Marshall, "Systematic review and meta-analysis: the incidence and prognosis of post-infectious irritable bowel syndrome," *Alimentary Pharmacology and Therapeutics*, vol. 26, no. 4, pp. 535–544, 2007.

[6] L. Öhman and M. Simrén, "Pathogenesis of IBS: role of inflammation, immunity and neuroimmune interactions," *Nature Reviews Gastroenterology and Hepatology*, vol. 7, no. 3, pp. 163–173, 2010.

[7] F. Guarner, R. Bourdet-Sicard, P. Brandtzaeg et al., "Mechanisms of disease: the hygiene hypothesis revisited," *Nature Clinical Practice Gastroenterology and Hepatology*, vol. 3, no. 5, pp. 275–284, 2006.

[8] W. E. Whitehead, O. Palsson, and K. R. Jones, "Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications?" *Gastroenterology*, vol. 122, no. 4, pp. 1140–1156, 2002.

[9] A. D. Sperber, Y. Atzmon, L. Neumann et al., "Fibromyalgia in the irritable bowel syndrome: studies of prevalence and clinical implications," *American Journal of Gastroenterology*, vol. 94, no. 12, pp. 3541–3546, 1999.

[10] M. B. Yunus, "Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes," *Seminars in Arthritis and Rheumatism*, vol. 36, no. 6, pp. 339–356, 2007.

[11] R. L. Levy, K. W. Olden, B. D. Naliboff et al., "Psychosocial aspects of the functional gastrointestinal disorders," *Gastroenterology*, vol. 130, no. 5, pp. 1447–1458, 2006.

[12] E. M. M. Quigley, P. Bytzer, R. Jones, and F. Mearin, "Irritable bowel syndrome: the burden and unmet needs in Europe," *Digestive and Liver Disease*, vol. 38, no. 10, pp. 717–723, 2006.

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Research Article

The Epidemiology of Functional Gastrointestinal Disorders in Mexico: A Population-Based Study

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Aims. The frequency of functional gastrointestinal disorders (FGIDs) in the general population of Mexico is unknown. *Methods.* To determine the prevalence of FGIDs, associated depression, and health care utilization, a population-based sampling strategy was used to select 500 households in the State of Tlaxcala, in central Mexico. Household interviews were conducted by two trained physicians using the Rome II Modular Questionnaire, a health-care and medication used questionnaire and the CES-D depression scale. *Results.* The most common FGIDs were IBS: 16.0% (95% CI: 12.9–19.5); functional bloating: 10.8% (8.2–13.9); unspecified functional bowel disorder: 10.6% (8.0–13.6); and functional constipation (FC): 7.4% (5.3–10.1). Uninvestigated heartburn was common: 19.6% (16.2–23.4). All FGIDs were equally prevalent among both genders, except for IBS ($P = 0.001$), IBS-C ($P < 0.001$), IBS-A/M ($P = 0.049$), and FC ($P = 0.039$) which were more frequent in women. Subjects with FGIDs reported higher frequencies of medical visits: 34.6 versus 16.8%; use of medications: 40.7 versus 21.6%; (both $P < 0.001$); and reported depression: 26.7 versus 6.7%, ($P < 0.001$). *Conclusion.* In this first population-based study of FGIDs in Mexico, heartburn, IBS, functional distension, and FC were common. Only IBS, IBS-C, IBS-A/M, and FC were more frequent in women. Finally, FGIDs in Mexico had an increased burden of health care utilization and depression.

1. Introduction

Functional gastrointestinal disorders (FGIDs) are very common and their global impact is often underestimated [1, 2] due to their limited associated mortality [3]. However, it is well documented that FGIDs have a negative impact on health-related quality of life (HRQOL) and have a burden of illness because of the number of physician visits, diagnostic tests, and secondary economic losses due to work absenteeism [4].

In Latin America, there are few studies that have estimated the prevalence and burden of FGIDs and the majority have been conducted in selected populations [5–7]. In Mexico, for example, only one study to date has evaluated the prevalence of all FGIDs using the Rome II Modular Questionnaire (RIIQ) but focused on a University population from Mexico City [8]. This study found that irritable bowel syndrome (FC) (35%), uninvestigated heartburn (35%), functional abdominal bloating, (21%) and functional constipation (FC) (19%) were frequent. Interestingly, uninvestigated dyspepsia was less common (8.0%) [8]. Also, IBS with diarrhea predominance (IBS-D) was less frequent compared to IBS with constipation (IBS-C): 4.6 versus 14.7% and the latter was four times more common in women than men [8]. A second study in Mexico in patients with IBS nationally cared for in private practice, confirmed the lower prevalence of IBS-D compared to IBS-C and although all IBS subtypes showed a female predominance, the percentage of men

among those with IBS-D was 1.7 to 2.4 higher than in the other subtypes [9]. Recently, our group reported the analysis of a RIIQ database, noting that the proportion of women among those fulfilling criteria for IBS and uninvestigated dyspepsia (67.8 y 85.4%, resp.,) was significantly higher than the proportion of women among the group not fulfilling criteria for any FGID (55.9%) [10]. In addition, compared to men with IBS, women reported more frequently symptoms related to constipation and abdominal distension [10].

We conducted a population-based study of FGIDs in Mexico, to our knowledge, the first such investigation. Based on our previous study among volunteers in Mexico [8], we hypothesized that uninvestigated heartburn, IBS, FC and uninvestigated dyspepsia would be the most common FGIDs and that all of these disorders together with IBS-C would be more common in women, while IBS-D would be more common in men. In addition, we included assessments of health care utilization and psychological burden.

2. Methods

From June 1st to October 31st, 2005, a population-based, cross-sectional study was conducted in the State of Tlaxcala, in central Mexico. In the 2000 population registry (census) of the *Instituto Nacional de Estadística y Geografía (INEGI)* [National Institute of Statistics and Geography], Tlaxcala had 962,646 inhabitants distributed in 60 cities/villages [11]. Anticipating an IBS prevalence ranging between 10 to 20% based on a systematic review of population-based studies in North America that did not include Mexico [12], considering a 10% precision of the outcome factor with a 99.99% confidence interval and a design effect of 1, a sample of 243 subjects was estimated. Therefore, we decided to survey a sample double that size. A population-based sample strategy was used to select 500 subjects representing approximately 0.05% of the State's population. The interviews were conducted in 500 randomly selected households and the number of subjects surveyed within each city/village was proportional to the number of their population. Exclusion criteria included pregnancy and major medical illness at the moment of the survey and a history of gastrointestinal surgery and/or significant psychiatric disease. Per protocol, if the first adult appearing in the household could not be interviewed due to exclusion criteria or recruitment failure, the neighboring household was selected.

Household interviews were conducted by two trained physicians. Demographic information included age, gender, occupation, and marital status. The RIIQ was used to assess abdominal symptoms and diagnose the FGIDs by the Rome II criteria [13]. The RIIQ had been previously translated and validated in Mexico and allowed us to determine the presence of all FGIDs [8]. We acknowledge that the RIIQ identifies uninvestigated heartburn including functional heartburn and gastroesophageal reflux (GER) [14]. The Rome II criteria require a medical evaluation with endoscopy and/or esophageal pH monitoring, to confirm cases with functional heartburn which was beyond the scope of the current protocol [15]. This is also applicable for dyspepsia, requiring upper endoscopy to rule out organic causes and diagnosed functional dyspepsia [16]. Therefore, subjects fulfilling criteria for heartburn or dyspepsia were designated herein as uninvestigated heartburn and uninvestigated dyspepsia, respectively.

Table 1: Demographic characteristics of the study population.

Item	Study population	95% CI
Age: (mean ± SD)	39.8 ± 16.3	38.7–41.2
Sex: *n* (%)		
(i) Women	305 (61.0)	56.6–65.3
(ii) Men	195 (39.0)	34.7–43.4
Occupation: *n* (%)		
(i) Homemaker	220 (44.0)	39.6–48.5
(ii) Employee	115 (23.0)	19.4–26.9
(iii) Self-employed	100 (20.0)	16.6–23.8
(iv) Student	30 (6.0)	4.1–8.5
(v) Manual labor	20 (4.0)	2.5–6.1
(vi) Other activities	15 (3.0)	1.7–4.9
Marital Status: *n* (%)		
(i) Married	303 (60.6)	56.2–64.9
(ii) Single	111 (22.2)	18.6–26.1
(iii) Civil Union	43 (8.6)	6.3–11.4
(iv) Widower	24 (4.8)	3.1–7.1
(v) Separated/Divorced	19 (3.8)	2.3–5.9

General questions regarding medical visits and medication use were included (have you consulted a physician for gastric, or intestinal problems? And, have you taken or are you currently taking any medication for your gastric or intestinal problems?). The Center for Epidemiological Studies Depression Scale (CES-D) [17] served as the instrument of psychological assessment. The CES-D is a 20 questions instrument commonly used to screen for symptoms of depression in the general population and has been validated in Mexico [18]. A total CES-D score from 0 to 14 is considered negative for depression, from 15 to 21 is considered mild to moderate depression, and a score higher than 22 is major depression [18]. Per standard, for the purpose of the current study, we used a threshold of ≥15 to identify subjects with depression.

The frequency of FGIDs is expressed in percentages with 95% Confidence Interval (95% CI). Categorical variables were analyzed by Chi-square and Fisher's exact test and continuous variables with the Students t test. A P value ≤ 0.05 was considered significant.

The protocol was approved by the local Institutional Review Board (IRB) for Health Research—2901—of the *Hospital General de Zona No. 1* of the *Instituto Mexicano del Seguro Social (IMSS)* in the State of Tlaxcala.

3. Results

The demographic characteristics of the study population are presented in Table 1. In the initial random sample of 500 households, 56 subjects were recruitment failures because of

lack of availability or refusal and 10 because of inaccurate census information. In addition, five subjects were excluded due to medical reasons. In each case, a subject was selected from a neighboring household, per protocol. In the study population, two-thirds were women and almost a half were homemakers.

Criteria for at least one FGID were fulfilled by 292 subjects (58.4%) while 208 (41.6%) were without a FGID diagnosis herein designated as "controls". The groups were similar in terms of age (mean ± SD): 40.3 ± 16.1 versus 39.5 ± 16.5 ($P = 0.568$); however, there were more women among those with FGIDs versus controls: 64.4% versus 56.2% ($P = 0.039$). Table 2 depicts the general frequency of each FGID, including a summary by gender. The most common diagnoses were uninvestigated heartburn followed by IBS, functional abdominal bloating, unspecified functional bowel disorder, and FC. Interestingly, dyspepsia was relatively uncommon.

When comparing the group with FGIDs versus controls, subjects with *levator ani* syndrome (mean ± SD: 54.6 ± 28.8 years old) and fecal incontinence (49.7 ± 19.3), were significantly ($P < 0.05$) older than controls (40.4 ± 16.1). The prevalence of the majority of the FGIDs was similar between women and men except for IBS, IBS-C, IBS Alternating/Mixed (IBS-A/M), and functional abdominal bloating, which were significantly more common among women.

Importantly, the burden of health care utilization and psychological disease was increased in those with FGIDs. Subjects with FGIDs reported higher number of medical visits: 35.0 versus 17.0% ($P < 0.05$) and use of medication for gastrointestinal symptoms: 41.0 versus 22.0% ($P < 0.05$). In addition, depression was more frequent in the group with FGIDs compared to controls: 26.4% versus 6.7% ($P < 0.001$) Table 3. Further, depression was present in 37.6% of the subjects with FGIDs that consulted for medical care versus 20.4% that did not consult ($P < 0.01$).

4. Discussion

To the best of our knowledge this is the first population-based study to estimate the prevalence of the FGIDs in Mexico using the Rome II criteria. The FGIDs were common in the general population as nearly sixty percent fulfilled criteria for at least one FGID. The most common diagnoses were uninvestigated heartburn, IBS, functional abdominal bloating, unspecified functional bowel disorders, and FC. As postulated, IBS, IBS-C, and IBS-A/M were all significantly more frequent in women than men and there was a trend for FC. Notwithstanding, functional abdominal bloating was also more common in women. Finally, compared to controls, subjects with FGIDs were twofold more likely to seek medical consultations and to use medications for GI symptoms, while depression was four times more likely.

4.1. Uninvestigated Heartburn. In our population, one-fifth of the subjects fulfilled criteria for heartburn. This finding is in agreement with those from other population-based studies that have reported a high frequency of GER-related symptoms. For example in Spain, in a telephone-based survey, Diaz-Rubio et al. found that 32% of the subjects reported GER symptoms [19]. In our study the diagnosis of heartburn was based only on symptom reporting with the RIIQ without additional diagnostic investigation, therefore the true prevalence of functional heartburn cannot be estimated. In a previous study in Mexico in patients fulfilling criteria for heartburn according to the RIIQ, 62.0% had GER confirmed by endoscopy and/or pH monitoring [20]; this study was limited by the fact that pH impedance testing was not used. Notwithstanding, based on those results, we may assume that of the 98 subjects that fulfilled criteria for heartburn in the present study, 61 (62.0%) will probably have true GER and 37 (38.0%) may have functional heartburn, thus estimating a prevalence of 7.4% (37/500) for functional heartburn in our population. This result is in agreement with a population-based study from Australia using Rome II criteria, reporting a prevalence of functional heartburn of 10.4% [21].

4.2. Uninvestigated Dyspepsia. The low frequency (7.0%) of dyspepsia is an interesting finding, which may reflect a true low-population prevalence of functional dyspepsia in Mexico and/or it may be related with aspects of the RIIQ in the assessment of functional dyspepsia. Similar to uninvestigated heartburn, subjects did not undergo endoscopy to rule out organic etiologies. Thus, we suggest that the prevalence reported herein corresponds to uninvestigated dyspepsia. This result is in accordance with our previous study among volunteers in Mexico City with the RIIQ, where dyspepsia was present in 8.0% of the subjects [8]. Furthermore, a similar study from Canada with the RIIQ found a very low prevalence of dyspepsia (1.8%) [22]. This contrasts with a study from Brazil that used modified Rome II criteria and found a 48% frequency of uninvestigated dyspepsia [23]. These observations suggest that in Mexico, dyspepsia is uncommon compared to other FGIDs such as IBS, understanding that the Rome II criteria may have inherent limitations with respect to the diagnosis of functional dyspepsia.

4.3. Irritable Bowel Syndrome. Globally, IBS is considered the most frequent FGID with a prevalence that ranges from 5 to 25% [1, 22]. This variability is probably related to the use of different diagnostic criteria between the studies, study designed differences (e.g., convenience samples versus population-based sampling), as well as true population differences. In fact, a recent joint conference of the Rome Foundation and the World Gastroenterology Organization (WGO) about the global perspective of IBS concluded that it was necessary to conduct population-based studies to estimate the frequency of this functional bowel disorder worldwide [24]. The 16.0% frequency of IBS in the current study is concordant with a parallel study that was conducted in Central America (Nicaragua) using Rome II criteria that reported a 13.2% prevalence [25] and with the 19.9% reported in a population-based study from South America (Colombia), using Rome III criteria [26]. In contrast, our

Table 2: Prevalence of functional gastrointestinal disorders.

FGID	All ($n = 500$)		Women ($n = 305$)	Men ($n = 195$)	P (women versus men)
	n	% (95% CI)	n (%)	n (%)	
	292	58.4 (53.9–62.8)	188 (61.6)	104 (53.5)	0.066
Esophageal disorders					
Globus	9	1.8 (0.8–3.4)	6 (2.0)	3 (1.5)	0.725
Rumination syndrome	4	0.8 (0.2–2.0)	2 (0.7)	2 (1.0)	0.651
Functional chest pain of presumed esophageal origin	15	3.0 (1.7–4.9)	11 (3.6)	4 (2.1)	0.320
Uninvestigated heartburn	98	19.6 (16.2–23.4)	57 (18.7)	41 (21.0)	0.521
Dysphagia	9	1.8 (0.8–3.4)	5 (1.6)	4 (2.1)	0.735
Gastroduodenal disorders					
Uninvestigated dyspepsia	35	7.0 (4.9–9.6)	23 (7.5)	12 (6.2)	0.553
(i) Ulcer-like	17	3.4 (2.0–5.4)	12 (3.9)	5 (2.6)	0.410
(ii) Dysmotility-like	18	3.6 (2.1–5.6)	11 (3.6)	7 (3.6)	0.992
Aerophagia	28	5.6 (3.8–8.0)	15 (4.9)	13 (6.7)	0.399
Functional vomiting	10	2.0 (1.0–3.6)	8 (2.6)	2 (1.0)	0.213
Bowel disorders					
IBS	80	16.0 (12.9–19.5)	62 (20.3)	18 (9.2)	**0.001**
(i) IBS-D	12	2.4 (1.2–4.2)	7 (2.3)	5 (2.6)	0.841
(ii) IBS-C	33	6.6 (4.6–9.1)	29 (9.5)	4 (2.1)	**0.001**
(iii) IBS-A/M	45	7.0 (4.9–9.6)	26 (8.5)	9 (4.6)	**0.003**
Functional abdominal bloating	54	10.8 (8.2–13.9)	41 (13.4)	13 (6.7)	**0.017**
Functional constipation	37	7.4 (5.3–10.1)	28 (9.2)	9 (4.6)	0.057
Functional diarrhea	7	1.4 (0.6–2.9)	3 (1.0)	4 (2.1)	0.322
Unspecified eunctional bowel disorder	53	10.6 (8.0–13.6)	30 (9.8)	23 (11.8)	0.488
Functional abdominal pain					
Functional abdominal pain syndrome	5	1.0 (0.3–2.3)	4 (1.3)	1 (0.5)	0.381
Unspecified functional abdominal pain	8	1.6 (0.7–3.1)	6 (2.0)	2 (1.0)	0.413
Biliary disorders					
Gallbladder dysfunction	6	1.2 (0.4–2.6)	5 (1.6)	1 (0.5)	0.259
Sphincter of oddi dysfunction	1	0.2 (0-1.1)	1 (0.3)	0 (0.0)	0.423
Anorectal disorders					
Functional fecal incontinence	23	4.6 (2.9–6.8)	13 (4.3)	10 (5.1)	0.652
(i) Soiling	14	2.8 (1.5–4.7)	7 (2.3)	7 (3.6)	0.392
(ii) Gross incontinence	9	1.8 (0.8–3.4)	6 (2.0)	3 (1.5)	0.725
Levator ani syndrome	7	1.4 (0.6–2.9)	3 (1.0)	4 (2.1)	0.322
Proctalgia fugax	31	6.2 (4.3–8.7)	22 (7.2)	9 (4.6)	0.240
Dyssynergia	10	2.0 (1.0–3.6)	8 (2.6)	2 (1.0)	0.213

IBS: irritable bowel syndrome, IBS-D: irritable bowel syndrome diarrhea predominant, IBS-C: irritable bowel syndrome constipation predominant, IBS-A/M: irritable bowel syndrome alternating/mixed. There were no differences in the prevalence of the different FGIDs between women versus men, except for IBS IBS-C IBS-A/M and functional abdominal bloating that were all more frequent among women and a trend for functional constipation.

prevalence is eight times higher than the one reported in a multinational study in Europe using Rome II criteria [1]. In that study, dyspepsia was also more common than IBS, with a prevalence that ranged from 15.1% to 23.9% [27, 28]. In the current study, IBS proved to be more frequent in women than men and in the IBS subtypes, IBS-C, and IBS-A/M. This gender difference did not hold up for IBS-D as has been reported in other studies [29]. Further, in this population-based study IBS-A/M is the most frequent subtype followed by IBS-C and IBS-D. This is consistent with our prior studies in Mexico [8, 9]. The higher frequency of IBS-C compared to IBS-D seems to be a common finding in Latin American

Table 3: Depression, medical visits, and use of medications by FGID.

Diagnosis		Age	Women	Depression (CES-D)	Medical visits for GI problems	Use of medications for GI problems
	n	(mean ± SD)	(%)	(%)	(%)	(%)
Esophageal disorders						
Globus	9	40.4 ± 12.0	66.7	11.1	11.1	44.4
Rumination syndrome	4	46.0 ± 11.2	50.0	75.0	50.0	50.0
Functional chest pain of presumed esophageal origin	15	39.4 ± 14.9	73.3	46.7	33.3	60.0
Uninvestigated heartburn	98	37.2 ± 13.8	58.2	26.5	45.9	44.9
Dysphagia	9	50.3 ± 17.9	55.5	44.4	55.6	55.6
Gastroduodenal disorders						
Uninvestigated dyspepsia	35	37.6 ± 14.7	65.7	17.1	25.7	40.0
(i) Ulcer-like	17	40.1 ± 18.3	70.6	17.6	23.5	41.2
(ii) Dysmotility-like	18	35.2 ± 10.4	61.1	16.7	27.8	38.9
Aerophagia	28	41.7 ± 19.7	53.6	50.0	39.3	53.6
Functional vomiting	10	32.2 ± 12.7	80.0	30.0	70.0	80.0
Bowel disorders						
IBS	80	40.4 ± 17.5	77.5	47.5	56.2	67.5
(i) IBS-D	12	43.3 ± 20.8	58.3	50.0	50.0	66.7
(ii) IBS-C	33	40.7 ± 20.1	87.9	60.6	66.7	69.7
(iii) IBS-A/M	45	39.3 ± 13.6	74.3	40.0	48.6	65.7
Functional abdominal bloating	54	37.0 ± 16.2	75.9	24.1	40.7	42.6
Functional constipation	37	37.6 ± 18.7	75.7	24.3	35.1	37.8
Functional diarrhea	7	42.3 ± 24.2	42.9	42.9	42.9	28.6
Unspecified functional bowel disorder	53	38.5 ± 15.9	56.6	13.2	17.0	26.4
Functional abdominal pain						
Functional abdominal pain syndrome	5	38.2 ± 9.6	80.0	100.0	60.0	60.0
Unspecified functional abdominal pain	8	35.4 ± 8.7	75.0	25.0	75.0	50.0
Biliary disorders						
Gallbladder dysfunction	6	27.7 ± 8.8	83.3	50.0	66.7	83.3
Sphincter of oddi dysfunction	1	27.0	100.0	0	0	0
Anorectal disorders						
Functional fecal incontinence	23	49.6 ± 19.2	56.5	52.2	65.2	60.9
(i) Soiling	14	45.4 ± 15.9	50.0	50.0	71.4	57.1
(ii) Gross incontinence	9	56.2 ± 23.0	66.7	55.6	55.6	66.7
Levator ani syndrome	7	54.6 ± 28.8	42.9	71.4	71.4	71.4
Proctalgia fugax	31	41.4 ± 16.5	71.0	61.3	45.2	54.8
Dyssynergia	10	42.3 ± 19.9	80.0	60.0	30.0	40.0

CES-D: center for epidemiological studies depression scale, GI: gastrointestinal, IBS: irritable bowel syndrome, IBS-D: irritable bowel syndrome diarrhea predominant, IBS-C: irritable bowel syndrome constipation predominant, IBS-A/M: irritable bowel syndrome alternating/mixed.

studies [26, 30], except for Argentina [31] where IBS-D is the predominant subtype. This latter discordance might relate to genetic and environmental influences in populations such as Argentina with a greater European influence. Also, in one of the first cross-cultural studies of IBS conducted in the USA, Mexico, Canada, England, Italy, Israel, India, and China, using the Bowel Symptom Scale (BSS), diarrhea was less frequent than constipation [32]. The Mexican subjects reported the highest score for constipation while those from China reported the highest score for diarrhea [32]. The higher frequency of IBS-D in China was confirmed in a recent study among patients with IBS using the Rome II criteria, in which 65.9% was diagnosed as IBS-D while 26.4% was diagnosed as IBS-C [33]. The contrasts between the

different studies underscore the importance of diagnostic criteria, study methodology, and subject populations, all important factors than can influence the reported frequencies of IBS and the IBS subtypes. Use of standard criteria and methodology is imperative in future studies to elucidate the worldwide frequency of IBS.

4.4. Functional Constipation. A recent systematic review and meta-analysis of population-based studies from around the world, with limited data from Latin America, reported a pooled prevalence of 14% (95% CI: 12–17) for FC. The prevalence of FC was lower in South East Asian studies and in those using the Rome II or III criteria [34]. The lower prevalence found in our study using the Rome II criteria [7.4% (5.3–10.1)] is concordant. In contrast, a recent meta-analysis that included the results from the current survey and those from other available studies in Mexico reported a pooled prevalence of FC of 14.4% (12.6–16.6). Although this meta-analysis found similar figures to those from the first systematic review [35], they are higher than the ones from the current survey, probably influenced by the inclusion of data from studies conducted in convenience samples in Mexico contrary to the current one using a population-based sampling strategy.

4.5. The Burden of FGIDs: Health Care Utilization and Depression. Psychological comorbidities such as anxiety and depression have been associated with FGIDs. For example, depression has been associated with GER symptoms [36, 37]; patients with IBS and functional dyspepsia [38]; IBS-C with higher symptoms severity [39, 40]; IBS with lower HRQOL [39, 40]. Although psychological comorbidities are frequent among FGID subjects that seek medical care, few studies have analyzed such associations in subjects with FGIDs from the community [41]. Furthermore, subjects with depression in the community report more frequently gastrointestinal symptoms such as abdominal pain, diarrhea, constipation, dyspepsia, and/or IBS [42]. In the current study, we used a validated instrument to screen for depression, and we confirmed that depression is four times more likely to be present among subjects with FGIDs than those without a FGID and in those that consulted compared to those who did not. This finding is in agreement with a study in primary care showing that severe depression was five times more likely among subjects with gastrointestinal symptoms [43]. With regard to IBS, we found that 47.5% of our subjects reported depression. This is consistent with a previous study among patients that consulted a referral center in Mexico, in which 46.0% had trait depression according to the Hospital Anxiety and Depression Scale (HAD) [44]. In summary, these results suggest that depression in subjects with FGIDs in the community is common and is more frequent among those that seek medical care.

The high frequency of FGIDs in the general population is remarkable and suggests that having at least one FGID is "normal". This finding is in agreement with data from a study that followed subjects for over 20 years in Olmsted County Minnesota and reported that 89% fulfilled criteria for at least one FGID [45]. Also, in this population-based cohort, health care utilization was increased in FGIDs and IBS subjects. One-third of the subjects with FGIDs had related medical care, thus they can be considered "patients". Among those with IBS, 56.2% had recent medical visits for GI symptoms, thereby also considered "patients". Our results are similar to those from other parts of the world [46]. In addition, almost 70% of the IBS subjects had used medications for their symptoms. These findings provide an indirect estimation of the IBS burden of illness in Mexico.

Our study has several limitations. It was conducted in a single State in Mexico; however, we consider that it is representative of the mestizo population which predominates in this country [47]. Secondly, we did not include an assessment of socioeconomic status or its possible relation to the FGIDs, nor to the consultation behavior. Third, while we did not screen for anxiety, we used a validated depression instrument, thereby strengthening our results. Lastly, the survey was conducted using the Rome II and not the more recent Rome III criteria. However, a Rome III-based epidemiological study is underway in Mexico and Central America and these results will allow us to further elucidate the FGIDs prevalence and potential instrument differences [48].

In conclusion, in this population-based study in Mexico, FGIDs and IBS are observed to be common with important gender differences for IBS and functional abdominal bloating. Among subjects with FGIDs and/or IBS, health care utilization is increased and a positive association with depression is observed. Further, studies of FGIDs epidemiology in Mexico and Latin America are warranted.

Disclosures

During the last 2 years, Dr. Aurelio López-Colombo has been a speaker for Nycomed and Takeda. Dr. Max Schmulson has served as a consultant for Procter and Gamble, Novartis, Schering-Plough, Alfa-Wasserman, and Janssen. He has been a speaker for Nycomed, Schering-Plough and Mayoli-Spindler, Alfa-Wasserman, and Janssen and has received research funding from Nycomed.

Specific Author Contributions

A. López-Colombo: he does the study conceptualizing and plans, analyzes and interprets the data, and drafts the paper and has approved the final paper. D. Morgan: He makes the study conceptualizing, plans and drafts the paper and has approved the final paper. D. Bravo-González: she coordinated the surveys and has approved the final paper. A. Montiel-Jarquín: he drafts the paper and has approved the final paper. S. Méndez-Martínez: he drafts the paper and has approved the final paper. M. Schmulson: he studies conceptualizing and planning, interprets the data, and drafts the paper. He has approved the final paper.

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References

[1] A. P. S. Hungin, P. J. Whorwell, J. Tack, and F. Mearin, "The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects," *Alimentary Pharmacology and Therapeutics*, vol. 17, no. 5, pp. 643–650, 2003.

[2] S. L. S. Halder, G. R. Locke, C. D. Schleck, A. R. Zinsmeister, L. J. Melton, and N. J. Talley, "Natural History of functional gastrointestinal disorders: a 12-year Longitudinal population-based study," *Gastroenterology*, vol. 133, no. 3, pp. 799–807, 2007.

[3] M. Dixon-Woods and S. Critchley, "Medical and lay views of irritable bowel syndrome," *Family Practice*, vol. 17, no. 2, pp. 108–113, 2000.

[4] N. Agarwal and B. M.R. Spiegel, "The effect of irritable Bowel syndrome on health-related quality of life and health care expenditures," *Gastroenterology Clinics of North America*, vol. 40, no. 1, pp. 11–19, 2011.

[5] C. Cornejo Zapata and J. Villarreal Menchola, "Relation between irritable bowel syndrome symptoms and depressive symptoms in hospitalized patients," *Revista de Gastroenterologia del Peru*, vol. 25, no. 2, pp. 156–160, 2005.

[6] G. Campos Hurtado, J. Villareal Menchola, C. Cornejo Zapata, and R. León Barúa, "Prevalence of Manning's symptoms in a Lima upper socioeconomic level population," *Revista de Gastroenterologia del Peru*, vol. 21, no. 4, pp. 301–305, 2001.

[7] L. Bujanda, M. A. Gutiérrez-Stampa, C. H. Caballeros, and M. E. Alkiza, "Gastrointestinal disorders in Guatemala and their relation with parasitic infections," *Anales de Medicina Interna*, vol. 19, no. 4, pp. 179–182, 2002.

[8] M. Schmulson, O. Ortíz, M. Santiago-Lomeli et al., "Frequency of functional bowel disorders among healthy volunteers in Mexico City," *Digestive Diseases*, vol. 24, no. 3-4, pp. 342–347, 2006.

[9] M. Schmulson, J. A. Vargas, A. Lopez-Colombo, J. M. Remes-Troche, and J. C. Lopez-Alvarenga, "Prevalence and clinical characteristics of the IBS subtypes according to the Rome III criteria in patients from a clinical, multicentric trial. A report from the Mexican IBS Working Group," *Revista de Gastroenterología de México*, vol. 75, pp. 427–438, 2010.

[10] M. Schmulson, M. Adeyemo, G. Gutiérrez-Reyes et al., "Differences in gastrointestinal symptoms according to gender in rome II positive IBS and dyspepsia in a latin American population," *American Journal of Gastroenterology*, vol. 105, no. 4, pp. 925–932, 2010.

[11] http://www.inegi.org.mx/sistemas/consulta_resultados/iter2000.aspx?c=27437&s=est.

[12] Y. A. Saito, P. Schoenfeld, and G. R. Locke, "The epidemiology of irritable bowel syndrome in North America: a systematic review," *American Journal of Gastroenterology*, vol. 97, no. 8, pp. 1910–1915, 2002.

[13] D. A. C. Drossman, N. J. Talley, W. G. Thompson, W. E. Whitehead, and The Rome II Multinational Working Team, "Research diagnostic questions for functional gastrointestinal disorders: Rome II modular questionnaire," in *Rome II The Functional Gastrointestinal Disorders*, K. S. Lawrence, Ed., pp. 670–688, Allen Press, 2nd edition, 2000.

[14] D. A. C. Drossman, N. J. Talley, W. G. Thompson, W. E. Whitehead, and The Rome II Multinational Working Team, "Research diagnostic questions for functional gastrointestinal disorders. Rome II modular questionnaire: investigator and respondent forms," in *Rome II The Functional Gastrointestinal Disorders*, K. S. Lawrence, Ed., pp. 669–688, Allen Press, 2nd edition, 2000.

[15] R. E. Clouse, J. E. Richter, R. C. Heading, J. Janssens, and J. A. Wilson, "Functional esophageal disorders," *Gut*, vol. 45, no. 2, supplement 2, pp. II31–II36, 1999.

[16] N. J. Talley, V. Stanghellini, R. C. Heading, K. L. Koch, J. R. Malagelada, and G. N. J. Tytgat, "Functional gastroduodenal disorders," *Gut*, vol. 45, no. 2, supplement 2, pp. II37–II42, 1999.

[17] R. L. Sawyer, "The CES-D scale: a self-report depression scale for research in the general population," *Applied Psychological Measurement*, vol. 1, pp. 385–401, 1977.

[18] C. González-Forteza, J. A. Jiménez-Tapia, L. Ramos-Lira, and F. A. Wagner, "Application of the revised version of the Center of Epidemiological Studies Depression Scale in adolescent students from Mexico City," *Salud Publica de Mexico*, vol. 50, no. 4, pp. 292–299, 2008.

[19] M. Diaz-Rubio, C. Moreno-Elola-Olaso, E. Rey, G. R. Locke, and F. Rodriguez-Artalejo, "Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population," *Alimentary Pharmacology and Therapeutics*, vol. 19, no. 1, pp. 95–105, 2004.

[20] M. Schmulson, "Heartburn according to Rome II in Spanish-Mexico: gastroesophageal reflux must be ruled out," *Revista de Gastroenterología de México*, vol. 74, pp. 74–76, 2009.

[21] P. M. Boyce, N. J. Talley, C. Burke, and N. A. Koloski, "Epidemiology of the functional gastrointestinal disorders diagnosed according to Rome II criteria: an Australian population-based study," *Internal Medicine Journal*, vol. 36, no. 1, pp. 28–36, 2006.

[22] W. G. Thompson, E. J. Irvine, P. Pare, S. Ferrazzi, and L. Rance, "Functional gastrointestinal disorders in Canada: first population-based survey using Rome II criteria with suggestions for improving the questionnaire," *Digestive Diseases and Sciences*, vol. 47, no. 1, pp. 225–235, 2002.

[23] G. B. M. L. Sander, C. F. Francesconi, M. H. I. Lopes, and J. Madi, "Unexpected high prevalence of non-investigated dyspepsia in Brazil: a population based study," *Gut*, vol. 56, supplement 3, p. A195, 2007.

[24] E. M. Quigley, A. D. Sperber, and D. A. Drossman, "WGO—Rome foundation joint symposium summary: IBS—the global perspective," *Journal of Clinical Gastroenterology*, vol. 45, no. 8, pp. 1–2, 2011.

[25] M. V. E. Benshoff, R. Peña, L. Cortes, P. Heidt, M. Caceres, and D.R. Morgan, "Post-infectious IBS in the "non-sterile" developing nation environment and the role of parasites burden, a population-based study in Central America," *Gastroenterology*, vol. 138, supplement 1, p. A104, 2008.

[26] D. F. Gómez Álvarez, J. G. Morales Vargas, L. M.A. Rojas Medina, S. C. Mújica Oviedo, P. A. Camacho López, and G. E. Rueda Jaimes, "Factores sociosanitarios y prevalencia del síndrome del intestino irritable según los criterios diagnósticos de Roma III en una población general de Colombia," *Gastroenterologia y Hepatologia*, vol. 32, no. 6, pp. 395–400, 2009.

[27] A. M. Caballero-Plasencia, S. Sofos-Kontoyannis, M. Valenzuela-Barranco, J. L. Martín-Ruiz, F. J. Casado-Caballero, and J. G. López-Mañas, "Irritable bowel syndrome in patients with dyspepsia: a community-based study in southern Europe," *European Journal of Gastroenterology and Hepatology*, vol. 11, no. 5, pp. 517–522, 1999.

[28] R. M. Zagari, G. R. Law, L. Fuccio et al., "Epidemiology of functional dyspepsia and subgroups in the Italian general population: an endoscopic study," *Gastroenterology*, vol. 138, no. 4, pp. 1302–1311, 2010.

[29] M. A. Adeyemo, B. M. R. Spiegel, and L. Chang, "Meta-analysis: do irritable bowel syndrome symptoms vary between men and women?" *Alimentary Pharmacology and Therapeutics*, vol. 32, no. 6, pp. 738–755, 2010.

[30] R. S.-V. G. Prochazka, M. Ojeda, S. Vila et al., "Prevalence of irritable bowel syndrome in students of a university in Lima-Peru," *The American Journal of Gastroenterology*, vol. 101, supplement, p. S476, 2006.

[31] J. A. I. G. Olmos, M. Guzmán, O. Gadea et al., "Irritable bowel syndrome: prevalence, comorbidity and impact. A population based study," *Gut*, vol. 59, supplement 3, p. A361, 2010.

[32] C. D. Gerson, M. J. Gerson, R. A. Awad et al., "Irritable bowel syndrome: an international study of symptoms in eight countries," *European Journal of Gastroenterology and Hepatology*, vol. 20, no. 7, pp. 659–667, 2008.

[33] X. Yao, Y. S. Yang, L. H. Cui et al., "Subtypes of irritablebowel syndrome on Rome III criteria : a multi-center study," *Journal of Gastroenterology and Hepatology*. In press.

[34] N. C. Suares and A. C. Ford, "Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis," *American Journal of Gastroenterology*, vol. 106, no. 9, pp. 1582–1591, 2011.

[35] T. J. M. Remes, T. J. L de la Cuesta, R. R Garibay, H. F. Iga, S. E. Moran, and M. Schmulson, "Guidelines for diagnosis and treatment of constipation in Mexico. A) Epidemiology (meta-analysis of the prevalence), pathophysiology and classification," *Revista de Gastroenterología de México*, vol. 76, pp. 126–132, 2011.

[36] E. Martín-Merino, A. Ruigómez, S. Johansson, M. -A. Wallander, and L. A. García-Rodriguez, "Study of a cohort of patients newly diagnosed with depression in general practice: prevalence, incidence, comorbidity, and treatment patterns," *Primary Care Companion to the Journal of Clinical Psychiatry*, vol. 12, no. 1, 2010.

[37] C. Jansson, H. Nordenstedt, M. A. Wallander et al., "Severe gastro-oesophageal reflux symptoms in relation to anxiety, depression and coping in a population-based study," *Alimentary Pharmacology and Therapeutics*, vol. 26, no. 5, pp. 683–691, 2007.

[38] L. Van Oudenhove, J. Vandenberghe, R. Vos, L. Holvoet, and J. Tack, "Factors associated with co-morbid irritable bowel syndrome and chronic fatigue-like symptoms in functional dyspepsia," *Neurogastroenterology and Motility*, vol. 23, no. 6, article e202, p. 524, 2011.

[39] M. R. A. Muscatello, A. Bruno, G. Pandolfo et al., "Depression, anxiety and anger in subtypes of irritable bowel syndrome patients," *Journal of Clinical Psychology in Medical Settings*, vol. 17, no. 1, pp. 64–70, 2010.

[40] A. Y. Thijssen, D. M. A. E. Jonkers, C. Leue et al., "Dysfunctional cognitions, anxiety and depression in irritable bowel syndrome," *Journal of Clinical Gastroenterology*, vol. 44, no. 10, pp. e236–e241, 2010.

[41] J. C. Y. Wu, "Community-based study on psychological comorbidity in functional gastrointestinal disorder," *Journal of Gastroenterology and Hepatology*, vol. 26, supplement 3, pp. 23–26, 2011.

[42] M. T. Hillilä, J. Hämäläinen, M. E. Heikkinen, and M. A. Färkkilä, "Gastrointestinal complaints among subjects with depressive symptoms in the general population," *Alimentary Pharmacology and Therapeutics*, vol. 28, no. 5, pp. 648–654, 2008.

[43] M. Mussell, K. Kroenke, R. L. Spitzer, J. B. W. Williams, W. Herzog, and B. Löwe, "Gastrointestinal symptoms in primary care: prevalence and association with depression and anxiety," *Journal of Psychosomatic Research*, vol. 64, no. 6, pp. 605–612, 2008.

[44] F. E. Reséndiz-Figueroa, O. M. Ortiz-Garrido, D. Pulido, D. Arcila-Martínez, and M. Schmulson, "Impact of the anxiety characteristics and depression on clinical aspects and quality of life in patients with irritable bowel syndrome," *Revista de gastroenterología de México*, vol. 73, no. 1, pp. 3–10, 2008.

[45] S. L. S. Halder, G. R. Locke, C. D. Schleck, A. R. Zinsmeister, L. J. Melton, and N. J. Talley, "Natural History of functional gastrointestinal disorders: a 12-year longitudinal population-based study," *Gastroenterology*, vol. 133, no. 3, article e1, p. 799, 2007.

[46] F. Cremonini and N. J. Talley, "Irritable bowel syndrome: epidemiology, natural history, health care seeking and emerging risk factors," *Gastroenterology Clinics of North America*, vol. 34, no. 2, pp. 189–204, 2005.

[47] I. Silva-Zolezzi, A. Hidalgo-Miranda, J. Estrada-Gil et al., "Analysis of genomic diversity in Mexican Mestizo populations to develop genomic medicine in Mexico," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 106, no. 21, pp. 8611–8616, 2009.

[48] D. R. S. F. Morgan, E. Pena, F. Mearin et al., "Multinational validation of the Spanish ROME III adult diagnostic questionnaire: comparable sensitivity and specificity to english instrument," *Gastroenterology*, vol. 38 supplement 1, p. S386, 2010.

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Clinical Study

Natural History of Irritable Bowel Syndrome in Women and Dysmenorrhea: A 10-Year Follow-Up Study

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Background. Studies have shown that women are more likely to have irritable bowel syndrome (IBS) and more women seek healthcare because of IBS than men. *Aim*. We wanted to examine the natural history of IBS and dysmenorrhea in women over a 10-year period and to assess the change in IBS after menopause. *Method*. A population-based postal study. A questionnaire was mailed to the same age- and gender-stratified random sample of the Icelandic population aged 18–75 in 1996 and again in 2006. *Results*. 77% premenopausal women had dysmenorrhea in the year 1996 and 74% in 2006. 42% of women with dysmenorrhea had IBS according to Manning criteria in the year 2006 and 49% in 1996. 26% of women with dysmenorrhea had IBS according to Rome III 2006 and 11% in the year 1996. In 2006 30% women had severe or very severe dysmenorrhea pain severity. More women (27%) reported severe abdominal pain after menopause than before menopause 11%. Women without dysmenorrhea were twice more likely to remain asymptomatic than the women with dysmenorrhea. Women with dysmenorrhea were more likely to have stable symptoms and were twice more likely to have increased symptoms. *Conclusion*. Women with IBS are more likely to experience dysmenorrhea than women without IBS which seems to be a part of the symptomatology in most women with IBS. IBS symptom severity seems to increase after menopause.

1. Introduction

Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habits and with features of disordered defecation [1]. Patients often experience additional symptoms such as bloating, sensation of incomplete evacuation, straining (constipation), and urgency (diarrhea) [2]. In the Western countries, more women than men seek health-care services for irritable bowel syndrome (IBS) [3, 4]. This can possibly be explained by factors involving physiological gender differences in gonadal hormones, stress reactivity, and inflammatory responses, as well as sociocultural differences in response to pain and/or bowel pattern changes [4]. In a recent study of men and women with IBS, the gender differences found were more complicated than a simple ration of men:women [5]. Women with IBS report more constipation, nausea, bloating, and extraintestinal and psychological symptoms than men with IBS [6]. Gender-related differences in gastrointestinal and somatic symptoms are apparent in persons with IBS but are most prominent in postmenopausal women [7]. Abdominal pain has been shown to be the most disruptive symptom in IBS and impacts on the quality of life in women with IBS [8]. The differences between genders in the occurrence of IBS could furthermore be the result of cultural, psychosocial, or healthcare access issues instead of purely physiologic differences [9].

Dysmenorrhea is a common conditions that can occur in 50–90% of women [10]. Dysmenorrhea is one of the most common complaints among women. It is defined as the presence of menstruation-associated spasmodic pain in the abdomen. Dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome are common complaints among women of reproductive age and are not consistently

associated with demographic risk factors [11]. Many women experience discomfort at the time of their periods. For most, this does not interfere with their daily lives or requires any special attention. However, for some women their monthly period is painful, problematic, and in some cases disabling. It can interfere with their lives because of the pain and inconvenience caused.

Dysmenorrhea severe enough to cause absence from work occurs in less than 5% of women [10]. Although improvement and worsening are equally likely for all women, improvement is more likely in women who bear children [10].

Population-based studies are essential for studying IBS since only a minority of IBS patients seek medical care [12]. Self-medication is common among these patients [12], and differences have been noted in IBS patients and nonpatients from the community [13, 14]. The great majority of IBS studies are patient or healthcare based. Women overall have a greater prevalence of IBS symptoms than men, particularly those associated with constipation [15]. Studies suggest that female sex hormones influence the severity of IBS symptoms [15]. A recent study suggests that an increase in gastrointestinal symptoms around the time of menses and early menopause occurs at times of declining or low ovarian hormones, suggesting that estrogen and progesterone withdrawal may contribute either directly or indirectly [16].

The objective of our study was to study the connection of IBS and dysmenorrhea in women and the change over a 10-year period. The secondary objective was to assess the change in IBS over menopause and the birth cohort effect of dysmenorrhea. The third objective was to assess the connection of functional gastrointestinal disorders (FGIDs) including functional dyspepsia (FD), heartburn and frequent abdominal pain (FAP), and dysmenorrhea severity.

2. Methods

2.1. Participants and Setting. In 1996 an epidemiological study of gastrointestinal diseases was performed in Iceland [17]. Involved were 2000 inhabitants in the age range of 18–75 years. The individuals were randomly selected from the National Registry. Equal distribution of sex and age was secured in each age group. In 2006 we attempted to contact all the individuals from 1996. A questionnaire was mailed to individuals at baseline, and the study questionnaire and an explanatory letter mailed to all eligible individuals. Reminder letters were mailed at 2, 4, and 7 weeks, using the Total Method of Dillman [18]. Individuals who indicated at any point that they did not want to participate in the study were not contacted further.

2.2. The Questionnaire. The bowel disease questionnaire (BDQ) [19, 20] was translated from English into Icelandic and modified for this study. The questionnaire was translated by two gastroenterologists and a pharmacist. A specialist in the Icelandic language at the University of Iceland made a linguistic modification. The questionnaire was piloted within a small group of IBS patients diagnosed by gastroenterologist.

The questionnaire was designed as a self-report instrument to measure symptoms experienced over the previous year and to collect the participant's past medical history [21].

The Icelandic version of the BDQ questionnaire addressed 47 gastrointestinal symptoms and 32 items that measure past illness, health care use, and socio-demographic and psychosomatic symptoms, together with a valid measure of non-GI somatic complaints, the somatic symptom checklist (SSC) [22]. There were only a few changes in the latter questionnaire (2006) which addressed 51 gastrointestinal symptoms and 33 items that measure past illness, health care use, and socio-demographic and psychosomatic symptoms. The questionnaire included questions on dysmenorrhea and the pain severity of dysmenorrhea.

2.3. Criteria to Identify Dysmenorrhea. Women were asked if they had menstruation. If they were menstruating, they were asked if they experienced dysmenorrhea in the beginning of their menstruation. Those who had dysmenorrhea were asked to state the magnitude of the dysmenorrhea pain; minor pain, medium pain, severe pain, very severe pain, and no pain. Menopause was identified in women who were menstruating in 1996 but reported that they did not menstruate in 2006.

2.4. Criteria to Identify IBS. The criteria for identification of IBS are presented in Table 1.

Diagnosis of IBS according to the Manning criteria [23] required two or more of the six symptoms listed in Table 1 and abdominal pain six or more times during the previous year [24, 25].

2.5. Transition between Disorders from the Initial to the Final Survey. A transition model used by Halder et al. was modified and applied for this study [21]. The responses from the initial (1996) and final (2006) surveys were matched for each subject to examine the changes between disorders at an individual level for the 6 categories (IBS, FD, heartburn, frequent abdominal pain, and no symptoms). A 5×5 table was used to model these multiple changes and collapsed into 6 groups, as illustrated in Figure 1. Those with the most symptoms were prioritized higher. Those who developed more symptoms and those who reported fewer symptoms could be categorised into groups. There were six patterns of symptoms, identified as follows: (1) symptom stability, (2) symptom increase, (3) symptom decrease, (4) symptom onset, (5) becoming asymptomatic, and (6) none of these symptoms.

2.6. Mortality Data. For the 2006 survey, we identified all deceased individuals with the assistance of the National Registry of Iceland.

2.7. Statistical Analysis. Tables were constructed for frequency and percentage. Categorical variables were summarized using frequency and percentage. Chi square test was

FGID in 1996	Proportion of FGID in 2006 based on primary survey disorder				
	FD (%)	IBS (%)	Heartburn (%)	Frequent abd. pain (%)	No symptoms
FD ($n = 29$) *FD ($n = 18$)*	62.1 *44.4*	17.2 *27.8*	6.9 *16.7*	0.0 *5.6*	13.8 *20.7*
IBS ($n = 37$) *IBS ($n = 29$)*	29.7 *17.2*	29.7 *37.9*	10.8 *13.8*	5.4 *10.3*	24.3 *20.7*
Heartburn ($n = 22$) *Heartburn ($n = 26$)*	22.7 *7.7*	22.7 *15.4*	22.7 *42.3*	4.5 *11.5*	27.3 *23.1*
FAP ($n = 4$) *FAP ($n = 10$)*	0.0 *0.0*	25.0 *30.0*	75.0 *10.0*	0.0 *10.0*	0.0 *50.0*
No symptoms ($n = 38$) *No symptoms ($n = 80$)*	7.9 *1.3*	15.8 *8.8*	15.8 *15.0*	5.3 *7.5*	55.3 *67.5*

Remaining asymptomatic
Became asymptomatic
Stable
Developed symptoms
Decreased symptoms
Increased symptoms

FGID-Functional gastrointestinal disorder
FD-Functional dyspepsia
IBS-Irritable bowel syndrome
FAP-Frequent abdominal pain

Figure 1: Transitions among symptom subgroups between the initial and final surveys. Women with dysmenorrhea, *women without dysmenorrhea.*

used to compare categorical variable. Type I error protection rate was set at 0.05. The exact P is listed in the tables and text. The statistical software SPSS (Statistical Package of Social Science) was used for data analysis.

2.8. Ethics. The National Bioethics Committee of Iceland and The Icelandic Data Protection Authority gave their permission for the research.

3. Results

3.1. Demographic Data of Involved Individuals. In 1996 the response rate was 66.8% (1336/2000). Of the 1336 individuals who participated in 1996, 81 were deceased by 2006, five subjects were unable to answer, mainly because of old age, and 70 could not be traced to a current address. This left 1180 individuals, out of which 799 responded in 2006 (Figure 2). The response rate in 2006 was 63.7% (799/1255). The mean age of the individuals in 1996 was 43 and in 2006 53; there was not a significant difference between those who responded 2006 and those who did not respond (NS). Women were more apt to respond than men in both years. A larger proportion of women responded again in 2006 (57.8%) than those who responded in 1996 but did not respond again in 2006 (49.8%, $P < 0.01$). The responders represented the population concerning sex and age distribution. The response rate was higher for older subjects than younger ones. There was no significant difference between those who responded or those who did not respond in the year 2006, whether they were diagnosed with IBS in the year 1996 or not. Age distribution and demographic details of the study cohort are presented in Table 2.

3.2. Dysmenorrhea (Painful Menstruation). Of those women who responded, 331 women reported menstruation in 1996 and 205 in the year 2006. A total of 254/331 (77%) in 1996 and 152/205 (74%) in 2006 reported dysmenorrhea (Table 3). Half of those reported medium severity of dysmenorrhea. Slightly more reported minor dysmenorrhea in the year 1996 than 2006. Slightly more reported severe or very severe dysmenorrhea (Figure 3).

3.3. Dysmenorrhea and Irritable Bowel Syndrome. One out of ten women with dysmenorrhea had IBS according to the Rome III criteria in the year 1996, and 5% of women without dysmenorrhea had IBS ($P = 0.170$) (Table 4). A total of 39/152 (26%) women with dysmenorrhea had IBS according to Rome III in the year 2006 and 14/152 (9%) of women without dysmenorrhea had IBS, with a statistical difference ($P = 0.013$).

Overall 105/254 (41.5%) of women with dysmenorrhea had IBS according to the Manning criteria in the year 1996, and one out of four without dysmenorrhea had IBS, with a statistical difference ($P = 0.014$). 49% of the women in the year 2006 of women with dysmenorrhea had IBS according to Manning and 33% of women without dysmenorrhea had IBS in the year 2006 ($P = 0.063$).

Table 1: Criteria to identify IBS.

Manning
Pain eased after BM
Looser stools at onset of pain
More frequent BM at onset of pain
Abdominal distension
Mucus per rectum
Feeling of incomplete emptying
Rome III criteria
Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months association with two or more of the following:
Improvement with defecation
Onset associated with a change in frequency of stool
Onset associated with a change in form (appearance) of stool
BMs, bowel movements.
Subgroups of Rome III: subjects fulfilling the Rome III criteria were divided into 4 subgroups according to their bowel habits:
(1) diarrhea-predominant (IBS-D), IBS-D is determined by predominantly loose or watery stools ≥25% of the time
(2) constipation- predominant (IBS-C), IBS-C is determined by predominantly hard or lumpy stools ≥25% of the time
(3) diarrhea and constipation (IBS-M), categories for mixed (mixed irritable bowel syndrome (IBS-M): meeting criteria for IBS-D and IBS-C ≥25% of time)
(4) no diarrhea or constipation, un-subtyped (un-subtyped irritable bowel syndrome (IBS-U): not meeting criteria for of IBS-C nor IBS-D, that is, both are <25% of the time).

Rome III: a close approximation of the Rome III criteria was used. The data were reevaluated retrospectively to conform to the Rome III criteria.

Table 2: Study population. Age and sex distribution.

	Population 2006 (%)	Respondents 2006 (%)
Gender		
Men	50.3	42.2
Women	49.7	57.8
Age		
28–35	19.5	14.52
36–45	24.9	20.40
46–55	22.8	22.15
56–65	15.6	19.52
66–75	10.4	15.14
76–85	6.8	8.26
Total number	$N = 173859$	$n = 799$

3.4. Dysmenorrhea and Other Functional Gastrointestinal Disorders. A total of 45/57 (79%) of those who had functional dyspepsia (FD) and 72/90 (80%) heartburn had dysmenorrheal, and 88% of those who had diarrhea and or constipation had dysmenorrhea (Figure 4). Altogether 39% of those who had FD and 41% of those who had diarrhea and/or constipation had severe or very severe dysmenorrhea. There was a significant statistical difference ($P < 0.01$) of dysmenorrhea between those who had FD and those who did not have FD. Those who had diarrhea and, or constipation had proportionally higher prevalence of dysmenorrhea than

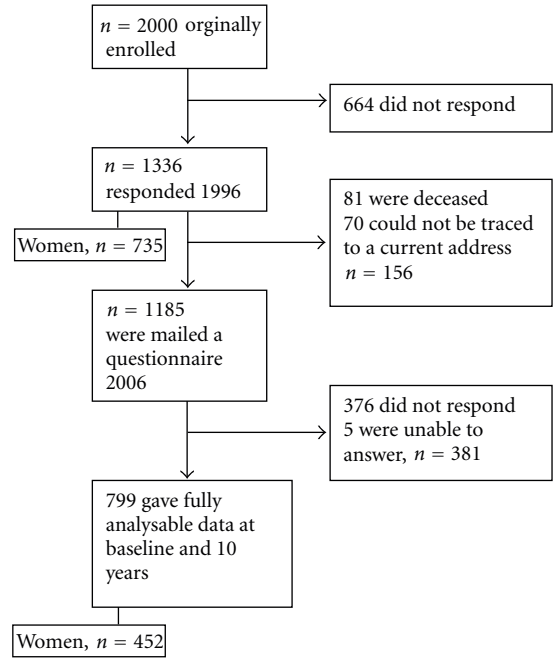

Figure 2: Flow of study participants.

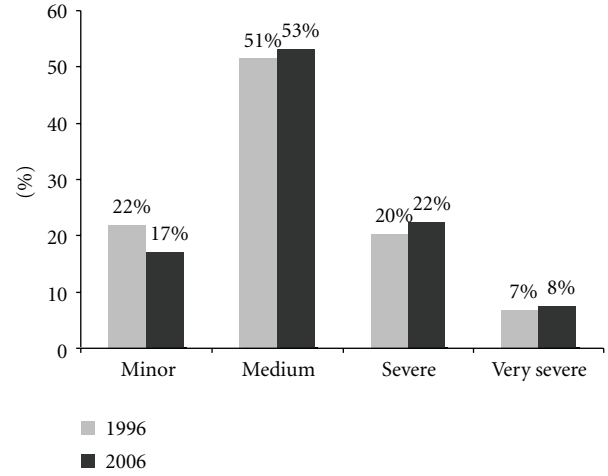

Figure 3: Distribution of dysmenorrhea severity (1996, $n = 254$, 2006, $n = 152$).

Table 3: Women with menstruation and dysmenorrhea.

	1996		2006	
Total women	446		444	
Women without menstruation	115	25.8%	239	53.8%
Women with menstruation	331	74.2%	205	46.2%
Women with dysmenorrhea	254	76.7%	152	74.1%

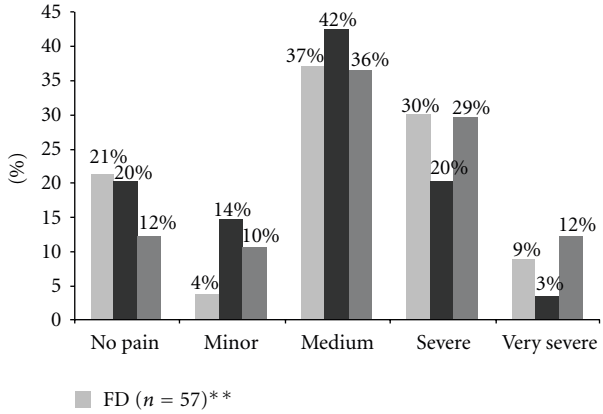

Figure 4: Functional gastrointestinal disorders and dysmenorrhea severity (2006, n = 152).

Table 4: Women with IBS according to Rome III and Manning and dysmenorrhea.

		1996	2006
Rome III	Dysmenorrhea	10.5%	25.7%
	Without dysmenorrhea	5.3%	9.4%
Manning	Dysmenorrhea	41.5%	48.6%
	Without dysmenorrhea	25.3%	33.3%

those who did not have diarrhea and or constipation ($P < 0.01$) (Figure 4).

3.5. Women with Dysmenorrhea in 1996 and after Menopause 2006, IBS, and Abdominal Pain Severity. In the year 1996, overall 64 women experienced dysmenorrhea but did not have periods in the year 2006. In the year 1996, 24/64 (38%) of those had IBS according to the Manning criteria and 41% in the year 2006 altogether. 6% experienced IBS according to Rome III criteria in the year 1996 and 13% in the year 2006. Figure 5 shows the changes in abdominal pain severity in women with dysmenorrhea in the year 1996 and after menopause in the year 2006.

3.6. Transition between Disorders from the 1996 and 2006 Surveys. As described in the method section, the groups in this analysis were defined as mutually exclusive, using the symptom hierarchy so that each subject appears in only one category for both the 1996 and 2006 surveys. There was a "no symptoms" category for those who did not meet any of the criteria applied for FGID. Due to the hierarchical classification, only a few participants occurred in some categories.

Transitions between disorders were explored in two ways, for women with dysmenorrhea and for women without dysmenorrhea (Figure 1). There was a substantial change

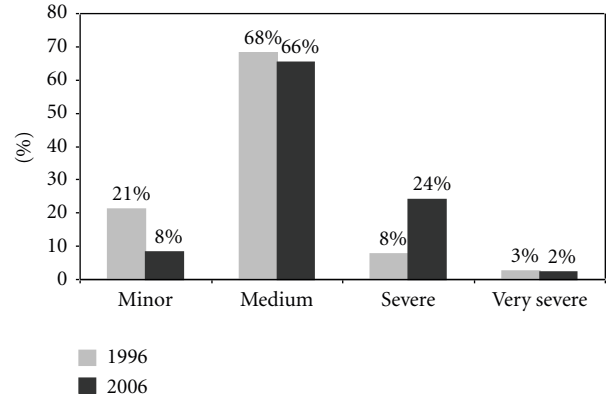

Figure 5: Abdominal pain in women with dysmenorrhea 1996 and after menopause 2006.

in numbers in all the categories between the two surveys. The group "no symptoms" was the most common in both transition models. For the women with dysmenorrheal, the FD was the most stable one. A total of 17% moved into the IBS group and 14% into the no symptom group. IBS was stable in 30% cases, and the same number moved into the FD group. One-fourth moved into the no symptom group. There were only 4 women in the heartburn group of women with dysmenorrhea. In women without dysmenorrheal, the stability of symptoms was greater than that for those who suffered from dysmenorrhea. 44% of the FD group was stable between the initial and final surveys. One out of four moved into the IBS group. The stability for the IBS group was 38%. 5/29 (17%) moved into the IBS group and 21% into the no symptom group. The highest stability (42%) was in the heartburn group.

The transitions were collected into six groups. Comparison of the differences between women with and without dysmenorrhea in those transition groups (Figure 6) showed that the greatest difference was between the two groups of women who remained asymptomatic. The women without dysmenorrhea were twice more likely to remain asymptomatic than the women with dysmenorrhea. The women with dysmenorrhea were also more likely to have stable symptoms at followup than women without dysmenorrhea. The women with dysmenorrhea were twice more likely to have increased symptoms than women without symptoms.

3.7. Birth Cohort Effect of Dysmenorrhea. There was no significant difference in prevalence between birth cohorts in women with dysmenorrhea nor in women without dysmenorrheal (Figure 7).

4. Discussion

The current study makes it possible for the first time to follow up women with and without dysmenorrhea over a ten-year period and to observe how the FGID symptoms are associated with dysmenorrhea.

Every three out of four women with menstruation in this study experience dysmenorrhea which is similar to other

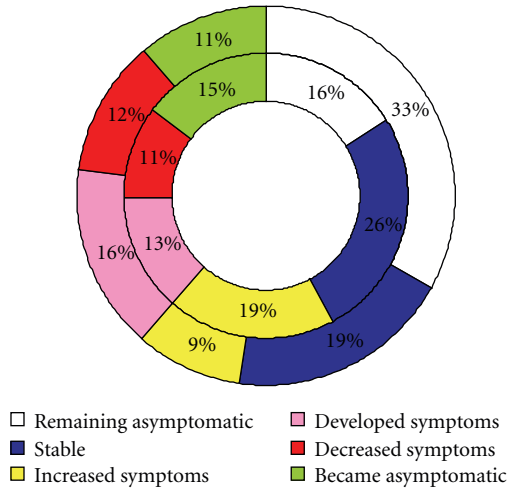

Figure 6: Six-group transition model, change from initial to the final survey. Women with dysmenorrhea ($n = 130$) in the inner circle and women without dysmenorrhea ($n = 163$) in the outer circle.

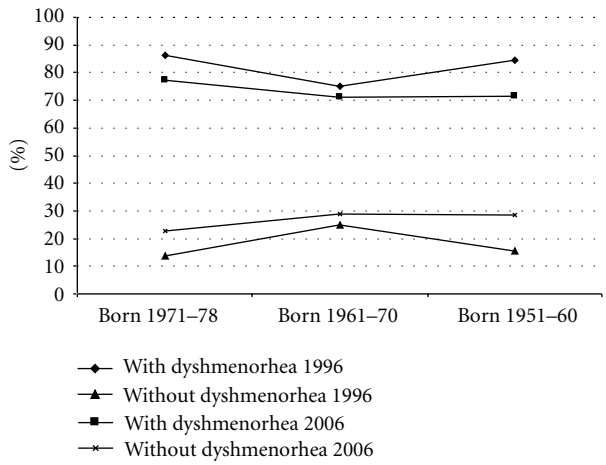

Figure 7: Birth cohort effect on the prevalence (%) in 10 years.

studies. Analysis of women with dysmenorrhea showed that they were more likely to have IBS, either based on the Rome III criteria and/or the Manning criteria. The Manning criteria were much more sensitive than the Rome criteria. There was an increase in prevalence in dysmenorrhea over the ten-year period for both women with IBS according to Rome III and Manning, with more increase in dysmenorrhea in the Rome III group.

A meta-analysis based on a small number of studies compared gastrointestinal symptoms in pre- and postmenopause women [15]. The authors concluded that there was insufficient evidence to determine the effect of menopausal status on IBS symptoms. The current study demonstrated an increase in prevalence in women having IBS after menopause using both IBS criteria. Increase in gastrointestinal symptoms around the time of menses and early menopause occurs at times of declining or low ovarian hormones, suggesting that estrogen and progesterone withdrawal may contribute either directly or indirectly [16]. One study has shown that gastrointestinal symptoms burden was higher in postmenopausal women than in men, but these differences mostly disappeared when controlled for age [7].

Women with dysmenorrhea report more gastrointestinal symptoms prior to or concurrent with uterine cramping pain at menses than women who are non-dysmenorrheic [26]. Gastrointestinal symptoms tend to be increased across all cycle phases in women with IBS compared to healthy women, but both groups demonstrated a similar increase in severity immediately prior to or at the onset of menses [27]. The current study compared the FGIDs and dysmenorrheal severity and demonstrated that the great majority of women with dysmenorrhea had other FGID symptoms than those related to IBS. Women reported more severe abdominal pain after menopause than before. One study has shown that abdominal pain is the most disruptive IBS symptom [8].

The current study observed the transition between symptoms and revealed substantial difference between women with and without dysmenorrhea. Women without dysmenorrhea remained more often asymptomatic than women with dysmenorrhea. FGID symptoms were more stable in 10 years for women with dysmenorrheal, and they also had more increase in symptoms than women without dysmenorrhea. This demonstrated a difference between those two groups of women. The prevalence of menstrually related symptoms has been shown to be high and appears to affect bowel patterns [26]. A recent meta-analysis revealed a significant menstrual cycle effect for loose stools, bloating, abdominal pain, stool frequency, and other changes in bowel habit [15].

The strength of our study was the use of a stable and homogeneous population. The sample was randomly selected from the National Registry of Iceland and represented the nation as a whole in selected age groups. Only a minority of IBS patients seek medical care, and population-based studies are therefore essential for studying IBS. The population of Iceland with approximately 300 thousand inhabitants represents 1% of the whole population from all around the country.

There are some limitations to our study. The subjects were not specifically interviewed or examined to evaluate the possibility of organic disease. However, the 10-year (postal) followup went some way to making an organic cause of symptoms unlikely. Information on women using the contraceptive pill is lacking from this study, and this could affect the study. Also information on endometriosis and other gynaecological problems is not addressed in this study but could affect the results. Furthermore, since the response rate was 67% in 1996 and 69% in 2006, a drop-out bias cannot be excluded. A similar mean age in the respondent group and the nonrespondent group does not indicate an age dropout bias in the study.

Conflict of Interests

The authors declare that they have no conflict of interests.

Acknowledgments

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References

[1] D. A. Drossman, *The Functional Gastrointestinal Disorders*, Degnon Associates, 3rd edition, 2006.

[2] A. P. S. Hungin, L. Chang, G. R. Locke, E. H. Dennis, and V. Barghout, "Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact," *Alimentary Pharmacology and Therapeutics*, vol. 21, no. 11, pp. 1365–1375, 2005.

[3] H. J. Chial and M. Camilleri, "Gender differences in irritable bowel syndrome," *Journal of Gender-Specific Medicine*, vol. 5, no. 3, pp. 37–45, 2002.

[4] M. Heitkemper and M. Jarrett, "Irritable bowel syndrome: does gender matter?" *Journal of Psychosomatic Research*, vol. 64, no. 6, pp. 583–587, 2008.

[5] J. Herman, V. Pokkunuri, L. Braham, and M. Pimentel, "Gender distribution in irritable bowel syndrome is proportional to the severity of constipation relative to diarrhea," *Gender Medicine*, vol. 7, no. 3, pp. 240–246, 2010.

[6] L. Chang and M. M. Heitkemper, "Gender differences in irritable bowel syndrome," *Gastroenterology*, vol. 123, no. 5, pp. 1686–1701, 2002.

[7] K. C. Cain, M. E. Jarrett, R. L. Burr, S. Rosen, V. L. Hertig, and M. M. Heitkemper, "Gender differences in gastrointestinal, psychological, and somatic symptoms in irritable bowel syndrome," *Digestive Diseases and Sciences*, vol. 54, no. 7, pp. 1542–1549, 2009.

[8] K. C. Cain, P. Headstrom, M. E. Jarrett et al., "Abdominal pain impacts quality of life in women with irritable bowel syndrome," *American Journal of Gastroenterology*, vol. 101, no. 1, pp. 124–132, 2006.

[9] M. M. Heitkemper and M. E. Jarrett, "Update on irritable bowel syndrome and gender differences," *Nutrition in Clinical Practice*, vol. 23, no. 3, pp. 275–283, 2008.

[10] A. M. Weissman, A. J. Hartz, M. D. Hansen, and S. R. Johnson, "The natural history of primary dysmenorrhoea: a longitudinal study," *BJOG*, vol. 111, no. 4, pp. 345–352, 2004.

[11] D. J. Jamieson and J. F. Steege, "The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices," *Obstetrics and Gynecology*, vol. 87, no. 1, pp. 55–58, 1996.

[12] J. G. Penston and R. E. Pounder, "A survey of dyspepsia in Great Britain," *Alimentary Pharmacology and Therapeutics*, vol. 10, no. 1, pp. 83–89, 1996.

[13] R. Jones and S. Lydeard, "Irritable bowel syndrome in the general population," *British Medical Journal*, vol. 304, no. 6819, pp. 87–90, 1992.

[14] H. B. El-Serag and N. J. Talley, "Systematic review: the prevalence and clinical course of functional dyspepsia," *Alimentary Pharmacology and Therapeutics*, vol. 19, no. 6, pp. 643–654, 2004.

[15] M. A. Adeyemo, B. M. R. Spiegel, and L. Chang, "Meta-analysis: do irritable bowel syndrome symptoms vary between men and women?" *Alimentary Pharmacology and Therapeutics*, vol. 32, no. 6, pp. 738–755, 2010.

[16] M. M. Heitkemper and L. Chang, "Do fluctuations in ovarian hormones affect gastrointestinal symptoms in women with irritable bowel syndrome?" *Gender Medicine*, vol. 6, no. 2, pp. 152–167, 2009.

[17] L. B. Olafsdóttir, H. Gudjónsson, and B. Thjódleifsson, "Epidemiological study of functional bowel disorders in Iceland," *Icelandic Medical Journal* , vol. 91, no. 4, pp. 329–333, 2005.

[18] D. Dillman, *Mail and Telephone Surveys: The Total Design Method*, John Wiley and Sons, 1978.

[19] N. J. Talley, S. F. Phillips, C. M. Wiltgen, A. R. Zinsmeister, and L. J. Melton III, "Assessment of functional gastrointestinal disease: the bowel disease questionnaire," *Mayo Clinic Proceedings*, vol. 65, no. 11, pp. 1456–1479, 1990.

[20] N. J. Talley, S. F. Phillips, L. J. Melton, C. Wiltgen, and A. R. Zinsmeister, "A patient questionnaire to identify bowel disease," *Annals of Internal Medicine*, vol. 111, no. 8, pp. 671–674, 1989.

[21] S. L. S. Halder, G. R. Locke, C. D. Schleck, A. R. Zinsmeister, L. J. Melton, and N. J. Talley, "Natural history of functional gastrointestinal disorders: a 12-year longitudinal population-based study," *Gastroenterology*, vol. 133, no. 3, pp. 799–807, 2007.

[22] V. Attanasio, F. Andrasik, E. B. Blanchard, and J. G. Arena, "Psychometric properties of the SUNYA revision of the Psychosomatic Symptom Checklist," *Journal of Behavioral Medicine*, vol. 7, no. 2, pp. 247–257, 1984.

[23] A. P. Manning, W. G. Thompson, K. W. Heaton, and A. F. Morris, "Towards positive diagnosis of the irritable bowel," *British Medical Journal*, vol. 2, no. 6138, pp. 653–654, 1978.

[24] N. J. Talley, A. R. Zinsmeister, C. Van Dyke, and L. J. Melton, "Epidemiology of colonic symptoms and the irritable bowel syndrome," *Gastroenterology*, vol. 101, no. 4, pp. 927–934, 1991.

[25] D. A. Drossman, "A questionnaire for functional bowel disorders," *Annals of Internal Medicine*, vol. 111, no. 8, pp. 627–629, 1989.

[26] S. V. Kane, K. Sable, and S. B. Hanauer, "The menstrual cycle and its effect on inflammatory bowel disease and irritable bowel syndrome: a prevalence study," *American Journal of Gastroenterology*, vol. 93, no. 10, pp. 1867–1872, 1998.

[27] M. M. Heitkemper, K. C. Cain, M. E. Jarrett, R. L. Burr, V. Hertig, and E. F. Bond, "Symptoms across the menstrual cycle in women with irritable bowel syndrome," *American Journal of Gastroenterology*, vol. 98, no. 2, pp. 420–430, 2003.

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Clinical Study

Irritable Bowel Syndrome and Psychiatric Disorders in Pakistan: A Case Control Study

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Background. The psychiatric disorders like anxiety and depression could have a profound influence on onset, expression, and course of Irritable bowel syndrome (IBS). *Aim*. To estimate the frequency and strength of association of common mental disorders (CMDs) in patients with IBS and patients with other chronic diseases, that is, migraine and hypertension. *Method*. This was a case control study. Individuals aged 18–70 years diagnosed as IBS were enrolled as cases. The control groups consisted of patients without IBS but diagnosed to have a chronic disease, that is, migraine or HTN. Self-Reporting Questonnaire-20(SRQ-20) was used as a screening tool for the detection of CMD. *Results*. 82 patients were enrolled in each group. Mean SRQ score was significantly higher in IBS group than controls (9.9 ± 4.5 versus 4.9 ± 3.6, $P < 0.001$). CMDs were more frequent (67.1% versus 22%) and the odds of CMD were 7.24 times higher among IBS patients than controls (95% CI 3.6–14.5, $P < 0.001$). No difference was found in frequency of CMDs among various subtypes of IBS. *Conclusion*. We found that CMDs are more common and strongly associated with IBS as compared to other chronic diseases. Early screening for CMDs might be useful for an effective management of IBS.

1. Introduction

Irritable bowel syndrome (IBS) is a common health problem which not only affects 10–20% of adult population worldwide [1] but also account for up to 25% outpatient workload of a gastroenterologist [2–4]. IBS is considered as a functional bowel disorder characterized by abdominal pain/discomfort which is relieved by defecation and associated with altered stool frequency and/or consistency, in the absence of structural, microbiological, and biochemical abnormalities [3, 5, 6]. The overall point prevalence of IBS in Asia varies from 4.4% to 10.4% in various communities [3, 7]. The exact prevalence of IBS in Pakistani population is unknown. However, the prevalence of IBS was found 34% in a study conducted in 508 college going students of Karachi, Pakistan [7]. Likewise, 45% of 1048 adults living in Karachi and Bahawalpur were found to be affected by IBS [8].

Despite conceptualization of several mechanisms, the exact cause of IBS remains uncertain. Currently, postulated mechanisms include exaggerated visceral hypersensitivity, gastrointestinal motor disturbances, and postinfectious IBS [5]. In addition, the brain gut axis has been suggested. Studies from different parts of the world have revealed underlying psychiatric disorders in 40–60% of IBS cases which is significantly higher than healthy control or controls with other chronic diseases [5, 9–15]. Moreover, in a study conducted in our hospital significantly high proportion of patients with functional dyspepsia were found to have common mental disorders as compared to controls (71.33% versus 15.33%, $P < 0.001$) [16]. Hence, the proper screening and management of associated common mental disorders in addition to the treatment is needed.

Common mental disorders (CMD) described as anxiety, depression, and somatoform disorders are the most frequent and disabling group of psychiatric states [17]. These CMDs like depression not only affect the quality of life but may potentially increase short-term mortality in cardiac patients [18]. Significant depressive symptoms have been reported in

patients affected by chronic illness [19] for example, 18% of patients with migraine was found affected by CMD [20] and almost 50% patients with depression was found to have hypertension (HTN) [21]. In Pakistan, the overall reported prevalence of anxiety and depressive disorders is 34%, which is yet another challenge for a resource poor country like Pakistan [22].

Individuals with IBS incur more direct health care costs than non-IBS patients, particularly for their nongastrointestinal complaints including psychiatric symptoms [9, 23]. Frequency of symptoms experienced, concern of serious underlying illness, lower quality of life, and coexisting health problems lead to frequent visits and extended investigations of IBS patients [2]. Furthermore, coexisting CMD with IBS may further deteriorate health resulting in absenteeism at work, increased health care cost thus has significant implications on economics for a poor country like Pakistan. To date there is no published data regarding frequency of CMD in patients with IBS from Pakistan. Hence, identification of associated psychiatric disorders may help in treatment and counseling of patients with IBS through early psychological or psychopharmacological interventions [6]. Therefore, it is imperative to know the frequency and strength of association of CMD in patients with IBS from our region.

Thus, the current study is designed to estimate the frequency and strength of association of common mental disorders (CMDs) in Pakistani patients with irritable bowel syndrome (IBS) and patients with other chronic diseases, that are, migraine and hypertension. It is hypothesized that among IBS cases the CMD is greater than controls.

2. Methods

2.1. Study Design and Setting. Two parallel case control studies [16] were conducted in 2009 in Gastroenterology clinics of The Aga Khan University Hospital (AKUH), Karachi, Pakistan. First was the current study designed to evaluate the frequency of CMDs in patients with IBS as compared to controls. The AKUH is a tertiary care hospital where patients are referred from all over the country for treatment. The current study was conducted in outpatient Gastroenterology and Neurology clinics from January–September 2009. Individuals aged 18–70 years who could read and understand Urdu (national language) or English were offered to participate. Those who agreed to participate and met the eligibility criteria were enrolled with their consent.

2.2. Selection of Cases and Controls. Individuals visiting our Gastroenterology clinics and already diagnosed to have IBS by a qualified gastroenterologist at AKUH were recruited randomly as "cases". However, those cases of IBS with diagnosed psychiatric disorders including CMD, other concomitant chronic diseases including HTN, DM, ischemic heart disease, and migraine, or had limited functional activity (i.e., functional class ≥ 2) were excluded. Diagnosis of IBS was made according to Room III criteria for IBS. Rome III criteria have been found useful and cost effective for diagnosing IBS in clinical practice, epidemiological surveys, physiological research and therapeutic trials [1, 6, 13]. Moreover, the IBS cases were also categorized into subtypes, that are, (1) IBS with constipation (IBS-C), (2) IBS with diarrhea (IBS-D), and (3) Mixed IBS (IBS-M) [1].

The control group was randomly selected from Neurology and Medicine clinics of AKUH. The control group comprised of patients who either have migraine diagnosed by a qualified neurologist or have HTN diagnosed based upon the Seventh Report of Joint National Committee (JNC VII) on Prevention, Detection, Evaluation, and Treatment of high blood pressure [24]. According to JNC VII Hypertension was defined as a mean of two or more properly measured seated BP readings of systolic BP $\geq$ 140–159 mmHg or diastolic BP $\geq$ 90–99 mmHg on each of two or more office visits [24]. Migraine was defined as lateralized, throbbing, or dull episodic headache occurring without preceding aura, sometimes associated with anorexia, nausea, vomiting, cognitive impairment, and blurring of vision [25].

Common mental disorders (CMD) describe the state of anxiety, depression, and psychosomatic disorders [17]. Based upon DSM IV criteria, diagnosis of major depression was made if an individual experienced five or more of the following symptoms for at least two consecutive weeks; (1) depressed mood, (2) loss of interest or pleasure in most or all activities, (3) insomnia or hypersomnia, (4) change in appetite or weight, (5) psychomotor retardation or agitation, (6) low energy, (7) poor concentration, (8) thoughts of worthlessness or guilt, and (9) recurrent thoughts about death or suicide. However, the individual diagnosed to have minor depression if experiences any two or four of the nine symptoms of major depression present most of the day, nearly every day, for at least two weeks, at least one being depressed mood or loss of interest/pleasure [26]. Anxiety disorder defined as an uncontrollable disposition to worry about one's welfare and that of one's immediate kin associated with wide range of physical and affective symptoms, changes in behavior, and cognition like arousal, vigilance, tension, irritability, and unrestful sleep [26, 27].

2.3. Screening for Common Mental Disorders. We used self-reporting questionnaire-20 (SRQ-20) which is one of the most widely used self-administered psychiatric questionnaires developed by Harding et al. [28] for World Health organization (WHO) to screen for CMD, especially in developing countries. It is available in at least 21 language translations including a validated Urdu version [29–32]. It has not only been validated but also adapted for cross-cultural use in Pakistan [30]. It is simple, easy to interpret and takes only few minutes to administer the questionnaire [30, 31, 33–36]. It consists of 20 questions and inquires about the presence of symptoms over the period of last 30 days [36]. Each item is scored 0 or 1. A score of 1 indicates the presence and 0 indicates the absence of symptoms with a maximum score of 20. Different cut off for SRQ scores has been used in different studies. However, a cutoff point of 8/9 (8 "yes" for a "control" and 9 "yes" for a "case") is common with sensitivity of about 80% and specificity of 75% [30, 31].

Thus, eligible patients were interviewed by a single interviewer to screen them for CMDs by using SRQ-20. Moreover,

Table 1: Comparison among patients with IBS and controls.

	Cases mean ± SD or *n* (%)	Controls mean ± SD or *n* (%)	95% confidence interval	*P* value
Age (years)	43.1 ± 12.1	39.9 ± 11.2	0.95–1.00	0.08
Gender				
Male	61 (74.4)	48 (58.5)	0.25–0.94	0.03
Females	21 (25.6)	34 (41.5)		
SRQ score	9.9 ± 4.5	4.9 ± 3.6	1.22–1.44	<0.001
CMDs				
Present	55 (67.1)	18 (22.0)	3.6–14.5	<0.001
Absent	27 (32.9)	64 (78.0)		

information regarding age, gender, marital status for cases and controls, and type of IBS for cases were also collected.

This was a prospective, case control study, conducted by maintain compliance with the Helsinki Declaration. This was an interview based study and study participants were interviewed after their informed consent and there was no intervention involved.

2.4. Statistical Analysis. Sample size was calculated by using EPI Info version 6 [37]. Assuming the prevalence of CMDs 40% in IBS group [11] and 18% in the control group [19, 20] we require 148 (74 individuals in each group) to detect a difference in the proportion of CMDs in IBS group versus control group with 80% power, at 5% significance level. Adding 10% refusals to the calculated sample size, we required target sample size of 164 (82 subjects in each arm).

Data was analyzed in SPSS version 16.0. Mean ± standard deviation were calculated for quantitative variables (age, SRQ score) and proportions (percentage) were calculated for categorical data (gender, subtypes of IBS). The baseline characteristics were compared in the two groups by using independent student *t*-test for continuous variable and chi-square or Fisher exact test for categorical variables wherever appropriate. The association of age with CMDs was checked by stratifying cases and controls on age. A P value < 0.05 was considered statistically significant. All P values were single sided. Furthermore, binary logistic was performed to see association between CMDs and subtypes of IBS.

3. Results

A total of 164 patients; 82 patients in each group were enrolled. Out of 82 patients in control group, 42 patients had HTN and 40 had migraine. In IBS group, the proportion of IBS-constipation, IBS-diarrhea, and IBS-mixed were 37 (45.1%), 29 (35.4%), and 16 (19.5%), respectively. No difference was observed in mean age among patients with IBS and controls (43.1 ± 12.1 versus 39.9 ± 11.2 years, 95% CI 0.9–1.0, $P = 0.08$). There was male predominance in both groups. Moreover, CMDs were more frequent among males affected by IBS than controls (74.4% versus 58.5%, 95% CI 0.3–0.9, $P = 0.03$) (Table 1).

Overall mean SRQ score was 7.4 ± 4.7 (range 0–18). Mean SRQ score was significantly higher in IBS group as compared to the control group (9.9 ± 4.5 versus 4.9 ± 3.6, 95% CI 1.22–1.44, $P < 0.001$) (Figure 1). Using the cut off 8/9 for SRQ score, common mental disorders were found in 55 (67.1%) of patients with IBS as compared to 18 (22%) of the control group. Moreover, the odds to be affected by CMDs were 7.2 times greater among IBS cases as compared to the control group (95% CI 3.6–14.5, $P < 0.001$). Furthermore, no difference was observed in frequency of CMDs among IBS cases and controls when both study groups were stratified on age (P value 0.6).

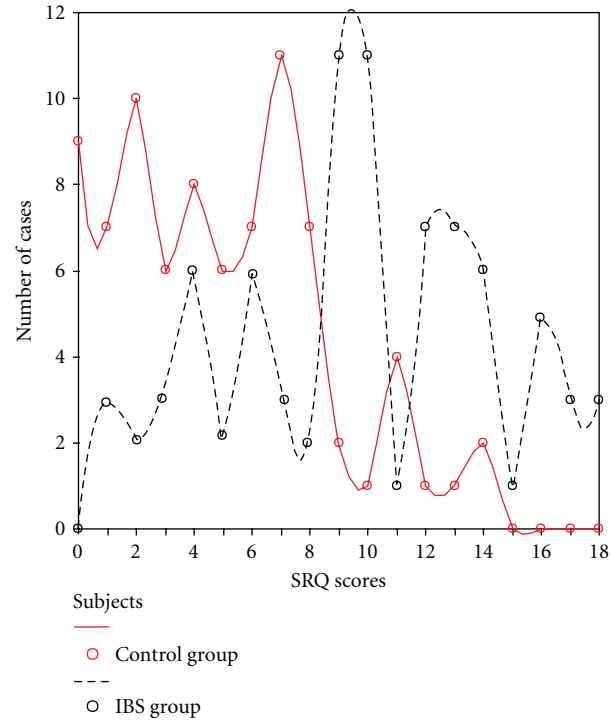

Figure 1: Comparison of SRQ-scores in IBS patients and controls.

Binary logistic was also performed to see an association of CMD with subtypes of IBS. No difference was found in distribution of age and gender among different subtypes of IBS. Mean SRQ score was 10.62 ± 4.56, 8.52 ± 4.52, and 10.13 ± 4.12 in IBS-C, IBS-D, and IBS-mixed group, respectively ($P = 0.16$). Likewise, no difference was observed in frequency of CMD among patients with IBS-C, IBS-D, and IBS-mixed (27 (73.0%) versus 16 (55.2%) versus 12 (75.0%), $P = 0.23$) (Table 2).

Table 2: Baseline demographic characteristics and CMD status of patients with different subtypes of IBS.

	IBS-C	IBS-D	IBS-mixed	*P* value
Gender*				
Male	25 (67.56%)	21 (72.4%)	15 (93.8%)	0.12
Female	12 (32.4%)	8 (27.6%)	1 (6.3%)	
Age (years)†	38.3 ± 10.13	42.6 ± 13.05	38.7 ± 9.67	0.26
Age categories (years)*				
18–34	14 (37.8%)	8 (27.6%)	6 (37.5%)	0.36
35–40	8 (21.6%)	9 (31.0%)	5 (31.3%)	
41–50	12 (32.4%)	5 (17.2%)	4 (25.0%)	
51–67	3 (8.1%)	7 (24.1%)	1 (6.3%)	
SRQ score†	10.62 ± 4.56	8.52 ± 4.52	10.13 ± 4.12	0.16
CMD present*	27 (73.0%)	16 (55.2%)	12 (75.0%)	0.23

*n (%), †mean ± SD.

4. Discussion

In this case control study, the distribution of age was comparable in both IBS and with chronic disease. Males were predominant among both cases and controls; however, the proportion of females was significantly higher in control group as compared to IBS group. Mean SRQ score and frequency of CMD were significantly higher in IBS group as compared to controls. We did not find difference in proportion of CMD and mean SRQ score among patients with IBS-C, IBS-D, and IBS-mixed. However, these findings were based upon post-hoc analysis and could be due to insufficient small sample size to assess this association.

The implications of our study are that there was a male predominance in both groups and CMDs were more frequent among male cases than controls. These findings are consistent with local studies conducted by Jafri and colleagues where IBS was found predominantly in males that is, 56% [8] and 48% (versus 42% in females) [7], respectively. Moreover, Healthcare seekers among IBS patients were predominantly males than females (56% versus 44%) [8]. Likewise, studies from neighboring country India have reported higher rates of IBS and dyspepsia among males than females [38, 39]. This might be due to possibility of male patients consulting doctors more often than females due to various sociocultural reasons here. Hence, in our study finding IBS more in males may suggest that the male preponderance for IBS is not a chance finding.

Our findings are consistent with Trikas and colleagues [10], who found depressive disorders more common among patients with IBS as compared to controls affected by cholelithiasis (36.1% versus 7.1%, $P = 0.016$). Likewise, 40 patients with IBS were compared with 32 patients with inflammatory bowel disease (IBD) and 34 healthy controls [40]. Prevalence of anxiety, depressive, and mood disorders as well as higher scores on anxiety and depression scales were found in IBS group as compared to the controls. Moreover, these findings were also true for patients with IBD as compared to healthy controls. In our study, the risk of CMD among patients with IBS was found 7.2 times higher than the controls. Moreover, we have used SRQ-20 to screen CMD in our study which is not only sensitive to detect depressive disorders but also detects anxiety and other somatoform disorders as well [19, 20]. However, conflicting results have also been reported in some studies.

In a cohort of 1037 young individuals in Dunedin, New Zealand [9], relationship between psychiatric disorders and IBS was investigated. Rome II and Manning criteria for IBS and modified version of Diagnostic interview Schedule was used to detect psychiatric disorders. No association was found between IBS and psychiatric disorders in this cohort. In contrast to this study where only young individuals of age 26 years were evaluated, individuals with age 18–70 years were evaluated in our study which may be a possible explanation for difference in frequencies of CMD in IBS. Another explanation may be that the first occurrence of IBS mostly occurs between 30–50 years of age [13]. Hence, the population under study represents a broad sample.

The limitations of our study include screening for CMD was based upon SRQ-20. It consists of symptoms experienced during last four weeks that could have led to some degree of recall bias. We found it better not match our cases and controls for age and gender. As age and gender are known risk factors for IBS and CMDs [5]. Moreover, prior local and regional studies had reported male preponderance for IBS. In case of matching for age and gender, association of age and gender could not be studied.

It has been suggested that cross-cultural research regarding molecular biology, genetic and psychosocial factors, disease manifestations, diagnosis and treatment, health seeking behaviors, health-related quality of life, all aspects of IBS could be affected by culture, and ethnicity and race. Hence, well-designed cross-cultural studies can help us to understand the epidemiology, pathophysiological mechanisms, and therapeutic interventions related to IBS [41, 42]. Pakistan is a developing country where political and economic instability is a major concern. Data from population-based studies indicate that a one-third of Pakistan's population has anxiety and depression [19, 39]. Despite the high burden of psychological problems, mental health is not given a priority in the National Health Policy and only 0.4% of health care budget is being allocated to mental health [43]. Although

cost-effective treatments exist for these disorders, required trained mental-health professionals are not available to deal with them. Public funded primary health care is ineffective and underresourced.

5. Conclusion

We found that CMDs is more common and strongly associated with IBS as compared to other chronic diseases including migraine and HTN. Hence, early screening for CMDs in IBS patients might be useful for an effective management of IBS.

Abbreviations

IBS: Irritable bowel syndrome
CMD: Common mental disorders
HTN: Hypertension
AKUH: Aga Khan University Hospital
IBS-C: IBS with constipation
IBS-D: IBS with diarrhea
IBS-M: Mixed IBS
JNC VII: Seventh Report of Joint National Committee VII
SRQ-20: Self-reporting questionnaire-20
WHO: World Health Organization.

Conflict of Interests

The authors declare they have no conflict of interests.

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References

[1] G. F. Longstreth, W. G. Thompson, W. D. Chey, L. A. Houghton, F. Mearin, and R. C. Spiller, "Functional Bowel Disorders," *Gastroenterology*, vol. 130, no. 5, pp. 1480–1491, 2006.

[2] A. C. Ford, D. Forman, A. G. Bailey, A. T. R. Axon, and P. Moayyedi, "Irritable bowel syndrome: a 10-yr natural history of symptoms and factors that influence consultation behavior," *American Journal of Gastroenterology*, vol. 103, no. 5, pp. 1229–1239, 2008.

[3] K. A. Gwee, S. Wee, M. L. Wong, and D. J. C. Png, "The prevalence, symptom characteristics, and impact of irritable bowel syndrome in an Asian urban community," *American Journal of Gastroenterology*, vol. 99, no. 5, pp. 924–931, 2004.

[4] Å. Faresjo, E. Grodzinsky, S. Johansson, M.-A. Wallander, T. Timpka, and I. Åkerlind, "Psychosocial factors at work and in every day life are associated with irritable bowel syndrome," *European Journal of Epidemiology*, vol. 22, no. 7, pp. 473–480, 2007.

[5] N. J. Talley, "Irritable bowel syndrome," *Internal Medicine Journal*, vol. 36, no. 11, pp. 724–728, 2006.

[6] L. J. C. D. Brandt, A. E. Foxx-Orenstei, L. R. Schiller et al., "An evidence-based systematic review on the management of irritable bowel syndrome; American College of Gastroenterology Task Force on IBS," *The American Journal of Gastroenterology*, vol. 104, supplement 1, pp. S1–S40, 2009.

[7] W. Jafri, J. Yakoob, N. Jafri, M. Islam, and Q. M. Ali, "Frequency of irritable bowel syndrome in college students," *Journal of Ayub Medical College*, vol. 17, no. 4, pp. 9–11, 2005.

[8] W. Jafri, J. Yakoob, N. Jafri, M. Islam, and Q. M. Ali, "Irritable bowel syndrome and health seeking behaviour in different communities of Pakistan," *Journal of the Pakistan Medical Association*, vol. 57, no. 6, pp. 285–287, 2007.

[9] N. J. Talley, S. Howell, and R. Poulton, "The irritable bowel syndrome and psychiatric disorders in the community: is there a link?" *American Journal of Gastroenterology*, vol. 96, no. 4, pp. 1072–1079, 2001.

[10] P. Trikas, I. Vlachonikolis, N. Fragkiadakis, S. Vasilakis, O. Manousos, and N. Paritsis, "Core mental state in irritable bowel syndrome," *Psychosomatic Medicine*, vol. 61, no. 6, pp. 781–788, 1999.

[11] R. L. Levy, K. W. Olden, B. D. Naliboff et al., "Psychosocial Aspects of the Functional Gastrointestinal Disorders," *Gastroenterology*, vol. 130, no. 5, pp. 1447–1458, 2006.

[12] W. E. Whitehead, O. Palsson, and K. R. Jones, "Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications?" *Gastroenterology*, vol. 122, no. 4, pp. 1140–1156, 2002.

[13] E. A. Mayer, "Clinical practice. Irritable bowel syndrome," *The New England Journal of Medicine*, vol. 358, no. 16, pp. 1692–1699, 2008.

[14] D. A. Drossman, D. C. McKee, R. S. Sandler et al., "Psychosocial factors in the irritable bowel syndrome. A multivariate study of patients and nonpatients with irritable bowel syndrome," *Gastroenterology*, vol. 95, no. 3, pp. 701–708, 1988.

[15] G. R. Locke III, A. L. Weaver, L. J. Melton III, and N. J. Talley, "Psychosocial factors are linked to functional gastrointestinal disorders: a population based nested case-control study," *American Journal of Gastroenterology*, vol. 99, no. 2, pp. 350–357, 2004.

[16] A. Sattar, M. Salih, and W. Jafri, "Burden of common mental disorders in patients with functional dyspepsia," *Journal of the Pakistan Medical Association*, vol. 82, no. 12, pp. 995–997, 2010.

[17] V. Patel, J. Pereira, and A. H. Mann, "Somatic and psychological models of common mental disorder in primary care in India," *Psychological Medicine*, vol. 28, no. 1, pp. 135–143, 1998.

[18] R. M. Carney, K. E. Freedland, and A. S. Jaffe, "Insomnia and depression prior to myocardial infarction," *Psychosomatic Medicine*, vol. 52, no. 6, pp. 603–609, 1990.

[19] H. A. Naqvi and M. M. Khan, "Pathway to psychiatric care in Karachi," *Journal of the College of Physicians and Surgeons Pakistan*, vol. 16, no. 6, pp. 438–439, 2006.

[20] J. Arehart-Treichel, "Depression, migraines show strong but unexplained link," *Psychiatric News*, vol. 41, no. 1, p. 32, 2006.

[21] H. Naqvi and M. M. Khan, "Depression in primary care: difficulties and paradoxes," *Journal of the Pakistan Medical Association*, vol. 55, no. 9, pp. 393–398, 2005.

[22] I. Mirza and R. Jenkins, "Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review," *British Medical Journal*, vol. 328, no. 7443, pp. 794–797, 2004.

[23] N. J. Talley, P. M. Boyce, and M. Jones, "Predictors of health care seeking for irritable bowel syndrome: a population based study," *Gut*, vol. 41, no. 3, pp. 394–398, 1997.

[24] A. V. Chobanian, G. L. Bakris, H. R. Black et al., "The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report," *Journal of the American Medical Association*, vol. 289, no. 19, pp. 2560–2572, 2003.

[25] "Nervous System Disorders," in *Current Medical Diagnosis and Treatment*, vol. 29, McGraw–Hill Lang, New York, NY, USA, 29th edition, 2010.

[26] American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders, Text Revision*, American Psychiatric Association, Washington, DC, USA, 4th edition, 2000.

[27] H. S. Akiskal, "Toward a definition of generalized anxiety disorder as an anxious temperament type," *Acta Psychiatrica Scandinavica, Supplement*, vol. 98, no. 393, pp. 66–73, 1998.

[28] T. W. Harding, M. V. de Arango, J. Baltazar et al., "Mental disorders in primary health care: a study of their frequency and diagnosis in four developing countries," *Psychological Medicine*, vol. 10, no. 2, pp. 231–241, 1980.

[29] N. Husain, R. Gater, B. Tomenson, and F. Creed, "Comparison of the personal health questionnaire and the self reporting questionnaire in rural Pakistan," *Journal of the Pakistan Medical Association*, vol. 56, no. 8, pp. 366–370, 2006.

[30] A. Rahman, Z. Iqbal, W. Waheed, and N. Hussain, "Translation and cultural adaptation of health questionnaires," *JPMA. The Journal of the Pakistan Medical Association*, vol. 53, no. 4, pp. 142–147, 2003.

[31] S. V. Chincholikar, "Use of SRQ in Psychiatric Epidemiology," *Indian Journal of Community Medicine*, vol. 29, no. 4, pp. 344–349, 2004.

[32] T. Harpham, M. Reichenheim, R. Oser et al., "Measuring mental health in a cost-effective manner," *Health Policy and Planning*, vol. 18, no. 3, pp. 344–349, 2003.

[33] K. Saeed, R. Gater, A. Hussain, and M. Mubbashar, "The prevalence, classification and treatment of mental disorders among attenders of native faith healers in rural Pakistan," *Social Psychiatry and Psychiatric Epidemiology*, vol. 35, no. 10, pp. 480–485, 2000.

[34] D. B. Mumford, F. A. Minhas, I. Akhtar, S. Akhter, and M. H. Mubbashar, "Stress and psychiatric disorder in urban Rawalpindi: community survey," *British Journal of Psychiatry*, vol. 177, pp. 557–562, 2000.

[35] B. S. Ali, "Validation of an indigenous screening questionnaire for anxiety and depression in an urban squatter settlement of Karachi," *Journal of the College of Physicians and Surgeons Pakistan*, vol. 8, no. 5, pp. 207–210, 1998.

[36] B. S. Ali and S. Amanullah, "A comparative review of two screening instruments; the Aga Khan University anxiety and depression scale and the self reporting questionnaire," *Journal of the Pakistan Medical Association*, vol. 48, no. 3, pp. 79–82, 1998.

[37] EPI Info, *a Word Processing Database and Statistics Program for Public Health [Computer Program]. Version 6*, Center for Disease Control and Prevention, Atlanta, Ga, USA, 1996.

[38] S. S. Shah, S. J. Bhatia, and F. P. Mistry, "Epidemiology of dyspepsia in the general population in Mumbai," *Indian Journal of Gastroenterology*, vol. 20, no. 3, pp. 103–106, 2001.

[39] U. C. Ghoshal, P. Abraham, C. Bhatt et al., "Epidemiological and clinical profile of irritable bowel syndrome in India: report of the Indian Society of Gastroenterology Task Force," *Indian Journal of Gastroenterology*, vol. 27, no. 1, pp. 22–28, 2008.

[40] M. Solmaz, I. Kavuk, and K. Sayar, "Psychological factors in the irritable bowel syndrome," *European journal of medical research*, vol. 8, no. 12, pp. 549–556, 2003.

[41] A. D. Sperber, "The challenge of cross-cultural, multi-national research: potential benefits in the functional gastrointestinal disorders," *Neurogastroenterology and Motility*, vol. 21, no. 4, pp. 351–360, 2009.

[42] M. J. Gerson, C. D. Gerson, R. A. Awad et al., "An international study of irritable bowel syndrome: family relationships and mind-body attributions," *Social Science and Medicine*, vol. 62, no. 11, pp. 2838–2847, 2006.

[43] A. A. Gadit, "Psychiatry in Pakistan: 1947–2006: a new balance sheet," *Journal of the Pakistan Medical Association*, vol. 57, no. 9, pp. 453–463, 2007.

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Research Article

Irritable Bowel Syndrome and Gastrointestinal Parasite Infection in a Developing Nation Environment

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Postinfectious IBS is defined in the industrialized world as IBS onset following a sentinel gastrointestinal infection. In developing nations, where repeated bacterial and parasitic gastrointestinal infections are common, the IBS pathophysiology may be altered. Our aim was to investigate the relationship between intestinal parasite infection and IBS in the "nonsterile" developing world environment. IBS subjects were identified from a population-based sample of 1624 participants using the Rome II Modular Questionnaire. Stool samples from cases and randomly selected controls were examined for ova and parasites. Logistic regression models explored the relationship between IBS and parasite infection. The overall IBS prevalence among participants was 13.2% (9.3% males, 15.9% females). There was no difference in parasite carriage between IBS cases and controls, 16.6% versus 15.4% ($P = 0.78$), nor among IBS subtypes. The pathophysiology of post-infectious IBS may be altered in the developing world as compared to industrialized nations and warrants investigation.

1. Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder which affects approximately 12% of persons globally [1, 2]. Several studies have examined the prevalence of IBS in different geographic regions, and in general, have found the prevalence of IBS to be higher in industrialized nations and lower in developing nations [3, 4]. This may be due to differences in diagnostic criteria and their translations, health care access and use, and other factors which differ between countries [4]. In his review, Kang suggests additional differences in host genetics, diet, and health belief models may contribute to the variability in the prevalence of IBS between countries [4]. Also in this review, the paucity of IBS investigations from Latin America is highlighted.

Postinfectious IBS (PI-IBS) is defined as the onset of IBS following a sentinel gastrointestinal infection, particularly infectious gastroenteritis [5, 6]. The prevalence of PI-IBS following infectious gastroenteritis ranges from 4% to 31%, with a pooled incidence of 10% [7, 8]. PI-IBS has been predominantly described for residents of the industrialized world in two scenarios: traveler's diarrhea and gastroenteritis outbreaks. Following these intestinal infections, there is a higher prevalence of diarrhea-predominant IBS (IBS-D) symptoms. Multiple pathogens have been implicated in the development of IBS in the so-called "sterile" environments of developed nations, including *E. coli, C. jejuni,* and *S. sonnei* [9–12]. Not all studies support a causative role of infectious gastroenteritis [13]. A number of nonbacterial pathogens have also been implicated in PI-IBS, including viral and parasitic organisms [14–17]. Several parasites including *E. histolytica*, *Giardia* spp., *B. hominis,* and *Trichinella* spp. have been discussed as contributing factors to the development of IBS, though the relationship is less well defined [14–21].

While the precise pathophysiology of PI-IBS is unknown, suggested factors include altered serotonin signaling activity, inflammation, malabsorption, and small intestinal bacterial overgrowth [10–12, 22]. Although it is apparent that the majority of gastrointestinal infections do not result in IBS, the incidence of IBS after infection may provide insight into the etiology of the disease and the "hygiene hypothesis" [23].

The effect of gastrointestinal infections on the development of IBS is largely unexplored in the developing world. The developing world environment may be considered "nonsterile," with the majority of the population exposed to intermittent acute infections beginning in infancy, and a subset with chronic gastrointestinal infections [24, 25]. For example, in Mexico, the overall prevalence of infection with *E. histolytica/E. dispar* in pregnant women has been estimated to be between 22 and 35%, with 15% of their children also infected [26]. The concept of the sentinel infection to trigger PI-IBS may not be applicable and, in addition, would be difficult to ascertain.

We examined the relationship between IBS and parasite infection using a population-based case-control design in the "nonsterile" developing nation environment in western Nicaragua. In this setting, parasite carriage may serve as a surrogate for repeated exposures to gastrointestinal pathogens and infection. As described below, the unique Health and Demographic Surveillance Site in León, Nicaragua (HDSS-León) was used to select a random population-based sample for identification of IBS cases and healthy controls.

2. Materials and Methods

2.1. Setting. The Center for Epidemiology and Health (CIDS) within the University of Nicaragua, León (UNAN-León) maintains HDSS-León for the region with a sampled population of over 200,000. HDSS-León, established by CIDS in 1993, includes approximately 11,000 households and 55,000 individuals, or 30% of the population of León municipality [27]. This is the only Latin American member of the INDEPTH network, an international network of demographic surveillance population cohorts in developing nations [28]. The region's population is Hispanic Mestizo ethnic origin, with less than 10% from indigenous groups. Half of the population is under the age of 15. Nicaragua consistently ranks among the poorest countries in Latin America, with a per capita gross national income of US$1000 [29]. In addition, parasite infection is known to be high in the León province of western Nicaragua [25, 30].

2.2. Study Design. The study utilized a population-based, nested case-control design with household interviews. The cross-sectional survey of the functional gastrointestinal disorders was performed with randomly selected individuals ($n = 1624$) within the HDSS-León. IBS cases were identified using the Rome II Modular Questionnaire that has been previously translated into Spanish and validated for Mexico and Central America [31, 32]. IBS cases were further characterized using the Rome II criteria as IBS-D, constipation-predominant (IBS-C), and alternating/mixed (IBS-A), for those not fulfilling criteria for either of the above categories. Within this cross-sectional survey ($n = 1.642$), we conducted a nested case-control study of IBS cases and healthy controls ($n = 359$). Healthy controls without IBS were randomly selected from the cross-sectional survey participants in a 1 : 1 ratio for stool collection and related study data. Cases and controls were interviewed by study team physicians.

Socioeconomic status was assessed using a validated poverty index which was calculated using the United Nation's unsatisfied basic needs measurement, based on housing, sanitation, education, and employment [33–35] and validated in Nicaragua [36, 37]. Specific factors related to the environment that were examined included water source, toilet or latrine use, household construction, and neighborhood.

2.3. Laboratory Analysis. Laboratory stool analysis was performed in the UNAN-León Center for Infectious Disease Research, by methods previously described [38]. The stool specimens were collected in labeled plastic vials without preservatives and examined in less than two hours. Stool samples were subjected to macroscopic examination, to check the consistency and to evaluate for the presence of blood, mucus, or adult helminth parasites. Specimens were examined by direct microscopy with saline and iodine by microbiologists. In addition to direct microscopy of fresh smears, formalin ethyl acetate sedimentation technique was used for detection of cysts and eggs, iron hematoxylin staining for amebas and flagellates, and modified Ziehl-Neelsen staining for detection of enteric coccidia. No additional tests for viral and bacterial infections were performed. These university-based microscopy methods have been shown to be highly reproducible in Nicaragua, and with comparable sensitivity to PCR methodology for detection of *Entamoeba* spp. [38].

Parasites were classified as either pathogenic or commensal, based upon internationally accepted classification [39]. The *E. histolytica/E. dispar* complex was classified as commensal for the primary analysis, because the prevalence of *E. dispar* exceeds that of *E. histolytica* (5 : 1) in Nicaragua [38]. We further performed a sensitivity analysis classifying either of these amoebas instead as pathogenic. Since no difference was found in the prevalence of the *E. histolytica/E. dispar* complex between IBS and controls (see Section 3), the molecular differentiation of the two species was not performed. Subjects with pathogenic parasitic infection on stool exam were offered treatment with antiparasitic medications per the local standard of care.

2.4. Statistical Analysis. Data was analyzed using SPSS version 12.0 statistical software (Chicago, IL, USA). Mantel-Haenszel odds ratios were calculated to determine the association between IBS and parasite infection. Possible confounding factors, including age, gender, poverty index, household water source, latrine or toilet use, household construction, and neighborhood, were examined. The current study was approved by the institutional review boards of the University of North Carolina, Chapel Hill and UNAN-León.

Table 1: Summary of the study population.

	IBS cases ($N = 163$)	Controls ($N = 194$)	P value	Total ($N = 357$)
Gender				
Male	24.5% (40)	31.4% (61)	0.16	28.3% (101)
Female	75.4% (123)	68.6% (133)		71.7% (256)
Age (in years)				
18–34	39.9% (65)	37.6% (73)		38.7% (138)
35–54	47.2% (77)	49.7% (98)	0.83	49.0% (175)
55–66	12.9% (21)	11.8% (23)		12.3% (44)
Household water source				
Municipal supply[†]	97.5% (159)	97.4% (189)	0.98	97.5% (348)
Other	2.5% (4)	2.6% (5)		2.5% (9)
Sanitary conditions				
Toilet	58.2% (95)	60.3% (117)	0.85	59.4% (212)
Latrine or none	41.7% (68)	39.6% (77)		40.6% (145)
Poverty index				
Basic needs met	63.8% (104)	71.1% (138)	0.20	67.8% (242)
basic needs unmet	36.2% (59)	28.9% (56)		32.2% (115)

[†] Municipal water source refers to water delivery to the household or nearby community source for at least 4 hours per day.

3. Results

3.1. Characteristics of the Participants. The overall prevalence of IBS in the population-based cross sectional study was 13.2%, with the prevalence of 15.9% in females and 9.3% in males. The IBS subsets were nearly evenly distributed: IBS-D 25%, IBS-C 32%, and IBS-A 43%. The characteristics of the study population ($n = 357$) are presented in Table 1. The median age was 39.0 years old with a range of 18 to 66. In the households, 68% had their basic needs met, 28% lived in poverty, and 4.0% lived in extreme poverty. Nearly all subjects lived in moderate-to-severe poverty by developed nation standards. Forty-one percent used latrines or did not have household sanitary facilities.

3.2. Association between IBS and Parasite Infection. The overall prevalence of parasitic infection in the nested case-control study population was 16.0%. Of the 214 identified IBS cases, 163 stool samples adequate for examination were obtained. Evaluable stool samples were obtained from 194 controls. No statistically significant association was found between the presence of parasites upon stool examination and the presence of IBS. Specifically, 16.6% of IBS cases and 15.4% of controls tested positively for parasite infection. Those with IBS had the same odds of parasitic infection as the controls (OR = 1.09, 95% CI 0.62, 1.91). Furthermore, when broken down by individual parasites, none showed a significant association with IBS, having a range of ORs from 0.75 (95% CI 0.36, 1.57) to 6.12 (95% CI 0.71, 52.8) (Table 2). Lastly, we found no association between parasite infection and IBS in the IBS subgroups: IBS-D (OR = 0.73, 95% CI 0.21, 1.99) and IBS-C (OR = 1.46, 95% CI 0.63, 3.16).

When the parasites were classified into the pathogenic or commensal groups, neither of the two groups showed an association with IBS prevalence (Table 2). As noted, differentiation of *E. histolytica* and *E. dispar* was not performed, and the *E. histolytica/E. dispar* complex was classified as commensal. A sensitivity analysis, classifying the *E. histolytica/E. dispar* complex as pathogenic, also resulted in no association between parasite infection and IBS in either the pathogenic or commensal groups.

In addition to parasite presence, other possible confounding factors were analyzed including water source, sanitation (toilet or latrine use), household construction, neighborhood, and socioeconomic status (poverty index). There were no statistically significant differences between IBS cases and controls for water source, sanitation, housing construction, neighborhood, or overall poverty index; therefore, these factors were not included in the final logistic regression model.

4. Discussion

This study found a lack of an association between IBS and parasite infection in the developing nation environment of Nicaragua, Central America. This is the one of first studies to utilize a population-based sampling frame and Rome criteria assessment to examine the phenomenon of IBS in a "nonsterile" developing population, where repeated exposure to gastrointestinal pathogens is common. The overall prevalence of IBS based upon the Rome II criteria in our population-based study ($n = 1.642$) was 13.2%. This is comparable to the prevalence reported in the community-based study conducted in Mexico (16.0%) and in other countries as reported by Kang [4, 40]. Importantly, the current study identified IBS cases from the community, rather than from a health care setting, potentially removing selection bias and related confounding factors that may be associated with access and health care seeking behaviors. We found a similar prevalence of parasite infection between IBS cases and controls suggesting that gastrointestinal infection and

Table 2: Parasite carriage among IBS cases and healthy controls.

Characteristic	IBS cases ($N = 163$)	Healthy controls ($N = 194$)	Parasite carriage OR (95% CI)	Total subjects ($N = 357$)
Any parasite (N)	27	30	1.09 (0.62–1.91)	57
Pathogenic parasite (N)	9	8	1.36 (0.51–3.61)	17
Individual parasites (N)				
B. hominis †	13	20	0.75 (0.36–1.57)	33
G. lamblia ‡	5	7	0.85 (0.26–2.72)	12
E. coli	15	16	1.14 (0.55–2.39)	31
E. histolytica ‡/*dispar*	18	26	0.81 (0.43–1.53)	44
I. butschlii	7	6	1.41 (0.46–4.27)	13
E. nana	9	7	1.56 (0.57–4.29)	16
C. mesnili	5	1	6.12 (0.71–52.82)	6
T. trichiura ‡	3	1	3.62 (0.37–35.13)	4
A. lumbricoides ‡	1	0	—	1
H. nana ‡	1	0	—	1

(1) Mantel-Haenszel odds ratios (ORs) were calculated to determine the association between IBS and parasite infection. Factors such as age, gender, poverty index, household water source, latrine or toilet use, and neighborhood were not confounders and were not included in the final model.
(2) Individuals may have been infected with more than one parasite.
(3) Individual parasites include *Blastocystis hominis, Giardia lamblia, Entamoeba coli, Entamoeba histolytica, Entamoeba dispar, Iodamoeba butschlii, Endolimax nana, Chilomastix mesnili, Trichuris trichiura*, *Ascaris lumbricoides, Hymenolepis nana.*
† Pathogenicity depends on parasite load; classified as commensal for the analysis.
‡ Denotes pathogen.

specifically, parasite infection, is unlikely to be a significant attributable risk factor to the development of IBS.

Our findings of a 20.2% prevalence of *Entamoeba* spp., 3.0% prevalence of *G. lamblia,* 0.6% prevalence of *A. lumbricoides,* and 1.8% prevalence of *T. trichiura* among IBS cases are in agreement with other regional studies of parasite prevalence, including prior investigations in Nicaragua [25]. A study from Guatemala reported a 2.7% prevalence of *G. lamblia* and a similar prevalence for the combination of *T. solium*, *A. lumbricoides,* and *T. trichuria* in IBS [41]. However, our study differed from a study in Pakistan, which found a higher prevalence of *B. hominis* and *D. fragilis* among IBS cases as compared to controls [42]. A similar study from Thailand noted prevalent *B. hominis* infection, yet no difference between IBS subjects and controls (13.6% versus 20%; $P = 0.87$) [43]. Interestingly, in an investigation in Pakistan, wherein a cohort of IBS subjects was followed over 48 weeks with monthly stool exams, spontaneous clearance of *E. histolytica* was noted in a subset (4/22) yet without symptom improvement [44].

In industrialized nations, emerging evidence suggests that PI-IBS may account for a measureable percentage of the total burden of IBS in the community [7, 8]. While the specifics of the pathogen, severity, and duration of the infection play a role, a range of host factors are also responsible for the initiation and maintenance of IBS following enteritis. Host factors include host susceptibility genotypes, inflammatory response, and the psychosocial dynamic. In developing nations where water supplies, sanitation, and food hygiene are compromised, repeated episodes of gastroenteritis and chronic gastrointestinal infection begin in infancy. A segment of the IBS population may have the equivalent of PI-IBS by the western model, but without a "sentinel infection." Alternatively, the pathophysiology model for IBS in developing nations may have a different balance of factors. In fact, per the hygiene hypothesis, gastrointestinal pathogen exposure in childhood may provide an element of immune tolerance and/or be protective and preclude the development of IBS per the western model [23]. Preliminary data from an ongoing multinational internet survey is also supportive: 21% of IBS patients in North America and Northern Europe may be considered "postinfectious" as compared to 14% in the rest of the world [45]. It is clear that chronic colonization by pathogens and commensals, which are prevalent infections in tropical environments, serves to regulate gastrointestinal inflammation and the immune response. Important examples include helminth colonization and ulcerative colitis [46], and *H. pylori* and asthma [47]. Similar studies investigating the relationship between parasites and IBS are needed in the northern hemisphere.

The current study was strengthened by the use of a population-based study design with household interviews, which helps to address issues of selection and reporting bias present in clinic-based samples. In addition, Nicaragua is an appropriate setting for the study, as it consistently ranks among the poorest countries in Latin America. In spite of the large initial community sample, our investigation may not have been sufficiently powered to detect a difference in infection prevalence and further study may be warranted. Our study may have been limited by the focus upon parasitic rather than bacterial infections. Given the exposure to multiple episodes of all forms of gastroenteritis and health system access issues for the majority of subjects, recall bias would have precluded true assessment of past bacterial infections. In addition, it is suggested that parasite carriage is a reasonable surrogate for exposure to gastrointestinal pathogens in this setting. Lastly, parasites were classified

as commensal or pathogen based on their ability to cause clinical disease. As noted, the characterization of intestinal parasites did not include the differentiation of *E. histolytica* and *E. dispar,* although this did not appear to be a factor based upon our sensitivity analysis.

5. Conclusions

In this population-based study, a significant difference was not observed in the prevalence of intestinal parasite infection among patients with IBS compared with healthy controls in the developing nation setting of Nicaragua. The reality of frequent gastrointestinal infections, and the lack of a "sentinel infection," may suggest an alternate PI-IBS pathophysiology model in this setting and warrants investigation.

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References

[1] H. R. Mertz, "Irritable bowel syndrome," *The New England Journal of Medicine*, vol. 349, no. 22, pp. 2136–2146, 2003.

[2] Y. A. Saito, P. Schoenfeld, and G. R. Locke III, "The epidemiology of irritable bowel syndrome in North America: a systematic review," *American Journal of Gastroenterology*, vol. 97, no. 8, pp. 1910–1915, 2002.

[3] K. A. Gwee, "Irritable bowel syndrome in developing countries—a disorder of civilization or colonization?" *Neurogastroenterology and Motility*, vol. 17, no. 3, pp. 317–324, 2005.

[4] J. Y. Kang, "Systematic review: the influence of geography and ethnicity in irritable bowel syndrome," *Alimentary Pharmacology and Therapeutics*, vol. 21, no. 6, pp. 663–676, 2005.

[5] D. Y. Rhodes and M. Wallace, "Post-infectious irritable bowel syndrome," *Current Gastroenterology Reports*, vol. 8, no. 4, pp. 327–332, 2006.

[6] M. Thabane and J. K. Marshall, "Post-infectious irritable bowel syndrome," *World Journal of Gastroenterology*, vol. 15, no. 29, pp. 3591–3596, 2009.

[7] H. A. Halvorson, C. D. Schlett, and M. S. Riddle, "Postinfectious irritable bowel syndrome—a meta-analysis," *American Journal of Gastroenterology*, vol. 101, no. 8, pp. 1894–1942, 2006.

[8] M. Thabane, D. T. Kottachchi, and J. K. Marshall, "Systematic review and meta-analysis: the incidence and prognosis of post-infectious irritable bowel syndrome," *Alimentary Pharmacology and Therapeutics*, vol. 26, no. 4, pp. 535–544, 2007.

[9] J. K. Marshall, M. Thabane, A. X. Garg, W. Clark, J. Meddings, and S. M. Collins, "Intestinal permeability in patients with irritable bowel syndrome after a waterborne outbreak of acute gastroenteritis in Walkerton, Ontario," *Alimentary Pharmacology and Therapeutics*, vol. 20, no. 11-12, pp. 1317–1322, 2004.

[10] S. Ji, H. Park, D. Lee, Y. K. Song, J. P. Choi, and S. I. Lee, "Post-infectious irritable bowel syndrome in patients with Shigella infection," *Journal of Gastroenterology and Hepatology*, vol. 20, no. 3, pp. 381–386, 2005.

[11] R. C. Spiller, "Role of infection in irritable bowel syndrome," *Journal of Gastroenterology*, vol. 42, supplement 17, pp. 41–47, 2007.

[12] S. Parry and I. Forgacs, "Intestinal infection and irritable bowel syndrome," *European Journal of Gastroenterology and Hepatology*, vol. 17, no. 1, pp. 5–9, 2005.

[13] A. Ilnyckyj, B. Balachandra, L. Elliott, S. Choudhri, and D. R. Duerksen, "Post-traveler's diarrhea irritable bowel syndrome: a prospective study," *American Journal of Gastroenterology*, vol. 98, no. 3, pp. 596–599, 2003.

[14] K. A. Wensaas, N. Langeland, K. Hanevik, K. Mørch, G. E. Eide, and G. Rortveit, "Irritable bowel syndrome and chronic fatigue 3 years after acute giardiasis: historic cohort study," *Gut*, vol. 61, no. 2, pp. 214–219, 2012.

[15] D. Stark, S. van Hal, D. Marriott, J. Ellis, and J. Harkness, "Irritable bowel syndrome: a review on the role of intestinal protozoa and the importance of their detection and diagnosis," *International Journal for Parasitology*, vol. 37, no. 1, pp. 11–20, 2007.

[16] R. Spiller and K. Garsed, "Postinfectious irritable bowel syndrome," *Gastroenterology*, vol. 136, no. 6, pp. 1979–1988, 2009.

[17] J. K. Marshall, M. Thabane, M. R. Borgaonkar, and C. James, "Postinfectious irritable bowel syndrome after a food-borne outbreak of acute gastroenteritis attributed to a viral pathogen," *Clinical Gastroenterology and Hepatology*, vol. 5, no. 4, pp. 457–460, 2007.

[18] R. Hussain, W. Jaferi, S. Zuberi et al., "Significantly increased IgG2 subclass antibody levels to Blastocystis hominis in patients with irritable bowel syndrome," *American Journal of Tropical Medicine and Hygiene*, vol. 56, no. 3, pp. 301–306, 1997.

[19] M. D'Anchino, D. Orlando, and L. De Feudis, "Giardia lamblia infections become clinically evident by eliciting symptoms of irritable bowel syndrome," *Journal of Infection*, vol. 45, no. 3, pp. 169–172, 2002.

[20] J. Yakoob, W. Jafri, N. Jafri et al., "Irritable bowel syndrome: In search of an etiology: role of Blastocystis hominis," *American Journal of Tropical Medicine and Hygiene*, vol. 70, no. 4, pp. 383–385, 2004.

[21] M. Soyturk, H. Akpinar, O. Gurler et al., "Irritable bowel syndrome in persons who acquired trichinellosis," *American Journal of Gastroenterology*, vol. 102, no. 5, pp. 1064–1069, 2007.

[22] A. C. Ford, B. M. Spiegel, N. J. Talley, and P. Moayyedi, "Small intestinal bacterial overgrowth in irritable bowel syndrome: systematic review and meta-analysis," *Clinical Gastroenterology and Hepatology*, vol. 7, no. 12, pp. 1279–1286, 2009.

[23] F. Guarner, R. Bourdet-Sicard, P. Brandtzaeg et al., "Mechanisms of disease: the hygiene hypothesis revisited," *Nature Clinical Practice Gastroenterology and Hepatology*, vol. 3, no. 5, pp. 275–284, 2006.

[24] C. Ximénez, P. Morán, L. Rojas, A. Valadez, and A. Gómez, "Reassessment of the epidemiology of amebiasis: state of the

art," *Infection, Genetics and Evolution*, vol. 9, no. 6, pp. 1023–1032, 2009.

[25] A. Téllez, W. Morales, T. Rivera, E. Meyer, B. Leiva, and E. Linder, "Prevalence of intestinal parasites in the human population of León, Nicaragua," *Acta Tropica*, vol. 66, no. 3, pp. 119–125, 1997.

[26] S. Weingerz and R. Avila, "Asymptomatic invasive amebiasis in pregnant women," *Ginecologia y Obstetricia de Mexico*, vol. 51, no. 318, pp. 277–279, 1983.

[27] R. Peña, W. Pérez, M. Meléndez, C. Källestål, and L. A. Persson, "The nicaraguan health and demographic surveillance site, HDSS-León: a platform for public health research," *Scandinavian Journal of Public Health*, vol. 36, no. 3, pp. 318–325, 2008.

[28] INDEPTH demographic network, Indepth Health and Demographic Surveillance Sites, 2011, http://www.indepth-network.org/index.php?option=com_content&task=view&id=649&Itemid=5.

[29] World Bank, "Nicaragua at a glance," 2011, http://devdata.worldbank.org/AAG/nic_aag.pdf.

[30] B. Leiva, E. Clasdotter, E. Linder, and J. Winiecka-Krusnell, "Free-living acanthamoeba and Naegleria spp. amebae in water sources of León, Nicaragua," *Revista de Biologia Tropical*, vol. 56, no. 2, pp. 439–446, 2008.

[31] D. A. Drossman, E. Corazziari, N. J. Talley, G. Thompson, and W. Whitehead, Eds., *Rome II, The Functional Gastrointestinal Disorders*, Degnon Associates, Inc., McLean, Va, USA, 2000.

[32] M. Schmulson, O. Ortíz, M. Santiago-Lomeli et al., "Frequency of functional bowel disorders among healthy volunteers in Mexico City," *Digestive Diseases*, vol. 24, no. 3-4, pp. 342–347, 2006.

[33] United Nations Development Program, *Human Development Reports*, Oxford University Press, Oxford, UK, 1990.

[34] J. Boltvinik, *Pobreza y Necesidades Básicas. Conceptos y Métodos de Medición*, United Nations Development Program, Caracas, Venezuela, 1990.

[35] J. Blotvinik, "La medición de la pobreza en América Latina," *Comercio Exterior*, vol. 41, pp. 423–428, 1991.

[36] M. R. Renzi and S. Agurto, *Situación Económica y Social de León, Managua y Granada*, Fundación Internacional Para el Desafío Económico Global (FIDEG), Managua, Nicaragua, 1993.

[37] M. R. Renzi and S. Agurto, *Mercado Laboral y Condiciones de Vida de la Población Urbana de Managua, León y Granada. Agosto-Diciembre 1992*, Fundación Internacional Para el Desafío Económico Global (FIDEG), Managua, Nicaragua, 1993.

[38] B. Leiva, M. Lebbad, J. Winiecka-Krusnell, I. Altamirano, A. Tellez, and E. Linder, "Overdiagnosis of entamoeba histolytica and entamoeba dispar in Nicaragua: a microscopic, triage parasite panel and PCR study," *Archives of Medical Research*, vol. 37, no. 4, pp. 529–534, 2006.

[39] Centers for Disease Control, "Parasites of the Intestinal Tract," 2011, http://dpd.cdc.gov/dpdx/HTML/Para_Health.htm.

[40] A. Lopez-Colombo, D. Bravo-Gonzáles, A. Corona-Lopez et al., "First community-based study of functional gastrointestinal disorders (FGID) in México using the Rome II modular questionnaire," *Gastroenterology*, vol. 130, supplement 2, p. A508, 2006.

[41] L. Bujanda, M. A. Gutiérrez-Stampa, C. H. Caballeros, and M. E. Alkiza, "Gastrointestinal disorders in Guatemala and their relation with parasitic infections," *Anales de Medicina Interna*, vol. 19, no. 4, pp. 179–182, 2002.

[42] J. Yakoob, W. Jafri, M. A. Beg et al., "Blastocystis hominis and Dientamoeba fragilis in patients fulfilling irritable bowel syndrome criteria," *Parasitology Research*, vol. 107, no. 3, pp. 679–684, 2010.

[43] A. Tungtrongchitr, S. Manatsathit, C. Kositchaiwat et al., "Blastocystis hominis infection in irritable bowel syndrome patients," *Southeast Asian Journal of Tropical Medicine and Public Health*, vol. 35, no. 3, pp. 705–710, 2004.

[44] P. Sinha, U. C. Ghoshai, G. Chouduri et al., "Does Entamoeba histolytica cause irritable bowel syndrome?" *Indian Journal of Gastroenterology*, vol. 16, no. 4, pp. 130–133, 1997.

[45] R. Spiller, T. Card, F. Mearin et al., "Incidence and characteristics of postinfectious IBS (PI-IBS): a multinational internet survey," *Gut*, vol. 59, supplement 3, p. A32, 2010.

[46] M. J. Broadhurst, J. M. Leung, V. Kashyap et al., "IL-22+ CD4+ T cells are associated with therapeutic Trichuris trichiura infection in an ulcerative colitis patient," *Science Translational Medicine*, vol. 2, no. 60, Article ID 60ra88, 2010.

[47] Y. Chen and M. J. Blaser, "Helicobacter pylori colonization is inversely associated with childhood asthma," *Journal of Infectious Diseases*, vol. 198, no. 4, pp. 553–560, 2008.

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Clinical Study

Benefits from Long-Term Treatment in Irritable Bowel Syndrome

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It is known that irritable bowel syndrome (IBS) is a chronic disease of cyclic nature characterized by recurrent symptoms. IBS patients should receive, as initial therapeutic approach a short course of treatment which, if effective, has the additional value of confirming the diagnosis. Long-term treatment should be reserved to diagnosed IBS patients with recurrent symptoms. Clinical trials with stabilized therapies and new active treatments showed an improvement of the symptoms over placebo that is often time-dependent but with high relapse rates (around 40%–50% when stopping treatment). Relapse is not always immediate after stopping treatment and the recent data from OBIS trial with otilonium bromide or with psychotherapy, showed that due to different chemico-physical characteristics of the drugs or the psychosomatic impact to the disease not all treatment gave the same relapsing rate if compared to placebo. Results of IBS clinical trials with different therapies tailored to the patient needs indicate that a cyclic treatment therapy is advisable to counteract the nature of the disease.

1. Natural History of IBS

In order to determine whether short- or long-term treatment is needed for irritable bowel syndrome (IBS), it is important to know the natural history of this disease. Various studies have looked at this. A Swedish group of researchers used a validated questionnaire to assess the course of IBS in over 1,000 patients with symptomatic IBS at the index assessment [1]. The questionnaire was administered again 1 and 7 years later, and at both time-points more than 50% of the people were still symptomatic with IBS (Figure 1). A further 25% of the patients had minor IBS symptoms, and the remaining had no longer symptoms. Similar results emerged from a survey in Olmsted County in a population of 1365 humans from which 166 were diagnosed as IBS patients [2]. In this case the follow-up was 12 years but again just over a quarter of the patients became symptom-free, whereas the remaining still had IBS symptoms. An international study followed changes in symptoms in a shorter time frame (12 weeks; [3]). Patients used an interactive telephone data entry system to report daily symptoms. The presence and duration of individual symptoms and their concomitant occurrence were determined on a total of 59 IBS patients. The main symptoms, such as pain, bloating, and change in stool form, were present in about 20% of the days. The mean duration of the symptoms was about 5 days for pain and bloating and between 1 and 2 days for the other symptoms. These results were confirmed in a large European study in which it was found that IBS patients were symptomatic for about one quarter of the days in a month [4]. Ford et al. [5] reported that of the 1402 individuals symptomatic at baseline, 404 (29%) remained in the same subgroup at 10 years while a large proportion of other patients changed subgroups altering their predominant symptoms and developing dyspepsia or gastrooesophageal reflux diseases. Symptom stability was more likely in males and older subjects.

Indeed, there is strong evidence that the pattern of IBS symptoms is cyclical; more than half of IBS patients is still symptomatic after up to 10 years, and symptoms wax and wane within days to weeks [6].

2. Symptom Course during and Relapse Rate after 3 Months of Treatment

Although IBS is clearly a chronic disease, the initial therapeutic approach is to give a short course of treatment (often 3 months), which if effective has the additional value of confirming the diagnosis. The symptom course during 3 months

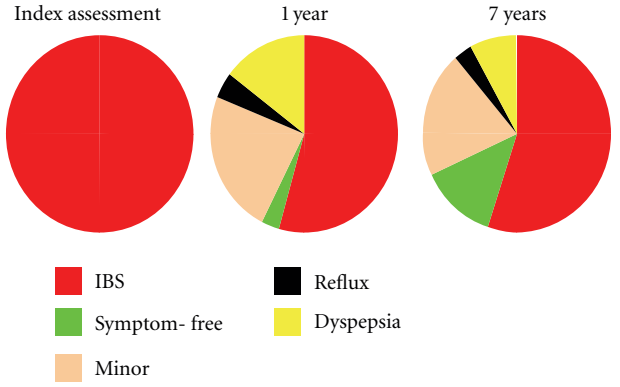

Figure 1: Representative diagram of the stability over time of IBS: percentage of the patients reporting IBS after 1 and 7 years from the first interview. Modified from [1].

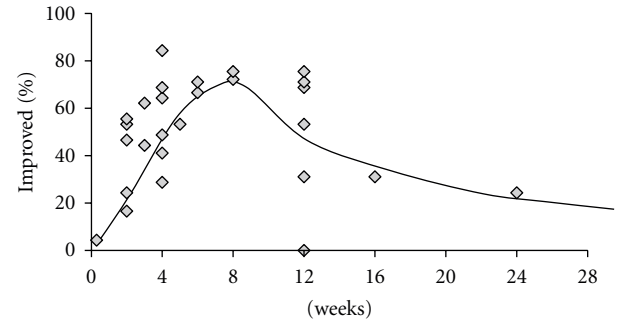

Figure 2: Placebo response plotted against length of trial for 27 randomised controlled trials performed during 1976–1998. There are not enough data points between 3–6 months, but it appears that the placebo response increases and then decreases with time, peaking at 8 weeks. Modified from [7].

of treatment and the relapse rate after such treatment have been revealed by the results of several drug trials.

A recent phase II study performed with linaclotide, an agonist of guanylate cyclase-C for the treatment of IBS patients with constipation (C), showed that all the doses utilised improved abdominal pain compared with placebo along the improvement of other intestinal habits [12]. The study was carried out on a total of 420 C-IBS and for a period of 12 weeks. The symptoms were progressively improved during the treatment time but their observation, 2 weeks after the treatment, revealed the return to baseline levels [12]. Lubiprostone, a prostaglandin E1 derivative that activates epithelial chloride channels and approved by FDA on 2008, has been tested in women with C-IBS. In one of the 3-month phase III trial ($n = 436$; [13]) the efficacy of this new drug was demonstrated over placebo group but at the conclusion of the 4-week randomised withdrawal period conducted in overall responders, 38% of patients who were randomised to continue lubiprostone and 40% of those who were randomised to placebo were reported to be monthly responders showing any difference between active treatment and placebo in this period [14].

In another IBS trial, patients were treated with the spasmolytic otilonium bromide or placebo for 4 months and the main symptoms were recorded. Not surprisingly, there were improvements in both groups, but the therapeutic gain (i.e., the difference between the improvements produced by otilonium bromide and placebo) persisted each month of treatment in terms of responder rate [15]. A similar schedule was applied for another recent study, and the results obtained on the effect of otilonium on pain frequency and bloating were found significant, and these symptoms improved progressively during the study [9]. This means that therapeutic gain is not limited to the first few weeks of treatment and it may be worthwhile continuing treatment even if it is not immediately successful. On the other hand, IBS trials are subjected to high placebo effect, typically between 30 and 60%, and this makes difficult to detect the therapeutic gain and interpretation of the results [7, 16, 17]. Two meta-analyses have shown that stringent entry criteria and an increased number of office visits are factors able to decrease the placebo response in a clinical trial [16, 17]. Being the psychosomatic part of the IBS, an important side of the disease, the reassuration and patient-practitioner relationship can give positive results. As seen in Figure 2, when the placebo response is plotted against the length of the study, a parabolic curve is drawn with the maximum of placebo response at around 6–8 weeks and a clear decline after approximately 12 weeks [7]. Therefore the placebo-controlled trials in IBS shall be realised with a time period of the active treatment superior to the 8 weeks as stated since from Rome II criteria definition [18].

In another study, 623 patients were assigned to treatment with alosetron, a 5HT-3 antagonist used for diarrhoea (D) predominant IBS, or with the spasmolytic mebeverine for 3 months [19]. Symptoms recurred in both treatment groups, during the 4-week follow-up period, with the relapse rate being between 30–45%. The patients who did not relapse in this period may have relapsed later or had a spontaneous improvement, compatible with the above described natural history of IBS. The relapse rate was also recorded in a German study of patients with C-IBS treated with 5-HT4 agonist tegaserod [20]. The study was carried out on more than 300 patients, and the primary efficacy parameter was the weekly satisfactory relief of the symptoms over the past week. Patients who responded to a 3-month course of this drug were taken off the medication and followed for 1 to 2 months. If symptoms recurred, they were retreated [8]. During the treatment period symptoms improved progressively. If treatment was withdrawn, the symptoms recurred and if treatment was restarted, the symptoms improved again (Figure 3). The relapse rate in the first month of treatment withdrawal exceeded 50%. Unfortunately in this trial the placebo response was not considered, and we cannot know the real therapeutic gain obtained during the follow-up period.

In this regard new findings come from the above-cited OBIS study of Clavè et al. [9] with otilonium bromide. After 12 weeks of treatment, both patients treated with the active treatment ($n = 82$) or those with placebo ($n = 80$) were followed for 3, 6, or 10 weeks. Only successful treated patients

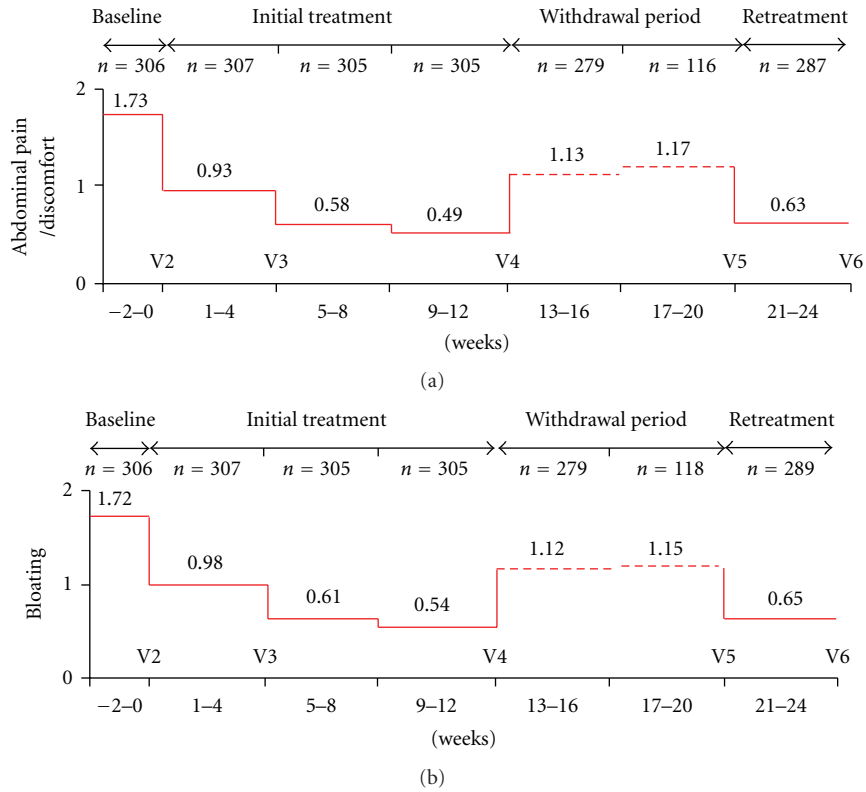

Figure 3: Mean abdominal pain/discomfort score (a) and bloating score (b) in patients cohort enrolled in retreatment phase with tegaserod. Modified from [8].

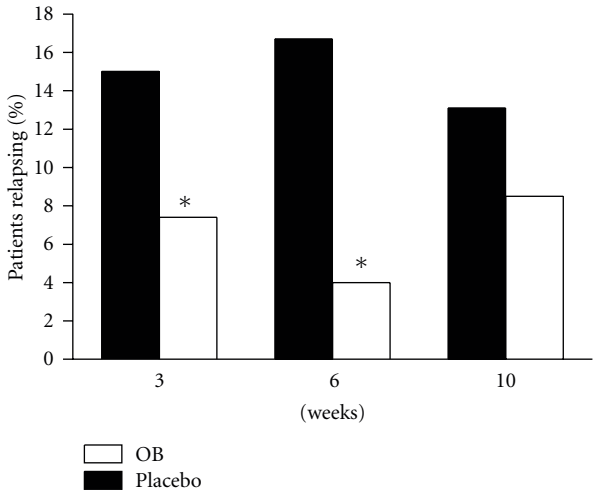

Figure 4: Percentage of the patients relapsing during the follow-up treatment free-period (at 3, 6, and 10 weeks) after 12 weeks treatment with placebo or otilonium bromide. $^*P < 0.05$ as compared to respective placebo group. From OBIS trial [9].

were eligible for this follow-up period. The results indicate the loss of therapeutic effect of placebo and the persistence of the effect of otilonium bromide since the percentage of relapsing patients at 3 and 6 weeks was significantly higher in the placebo group (Figure 4). Probably the chemicophysical characteristics of this drug and its affinity for colonic smooth muscle [21] may be factors influencing the extension of the benefits due to the treatment that was not observed with other drugs.

In summary, the therapeutic gain from active treatment may extend beyond 4 weeks, but relapse rates are high (around 40% when stopping treatment after 3 months); relapse is not always immediate after stopping treatment.

3. Symptom Course and Relapse Rate after One Year of Treatment

Other studies have determined the effect of long-term treatment on the symptom course and relapse rate of IBS. In a continuation of the study with tegaserod above cited [8], the therapeutic gain was maintained over the entire 1-year period of active treatment in a total of 451 C-IBS patient who completed the trial [22]. Another study using otilonium bromide has prolonged the active treatment up to a period of 2 years [10]. In this study otilonium was compared to fiber-rich diet in 114 patients suffering from IBS. Both abdominal pain and the intestinal function improved (Figure 5) progressively during the study confirming that the long-term treatment is useful and particularly with the use of safe drugs such as otilonium that thanks to its physico-chemical characteristics cannot be absorbed by the systemic circulation and act locally in the gut like the majority of

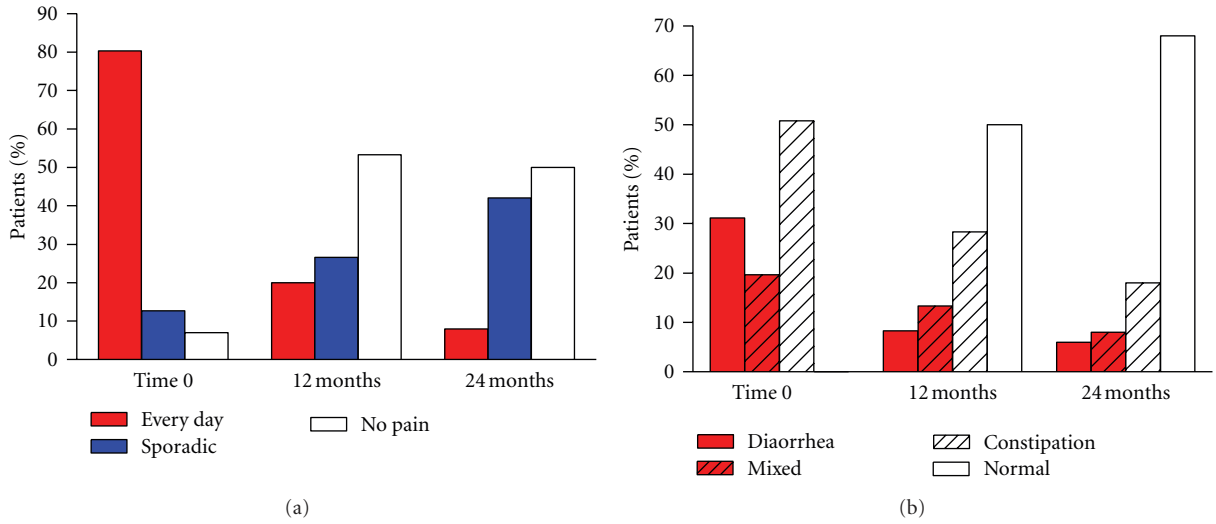

Figure 5: Effect of long-term treatment with otilonium bromide on pain episodes (a) and bowel habits (b) reported by patients. Modified from [10].

quaternary ammonium derivatives [21]. In another long-term study with the use of alosetron, 714 women with severe D-IBS were treated [11]. Randomised patients received either alosetron 1 mg ($n = 351$) or placebo ($n = 363$) twice a day during a 48-week double-blind study. The primary endpoint was the 48-week average rate of adequate relief of IBS pain and discomfort. Alosetron-treated patients had significantly greater adequate relief than placebo-treated patients ($P < 0.05$) in 9 of 12 months and significantly greater urgency control ($P < 0.001$) every month (Figure 6). Placebo effect peaked after 1 month of treatment and was stable for the other months at around 40%. It is noteworthy that when treatment was stopped, relapse occurred in nearly half of the patients after 1 month of observation.

The benefit of active treatment can be maintained for up to 1 year or more, but the relapse rate after treatment withdrawal following long-term therapy (1-year) is still high, being around 40%.

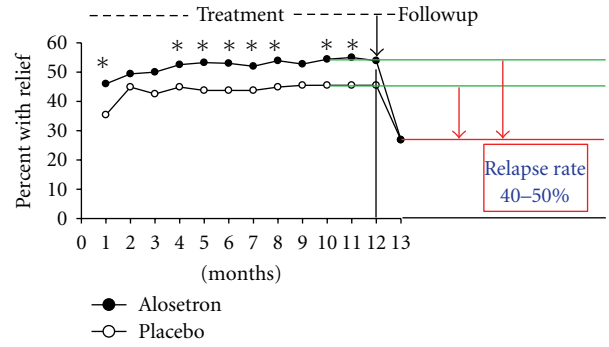

Figure 6: Effect of 1-year treatment with alosetron or placebo and percentage of patients with adequate relief after 1 month of followup. $^*P < 0.05$ as compared to respective placebo group. Modified from [11].

4. Symptom Course during and after Psychotherapy

Interestingly, the symptom course and relapse pattern after psychotherapy seem to differ from those after drug treatment. In one trial, 101 IBS patients received standard medical therapy with or without psychotherapy administered over a 3-month period [23]. During the 3-month intervention period, the improvement was greater in the psychotherapy group than that in the control group. Subsequently, in a 1-year treatment-free followup, the improvement continued in the psychotherapy group, whereas symptoms recurred in the controls, returning to their initial state.

5. Approach to the Patient

The type of IBS treatment must be tailored to patients' needs. Some patients require only "single-shot" treatment. They have symptoms for 1 or 2 days and do not need an entire treatment course. Others have symptoms for a couple of days or weeks and need a course of treatment. Yet others have more or less continuous symptoms and need long-term treatment. Not all types of treatments are suitable for all applications. Spasmolytics, laxatives, and loperamide are suited for all three types of treatment: single-shot treatment, a limited course of treatment, and a long-term treatment. Prokinetics, on the other hand, are not suitable for "single-shot" treatment—they need some days to work. Antidepressants must be given for some months or even years with a look to their potential side effects. Finally, psychotherapy is administered over a couple of weeks, but it is not usually continued for months or years.

6. Short- and Long-Term Treatment: Advantages

There are advantages of both short-term and long-term treatment. The arguments in favour of long-term treatment are that more than half of IBS patients continue to have

symptoms over many years, and the therapeutic gain of a pharmacological treatment continues for weeks or months. The relapse rate after stopping treatment is high (around 50%). Furthermore, some treatments require quite a long time to work. The arguments in favour of a short-term treatment are that about half of the patients improve over time and do not, therefore, need prolonged treatment. Although the relapse rate after treatment suspension is high, about 50% of patients do not relapse and most relapses do not occur immediately, a treatment-free interval can be gained. Some treatments, such as psychotherapy, can have long-lasting effects. The different dimensions of symptoms (intensity, frequency, and specificity) in a given patient also determine the best therapeutic approach. For example, a symptom may be of mild, moderate, or severe intensity, requiring only reassurance in some patients, an intervention in others, or in the most severe cases, multimodal intervention. Likewise, occasional, intermittent, or continuous symptoms will dictate whether on-demand treatment, a limited course of treatment or continuous treatment is necessary. The specific symptom will govern the choice of the appropriate drug. In conclusion, the drug of first choice is selected based on the dominant symptom. If this treatment is unsuccessful, the drug can be changed. If the treatment is successful, it can be suspended after a limited course. If a relapse occurs, treatment should be resumed with the same drug. If, however, the patient remains in remission he or she will not receive unnecessary treatment.

References

[1] L. Agréus, K. Svärdsudd, N. J. Talley, M. P. Jones, and G. Tibblin, "Natural history of gastroesophageal reflux disease and functional abdominal disorders: a population-based study," *The American Journal of Gastroenterology*, vol. 96, no. 10, pp. 2905–2914, 2001.

[2] S. L. S. Halder, G. R. Locke III, C. D. Schleck, A. R. Zinsmeister, L. J. Melton III, and N. J. Talley, "Natural history of functional gastrointestinal disorders: a 12-year longitudinal population-based study," *Gastroenterology*, vol. 133, no. 3, pp. 799–807, 2007.

[3] B. Hahn, M. Watson, S. Yan, D. Gunput, and J. Heuijerjans, "Irritable bowel syndrome symptom patterns: frequency, duration, and severity," *Digestive Diseases and Sciences*, vol. 43, no. 12, pp. 2715–2718, 1998.

[4] A. P. S. Hungin, P. J. Whorwell, J. Tack, and F. Mearin, "The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects," *Alimentary Pharmacology & Therapeutics*, vol. 17, no. 5, pp. 643–650, 2003.

[5] A. C. Ford, D. Forman, A. G. Bailey, A. T. R. Axon, and P. Moayyedi, "Fluctuation of gastrointestinal symptoms in the community: a 10-year longitudinal follow-up study," *Alimentary Pharmacology & Therapeutics*, vol. 28, no. 8, pp. 1013–1020, 2008.

[6] G. Ragnarsson and G. Bodemar, "Pain is temporally related to eating but not to defaecation in the irritable bowel syndrome (IBS). Patients' description of diarrhoea, constipation and symptom variation during a prospective 6-week study," *European Journal of Gastroenterology and Hepatology*, vol. 10, no. 5, pp. 415–421, 1998.

[7] R. C. Spiller, "Problems and challenges in the design of irritable bowel syndrome clinical trials: experience from published trials," *The American Journal of Medicine*, vol. 107, no. 5, pp. 91S–97S, 1999.

[8] S. Müller-Lissner, G. Holtmann, P. Rueegg, G. Weidinger, and H. Löffler, "Tegaserod is effective in the initial and retreatment of irritable bowel syndrome with constipation," *Alimentary Pharmacology & Therapeutics*, vol. 21, no. 1, pp. 11–20, 2005.

[9] P. Clavé, M. Acalovschi, J. K. Triantafillidis et al., "On behalf of the OBIS Study Investigators: randomised clinical trial: otilonium bromide improves frequency of abdominal pain, severity of distension and time to relapse in patients with irritable bowel syndrome," *Alimentary Pharmacology & Therapeutics*, vol. 34, no. 4, pp. 432–442, 2011.

[10] M. Villagrasa, J. Boix, P. Humbert, and J. C. Quer, "Aleatory clinical study comparing otilonium bromide with a fibre-rich diet in the treatment of irritable bowel syndrome," *Italian Journal of Gastroenterology*, vol. 23, no. 8, supplement 1, pp. 67–70, 1991.

[11] W. D. Chey, W. Y. Chey, A. T. Heath et al., "Long-term safety and efficacy of alosetron in women with severe diarrhea-predominant irritable bowel syndrome," *The American Journal of Gastroenterology*, vol. 99, no. 11, pp. 2195–2203, 2004.

[12] J. M. Johnston, C. B. Kurtz, J. E. MacDougall et al., "Linaclotide improves abdominal pain and bowel habits in a phase IIb study of patients with irritable bowel syndrome with constipation," *Gastroenterology*, vol. 139, no. 6, pp. 1877–1886, 2010.

[13] N. J. Carter and L. J. Scott, "Lubiprostone: in constipation-predominant irritable bowel syndrome," *Drugs*, vol. 69, no. 9, pp. 1229–1237, 2009.

[14] W. D. Chey, R. J. Saad, R. M. Panas, A. Wable, and R. Ueno, "Discontinuation of lubiprostone treatment for irritable bowel syndrome with constipation is not associated with symptom increase or recurrence: results from a randomised withdrawal study," *Gastroenterology*, vol. 134, no. 4, supplement 1, p. A401, 2008.

[15] M. Glende, A. M. Morselli-Labate, G. Battaglia, and S. Evangelista, "Extended analysis of a double-blind, placebo-controlled, 15-week study with otilonium bromide in irritable bowel syndrome," *European Journal of Gastroenterology and Hepatology*, vol. 14, no. 12, pp. 1331–1338, 2002.

[16] T. J. Kaptchuk, J. M. Kelley, L. A. Conboy et al., "Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome," *British Medical Journal*, vol. 336, no. 7651, pp. 999–1003, 2008.

[17] A. C. Ford and P. Moayyedi, "Meta-analysis: factors affecting placebo response rate in the irritable bowel syndrome," *Alimentary Pharmacology & Therapeutics*, vol. 32, no. 2, pp. 144–158, 2010.

[18] E. Corazziari, P. Bytzer, M. Delvaux et al., "Consensus report: clinical trial guidelines for pharmacological treatment of irritable bowel syndrome," *Alimentary Pharmacology & Therapeutics*, vol. 18, no. 6, pp. 569–580, 2003.

[19] R. H. Jones, G. Holtmann, L. Rodrigo et al., "Alosetron relieves pain and improves bowel function compared with mebeverine in female nonconstipated irritable bowel syndrome patients," *Alimentary Pharmacology & Therapeutics*, vol. 13, no. 11, pp. 1419–1427, 1999.

[20] H. Nyhlin, C. Bang, L. Elsborg et al., "A double-blind, placebo-controlled, randomised study to evaluate the efficacy, safety and tolerability of tegaserod in patients with irritable bowel syndrome," *Scandinavian Journal of Gastroenterology*, vol. 39, no. 2, pp. 119–126, 2004.

[21] S. Evangelista, "Quaternary ammonium derivatives as spasmolytics for irritable bowel syndrome," *Current Pharmaceutical Design*, vol. 10, no. 28, pp. 3561–3568, 2004.

[22] S. Müller-Lissner, M. A. Kamm, A. Musoglu, D. L. Earnest, C. Dunger-Baldauf, and M. A. Shetzline, "Safety, tolerability, and efficacy of tegaserod over 13 months in patients with chronic constipation," *The American Journal of Gastroenterology*, vol. 101, no. 11, pp. 2558–2569, 2006.

[23] J. Svedlund, I. Sjödin, J. Ottosson, and G. Dotevall, "Controlled study of psychotherapy in irritable bowel syndrome," *The Lancet*, vol. 2, no. 8350, pp. 589–592, 1983.

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Review Article

The Importance of Relationships in Patients with Irritable Bowel Syndrome: A Review

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Chronic illnesses such as irritable bowel syndrome are not experienced by patients in isolation. They live in a context of relationships, including spouses and partners, other family members, friends and business associates. Those relationships can have an effect, both positive and negative, on the course of illness and may also be affected by the experience of living with a chronic illness like IBS. We review the general literature regarding the effect of relationship factors on chronic illness followed by a focus on IBS symptomatology. We then discuss the challenges experienced by partners of IBS patients, followed by the effects of spousal violence, the particular relationship of mothers with IBS and their children, the effects of social support, and the importance of family dynamics and IBS. The final segment includes conclusions and recommendations. The topic, relationships and IBS, may have a significant effect on the lives of IBS patients and deserves more attention than it has received.

1. Introduction

Irritable bowel syndrome (IBS) is recognized as an illness in which symptoms may be caused by biological, psychological, and social factors. This paper will focus on the effect of a patient's relationships (family, friends, and work) on the IBS illness experience. This is a subject that has not received sufficient attention in the medical literature. IBS does not occur in a vacuum but in a context of interactions with others. Being aware of those interactions, by the patient and by the physician, may improve patient care.

2. Relationships and Health

There is an extensive literature regarding the effect of intimate relationships on health status. An excellent review of marriage and health by Kiecolt-Glaser and Newton [1] describes a number of conditions such as rheumatoid arthritis and hypertension as well as immunological function that may be affected directly by a marital relationship. Of course, this effect may be both positive and negative. Hostile communication in marriage appears to have a deleterious effect on health, in contrast to positive or problem-solving behavior [2]. Effects are more significant for women than for men. For example, one study explored the effect of marital discord on mortality and found that equality in decision making and companionship in marriage were protective against mortality in women, while there was no such effect in men [3]. Why might women be more vulnerable to the effects of conflict in marriage than men? Women are more focused on the relational aspects of marriage than men and are more attuned to its emotional quality. Thus, they are more greatly affected by hostility and problems within a marriage [4]. Being unhappy in marriage may result in psychological problems such as depression, which may adversely affect health status [5]. This effect appears to be "bidirectional" with poor marriages increasing depression and depression decreasing the quality of the marriage [6].

Pain is one of the dominant symptoms of IBS. Studies of patients with low-back pain suggest that the relationship between pain solicitousness on the part of a spouse may have beneficial effects in a happy marriage but adverse

effects in an unhappy marriage [7]. Open communication is extremely important in relation to pain management. A coping skills training program for couples focused on women suffering from arthritic knee pain which emphasized communication about the illness experience, resulted in less physical disability and pain behavior in the wife after one year, compared to a control group [8].

2.1. The IBS Patient and Family Relationships. The association between the quality of intimate relationships and the severity of IBS symptoms has been studied utilizing the Quality of Relationship Inventory (QRI), a validated 25-question self-report measure [9]. The QRI has three stems, support, depth, and conflict. It was included in an international survey that addressed psychosocial cross-cultural issues in IBS [10]. The eight-country survey included New York City, Mexico City, Montreal, England, Bari, Italy, Beersheva, Israel, Kolkata, India, and Beijing, China. 239 patients completed four questionnaires including the QRI, a Mind-Body Attribution Scale, an SF-36 quality of life scale, and the Bowel Symptom Scale (BSS). The BSS Likert scale included self-report of the major symptoms of IBS, abdominal pain, diarrhea, constipation, and bloating. In one report, patient and physician SSS scores were compared and there was no significant difference [11]. QRI results for support, depth, and conflict were correlated with BSS symptom severity. The hypothesis was that support and depth would be positive attributes, while conflict would have a negative impact on IBS.

The results confirmed the hypothesis. Aggregate results for all eight study sites showed that relationship support and depth correlated with lower symptom scores ($P < .01$). In contrast, relationship conflict correlated with higher symptom scores ($P < .001$). The support and depth results can be interpreted in two ways. Clearly, support and depth may be beneficial to the patient and lead to lower symptom scores. However, a patient with lower scores may elicit less anxiety or distress from intimate others, which could access greater support and depth of connection. Through multiple regression analysis, it was found that conflict was a unique predictor of higher scores ($P = .01$). This result is consistent with the marital studies mentioned above but this was the first publication to show an effect of relationship quality on symptom severity in IBS.

The strength of this study included the relatively large number of subjects and the strength of the statistically significant differences. A possible weakness was the inclusion of IBS patients from many different geographic locations where untested variables may have varied considerably, affecting relationship quality in different ways. Also, most patients were seen at tertiary centers, so the results may not apply to nonconsulters with milder forms of IBS.

The Quality of Relationship Inventory has been used in one other IBS study, in an attempt to see whether relationship issues might affect response to treatment. 75 IBS patients entered a biweekly seven session group of IBS hypnotherapy treatment program and completed the QRI before initiation of therapy [12]. Treatment consisted of a gut-focused hypnotherapy protocol developed by Whorwell et al. [13] and modified by Palsson [14]. The QRI was administered to see whether support, depth, or conflicted intimate relationships might impact the responsiveness of a patient to hypnotherapy in a group setting. The hypothesis was that relationship support and depth might enhance responsiveness to hypnotherapy in a group setting, while conflict might have a negative impact. The patients were followed for one year after the final therapy session. They completed the IBS Symptom Severity Scale (SSS) [15] before treatment began and twelve months later. The SSS measures improvement or worsening of symptoms at the one-year mark was correlated with the QRI results. Contrary to the hypothesis, relationship conflict correlated significantly with improvement in symptom score ($P = .07$).

While this might seem counterintuitive, it is possible that patients experiencing conflict in their personal relationships may represent a group of patients who can benefit from the calming effect of hypnotherapy, reducing their sensitivity to conflict. In addition, they might have found the supportive environment of the group process to be beneficial, making them more responsive to hypnotherapeutic ideation.

Strengths of this study included a relatively large number of subjects, long-term followup, and a high return rate (>90%) of questionnaires at the one-year mark. Weaknesses included lack of a control group without hypnotherapy and the fact that relationship quality was a secondary goal of the study.

2.2. Partners and IBS. The focus of another research study was the degree of burden experienced by the partner of an IBS patient. Wong et al. [16] administered the Zarit Burden Interview as well as the Relationship Satisfaction Scale to 152 partners (mostly male) of IBS patients. A healthy control partner population was included in this study. The goal was to determine the degree of experienced burden, how burden was affected by severity of the patient's symptoms, and whether relationship satisfaction and sexual satisfaction were also affected by having a partner with IBS. Results showed that burden scores for IBS partners were double the score of a control partner population ($P = .0002$) and were significantly correlated with disease severity in the IBS partner. Partner satisfaction and sexual satisfaction also correlated significantly with burden scores, but this was found in the control population as well, so this is not unique to IBS.

In one other report, 3090 subscribers to an IBS publication, 86% of whom were diagnosed with IBS by their physician, were mailed a questionnaire that included questions about personal relationships [17]. Of the 1595 subjects who responded, 75% were either married or cohabiting. Of that population, 6% felt that having IBS affected their partner's love and consideration for them, 19% felt that their partners had difficulties with their physical relationship, and 45% thought that IBS interfered with their sex life. These results, though representing a large sample, must be read with caution because there was only a 50% response rate and IBS diagnosis was based on self-report without verification.

2.3. The IBS Patient and Spousal Violence. A unique population study in Nicaragua examined the effect of spousal violence (sexual and physical), on the prevalence of IBS [18]. A number of studies have demonstrated that a childhood history of sexual abuse is more common in patients with IBS than in controls [19]. It should be noted that this is not unique to IBS since the same association has been reported in patients with inflammatory bowel disease [20]. In the Nicaraguan study, a randomly selected representative sample of 960 women were surveyed utilizing questionnaires that documented Rome II criteria for the diagnosis of IBS, as well as a measure of intimate partner violence. Physical violence was found in 14.8% and sexual violence in 4.4% of responders. Comparing women with and without IBS, there was a significant difference in violence history with odds ratios of 2.08 for physical and 2.85 for sexual abuse.

Strengths of this study included a large number of subjects, the use of personal interviews, and a random sampling technique. Since Nicaragua has had a particularly traumatic history, with prolonged armed struggle against both the dictator, Somoza, and against the Contras, these results may not be applicable to other countries in the developing world.

2.4. Mothers with IBS and Their Children. The effect of maternal IBS illness on children has been studied. Beyond the influence of familial genetics [21], the development of IBS in children and other illness behavior is seemingly influenced by the relationship between a mother with IBS and her children. In an important study [22], 208 mothers with IBS and their 296 children (average age 11.9 years) were compared to 241 mothers without IBS and their 335 children. Children and mothers were independently interviewed and assessed for stress experience, psychological status, level of pain, and coping skill. Mothers also completed a measure of solicitousness. Questionnaires to children were administered orally. When children with mothers with IBS were compared to children with healthy mothers, there was increased frequency of stomach aches, non-GI physical complaints, more time lost from school and more frequent physician visits in the IBS group. Maternal solicitousness was not associated with the presence or frequency of stomach aches but it was correlated with school absence. Solicitousness also did not effect non-GI illness reporting.

It is psychologically understandable and predictable that mothers suffering from IBS would be more sensitive to, and aware of, gastrointestinal discomfort in their children, but this sensitivity might lead to an increased focus on gastrointestinal complaints voiced by their children. Moreover children of mothers with IBS may feel identified with their mother's discomfort or may inevitably absorb anxiety due to IBS distress. Thus far, there have been no reports on fathers with IBS and their children.

2.5. Social Support and IBS. There have been other investigations of IBS and relationships, mostly limited to the realm of general social support, in contrast to intimate relationships. Social support describes the network of resources available to someone when they are facing difficulties in life and expands beyond intimate relationships to friends, neighbors, colleagues, and community.

In one publication regarding social support and IBS, Jones et al. [23] asked patients to complete a composite measure of social support, the Interpersonal Support Inventory List. This is a 40-item measure that has been validated in other health research studies. The patient population consisted of 74 patients with IBS (out of 145 recruited), 48 patients with inflammatory bowel disease (out of 74 recruited), and 55 controls. Both the IBS group and the IBD group had significantly lower scores than the controls, indicating poor social support. It is noteworthy that there was no significant difference between IBS and IBD patients. There was also no significant difference in psychological disturbance or quality of life suggesting that IBS and IBD have similar psychosocial profiles. It should be noted that the results were cross-sectional, not sequential, so it is not known whether having IBS affects social support or vice versa.

Another study compared social support in IBS and chronic headache [24]. A structured interview technique was employed and patients were asked about helpful and unhelpful support from intimate others, family members, friends, acquaintances, and physicians. Support was divided into tangible assistance such as information and practical advice and emotional support. Both groups of patients found tangible support to be more helpful than emotional support. However, tangible assistance was less important to IBS patients than those with headaches, which the authors suggest may be related to the embarrassing nature of IBS symptoms.

The finding that social support is reduced in chronic illness may represent the acute needs that a patient experiences, which may exceed ordinary social relationships. On the other hand, reduction in social support might indicate the difficulties that healthy people experience in relating to someone with a chronic illness, such as anxious identification with illness, a sense of guilt about being well, or perhaps unresolved childhood difficulties in dealing with parental illness.

2.6. Family Dynamics and IBS. The first study that incorporated an investigation of family relationships affecting symptomatology in IBS was a collaborative psychologist-gastroenterologist treatment program, using a biweekly three session model based on discussion between patient and both professionals [25]. Sixteen patients with IBS entered the therapy are of the study and were compared to 8 IBS controls, who received usual medical treatment. During the course of the three-session therapy, it became clear that a patient's relationships had an effect on their illness experience. Examples included spousal conflict, poor personal health care on the part of a parent during childhood, and the occasional eliciting of a history of abuse during childhood. For example, one patient reported highly dismissive attitudes on the part of his spouse who discredited the physiological reality of gut hypersensitivity. Another patient described the pervasive

anxiety of her childhood in which a diabetic parent suffered multiple medical crises, which, it seemed, left her with a high level of anxiety about managing medical illness. The novel use of a three-generational genogram during one of the sessions was very revealing, exposing not only psychological dynamics, but also the frequency of chronic gastrointestinal symptoms in other family members. An important part of the treatment was an exploratory discussion of relationship issues, which appeared to contribute, at least in part, to the success of this program.

The collaborative model proved to be highly successful, resulting in a statistically significant decrease in IBS symptoms, as measured by a two-week daily diary [26], comparing results before onset of therapy to three months after termination. All three major symptoms of IBS, abdominal pain, diarrhea, and constipation were reduced ($P < .05$), as well as global improvement, measured by self-assessment ($P < .0002$). Results were also significantly better than the medically treated IBS control group ($P < .05$).

Strengths of this study included a medically treated control group, the use of a two-week daily diary for recording of symptoms as well as a global assessment scale, and, a three-month followup. The main weakness was the small number of subjects.

One of the conundrums of IBS research concerns the measurement of symptoms. In the above three studies, three different measures were used. All three have been validated with high reliability quotients [11, 15, 26]. While the two-week daily diary is the most rigorous, it is also more burdensome on the patient than the other two. The SSS is more comprehensive than the BSS and is currently the most commonly used symptom measure.

Insights from this collaborative model were then applied to a successful five-session group program conducted by both a clinical psychologist and a gastroenterologist [27]. One session was led by the gastroenterologist, two by the psychologist, one by a nutritionist, and the last session by both psychologist and gastroenterologist. The psychologist emphasized the importance of context, that IBS is a multiperson phenomenon. Some patients clearly benefited from supportive relationships, while others suffered from accusatory or blaming interactions such as "Can't you relax more?", or "You're eating all the wrong foods!". One patient talked about a scenario that took place when she and her husband were about to get into their car when he would ritualistically ask whether the patient was ok or whether she wanted to use the bathroom. While the husband thought he was being helpful, he was actually increasing the patient's anxiety regarding the car ride and interfering with her own self-regulation. These examples demonstrate the complexity of relationship effects on IBS. A three-generational genogram was employed again, including observations about how family members coped with illness.

A pilot study of one of the groups found statistically significant improvement in IBS symptoms at the end of the five sessions ($P < .05$). However, this involved a small number of patients with no long-term followup.

3. Conclusions and Recommendations

These reports, while few in number, support the premise that relationships may have an impact on the IBS illness experience and may even have an effect on response to treatment. The findings reviewed require rigorous confirmation and extension into other areas of research. What are the parameters of relationships that affect the psychological status of a patient? Is compliance with treatment affected? Can couple or family counseling improve the clinical course of the IBS patient?

What recommendations should be made on the basis of all of these studies? Doctors should enquire whether family members and intimate others are sufficiently educated about IBS, and whether they are supportive to the patient or whether there are problems that can be addressed. At the least, it may be helpful for IBS patients to understand that people who are close to them can have a positive or a negative effect on their symptoms. In some circumstances, it may be helpful to have family members present during a consultation. Finally, if it is clear that family relationships are detrimental, or if there is partner confusion about how to be more helpful, referral to a family therapist should be recommended. Family treatment is generally time limited and is highly effective in mobilizing coping strengths.

Conflict of Interests

The authors have no conflict of interests.

References

[1] J. K. Kiecolt-Glaser and T. L. Newton, "Marriage and health: his and hers," *Psychological Bulletin*, vol. 127, no. 4, pp. 472–503, 2001.

[2] A. J. Zautra, J. M. Hoffman, K. S. Matt et al., "An examination of individual differences in the relationship between interpersonal stress and disease activity among women with rheumatoid arthritis," *Arthritis Care and Research*, vol. 11, no. 4, pp. 271–279, 1998.

[3] J. H. Hibbard and C. R. Pope, "The quality of social roles as predictors of morbidity and mortality," *Social Science and Medicine*, vol. 36, no. 3, pp. 217–225, 1993.

[4] S. E. Cross and L. Madson, "Models of the self: self-construals and gender," *Psychological Bulletin*, vol. 122, no. 1, pp. 5–37, 1997.

[5] S. R. H. Beach, F. D. Fincham, and J. Katz, "Marital therapy in the treatment of depression: toward a third generation of therapy and research," *Clinical Psychology Review*, vol. 18, no. 6, pp. 635–661, 1998.

[6] B. H. Brummett, J. C. Barefoot, J. R. Feaganes et al., "Hostility in marital dyads: associations with depressive symptoms," *Journal of Behavioral Medicine*, vol. 23, no. 1, pp. 95–105, 2000.

[7] H. Flor, C. Breitenstein, N. Birbaumer, and M. Furst, "A psychophysiological analysis of spouse solicitousness towards pain behaviors, spouse interaction, and pain perception," *Behavior Therapy*, vol. 26, no. 2, pp. 255–272, 1995.

[8] F. J. Keefe, D. S. Caldwell, D. Baucom et al., "Spouse-assisted coping skills training in the management of knee pain in osteoarthritis: long-term follow-up results," *Arthritis Care and Research*, vol. 12, no. 2, pp. 101–111, 1999.

[9] G. R. Pierce, I. G. Sarason, and B. R. Sarason, "General and relationship-based perceptions of social support: are two constructs better than one?" *Journal of Personality and Social Psychology*, vol. 61, no. 6, pp. 1028–1039, 1991.

[10] M. J. Gerson, C. D. Gerson, R. A. Awad et al., "An international study of irritable bowel syndrome: family relationships and mind-body attributions," *Social Science and Medicine*, vol. 62, no. 11, pp. 2838–2847, 2006.

[11] A. Bensoussan, N. J. Talley, M. Hing, R. Menzies, A. Guo, and M. Ngu, "Treatment of irritable bowel syndrome with Chinese herbal medicine: a randomized controlled trial," *Journal of the American Medical Association*, vol. 280, no. 18, pp. 1585–1589, 1998.

[12] C. D. Gerson, J. Gerson, and M.-J. Gerson, "Group hypnotherapy for irritable bowel syndrome with long-term follow-up," *International Journal of Clinical and Experimental Hypnotherapy*. In press.

[13] P. J. Whorwell, A. Prior, and E. B. Faragher, "Controlled trial of hypnotherapy in the treatment of severe refractory irritable-bowel syndrome," *The Lancet*, vol. 2, no. 8414, pp. 1232–1234, 1984.

[14] O. S. Palsson, "Standardized hypnosis treatment for irritable bowel syndrome: the North Carolina protocol," *International Journal of Clinical and Experimental Hypnosis*, vol. 54, no. 1, pp. 51–64, 2006.

[15] C. Y. Francis, J. Morris, and P. J. Whorwell, "The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress," *Alimentary Pharmacology and Therapeutics*, vol. 11, no. 2, pp. 395–402, 1997.

[16] R. K. Wong, D. A. Drossman, C. B. Morris et al., "Irritable bowel syndrome causes increased partner burden: a comparative study," *Gastroenterology*, vol. 140, no. 5, supplement 1, pp. S463–S464, 2011.

[17] D. B. Silk, "Impact of irritable bowel syndrome on personal relationships and working practices," *European Journal of Gastroenterology and Hepatology*, vol. 13, no. 11, pp. 1327–1332, 2001.

[18] S. Becker-Dreps, D. Morgan, R. Peña, L. Cortes, C. F. Martin, and E. Valladares, "Association between intimate partner violence and irritable bowel syndrome: a population-based study in Nicaragua," *Violence Against Women*, vol. 16, no. 7, pp. 832–845, 2010.

[19] N. J. Talley, S. L. Fett, and A. R. Zinsmeister, "Self-reported abuse and gastrointestinal disease in outpatients: association with irritable bowel-type symptoms," *American Journal of Gastroenterology*, vol. 90, no. 3, pp. 366–371, 1995.

[20] J. Leserman, D. A. Drossman, and Z. Li, "The relationship of abuse history with health status and health care use in a referral GI clinic," *Gastroenterology*, vol. 104, Article ID A541, 1993.

[21] R. L. Levy, K. R. Jones, W. E. Whitehead, S. I. Feld, N. J. Talley, and L. A. Corey, "Irritable bowel syndrome in twins: heredity and social learning both contribute to etiology," *Gastroenterology*, vol. 121, no. 4, pp. 799–804, 2001.

[22] R. L. Levy, W. E. Whitehead, L. S. Walker et al., "Increased somatic complaints and health-care utilization in children: effects of parent IBS status and parent response to gastrointestinal symptoms," *American Journal of Gastroenterology*, vol. 99, no. 12, pp. 2442–2451, 2004.

[23] M. P. Jones, S. Wessinger, and M. D. Crowell, "Coping strategies and interpersonal support in patients with irritable bowel syndrome and inflammatory bowel disease," *Clinical Gastroenterology and Hepatology*, vol. 4, no. 4, pp. 474–481, 2006.

[24] R. Martin, G. M. Davis, R. S. Baron, J. Suls, and E. B. Blanchard, "Specificity in social support: perceptions of helpful and unhelpful provider behaviors among irritable bowel syndrome, headache, and cancer patients," *Health Psychology*, vol. 13, no. 5, pp. 432–439, 1994.

[25] C. D. Gerson and M. J. Gerson, "A collaborative health care model for the treatment of irritable bowel syndrome," *Clinical Gastroenterology and Hepatology*, vol. 1, no. 6, pp. 446–452, 2003.

[26] B. Greene and E. B. Blanchard, "Cognitive therapy for irritable bowel syndrome," *Journal of Consulting and Clinical Psychology*, vol. 62, no. 3, pp. 576–582, 1994.

[27] M. J. Gerson and C. D. Gerson, "A collaborative family-systemic approach to treating chronic illness: irritable bowel syndrome as exemplar," *Contemporary Family Therapy*, vol. 27, no. 1, pp. 37–49, 2005.