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A Simultaneous Multidisciplinary Evaluation of Irritable Bowel Syndrome in Egyptian Patients: Dietary, Psychiatric, Microbiologic and Autonomic Aspects

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Abstract

Background and Aim: Irritable bowel syndrome (IBS) is a common medical disorder that may be severe enough to impair the quality of life. This study aimed to assess the role of each of dietary, psychiatric, autonomic, and microbiology background and their interactions in Egyptian patients with IBS. **Patients and Methods:** Forty adult patients diagnosed with IBS, equally divided into 2 groups the diarrhea predominant and the constipation predominant, were recruited from the Endoscopy Unit. Dietary assessment was done by monthly food frequency questionnaire. Psychiatric assessment was done by both the Eysenck Personality Questionnaire (EPQ) and Hopkins Symptom Checklist (HSCL-90). Microbiologic evaluation was done by faecal cultures and neurophysiologic autonomic evaluation was done via the sympathetic skin response and the parasympathetic R-R interval variation. Another 20 healthy subjects were included as control group. **Results:** All IBS patients were young, with significant female predominance (P = 0.007), particularly in IBS-C group (20/20; 100%, P = 0.003). Psychologically, abnormal scores of neuroticism, extraversion and criminality, and depression, obsessive compulsion, somatization, sensitivity and anxiety in both IBS groups with particularly extraversion, criminality and depression were significantly higher in constipation subtype. Microbiologically, Bacteroids were significantly related to IBS, while Klebsiella was significantly deficient without significant difference between its groups. On the contrary, neither diet nor autonomic activity

showed any significant relation. **Conclusions:** IBS is a disorder induced by many factors and affected by several interacting agents, thus revealing controversial results when studied simultaneously.

Keywords

Irritable Bowel Syndrome (IBS), Eysenck Personality Questionnaire (EPQ), Hopkins Symptom Checklist (HSCL-90), Microbiota, Autonomic Activity

1. Introduction

Irritable bowel syndrome (IBS) is a common functional intestinal disorder constituting a major health complaint and is the most commonly diagnosed gut disease [1].

Pathogenesis of IBS is multifactorial: dietary (food sensitivity and carbohydrate malabsorption), microbiologic (altered fecal microbiota, bacterial overgrowth, and post infectious reactivity), and neurophysiologic (brain-gut interaction, altered gut motility, visceral hypersensitivity, intestinal inflammation) [2].

Patients may correlate ingestion of certain foods with their IBS complaints [1]. Dietary fermentable oligo-di-monosaccharides and polyols (FODMAP), a group that includes fructose, fructans, mannitol, lactose, xylitol, sorbitol, and galactans induces increased and prolonged hydrogen production in the intestine thus influencing the methane production, and eventually inducing local and systemic symptoms of IBS [2]. Conversely, low dietary FODMAP is effective in controlling IBS symptoms [3]. However, excessive diet restriction may lead to nutritional deficiencies. The suspected food is identified by the recurrence of symptoms once reintroduced in diet after being temporarily eliminated [4].

Anxiety, depression, and somatoform disorders are obviously associated with IBS [5] [6]. Ten percent of the varied bowel symptoms are attributed to stress [6]. The psychiatric role in the pathogenesis of IBS was proved by the significant resolution by psychologic treatment [6], and the symptomatic relief by cognitive and hypnotherapies, and dynamic psychotherapy [7].

The role of small intestinal bacterial overgrowth in the pathogenesis of IBS was proved by the resolution of IBS when eradicated by antibiotics in 48% of subjects [8]. However, the benefit of antibiotics is transient and their exact mode of action is not clear whether treating small bowel bacterial overgrowth or altering gut microbiota [4].

Functional bowel disorders are associated with autonomic disturbance [9] [10]. Heart rate variability (HRV) has considerable potential to assess the role of autonomic nervous system (ANS) fluctuations in normal healthy individuals and in patients [11], and skin sympathetic response (SSR) is a simple bed side test strongly correlated with diseases where dysautonomia was incriminated [12]. ANS assessment may be considered a new modality for clinical management of IBS [13].

This study aimed at evaluating the dietary, psychiatric, microbiologic and autonomic nervous activity of IBS patients.

2. Patients and Methods

This was a cohort simultaneous multidisciplinary evaluation of IBS. The study included patients attending the colonoscopy room at Gastrointestinal (GI) Endoscopy Unit, Kasr El-Ainy, Faculty of Medicine, Cairo University, Egypt and presented with variable lower, non-alarming GI symptoms, and with normal colonic macroscopic and microscopic examination. Colonoscopic biopsies were done to exclude any organic pathology including those with normal overlying mucosa. Upper endoscopy with duodenal biopsy was done in cases simulating IBS like Celiac disease.

2.1. Inclusion Criteria

- Adult patients (≥ 18 years old);
- Both genders;
- Fulfilling the Rome III criteria [14] [15] *i.e.* at least three months of continuous or recurrent abdominal pain or discomfort that has two or more of the following features: improvement with defecation, association with a change in the frequency, and a change in stool form.

2.2. Exclusion Criteria

All organic colonic diseases that may simulate IBS clinical picture and any medications that may interfere with the applied tests of the test whether directly or indirectly.

- Celiac serology;
- Organic GI pathology;
- Alarming symptoms (e.g. significant weight loss, bloody diarrhea, cachexia).
- Organic neurologic affection;
- Medical condition affecting the brain—gut neurogenic pathways or any form of neuropathies; Special habits (alcoholism), Endocrinal, Cardiovascular diseases;
- Medications interfering with tests carried out.

Patients were equally divided into two groups according to their predominant motion; IBS-D and IBS-C. Twenty healthy volunteers participated in this work as control group.

All enrolled patients and control subjects were subjected to:

1) Full history taking: a) Complaint: constipation vs. diarrhea, frequency, passage of blood, mucous in stools, site of pain, distension, flatus, tenesmus, anal itching, passage of worms. b) Medical history. c) Dietary history e.g. Monthly food frequency questionnaire about common fermentable oligo-di-monosaccharides and polyols (FODMAP) foods in Egypt. It was composed of ingestion of beans, lentils/peas, refined bread, milk/dairy products, skinned vegetables/fruits, coffee,

sweets/candies, carbonated beverages, cakes/cookies/pasta, rice, and large fatty meals. **2) Thorough clinical examination:** a) General, b) Psychiatric assessment: The psychological profile of the patients was done provided that the Arabic certified translation was attached, by utilizing the following two tests. i) The Eysenck Personality Questionnaire (EPQ) [16]. It is composed of 90 statements of which subjects respond by "Yes" or "No". It has 5 scales that measure the dimensions of psychoticism, neuroticism, extraversion-introversion, lie, and criminality, provided that each one has its normal psychological range, and ii) The Hopkins Symptom Checklist (HSCL-90) scale [17]. It is a self-rating test to indicate how much he/she is distressed by each of 90 possible symptoms. This test is further scored for 9 clinical scales: somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Scale > 20 is considered significantly positive. **3) Investigatory work up:** a) Microbiologic assessment: Faecal microbiota were examined by repeated stool cultures to exclude infectious causes, and to identify faecal microbiota regarding type and count. Stool samples were cultured on i) a panel of selective and enriched media under aerobic and anaerobic conditions. Isolated microorganisms will be phenotypically identified by conventional biochemical testing and ii) an automated bacterial identification system; namely the VITEK® 2 system (bioMérieux). Representative species of fecal bacterial flora will be cultured quantitatively, and further categorized as mild ($1 - 999 \times 10^5$ CFU)/ml), moderate ($1000 - 99{,}999 \times 10^5$ CFU/ml) & high ($\geq 100{,}000 \times 10^5$ CFU/ml). b) Biochemical blood routine tests, c) Imaging *i.e.* Abdominal Ultrasound. d) Neurophysiologic Autonomic activity assessment: Autonomic activity is assessed by sympathetic skin response (SSR) [18], and R-R interval variation (RRIV) [11] which are noninvasive procedures to assess the autonomic nervous functions. SSR and RRIV were recorded using a Nihon Kohden Neuropack apparatus® (Tokyo, Japan) in the Clinical Neurophysiology Unit, Kasr AlAiny Hospital. i) The SSR was recorded from the upper limb by attaching surface electrodes on the right hand with application of electrically stimuli to the left wrist. For the SSR the onset latency in seconds was calculated. ii) The RRIV was acquired at rest (RRIV) and during deep breathing (RRIV-D) [19]. The coefficient of variation (CV) was calculated to represent the RRIV. e) Statistical analysis: Data were entered on the computer using "Microsoft Office Excel Software" program (2010) for windows. Data were then transferred to the Statistical Package of Social Science Software program, version 23 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) to be statistically analyzed. Data were presented using range, mean, standard deviation (SD) and median for quantitative variables, and frequency and percentage for qualitative ones. Comparison between groups was performed using Kruskal Wallis test with Mann Whitney test for pairwise comparisons for quantitative variables and Chi square or Fisher's exact test for qualitative ones. Spearman correlation coefficients were calculated to assess the association between different quantitative and

ordinal variables. $P < 0.05$ is considered statistically significant. In non-normally distributed data, P value was calculated via non parametric test. f) Ethical consideration: This study was conducted according to the declaration of Helsinki and was approved by the ethical committee of Tropical Medicine Department, Faculty of Medicine, Cairo University. A fully informative consent was signed by the IBS patients and control subjects but it was not presented for the personal data that may identify the patients.

3. Results

This study included 40 adult patients who attended the colonoscopy room of the Gastrointestinal Endoscopy Unit at Kasr El-Ainy Hospital, Faculty of Medicine, Cairo University. They were diagnosed to have IBS according to Rome III criteria. They were enrolled from June 2016 to January 2018 out of 335 referred colonoscopy cases (11.94%).

The 40 IBS patients were divided into two equal groups; IBS-D and IBS-C, and 20 other healthy subjects serving as control group.

The basic personal data and complaints are shown in Table 1. All of the patients were young, insignificantly and mildly older IBS-C group, and predominantly females, particularly in IBS-C. Course of the complaint in both IBS groups was stationary. All of them were clinically free.

Dietary assessment of the studied groups is shown in Table 2. None of the questioned food types was significantly related to any of the studied groups.

The psychiatric assessment of the studied groups via EPQ scale and HSCL-90 in terms of their absolute score is shown in Table 3. All the parameters, except extraversion and lie of EPQ, were significantly higher in both IBS groups, and mostly with insignificant interdifference.

However, for many of the recorded scores lied within the normal psychologic range, the percent of patients who recorded abnormal psychiatric scores in EPQ and HSCL-90 were illustrated in Figure 1 and Figure 2 respectively to show the true and definite psychiatric trait.

Table 1. Basic personal data and complaint of the studied IBS patients.

Basic personal data and complaint[a]		IBS-D n = 20	IBS-C n = 20	Control n = 20	P value			
					P1	P2	P3	P4
Personal	Age in years	32.9 ± 10.1	34.2 ± 9.5	32.7 ± 7.7	0.921	0.807	0.914	0.674
	Males/females	8/12 (40/60)	0/20 (0/100)	4/16 (20/80)	**0.007**	**0.003**	0.301	0.106
Complaint	Onset in months	47.1 ± 39.1 36 (6 - 144)	63.4 ± 70.6 30 (6 - 240)					
	Pattern	2 - 4 motions/day 3 (2 - 3)	Once within 2 - 5 days 3 (3 - 4)					

[a]Quantitative parameters are expressed in mean ± standard deviation, median (Inter quartile range), while qualitative parameters are expressed in number (percent). IBS-D = Irritable bowel disease-diarrhea, IBS-C = Irritable bowel disease-constipation. P1 = overall, P2 = IBS-D versus IBS-C, P3 = IBS-D versus control, P4 = IBS-C versus control.

Table 2. Nutritional assessment via diet questionnaire of the studied groups.

Foods of Diet Questionnaire	IBS-D (n = 20)		IBS-C (n = 20)		Control (n = 20)		P value (overall)
	Prevalence n (%)	Frequency Mean ± SD median (IQR)	Prevalence n (%)	Frequency Mean ± SD median (IQR)	Prevalence n (%)	Frequency Mean ± SD median (IQR)	
Beans	19 (95)	21 ± 10.2 25 (12 - 30)	17 (85)	19.4 ± 12.2 23 (10 - 30)	20 (100)	16.3 ± 11.7 12 (6 - 30)	0.425
Lentils	16 (80)	4.8 ± 9 1.5 (1 - 2.5)	16 (80)	6.4 ± 11.1 1 (1 - 2)	19 (95)	1.4 ± 0.8 1 (1 - 2)	0.742
Refined bread	1 (5)	1.5 ± 6.7 0 (0)	0 (0)	0 ± 0 0 (0)	0 (0)	0 ± 0 0 (0)	0.368
Milk & dairy products	20 (100)	12.8 ± 10.8 8 (3.5 - 23)	19 (95)	16.6 ± 15.4 10 (5.5 - 30)	20 (100)	15.3 ± 10.2 12 (8 - 30)	0.528
Skinned vegetables	2 (10)	1.1 ± 4.5 0 (0)	1 (5)	0.1 ± 0.2 0 (0)	3 (15)	2.5 ± 7.2 0 (0)	0.528
Skinned fruits	0 (0)	0 ± 0 0 (0)	0 (0)	0 ± 0 0 (0)	2 (10)	1.6 ± 6.7 0 (0)	0.131
Sweets & candies	19 (95)	4.3 ± 4.7 2 (1 - 8)	19 (95)	4.8 ± 6.6 2 (1 - 8)	19 (95)	4.7 ± 3 4 (2 - 8)	0.470
Coffee	17 (85)	17.3 ± 16 14 (1.5 - 30)	16 (80)	19.8 ± 24.8 8 (2.5 - 30)	18 (90)	15.9 ± 16.5 8 (3 - 30)	0.957
Carbonated drinks	20 (100)	13.1 ± 10 12 (4 - 16)	18 (90)	10.3 ± 9.7 8 (2 - 12)	19 (95)	12 ± 10.2 8 (5 - 14)	0.523
Rice	20 (100)	25.7 ± 6.3 30 (20 - 30)	20 (100)	25.5 ± 8.5 30 (25 - 30)	20 (100)	19.6 ± 10 14 (12 - 30)	0.052
Cake, cookies, pasta	20 (100)	19.8 ± 16.1 14 (8 - 30)	20 (100)	17.6 ± 9.5 16 (10 - 30)	20 (100)	11.5 ± 6 10 (8 - 14)	0.081
Large fatty meal	18 (90)	2.7 ± 3.8 1 (1 - 2)	14 (70)	3.4 ± 6.8 1 (0 - 3)	14 (70)	2.4 ± 6.5 1 (0 - 1.5)	0.305

IBS-D = Irritable bowel syndrome diarrhea predominant, IBS-C = Irritable bowel syndrome constipation predominant, SD = Standard deviation, IQR = Interquartile range.

Table 3. Psychiatric assessment of the studied groups in terms of its absolute score.

Psychologic assessment		Mean ± SD Median (IQR)			P value			
		IBS-D (n = 20)	IBS-C (n = 20)	Control (n = 20)	P1	P2	P3	P4
EPQ scale	Psychotism	5.9 ± 2.3 6 (4 - 7)	6.1 ± 1.8 6 (5 - 7)	5.8 ± 2.1 5.5 (4 - 7.5)	0.817	0.601	0.946	0.565
	Neuroticism	18.1 ± 3.5 19 (15.5 - 21)	20.4 ± 1.1 20.5 (20 - 21)	14.5 ± 3.8 15 (12 - 16.5)	**<0.001**	**0.021**	**0.003**	**<0.001**
	Extraversion	7.9 ± 5.2 6.5 (4 - 11.5)	5.7 ± 3.4 5.5 (2.5 - 8)	13 ± 4 13 (10 - 16.5)	**<0.001**	0.222	**0.002**	**<0.001**
	Lie	9.9 ± 2.7 9.5 (8.5 - 12)	11.3 ± 2.2 11 (10 - 12.5)	10.6 ± 2.5 10.5 (9 - 11.5)	0.110	0.129	0.435	0.170
	Criminality	15.6 ± 2.1 15.5 (14 - 16.5)	17.1 ± 2 17 (16 - 18)	13 ± 3.7 11.5 (10 - 16)	**0.001**	**0.013**	**0.014**	**0.001**
HSCL-90	Psychoticism	14.7 ± 5.7 13.5 (11 - 18.5)	15.9 ± 5.1 15 (12.5 - 18)	7.8 ± 4 7 (5 - 9.5)	**<0.001**	0.481	**<0.001**	**<0.001**
	Paranoia	9.4 ± 2.7 9 (8 - 11)	9.9 ± 2 10 (9 - 11)	6.4 ± 2.7 6 (4 - 9)	**<0.001**	0.206	**0.003**	**<0.001**
	Phobic anxiety	8.4 ± 4.1 9 (5 - 10)	8.7 ± 4.1 8 (6 - 12)	3.3 ± 2.4 3 (2 - 4)	**<0.001**	0.664	**<0.001**	**<0.001**
	Hostility	6.7 ± 3.1 6 (5 - 8)	7.1 ± 2.4 7 (5 - 9)	3.9 ± 0.8 4 (3 - 4)	**<0.001**	0.530	**<0.001**	**<0.001**
	Anxiety	15.7 ± 5.5 16 (11.5 - 18.5)	18.2 ± 5.8 19 (14.5 - 22)	9.4 ± 3.4 10 (8 - 10.5)	**<0.001**	0.143	**<0.001**	**<0.001**
	Depression	27.4 ± 7 27.5 (24.5 - 31)	29.3 ± 5.4 29.5 (28 - 31)	17.7 ± 4.2 19 (14 - 20)	**<0.001**	0.232	**<0.001**	**<0.001**
	Interpersonal sensitivity	17.7 ± 5.4 20 (16.5 - 21)	19.5 ± 4.4 19 (17 - 21)	12.5 ± 3.8 13 (10 - 16)	**<0.001**	0.849	**0.001**	**<0.001**
	Obsessive compulsive	19.9 ± 3.9 20 (19 - 22)	20.2 ± 3.4 20.5 (18 - 22)	13.9 ± 3.6 14.5 (13 - 16)	**<0.001**	0.744	**<0.001**	**<0.001**
	Somatization	19.7 ± 8.4 17.5 (13.5 - 22)	20.7 ± 8.7 18 (15 - 25.5)	8.1 ± 3.5 8.5 (6 - 10.5)	**<0.001**	0.645	**<0.001**	**<0.001**

EPQ = Eysenck's personality questionnaire, HSCL-90 = Hopkins symptom checklist, IBS-D = Irritable bowel disease-diarrhea, IBS-C = Irritable bowel disease-constipation, SD = Standard deviation, IQR = Interquartile range, P1 = overall, P2 = IBS-D versus IBS-C, P3 = IBS-D versus control, P4 = IBS-C versus control.

Fecal microbiota of the studied groups by the conventional cultures and the automated VITEK test are shown in Table 4. Aspergillus was significantly high in IBS-C however fungal detection was generally very low.

The ANS assessment of the studied groups is shown in Table 5. Neither the sympathetic nor the parasympathetic showed statistically significant relation with any of the studied groups.

Correlation tests were done between every 2 of the 4 studied aspects in which IBS groups were merged together for 1) most of the previous results showed a significant difference between each of IBS groups and the control one but not between them, and 2) the rather small number of patients. Significant correlations were found in very few items. Correlation results were expressed in many and lengthy tables, thus not included in the manuscript.

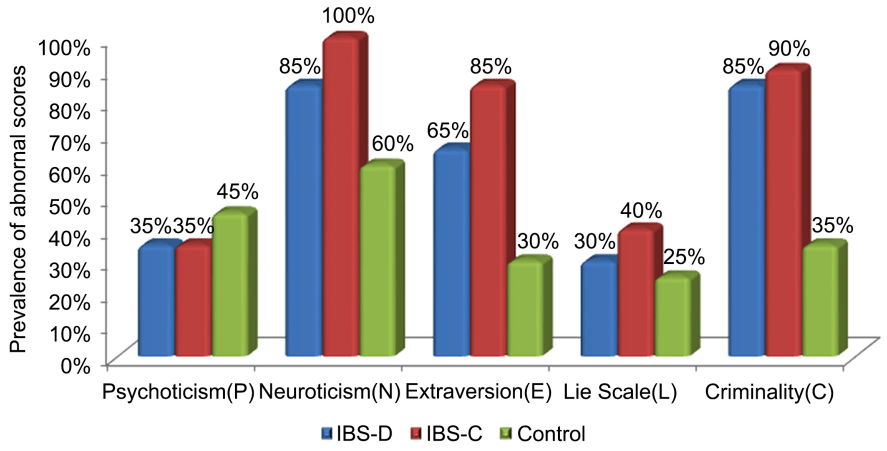

Figure 1. Prevalence of abnormal Eysneck personality questionnaire (EPQ) scores in the three studied groups [P (overall) = 0.754, 0.004, 0.002, 0.583, and <0.001 respectively].

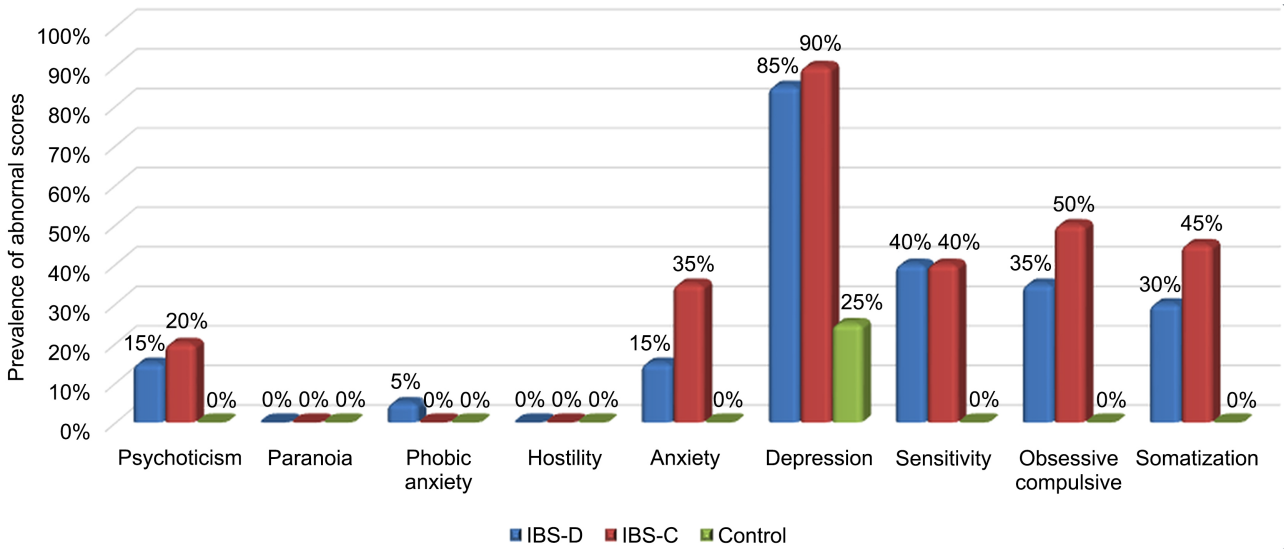

Figure 2. Prevalence of abnormal Hopkins symptom checklist (HSCL-90) scores in the three studied groups (Neither paranoia nor hostility was recorded abnormally in any of the studied groups) [P (overall) = 0.122, 1.00, 0.362, 1.00, 0.012, <0.001, 0.004, 0.002, and 0.004 respectively].

Table 4. Fecal microbiota of the studied groups.

Organisms' species by standard culture	IBS-D (n =20)				IBS-C (n = 20)				Controls (n = 20)				P value (Overall)
	Prevalence (%)	Degree			Prevalence (%)	Degree			Prevalence (%)	Degree			
		Mild	Moderate	Marked		Mild	Moderate	Marked		Mild	Moderate	Marked	
Coliform (enterobacterica)	95	15.8	42.1	42.1	95	15.8	68.4	15.8	95	26.3	36.8	36.8	1.000
E. col	90	16.7	38.9	44.4	95	26.3	63.2	10.5	90	22.2	44.4	33.3	0.804
Klebsiella	25	40	20	40	25	80	20		60	25	41.7	33.3	**0.030**
Other (non fermenters)	10		50	50	30	66.7	33.3		10	50	50		0.235
Aerobic gram positive	80	25	56.3	18.8	95	31.6	63.2	5.3	85	52.9	35.3	11.8	0.364
Staphylococci	55	27.3	72.7		50	70	30		55	54.5	36.4	9.1	0.176
Enterococci	65	30.8	61.5	7.7	70	28.6	64.3	7.1	85	64.7	35.3		0.216
Diphtheroid	35	57.1	42.9		30	83.3	16.7		10	50	50		0.155
Bifidobacterium	5		100		20		100		5			100	0.180
Eubacterium	60	25	41.7	33.3	80	18.8	50	31.3	80	6.3	43.8	50	0.256
Veillonella	40	37.5	62.5		50	20	70	10	65	61.5	38.5		0.281
Peptostreptococci/Ruminococcus	60	16.7	66.7	16.7	75	6.7	73.3	20	65	7.7	76.9	15.4	0.592
Fusobacterium	35	28.6	57.1	14.3	40	50	37.5	12.5	65	7.7	76.9	12.5	0.125
Bacterotides	85	17.6	52.9	29.4	90		33.3	66.7	60	8.3	50	41.7	**0.048**
Prevotella	50	20	50	30	40		75	25	55	9.1	45.5	45.5	0.627
Clostridium	50	30	40	30	70	7.1	57.1	35.7	65		53.8	46.2	0.400
Actinomyces	20	75	25		5		100		15	100			0.364
Fungus	10	50	50		35	85.7	14.3		5		100		**0.024**
Candida	5				5								
Aspergillus	5				30								**0.007**
Organisms' species by VITIC culture													
	Serratia		0				2 (10)				0		0.126
Non fermenters	**Proteus**		1 (5)				1 (5)				1 (5)		1.000
	Pseudomonas		1 (5)				3 (15)				0		0.153

Continued

Veillonella	**Megasheria**	0	1 (5)	0	0.362
Peptostreptococci	***Peptoniphilus asaccharolytica***	0	0	1 (5)	0.362
Fusobacterium	***F. mortiferum***	0	1 (5)	0	0.362
Bacteroids	***B. fragilis***	2 (10)	6 (30)	1 (5)	0.064
	B. vulgatus	0	1 (5)	0	0.362
	B. ovatus	0	3 (15)	0	0.129
	B. thetaiotamicron	0	1 (5)	0	0.362
	B. stercoris	0	0	1 (5)	0.362
	Parabacteroids distasonis	1 (5)	0	0	0.362
Prevotella	***P. melaninogenica***	1 (5)	1 (5)	1 (5)	1.000
	P. oralis	7 (35)	6 (30)	6 (30)	0.926
Clostridium	***C. sordelii***	1 (5)	2 (10)	0	0.349
	C. perfringens	2 (10)	0	0	0.126
	C. Clostridioforme	0	1 (5)	0	0.362
	C. sporogenes	0	0	2 (10)	0.126

Table 5. The autonomic activity in the three studied groups.

Autonomic parameters		**Mean ± SD Median (IQR)**			**P value**
		IBS-D (n = 20)	**IBS-C (n = 20)**	**Control (n = 20)**	
Para Sympathetic (coefficient)	**RRIV**	7.7 ± 8.3 4.1 (2.3 - 10.8)	9 ± 10.9 4.8 (2.5 - 8.3)	8.5 ± 8.2 4.5 (3.3 - 10.5)	0.875
	RRIV-D	18.5 ± 10.8 19.7 (12.1 - 27)	28.1 ± 24.1 20.1 (9.5 - 5.8)	19.7 ± 13.5 15.1 (11.2 - 26.8)	0.657
Sympathetic	**SSR in seconds**	2.5 ± 1.6 1.8 (1.2 - 4.1)	1.3 ± 0.5 1.3 (1 - 1.5)	1.8 ± 1.6 1.3 (1 - 1.7)	0.079

RRIV: R-R interval variation, RRIV-D: R-R interval variation during deep breathing, SSR: Sympathetic skin response.

Beans showed the broadest (6/9 items) significant negative correlation with HSCL-90. Lentils were positively correlated with Enterococci and Actinomyces, sweets and candies were positively correlated with Klebsiella, rice was negatively correlated with *Staph. aureus*. Large fatty meals were positively correlated with the parasympathetic activity at both rest and deep breath tests, but neither food nor psychiatric assessment showed significant correlation with the sympathetic activity. Sympathetic activity was positively correlated with *Staph. aureus*, and negatively correlated with Prevotella, while the parasympathetic activity showed positive correlation with Klebsiella at rest.

4. Discussion

IBS is the clinical challenge in this century. It is the most commonly diagnosed GI disorder [20]. IBS is the most common complaint in gastroenterology clinics [1] [20].

In this study, the prevalence of IBS among patients referred to colonoscopy unit was 11.94%. This percent was close to prevalence in several previous studies. Drossman *et al.*, 2002 stated that almost 12% of IBS patients sought medical advice at primary care centers constituting the largest group in gastroenterology clinics [1], Talley, 1999 found that approximately 10% - 15% of the general population have IBS [21], and Spiller *et al.*, 2007 stated that it affects 5% - 11% of population of most countries [22]. It is worth mentioning that that percent in this study is like the iceberg overlying a huge number of masked patients, because the included patients are those who suffered from symptoms that were severe enough to be evaluated colonoscopically. Those with mild and moderate symptoms, besides those who do not seek medical advice were beyond our scope. Higher prevalence was reported by Meleine & Matricon, 2014 who recorded a prevalence of one IBS patient in five people at some point in their lives, and this ratio has a significantly negative impact of both quality of life and the utility of health care centers [23].

All of the IBS patients in this study were young (mean age = 33.6 ± 9.7 years, IBS-D slightly younger). This agreed with Spiller et al who diagnosed IBS peak in 3rd and 4th decades [22].

Females were significantly predominant in IBS patients in this study (P = 0.007), particularly in IBS-C who were all females (P = 0.003), while all IBS male patients belonged to IBS-D. This was found in many previous results [21] [22]. That was explained by Meleine & Matricon who stated that the fluctuation of ovarian hormones along the menstrual cycle affects the sensorimotor gastrointestinal function. They influence IBS onset and the pattern of its symptoms. They alter pain processing and perception by interacting with both the neuromodulatory and emotional systems. They also modulate the susceptibility and hyper-responsiveness to stress which promote immune activation or impair gut barrier function [23]. Hattori & Fukudo, 2006 stated that females have lower pain threshold, and conversely males have greater sympathovagal balance in re-

sponse to visceral stimulation who found 2/3 of their IBS patients were females [24]. Also, Heitkemper & Jarrett, 2008 found IBS patients seeking medical advice are mainly women for several reasons; inherent different gonadal hormones, inflammatory responses, stress reactivity, and sociocultural differences in response to pain and/or bowel pattern changes [25].

In this study none of the foods was related to IBS symptoms which were contrary to the previous results. Patients correlated foods such as caffeine, fatty foods, carbonated foods, or gas-producing foods, and alcoholic beverages as the etiology of their complaints [1]. Food plays a critical role in pathogenesis of IBS, and most patients associated its onset or exacerbation of its symptoms after certain meals. Conversely, diet low in fermentable, poorly absorbed carbohydrates and sugar alcohols is beneficial in resolving IBS symptoms [26]. In addition, increasing dietary content of soluble fiber (psyllium) significantly relieves and reduces the severity of symptoms, to the contrary the insoluble fiber (bran) worsens those symptoms [27]. Similarly, low-FODMAP diet had a favourable impact on IBS symptoms, especially abdominal pain and bloating [28]. Also, rye bread low-FODMAP helps IBS patients control their symptoms and reduces gas distension [29]. However, this finding was limited by the inability to identify the exact amount or weight of the consumed type of food by the patients, besides their similar nutritional habit.

Abnormally higher scores of neuroticism, extraversion and criminality of EPQ, and anxiety and depression of HSCL-90 were significantly recorded in IBS, where extraversion and criminality of EPQ and depression of HSCL-90 were significantly higher in IBS-C. That agreed with previous studies e.g. Chakraborti et al who proved neuroticism, hypochondriasis and depression significantly found in IBS patients compared to control subjects [29], and Zhang *et al.*, 2018 who reported more frequent and severer depressive symptoms than healthy controls, particularly in female patients and younger age [30]. On the other hand, the findings in this study partially agreed with other studies e.g. Lee *et al.* 2017, and Geng *et al.* 2018 who stated that depression and anxiety levels are higher in IBS patients than in healthy controls, regardless IBS type [31] [32]. Anxiety and depression scores and overall symptom profiles are not significantly different in IBS subtypes. Moreover, anxiety and depression do not appear to be strongly associated with symptom severity, although they may interact with other psychological drivers of severity such as poor adapting skills [33], thus, the efficient mindfulness-based training remarkably reduces symptom severity and improves quality of life [34].

In this study, only few microbiota showed significant difference between IBS and control subjects. Bacteriodes were significantly high while Klebsiella was significantly low in both IBS groups. On the other hand, Aspergillus was significantly high in IBS-C group; however, fungal detection was generally low. Role of intestinal dysbiosis was proved in many studies but with different and even contradictory results [35] e.g. Jeffery *et al.*, 2012 reported significant decrease of

Bacteroids in IBS [36], Si *et al.*, 2004 found significant increase and decrease of Enterobacteriaceae and Bifidobacterium respectively in IBS patients compared with healthy controls [37], Kennedy *et al.*, 2014 found significantly lower Bifidobacteria and Lactobacilli [36], and Mättö *et al.*, 2005 found slightly higher numbers of coliforms as well as an increased aerobe: anaerobe ratio in IBS [38]. Also, Bifidobacteria were higher in IBS-C yet insignificantly. As a probiotic, *Bifidobacterium infantis* 35624 efficiently improved IBS symptoms like bloating/distention, abdominal pain/discomfort, and/or bowel movement [39]. However, probiotics showed controversial results in pathogenesis and treatment of IBS that need to be further clarified [40].

Neither the sympathetic nor the parasympathetic activities, the two components of the ANS, were significantly related to IBS. This agreed with several studies [41] [42] [43] [44] [45], for the applied autonomic activity tests in this study do not reflect the gastrointestinal vagal tone [46]. To the contrary, other studies proved the role of ANS dysfunction in the pathophysiology of IBS [13] [47] [48].

In this study, correlative tests were done between each two studied aspects including all their items. Both diet and faecal micobiota showed few significant intercorrelation and with psychiatric and autonomic activity parameters as well. The diet provides elements for microbial fermentation, and consequently triggering IBS symptomatology. In addition, definite interaction between certain foods and the intestinal microbiota is likely one of the explanations for the inconclusive findings among studies comparing the microbiota composition in IBS patients and healthy subjects [49]. Thus, Harper *et al.* 2018 recommended combined therapy of probiotics and low FODMAP diet as the ideal treatment strategy for IBS [50].

Only psychiatric-autonomic correlation study was completely insignificant. That was contrary to Salvioli *et al.*, 2015 who confirmed that correlation [13].

5. Conclusion

In this study, psychiatric assessment was the major parameter influencing the pathogenesis of IBS, with incorporation of few micobiota.

Limitation of the Study

The small number of the included patients for it took us carrying out 335 colonoscopies within one and half year to enroll the designed 20 IBS-D and 20 IBS-C patients to be subjected to the four parameters simultaneously. Also, the applied food frequency questionnaire did not cover all types of foods or fluids nor specify the exact quantity of the ingested type.

Disclosure Statement

All the authors declare that this study is not published or submitted for publication in any other journal. They all approved this manuscript. They also declare

that it is unfunded with no conflict of interest whether personal or financial.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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