

Colonoscopic Findings in Patients Fulfilling ROME IV Criteria of Irritable Bowel Syndrome with or without Recently Discovered Alarming Features

Hala M. Elfeky, Rasha M. Abd Rabh, Mostafa E. Fouad, Tamer E. Elazab

Department of Hepatology,
Gastroenterology and Infectious
Diseases, Faculty of Medicine
Benha University, Egypt.

Corresponding to: Department
of Hepatology, Gastroenterology
and Infectious Diseases, Faculty
of Medicine Benha University,
Egypt.

Email:
Shireenmohsen12@gmail.com

Received: 5 December 2023

Accepted: 6 January 2024

Abstract

Background: Irritable bowel syndrome (IBS) is a common gastrointestinal disorder characterized by recurrent abdominal pain and altered bowel habits. Identifying organic diseases in patients with IBS is crucial, especially when alarming features are present. **This study aimed to** assess colonoscopic findings in patients fulfilling ROME IV Criteria of Irritable Bowel Syndrome with or without Recently Discovered alarming features. **Methods:** This cross-sectional study was conducted on sixty consecutive patients with IBS who fulfilled the Rome IV criteria. The patients were divided into two groups: Group A (IBS without alarming features) and Group B (IBS with alarming features). Detailed history, clinical examination, laboratory investigations in the form of complete blood count and full colonoscopy with biopsy were performed. The colonoscopic and histopathological findings were analyzed to determine the presence of organic diseases. **Results:** Group B exhibited significantly higher occurrences of bleeding per rectum, weight loss, and pallor compared to Group A. Colonoscopic findings revealed a higher prevalence of adenomatous polyps in Group B, whereas Group A showed higher rates of normal findings and lymphocytic colitis. Age above 50 years may have association with organic colonic diseases. **Conclusion:** Absence of alarming features cannot exclude organic colonic diseases in IBS patients, influencing clinical management.

Keywords: Colonoscopic; ROME IV; Irritable Bowel Syndrome; Alarming Features.

Introduction

Functional bowel disorders (FBD) are highly prevalent disorders found worldwide. These disorders have the potential to affect all members of society,

regardless of age, sex, race or socioeconomic status. Irritable bowel syndrome (IBS) occurs as recurrent

abdominal pain that is related to defecation and associated with a change in frequency and/or form of stool in the absence of any other disease to cause these sorts of symptoms. It is one of the disorders of (FBD) (1).

IBS is a common disease occurring at all geographical latitudes. The prevalence of IBS in the global population is estimated at 11%. The prevalence of IBS in women is about twice as high as in men. Half of patients report their first symptoms before the age of 35 years (2).

The current recommended diagnostic criteria for IBS are the Rome IV criteria: recurrent abdominal pain (at least 1 day per week in the last 3 months) associated with 2 or more of the following criteria (2): 1. Related to defecation, 2. Associated with a change in frequency of stool. 3. Associated with a change in form (appearance) of stool. Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis (3).

IBS is then subtyped according to the abnormality of stool consistency, including constipation-predominant (IBS-C, > 25% hard stools and < 25% loose stools), diarrhea predominant (IBD-D, >25 % loose stools and <25 % hard stools), mixed bowel habits (IBS-M, > 25% loose stools and > 25% hard stools); and unclassified (IBS-U, <25% loose stools and <25% hard stools) (3).

There is symptomatic overlap between IBS patients and other gastrointestinal diseases.

Inflammatory bowel diseases, including ulcerative colitis and Crohn's disease, are of concern when a patient with IBS symptoms is evaluated. Studies suggest that more than a third of patients with inflammatory bowel disease fulfill the Rome criteria for IBS (4).

For IBS-C patients, colorectal cancer is a common concern; Case control study found that patients with chronic constipation have a significantly higher prevalence and incidence of colorectal cancer and benign colorectal neoplasm (5).

Collagenous and lymphocytic colitis are more difficult to distinguish from IBS because patients present with chronic watery diarrhea and often no weight loss. In addition, these forms of colitis have a completely normal endoscopic appearance (6).

Management guidelines for IBS recommend that, in a patient who reports abdominal pain associated with a change in stool consistency or number of motions, the diagnosis could be reached using symptom-based diagnostic criteria without the need for exhaustive investigations (7).

However, interest in the potential for missed organic GI lesions in patients diagnosed with IBS has increased over the last years (8).

The purpose of this study was to assess colonoscopic findings in patients fulfilling ROME IV Criteria of Irritable Bowel Syndrome with or without Recently Discovered alarming features.

Patients and methods

This cross-sectional study included sixty consecutive patients with irritable bowel syndrome fulfilling Rome IV criteria with or without alarming features. The study was carried out at Hepatology, Gastroenterology and Infectious Diseases Department in Benha University Hospital, during the period from July 2022 to December 2022.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Inclusion criteria were patients of both sex who attended to the endoscopy unite of Hepatology, Gastroenterology and Infectious Diseases Department at Benha University Hospital with irritable bowel syndrome fulfilling Rome IV criteria (9), recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with two or more of the following: Related to defecation (may be increased or unchanged by defecation). Associated with a change in stool frequency. Associated with a change in stool form or appearance, with or without alarming features like (Hematochezia, family history of colon cancer, family history of inflammatory bowel disease, anemia, positive fecal occult blood test, unexplained weight loss ≥ 10 pounds, severe persistent constipation that is unresponsive to treatment, new

onset constipation in an elderly patient) (10).

Exclusion criteria were prior abdominal surgeries, previously identified comorbidities that could explain their gastrointestinal (GI) symptoms, patients who had undergone colonoscopy is past six months, pregnant women, previously diagnosed colorectal cancer, previously diagnosed IBD, recent history of non-steroidal anti-inflammatory drugs and patients with known thyroid disorders.

Grouping: Patients were selected and divided into two equal groups: **Group A:** 30 patients fulfilled Rome IV criteria of irritable bowel syndrome without alarming features. **Group B:** 30 patients fulfilled Rome IV criteria of irritable bowel syndrome with alarming features that appeared within one month for weight loss and within three months for anemia before inclusion in the study.

All studied cases were subjected to the following: Detailed history taking, including [Personal history; name, age and gender, Present history: course of the disease and duration, Past history of any medical condition or previous hospital admission and Family history of similar condition]. **Full clinical examination: General examination including** [Pallor and Vital signs: pulse, blood pressure, respiratory rate and temperature]. **Laboratory investigations** [complete blood count].

All patients underwent full colonoscopy. Bowel preparation was

done, using oral magnesium citrate for 2 days prior to the procedure, or polyethylene glycol for 1 day prior to the procedure (depending on patient and physician preference). Patient fasted for 16-24 hours (water and fiber free juices were allowed), patients underwent 3 enemas using hypertonic solution of sodium phosphates the day before the procedure. Pentax colonoscopes (Pentax Canada, Inc.) were used for colonoscopy (5).

The following findings were defined as being consistent with organic disease at colonoscopy: evidence of colitis (inflammation or ulceration), colorectal carcinoma, masses or strictures. Multiple biopsies were taken from all cases from right and left colon and according to defined lesions, prepared for microscopic examination as formalin fixed paraffin embedded tissue. Sections were cut at 4 μ m and stained with hematoxylin and eosin dye, then interpreted by an experienced histopathologist. Organic diseases at histopathological examination of biopsy specimens were searching for microscopic colitis, ulcerative colitis, Crohn's disease, colonic or rectal carcinoma (11).

Individuals with no evidence of organic disease at both colonoscopy and histopathological examination of biopsy specimens were classified as exhibiting no organic GI disease, while those with evidence of organic disease at either colonoscopy or histopathological examination of biopsy specimens were classified as exhibiting organic GI disease.

Approval code: Ms.10.4.2022

Sample size

The recruitment size for the present study was established based on data published by a study in 2020 (12). The study disclosed that the prevalence of IBS with the Rome IV criteria across 34 countries, involving 82,476 individuals, was 3.8% (95% CI 3.1–4.5). Using OpenEpi software, with an alpha error of 0.05, 80% power, and a confidence level of 95%, the minimum required sample size was calculated to be 60.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test and ANOVA (F) test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Results

The personal history (age, sex and special habits of medical importance and occupation) were insignificantly different between both groups. Regarding clinical presentation, all patients in both groups suffered from abdominal pain. Bleeding per rectum, weight loss and pallor were significantly higher in group B. Other complaint like chronic constipation,

chronic diarrhea, distention, fatigue, fecal strain and Mucorhea were insignificantly different between both groups. There was no significant difference between the studied groups regarding proton pump inhibitor intake, comorbidities as hypertension and diabetes mellitus. **Table 1**

IBS subtypes (constipation predominant IBS, diarrhea predominant IBS and mixed subtype) had insignificant differences between both groups. **Figure 1**

Hemoglobin was slightly lower in group B compared to group A, however it was statistically insignificant ($P=0.066$) also white blood cells and platelet count were insignificantly different between both groups. Normal colonoscopic findings were significantly higher in group A compared to group B ($P=0.0008$). There was insignificant difference between the studied groups regarding the colonoscopic findings (hyperaemic mucosa, polyps, diverticulae and ulcerations) however, organic diseases representing in (26.66%) of the cases which has no alarming features (group A). **Table 2, Figure 2**

Lymphocytic colitis was significantly higher in group A compared to group B (p value= 0.016) while adenomatous polyps were significantly higher in group B compared to group A. Whereas other histopathological findings (hyperplastic, inflammatory polyps and ulcerative colitis) were insignificantly different between the studied groups. **Table 3**

There was a significant relationship between organic diseases and age above 50 years (P value=0.0044) whereas there was an insignificant relationship between organic diseases and both sex and smoking. **Table 4**

Organic causes (Polyps, diverticulae, ulcerative colitis and lymphocytic colitis) were insignificantly different between patients according to IBS subtypes. **Table 5**

Regarding to relation between presence of alarming features and organic colonic diseases, there was a statistically significant relation regarding Bleeding per rectum and presence of organic colonic diseases ($p<0.001$). **Table 6**

Table 1: Demographic and clinical data of the studied groups

		Group A (n=30)	Group B (n=30)	T test /X²	P value
Age (years)	Mean ± SD	44.3 ± 16.42	44.8 ± 13.87	0.174	0.873
	Range	18 - 80	18 - 75		
Sex	Male	17 (56.67%)	18 (60%)	0.069	0.793
	Female	13 (43.33%)	12 (40%)		
Special habits	Smoking	5 (16.67%)	6 (20%)	0.111	0.739
	No special habits	25 (83.33%)	24 (80%)		
Clinical presentation					
Abdominal pain		30 (100%)	30 (100%)	--	--
Chronic constipation		18 (60%)	11 (36.67%)	3.270	0.0705
Chronic diarrhea		12 (40%)	17 (56.67%)	1.669	0.1965
Alternating chronic diarrhea and constipation		0 (0%)	2 (6.67%)	0.741	0.491
Bleeding per rectum		0 (0%)	23 (76.67%)	37.297	<0.001
Weight loss		0 (0%)	9 (30%)	10.59	0.001
Pallor		0 (0%)	5 (16.67%)	5.455	0.02
Abdominal distention		10 (33.33%)	11 (36.67%)	0.073	0.787
Fatigue		0 (0%)	3 (10%)	3.158	0.237
Faecal strain		3 (10%)	4 (13.33%)	0.162	1.0
Menorrhoea		2 (6.67%)	6 (20%)	2.308	0.254
Proton pump inhibitor intake		2 (6.67%)	2 (6.67%)	0	1
Hypertension		4 (13.33%)	1 (3.33%)	1.96	0.353
Diabetes Mellitus		4 (13.33%)	0 (0%)	2.411	0.112

Table 2: Laboratory and colonoscopic findings of the studied groups

		Group A (n=30)	Group B (n=30)	Test of sig. test	P value
Hb (g/dL)	Mean \pm SD	12.6 \pm 0.94	11.9 \pm 1.43	t= 2.240	0.066
	Range	11 - 15	7.8 - 15		
WBCs (*10 ³ cells/ μ L)	Mean \pm SD	7.6 \pm 2.59	6.5 \pm 2.88	t= 1.576	0.120
	Range	3.7 - 13.5	3.36 - 13.45		
PLT (*10 ³ cells/ μ L)	Mean \pm SD	151.3 \pm 54.95	147.3 \pm 24.27	t= 0.365	0.717
	Range	101 - 377	110 - 198		
Hyperaemic mucosa		1 (3.33%)	5 (16.67%)	X ² = 2.963	0.0852
Polyps		6 (20%)	12 (40%)	X ² =2.857	0.0910
Diverticulae		1 (3.33%)	2 (6.67%)	X ² =0.3509	0.5536
Ulcerations		0 (0%)	2 (6.67%)	X ² =0.741	0.491
Normal Colonoscopic findings		22 (73.3%)	9 (30%)	X ² =11.279	0.0008

Hb: haemoglobin, PLT: platelet count, WBCs: white blood cells

Table 3: Histopathological findings of the studied groups

				Group A (n=30)	Group B (n=30)	X2	P value
Polyps	Hyperplastic			1 (3.3%)	4 (13.3%)	1.964	0.1611
	Inflammatory			1 (3.3%)	3 (10%)	1.071	0.3006
Adenomatous	Villous	Low grade dysplasia		0 (0%)	2 (3.33%)	7.867	0.0196*
		High grade dysplasia		1(3.3%)	0 (0%)		
	Tubular	Low grade dysplasia		3 (6.7%)	3 (6.7%)		
		High grade dysplasia		0 (0%)	0 (0%)		
Ulcerative colitis				0 (0%)	4 (13.3%)	0.112	0.112
Lymphocytic colitis				24(80%)	14(46.7%)	7.177	0.0074*

*: statistically significant as P value <0.05

Table 4: Relationship between organic diseases and demographic data

		Organic diseases		X2	P value
		present	Not present		
Age (years)	18-50	12	24	8.109	0.0044*
	>50	17	7		
Sex	Male	19	16	1.192	0.275
	Female	10	15		
Smoking	yes	7	4	1.2631	0.2611
	no	22	27		

*: statistically significant as P value <0.05

Table 5: Prevalence of organic causes in the studied patients according to IBS subtypes

	Diarrhea predominant IBS (n=29)	Constipation predominant IBS (n=29)	Mixed subtype (n=2)	P value*
Polyps	8 (27.59%)	7 (24.14%)	0 (0%)	0.952
Diverticulae	1 (3.45%)	2 (6.9%)	0 (0%)	
Ulcerative colitis	2 (6.9%)	2 (6.9%)	0 (0%)	
Lymphocytic colitis	18 (62.07%)	18 (62.07%)	2 (100%)	

* chi-square was used for comparison.

Table 6: Relation between presence of alarming features and detection of organic colonic diseases

N=30	Polyps	Diverticulae	Ulcerative colitis	Lymphocytic colitis	X2	P value
Weight loss	2 (3.3%)	3 (5%)	1 (1.67%)	3 (5%)	1.27	0.736
Bleeding per rectum	14 (23.3%)	1 (1.67%)	1 (1.67%)	7 (11.67%)	22.1	<0.001
Anaemia	2 (3.3%)	0 (0%)	2 (3.3%)	1 (1.67%)	2.25	0.523

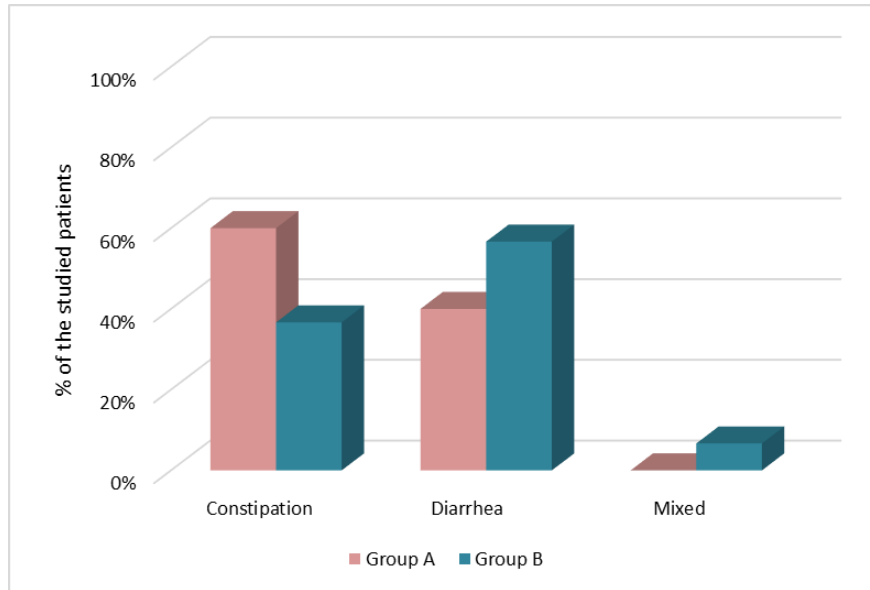


Fig. 1: IBS subtypes between the studied groups

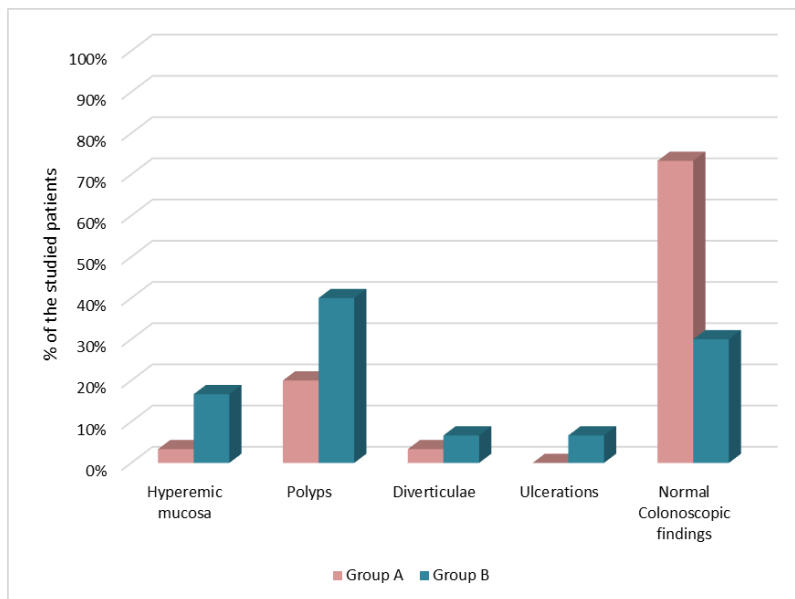


Fig. 2: Colonoscopic findings of the studied groups

Discussion

This study aimed to assess colonoscopic findings in patients fulfilling ROME IV criteria of irritable bowel syndrome with or

without recently discovered alarming features.

The personal history, including age, sex, special habits, and occupation, showed no

significant differences between the groups. Similarly, in a study (13) aligning with the present study, demographic characteristics, including age, gender, BMI, and lifestyle factors, did not significantly differ between their identified groups. In a cross-sectional study (5) with two groups meeting Rome IV criteria for IBS; the authors found no significant demographic distinctions between their participants with and without alarm features.

In terms of IBS subtypes, our study reported that 48.3% had IBS with constipation (IBS-C), another 48.3% had IBS with diarrhea (IBS-D), while 3.3% exhibited mixed IBS (IBS-M), and none had unclassified IBS (IBS-U), with no significant differences between the groups. Similarly, a study (5) found proportions of 42% IBS-D, 26% IBS-C, 28% IBS-M, and 4% IBS-U, with organic lesions present in varying percentages across these subtypes. These results coincide with another study (14), which observed varying proportions of IBS subtypes, emphasizing the diversity in subtype distribution across different populations and locations. Of note, the distribution of IBS subtypes differs in different studies, and probably depends on the population evaluated, geographic location and the definition for each subtype (15). IBS-M was the largest bowel habit subgroup in population-based studies performed in UK and the United States (16, 17), while IBS-C was the most frequent among Iranian adults (18), and IBS-D the most frequent in tertiary hospitals in China (19).

There was insignificant difference between the studied groups regarding the colonoscopic findings including hyperemic mucosa, polyps, diverticulae and ulcerations but there were some cases that represent (26.66%) from the cases with no alarming features have organic colonic diseases. Lymphocytic colitis was significantly higher in group A compared to group B (p value= 0.016) whereas villous adenomatous polyps were significantly higher in group B compared to group A. Other histopathological findings (hyperplastic, inflammatory polyps and ulcerative colitis) were insignificantly different between the studied groups.

Interestingly, a study revealed that microscopic colitis was the predominant organic disease among studied patients; 4/11 patients (36.4%). Three patients had colorectal cancer (27.3%), two patients had ulcerative colitis (18% of organic lesions detected), patient with solitary rectal ulcer (9.1%) and patient had Crohn's disease (9.1%) (5).

Contrarily, a study examined the yield of colonoscopy in a cohort of secondary care patients meeting criteria for IBS found that Crohn's disease was the predominant organic disease, followed by coeliac disease (4 subjects [2.9%]), and microscopic colitis (3 subjects [2.2%]).

In the current study, there was a significant relationship between organic diseases and age above 50 years (P value=0.027) whereas there was an insignificant

relationship between organic causes and other demographic data (smoking).

Supporting the present results, a study evaluated the predictive value of alarm symptoms for dyspeptic patients based on Rome IV criteria. They found that, alarm symptoms were of limited value in differentiating organic dyspepsia and organic upper GI diseases from functional dyspepsia. Age (Odds ratio (OR) = 1.056, P = 0.012) was independent predictors for organic upper GI diseases (20).

A study on a total of 568 consecutive patients (63% female; mean age 44.7 years) to establish the value of alarm features in differentiating between organic disease and irritable bowel syndrome (IBS) and functional dyspepsia (FD). They suggested that onset age > 50 years and blood stains on toilet paper had good predictive value for organic disease (21).

In China, some authors showed that onset age > 40 years, bleeding per rectum, melena and anemia helped distinguish organic disease from functional disease (22), while another study found that hematochezia, emaciation and anemia helped distinguish the two (23).

Regarding the association between organic causes and age, several studies have reported a higher prevalence of organic gastrointestinal conditions in older individuals. A study found that advanced age was associated with an increased risk of organic pathologies in patients undergoing colonoscopy. So there is significant relationship between organic

causes and age in the context of IBS patients (24).

However, the lack of significant relationships between organic causes and other demographic factors, such as sex and smoking, is somewhat contradictory to certain findings in the literature. Some studies have suggested that certain gastrointestinal conditions, including inflammatory bowel disease (IBD), may exhibit sex-specific differences in terms of prevalence and clinical characteristics. For example, a study reported a slightly higher prevalence of Crohn's disease in females compared to males (25).

It is worth noting that the existing research on the relationship between demographic factors and organic causes in IBS patients is diverse, and different studies may yield conflicting results. Additionally, the findings from the present study may be influenced by factors such as sample size and patient population.

Parallel to the current results, a study explored the relationship between IBS subtypes and organic causes, and their findings align with the present results. They reported no significant differences in organic causes based on IBS subtypes, regardless of the presence or absence of alarming features (2).

Interestingly, a cross-sectional study compared the prevalence of structural colonic lesions in patients with suspected non-constipation-predominant IBS and healthy volunteers and determined the yield of rectosigmoid biopsies in patients

with suspected IBS. They revealed that in the control group, the most common findings were polyps (34.4%) followed by diverticulae (21.3%), and hemorrhoids (16.4%). Healthy controls had a significantly higher prevalence of polyps and diverticulosis compared with patients with suspected IBS (34.4% vs. 14.6%, $P < 0.0001$ and 21.3% vs. 8.8%, $P=0.0001$, respectively) (26).

Among patients with IBS-D, organic lesions were present in 12 (28.5%); among patients with IBS-C, organic lesions were present in 11 (30.5%); among patients with IBS-M, organic lesions were present in nine (29.0%) and among patients with IBS-U, organic lesions were present in seven (22.5%). The difference was not statistically significant ($P=0.89$) (27).

The percentage of organic colonic diseases varied with each IBS subtype where the most common subtype that exhibited organic disease was IBS-D group. This disagreed with result of another study (11). A study stated that the most common subtype that exhibited organic disease was IBS-C group (27). This variation in results may be attributed to difference in sample size and the different nature of organic colonic diseases detected.

Conclusion

Patients meeting Rome IV criteria for IBS without alarming features may have organic colonic diseases. Absence of alarming features cannot exclude organic colonic diseases in IBS patients, influencing clinical management.

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To cite this article: Hala M. Elfeky, Rasha M. Abd Rabh, Mostafa E. Fouad, Tamer E. Elazab. Colonoscopic Findings in Patients Fulfilling ROME IV Criteria of Irritable Bowel Syndrome with or without Recently Discovered Alarming Features. *BMFJ* 2024;41(1):21-33.