Irritable Bowel Syndrome and Inflammatory Bowel Disease: Is There a Link?

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Abstract: Background: Symptoms of irritable bowel syndrome and inflammatory bowel disease can overlap. Whether irritable bowel syndrome can hide an organic disorder as inflammatory bowel disease is still questionable. We aimed to estimate the frequency of detection of inflammatory bowel disease in Egyptian patients with clinically diagnosed irritable bowel syndrome. **Materials and Methods:** We prospectively included 90 patients with clinically diagnosed irritable bowel syndrome according to Rome III criteria. For all included patients, complete blood count, erythrocyte sedimentation rate, C-reactive protein, stool analysis and stool culture were done. Besides these laboratory investigations, abdominal ultrasonography and colonoscopy with colonic biopsies were performed. **Results: I**nflammatory bowel disease was detected in 18.9% among the included patients. While irritable bowel syndrome was confirmed in 57.8%, no significant difference between irritable bowel syndrome and inflammatory bowel disease patients as regard the age, gender and symptomatology such as abdominal pain, bloating, diarrhea and constipation. A highly significant difference was found regarding the used laboratory tests, ultrasonographic and colonic examinations between irritable bowel syndrome and inflammatory bowel disease patients. **Conclusion:** A considerable percentage of inflammatory bowel disease patients could be detected among patients with clinically diagnosed irritable bowel syndrome. Laboratory tests and ultrasonographic examination can help primarily to discriminate the two conditions although colonoscopy with colonic biopsy remains the gold standard in diagnosis of inflammatory bowel disease. [Report and Opinion. 2010;2(3):44-50]. (ISSN: 1553-9873).

Key Words: Irritable bowel syndrome (IBS), Inflammatory bowel disease (IBD), Rome criteria

1. Introduction:

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by chronic abdominal pain, discomfort, bloating, and alteration of bowel habits in the absence of any organic cause. Diarrhea or constipation may predominate, or they may alternate (classified as IBS-D, IBS-C or IBS-A, respectively) [1].IBS is not associated with any definitive biochemical, structural, or serologic abnormalities that define its presence. Because the symptoms of IBS are common to a number of other gastrointestinal conditions, IBS was long considered a "diagnosis of exclusion" [2].

An international group of experts in functional GI motility disorders convened to develop symptom-based criteria, known as the Rome criteria. Overall, the Rome I and II criteria are considered useful for standardizing enrollment of patients into clinical trials. However, many clinicians believe that these criteria are too restrictive for use in clinical practice [3]. The less restrictive symptom timeframe requirements of the Rome III guidelines make them more clinically practical than the previous iterations. Rome III criteria require symptoms to originate for 6 months prior to diagnosis, and be currently active for 3 months [4]

Inflammatory bowel disease (IBD) is a group of chronic, autoimmune and inflammatory disorder of the large and small intestine. The major types of IBD are Ulcerative colitis (UC) and Crohn's disease (CD) [5].

There is a considerable overlap between symptoms in patients with IBS and IBD. Furthermore, IBS-like symptoms are frequently reported in patients before the diagnosis of IBD [6]. Whether irritable bowel syndrome can hide an organic disorder as inflammatory bowel disease is still questionable.

We aimed in this study to estimate the frequency of detection of IBD in Egyptian patients with clinically diagnosed irritable bowel syndrome.

2. Materials and Methods:

2.1. Patients: Ninty patients, clinically diagnosed to have IBS, were included in this prospective study. Based on Rome III criteria for functional gastrointestinal disorders, (C1 of Rome III Functional Gastrointestinal Disorders), IBS is defined as abdominal discomfort or pain that originates 6 months prior to diagnosis and be currently active for 3 months [4]. This abdominal pain had two out of three of these features:

- Relieved with defecation; and/or

- Onset associated with a change in frequency of stool; and/or
- Onset associated with a change in form (appearance) of stool.

The patients were attended to Gastroenterology and Endoscopy Unit, Ain Shams University Hospitals between November 2008 and October 2009.

The patients excluded were those with known IBD, history or diagnosis of colorectal cancer, refusal of colonoscopy or participation in the study and incomplete colonoscopic examination.

2.2. Ethical consideration: This study has been performed in accordance with the ethical standards. Informed consents were obtained from all participants. Voluntary participation and the right to refuse participation were emphasized.

2.3. Methodology: After informed consent, all patients were subjected to full history taking, clinical examination, laboratory investigations in the form of (complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and abdominal ultrasound (U/S). Colonoscopic examination was performed by using Pentax Videocolonoscope. Multiple colonic biopsies were obtained and stained with Hematoxylin and Eosin stain for histopathological examination.

2.4. Statistical methods: SPSS statistical software package (V. 17.0, Echo soft Corp., USA, 2008) was used for data analysis. Data were expressed as Mean±SD for quantitative measures and both number and percentage for categorized data.The following tests were done:

1. Comparison between two independent mean groups for parametric data using Student t test.
2. Comparison between two independent groups for non-parametric data using Wilcoxon Rank Sum test.
3. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at 0.05 was considered significant while at 0.01 and 0.001 are highly significant.

4. Logistic Multi-Regression analysis was used to search for a panel (independent parameters) that can predict the target parameter (dependant variable). By using logistic stepwise multi-regression analysis, we can get the most sensitive ones that predict the dependant variable. They can be sorted according to their sensitivity to discriminate according to their p values.

3. Results:

The included patients were 55 males and 35 females, their ages ranged between 19-65 years (Mean±SD=38.29±11.88). Colonoscopic and colonic biopsies were obtained from all subjects. According to histopathological findings, the patients were categorized as shown in table (1).

Table 1. Distribution of the study cases according to histopathological findings

Histopathological Findings	no	%
Normal Histopathology (IBS cases)	52	57.8
Non Specific colitis	16	17.8
Bilharzial colitis	3	3.3
IBD (13 cases UC and 4 cases CD)	17	18.9
Cancer Colon	2	2.2

Table 2. Stool analysis in IBS and IBD groups

Stool Analysis	IBS		IBD		P value
	no	%	no	%	
Negative	45	86.54	6	31.3	<0.001
Occult Blood	0		7	41.2	
Entamaeba histolytica cysts	7	13.46	2	11.67	
Pus cells	0		2	11.67	

Table 3. Comparison between IBS and IBD cases in relation to Hb concentration, WBCs, platelet counts and ESR.

	IBS	IBD	P value
Hb[a]	13.07±1.45	11.2±1.8	0.001
WBCs count[b]	6069.2±1456.2	8629.4±2766.7	0.002
Platelet count	276.4±55.2	444±69.4	0.000
ESR	11.6±7.4	49.8±29.6	0.000

a=Haemoglobin concentration b=White blood cell count

Table 4. Comparison between IBS and IBD cases in relation to CRP

CRP	IBS		IBD		P value
	no	%	no	%	
+ve	3	5.8	9	52.9	0.000
-ve	49	94.2	8	47.1	

Table 5. Comparison between IBD and IBS cases in relation to U/S findings

U/S Findings	IBS		IBD		P value
	no	%	no	%	
Bowel wall thickening	0		13	76.5	0.000
No bowel wall thickening	52	100	4	23.5	

Table 6. Comparison between IBD and IBS cases in relation to colonoscopic findings

Colonoscopic Findings	IBS		IBD		P value
	no	%	no	%	
Normal	46	88.46	0		<0.001
Spastic Colon	6	11.54	0		
Hyperaemic mucosa	0		4	23.53	
Colonic Erosions	0		2	11.76	
Colonic Ulcerations	0		11	64.71	

Table 7. Logistic Stepwise multi-regression analysis for discrimination between IBD and IBS

Parameter	Regression coefficient	P	F-ratio	Sig.
WBCs Count	+0.0026	0.1102		
Platelet Count	+0.4017	0.0000		
ESR	+0.0091	0.1799	49.3	<0.001
CRP	+0.0089	0.2212		
U/S findings	+0.5869	0.0000		

4. Discussion:

Patients presented to gastroenterology clinics with symptoms suggestive of lower-bowel disorders often require extensive investigation to differentiate functional from organic disease [7]. Although they cause similar symptoms, IBS and IBD are different conditions, with different courses, different treatment options and different outcomes [8].

Among our patients, IBS and IBD were detected in 57.8 and 18.9% respectively. Garcia et al. [9] reported a significant increased risk of detecting IBD in patients initially diagnosed with IBS (relative risk 16.3%) during a mean follow-up period of 3 years. In a recent case–control study, the association of the risk of developing IBD in subjects with symptoms of infectious gastroenteritis and IBS was elucidated. An approximately five-fold increase in IBD risk was noted for individuals with a previous diagnosis of IBS [10]. These results showed the relative risk in individuals with a previous episode of IBS symptoms for the development of IBD. Therefore IBS may hide an organic disease and an association between IBS and IBD could be found.

It was found that; in a proportion of patients later diagnosed with IBD, however, initial symptoms may be attributed to a functional gut disorder [11].It is well reported that patients with IBD often complain of IBS symptoms for several years before the diagnosis of IBD, and symptoms of IBS will occasionally occur in patients with IBD who are in remission [12-14]. While Farrokhyar et al [15] reported that; IBD in remission had a high rate of IBS-type symptoms in up to 26% of the patients.

Infectious gastroenteritis may be one of the important factors in the development of IBS, with affected individuals often categorized as having post-infectious IBS (PI-IBS), and is linked to the onset of symptoms in approximately 10–20% of patients diagnosed with IBS [16].Recently, infectious gastroenteritis has also been suggested to be associated with the development of IBD, and various studies have suggested that individuals with IBS or IBS-like symptoms may be susceptible to initiation of IBD [17].This adds a more support to the association between IBS and IBD.

Minderhoud et al. [18] reported that IBS symptoms were present in 41.7% and 31.5% of patients with Crohn's disease (CD) and ulcerative colitis (UC), respectively, but only in 7.6% of healthy controls. These findings are consistent with the hypotheses that

subclinical inflammation and immune activation that precede the expression of IBD result in symptoms of IBS. This previous immune activation and inflammation are followed by gut dysfunction and the generation of IBS symptoms.

In accordance, our results showed no significant difference between both groups regarding the symptomatology as abdominal pain, bloating, diarrhea and constipation. The Rome III criteria, in conjunction with careful history-taking and thorough physical examination, can be applied as part of the stepwise, symptom-based approach to diagnosing IBS . This raises the physicians' attention to the presence of alarm features (eg, bloody stool, weight loss).It is potentially indicative of organic disease and necessitates further evaluation [2].

Discriminating IBS from IBD, especially with mild disease activity, is a common clinical challenge [19].The clinical Laboratory plays an important role in differentiating these disorders [8].

Anaemia has been recognized as a key symptom of IBD. For a long time, the only laboratory parameter included in disease activity scores (such as the Crohn's disease activity index) was the haematocrit / haemoglobin ratio. Intestinal bleeding (either visible or occult blood) is a major symptom of the disease itself and anaemia is a consistent clinical feature of IBD [20]. This is in agreement with our study as the mean±SD of HB concentration showed significant reduction in the IBD than in IBS group (11.2±1.8) and (13.07±1.45) respectively.

Beside anemia, thrombocytosis and leukocytosis are common hematological abnormalities in IBD patients and can be seen in up to half of the patients with active disease. Thrombocytosis is postulated to result from circulating inflammatory cytokines that stimulate platelet production. Similarly, leukocytosis can occur as a result of generalized inflammation [21]. Association between thrombocytosis and both CD and UC has been recognized for many years [22]. Beattie et al. [23] found that the platelet count was increased in 88% of patients with CD and in 70% with UC. This is in keeping with our study as platelet count showed highly significant elevation in the IBD than in IBS cases.

In agreement with our study, Sabery and Bass [24] studied the use of ESR and HB concentration in comparison to serologic markers as screening test for IBD. They found that, serologic testing for IBD had 60% sensitivity and 92% specificity while positive laboratory test for anemia or an elevated ESR had 83% sensitivity and the combination of anemia and elevated ESR had 96% specificity.

CRP is one of the most important proteins up-regulated during an acute-phase stimulus in humans [25]. Our study showed a highly significant positive correlation between IBD cases and positive CRP in comparison to IBS cases. Matching with our results, Poullis et al [7] reported CRP to be a good marker in differentiating IBD from IBS among individuals referred for symptoms suggestive of lower bowel disease. In addition, ESR was proved to be the second best marker in such differentiation. The sensitivity of CRP for detection of IBD ranges between 50% and 60% for UC and between 70% and 100% for CD [7-26]. Also, Henriksen et al. [27] reported that, CRP levels at diagnosis were related to the extent of disease in patients with UC. However, other markers of inflammation such as ESR give reliable information on IBD activity; their longer half life and interference with other factors make them less useful in clinical practice compared with CRP [28].

Ileocolonoscopy represents the diagnostic standard in the work-up of patients with IBD. Because of the invasiveness and pain sensation during colonoscopy, patients are often reluctant to be colonoscoped [29].It was found that, in the hands of an experienced radiologist, U/S can be very accurate for the detection of IBD [30].

Trans-abdominal U/S is clinically useful in the initial diagnosis of IBD by evaluating bowel wall thickness and surrounding structures including peri-intestinal inflammatory reaction, extent and localization of involved bowel segments and detection of extra-luminal complications such as fistula, abscesses, carcinoma and ileus [31].

The criterion that is most extensively used for the diagnosis of CD is bowel wall thickening. In most studies, the bowel wall is considered to be thickened when thickness exceeds 3 mm [32]. Bowel wall thickening is considered to be a characteristic feature of UC as well [33]. Parente et al. [34] studied the role of early U/S in detecting inflammatory intestinal disorders. The main organic disorders found were CD (56%), ulcerative/indeterminate colitis (30%). These results are in agreement with our study as bowel wall thickening by U/S was found in 13 out of 17 IBD patients (76.5%).

Among our patients, WBCs (>6700); Platelets count (>318 000); ESR (>21); positive CRP and U/S findings (bowel wall thickening) were the most sensitive predictors for differentiation of IBD from IBS. Accordingly, CBC, ESR, CRP and U/S can be used as

non invasive screening tools when diagnosis of IBD was suspected.

Colonoscopy with multiple biopsy specimens is well established as the first line procedure for diagnosing colitis. It represents the diagnostic standard in the work-up of patients with inflammatory bowel diseases [35]. In our study colonoscopy showed abnormal endoscopic findings in 100% of IBD cases with accuracy of 100% in diagnosing IBD in comparison to abnormal findings in only 11.54% of IBS patients.

In conclusion, a considerable percentage of IBD patients could be detected among patients with clinically diagnosed IBS. Laboratory tests and ultrasonographic examination can help primarily to discriminate the two conditions although colonoscopy remains the gold standard in diagnosing IBD. Additional studies are necessary to understand the overlap among IBS and IBD, which may lead to the development of new therapeutic tools for patients with IBS and IBD.

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References

[1] Mayer EA. Clinical practice. Irritable bowel syndrome. N. Engl. J. Med 2008; 358(16): 1692-9.
[2] Brandt LJ, Bjorkman D, Fennerty MB, Locke GR, Olden K and Peterson W.Systematic review on the management of irritable bowel syndrome in North America. Am J Gastroenterol 2002; 97: 7–26.
[3] Thompson WG, Longstreth GF, Drossman DA, et al. Functional bowel disorders and functional abdominal pain. Gut 1999; 45: 43–47.
[4] Drossman DA. The functional gastrointestinal disorders and the Rome III process. Gastroenterology 2006; 130:1377–1390.
[5] Summers RW, Elliott DE, Qadir K, Urban JF Jr, Thompson R and Weinstock JV. Trichuris suis seems to be safe and possibly effective in the treatment of inflammatory bowel disease. Am. J. Gastroenterol 2003; 98(9): 2034-41.
[6] Schoepfer AM, Trummler M, Seeholzer P, Seibold-Schmid B, MSc and Seibold F. Discriminating IBD from IBS: Comparison of the test performance of fecal markers, blood leukocytes, CRP, and IBD antibodies. Inflamm Bowel Dis 2007; 14(1), 32:39.
[7] Poullis AP, Zar S, Sundaram KK, Moodie SJ, Risley P, Theodossi A, et al. A new, highly sensitive assay for CRP can aid the differentiation of inflammatory bowel disorders from constipation and diarrhea predominant functional bowel disorders. Eur J Gastroenterol Hepatol. 2002; 14:409-412.
[8] Moore E. IBS vs. IBD and other tummy aches, MLO 2007; 13-18.
[9] Garcı´a Rodrı´guez LA, Ruigo´mez A, Wallander MA, Johansson S and Olbe L. Detection of colorectal tumor and inflammatory bowel disease during follow-up of patients with initial diagnosis of irritable bowel syndrome. Scand J Gastroenterol. 2000; 35:306–11.
[10] Porter CK, Tribble DR, Aliaga PA, Halvorson HA and Riddle MS. Infectious gastroenteritis and risk of developing inflammatory bowel disease. Gastroenterology. 2008; 135:781–6.
[11] Isgar B, Harman M, Kaye MD and Whorwell PJ. Symptoms of irritable bowel syndrome in ulcerative colitis in remission. Gut 1983; 24(3):190–2.
[12] Talley NJ. Irritable bowel syndrome. Intern Med J. 2006; 36:724–8.
[13] Spiller R. Clinical update: irritable bowel syndrome. Lancet. 2007; 369:1586–8.
[14] Spiller R, Aziz Q, Creed F, Emmanuel A, Houghton L, Hungin P, et al. Guidelines on the irritable bowel syndrome: mechanisms and practical management. Gut. 2007; 56:1770–98.
[15] Farrokhyar F, Marshall JK, Easterbrook B, Irvine EJ. Functional gastrointestinal disorders and mood disorders in patients with inactive inflammatory bowel disease: prevalence and impact on health. Inflamm Bow Dis 2006; 12:38–46.
[16] Dupont AW. Post-infectious irritable bowel syndrome. Curr Gastroenterol Rep. 2007; 9:378–84.
[17] Ishihara S, Aziz M, Oshima N, Mishima Y, Imaoka H Moriyama I, et al. Irritable bowel syndrome and inflammatory bowel disease: infectious gastroenteritis-related disorders? Clin J Gastroenterol 2009; 2:9–16.
[18] Minderhoud IM, Oldenburg B, Wismeijer JA, van Berge Henegouwen GP and Smout AJ. IBS-like symptoms in patients with inflammatory bowel disease in remission; relationships with quality of life and coping behavior. Dig Dis Sci 2004; 49(3):469–74.
[19] Bercik P, Verdu EF, Collins SM. Is irritable bowel syndrome a low grade inflammatory bowel disease? Gastroenterol Clin North Am. 2005; 34:235–245.
[20] Gasche C, Lomer MC, Cavill I and Weiss G. Iron anaemia and inflammatory bowel diseases. Gut 2004; 53(8): 1190-1197.

[21] Larsen TB, Nielsen JN, Fredholm L, Lund ED, Brandslund I, Munkholm P and Hey H. Platelets and anticoagulant capacity in patients with inflammatory bowel disease. Pathophysiol Haemost Thromb. 2002; 32(2):92-6.
[22] Harries AD, Beeching SJ, Rogerson SJ and Nye FJ.The platelet count as a simple measure to distinguish inflammatory bowel disease from infective diarrhea. J Infect 1991; 22: 247-50.
[23] Beattie RM, Walker-Smith JA and Murch SH. Indications for investigation of chronic gastrointestinal symptoms. Arch Dis Child 1995; 73: 354-5.
[24] Sabery N and Bass D. Use of serologic markers as a screening tool in inflammatory bowel disease compared with elevated erythrocyte sedimentation rate and anemia. Pediatrics 2006; 119: 193-199.
[25] Vermeire S, Assche GV and Rutgeerts P. C-Reactive protein as a marker for inflammatory bowel disease. Inflamm Bowel Dis 2004; 10: 661-665.
[26] Shine B, Berghouse L, Jones JE, Landon J. C-reactive protein as an aid in the differentiation of functional and inflammatory bowel disorders. Clin Chim Acta. 1985; 148:105–109.
[27] Henriksen M, Jahnsen J, Lygren I, Stray N, Sauar J, Vatn MH.C-reactive protein: a predictive factor and marker of inflammation in inflammatory bowel disease. Results from a prospective population-based study. Gut 2008; 57(11):1518-23.
[28] Vermeire S, Assche GV and Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? .Gut. 2006; 55(3): 426–431.
[29] Pascu M, Roznowski AB, Muller HP, Adler A, Wiedenmann B and Dignass AU. Clinical relevance of transabdominal ultrasonography and magnetic resonance imaging in patients with inflammatory bowel disease of the terminal ileum and large bowel. Inflamm. Bowel Dis 2004; 10(4): 373-82.
[30] Rispo A, Imbriaco M, Celentano L, Cozzolino A, Camera L and Mainenti PP . Noninvasive diagnosis of small bowel Crohn's disease: combined use of bowel sonography and Tc-99m-HMPAO leukocyte scintigraphy. Inflamm Bowel Dis 2005; 11: 376-382.
[31] Dietrich CF. Significance of abdominal ultrasound in inflammatory bowel disease. Dig Dis. 2009; 27(4):482-93.
[32] Bru C, Sans M, Defelitto MM, Gilabert R, Fuster D and Liach J .Hydrocolonic sonography for evaluating inflammatory bowel disease. AJR 2001; 177: 99–105.
[33] Limberg B and Osswald B. Diagnosis and differential diagnosis of ulcerative colitis and Crohn's disease by hydrocolonic sonography. Am J Gastroenterol 1994; 89: 1051–1057.
[34] Parente F, Greco S, Molteni M, Cucino C, Maconi G and Sampietro GM. Role of early ultrasound in detecting inflammatory intestinal disorders and identifying their anatomical location within the bowel. Aliment Pharmacol Ther 2003; 18(10): 1009-1016.
[35] Geboes K, Ectors N, D'Haens G. et al Is ileoscopy with biopsy worthwhile in patients presenting with symptoms of inflammatory bowel disease? Am J Gastroenterol 1998. 93201–206.

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