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

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**Abstract:**

**Background and Study Aim**: Symptoms of irritable bowel syndrome and inflammatory bowel disease can overlap. Whether irritable bowel syndrome can hide an organic disorder as inflammatory bowel disease still questionable. We aimed to estimate the frequency of detection of inflammatory bowel disease in Egyptian patients with clinically diagnosed irritable bowel syndrome.

**Patients 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.

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

**1.Introduction:**

Irritable bowel syndrome (IBS) is a [functional bowel disorder](http://en.wikipedia.org/wiki/Functional_bowel_disorder) characterized by chronic [abdominal pain](http://en.wikipedia.org/wiki/Abdominal_pain), discomfort, bloating, and alteration of bowel habits in the absence of any organic cause. [Diarrhea](http://en.wikipedia.org/wiki/Diarrhea) or [constipation](http://en.wikipedia.org/wiki/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 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. Patients 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 originate 6 months prior to diagnosis andbe currently active for3 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 Exclusion Criteria:

1. Patients with known IBD.
2. Patients presenting with symptoms suggestive of IBD.
3. Patients with history or diagnosed colorectal cancer.

 4- Patients refusing colonoscopy or refusing to participate in the study.

 5- 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). All of them were colonoscopic and colonic biopsies were obtained. 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 |

 CD= Crohn's disease UC=Ulcerative colitis

Patients with normal histopathological findings represented the group of IBS.The mean±SD of ages showed no significant difference between IBS and IBD cases, (38.4±12.54) and (37.2±8.5) years respectively. Also no significant difference between them as regard the gender and symptomatology such as abdominal pain, bloating, diarrhea and constipation.

A highly significant difference was found between IBS and IBD cases regarding the stool analysis (Table 2). Occult blood was detected in 41.2% of IBD and none of IBS cases. Negative results were obtained for stool culture of all IBS and IBD cases.

**Table (2):** Stool analysis in IBS and IBD groups:

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

There was a highly significant difference between IBS and IBD cases regarding low HB concentration, increased WBCs, increased platelet counts and elevated ESR (Table 3).

**Table (3):** Comparison between IBS and IBD cases in relation to HB

Concentration, WBCs, platelet counts and ESR:

|  |  |  |  |
| --- | --- | --- | --- |
|  | IBS | IBD | P value |
| HBa | 13.07±1.45 | 11.2±1.8 | 0.001 |
| WBCs countb | 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

A highly significant difference was detected between IBD cases in comparison to IBS cases as regard to positive CRP.

**Table (4):** Comparison between IBS and IBD cases in relation to CRP:

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

There was a positive correlation between IBD and abnormal U/S findings with statistically significant difference between IBD and IBS cases.

**Table (5):** Comparison between IBD and IBS cases in relation to U/S findings:

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

Abnormal colonscopic findings (as mucosal hyperaemia, erosions and ulcerations) were detected in all IBD cases with a highly significant difference than IBS cases.

**Table (6):** Comparison between IBD and IBS cases in relation to colonoscopic findings:

|  |  |  |  |
| --- | --- | --- | --- |
| Colonoscopic Findings |  IBS |  IBD | P value |
| no | % | no | % |  <0.001 |
|  **Normal**  | 46 | 88.46 | 0 |  |
| 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 CountPlatelet CountESRCRPU/S findings | +0.0026+0.4017+0.0091+0.0089+0.5869 | 0.11020.00000.17990.22120.0000 | 49.3 | <0.001 |

Logistic stepwise multi-regression analysis showed that WBCs (>6700); Platelets count (>318 000); ESR (>21); positive CRP; U/S findings (shifting from normal to bowel wall thickening) are the most sensitive predictors for IBD from those with IBS (F-ratio = 49.3, p<0.001).

**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 symptomsin 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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