***Original Research Article***

# PsychimmunologicalAspects and Quality of Life in Patients with Irritable Bowel Syndrome


## Abstract

**Background**:Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder and may coexist with psychiatric disorders. We aimedto establish new directions for diagnosis of psychiatric disorders in IBS patients by assessment of the quality of life(QOL) andthe immunological role in IBS.

**Methods:**This study was carried out on 80 subjects aged from 18 to 65 years old, both sexes, assigned into two groups: group I included 60 patients were diagnosed with IBS according to ROM-IV diagnostic criteria and were further divided according to age into two groups, first group is (18-40) years and second group is (41-65) years. Group II: Included 20 subjects as a healthy Control group.

**Results:**The younger age group of patients with IBShave a significantlybetter overall QOL and its domains than the older age group. Hamilton Rating Scale of Depression scores were significantly higher in female patients and older age groups.Patients with psychiatric comorbidity had a lower QOLand its domains than patients without psychiatric comorbidity with a significant difference between both groups. There was a significant difference in serum Interlukin-6 between patients with IBS and healthy control group. Also in serum Interlukin-6 patients with IBScomorbid psychiatric disorders and patients without psychiatric comorbidity with.

**Conclusions:**Psychiatric symptoms are presented earlier in Egyptian IBS. A higher percentage of psychiatric disorders are presented with severe forms of IBS affecting the prognosis of IBS and subsequently the QOLand health costs.

**Keywords:**Psych immunological Aspects, Irritable Bowel Syndrome, Quality of Life

**Introduction:**

Irritable bowel syndrome is a functional gastrointestinal disorder with significant morbidity, resulting from the interaction of physiological, psychological, social, cultural and behavioral factors. Irritable bowel syndrome accounts for 50% of patients who visit general practitioners for gastrointestinal related complaints[1].

Brain-gut axis refers to bidirectional continuous communication between the enteric nervous system and CNS, including the hypothalamic-pituitary-adrenal axis. Various neurotransmitters, neuropeptides, and other neuromodulators are present in both the brain and the gut. Gastrointestinal homeostasis is dependent on a functional equilibrium between these pathways. Activation of the 5-HT3 receptor subtype results in enhanced motility, secretion, and sensation, whereas activation of the 5-HT4 receptor subtype has various excitatory and inhibitory effects [2].

Abnormalities in the 5-HT reuptake transport system have been found in irritable bowel syndrome patients. Studies have shown that 5-HT plays a critical role in gastrointestinal motility, visceral sensitivity, gastrointestinal immune function, and blood flow. Polymorphism of the 5-HT2A receptor gene may be associated with the development of irritable bowel syndrome [3].

In the absence of a measurable biological index of irritable bowel syndrome, health-related quality of life (HRQoL) has emerged as an ideal measure for use in clinical trials and studies [4].

The prevalence of irritable bowel syndrome in psychiatric disorders has been found to be 29% in major depression, 44% in panic disorder, 32% in generalized anxiety disorder, 36% in post-traumatic stress disorder, and 17% in schizophrenia. In a recent study, only 37% of patients with irritable bowel syndrome who were treated met the criteria for clinical

depression, yet 38% contemplated suicide because of their symptoms (5% attempted suicide) [5].

High prevalence rates of subthreshold psychiatric symptomatology of anxiety and obsessive-compulsive disorders were found in patients with functional gastrointestinal disorders, which are likely to influence the expression of gastrointestinal symptoms [6].

Studies supported that irritable bowel syndrome patients have high level of neuroticism which might influence coping strategies like catastrophizing and somatization. Studies found that many irritable bowel syndrome sufferers score high in the personality trait alexithymia, bodily preoccupation, hypochondriacal beliefs and phobias[7].

The aim of this work wasto establish new directions for diagnosis of psychiatric disorders in patients with irritable bowel syndrome by throwing the light on the nature of comorbidity between psychiatric disorders and irritable bowel syndrome, assessment of the quality of life in irritable bowel syndrome, assessment of the immunological role in irritable bowel syndrome.

**Patients and Methods:**

This study was carried out on 80subjects aged from 18 to 65 years old, both sexes, categorized into two groups: group I included 60 patients were diagnosed with irritable bowel syndrome according to ROM-IV diagnostic criteria and were further divided according to age into two groups, the first group is (18-40) years and the second group is (41-65) years. Group II: included 20 subjects as healthcontrol.

The study was done from October 2018 to October 2021 after approval from the Ethical CommitteeTanta University Hospitals. An informed written consent was obtained from the patients.

Exclusion criteria were inflammatory bowel diseases excluded by colonoscopy and Faecal Calprotectin, colorectal masses excluded by history, clinical examination and colonoscopy, evidence of overt gastrointestinal bleeding, Subjects above 65 years to exclude other factors that may affect cognition, intellectual disability which interfere with proper psychiatric assessment, medical or neurological disorders excluded by routine medical and neurological examinations, substance use disorders, pregnancy.

All patients were subjected to: History taking, clinical and neurological examination.

**GIT assessment**

1-Rome IV criteria for irritable bowel syndrome[8].

The criteria imply the presence recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with two or more of: Related to defecation, associated with a change in frequency of stool, associated with a change in form (appearance) of stool.

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The questionnaire was adopted from previously validated and published questionnaires[9]. The Arabic translated version was adopted from previously published studies with an official permission obtained from the Rome Foundation, Inc. [10].

The criteria had an excellent specificity of 97.1% and a moderate sensitivity of 62.7% from 9 gastroenterology clinics. The same study also assessed a 1month test-retest reliability of the criteria and found the same diagnoses were reproducible in about 75% of patients [11].

**Faecal Calprotectin by ELISA [12]:**

Quantitative test carried out in the stool through using mononclonal anti-calprotectin antibodies. Faecal sampling for measurement of calprotectin level was carried out before endoscopy and its levels were determined by ELISA test on 50–100 mg of faeces. Samples were stored in plain tubes without chemical or biological additives, between 2-8℃. The test

allows for the selective measurement of calprotectin antigen by sandwich ELISA. A monoclonal capture antibody highly specific to calprotectin heterodimeric and polymeric complexes, respectively, was coated to the microtitre plate (1st antibody)and were incubated at room temperature for 30 minutes. After a washing step, a detection antibody (2nd antibody, anti-calprotectin antibody) conjugated with horseradish peroxidase detected the calprotectin molecules bound to the monoclonal antibody coated on the plate. After incubation and a further washing step, tetramethylbenzidine was added (promoting a blue colour) prior to a stopping reaction (yellow colour). Absorption was measured at 450 nm (QUANTA Lite Calprotectin ELISA kit. INOVA)

Calprotectin concentrations of 50.0 mcg/g and lower are not suggestive of active inflammatory process within the gastrointestinal system. Concentrations between 50.1-120.0 mcg/g may represent a mild inflammatory process, such as treated inflammatory bowel disease or associated with non-steroidal anti-inflammatory drug or aspirin usage. Concentrations >120.0 mcg/g are suggestive of inflammatory bowel disease [13].

**Colonoscopy for exclusion of inflammatory bowel diseases [14]:**

Bowel preparation was done, using oral magnesium citrate for 2 days before the procedure. Patients fasted for 16-24 hours (water and fiber free juices were allowed), patients underwent special oral laxatives such as polyethylene glycol and enema for cleansing, and under cautious sedation using midazolam.

**Irritable Bowel Syndrome Quality of Life Questionnaire Scale (IBS-QOL)** [9]:

The questionnaire is a 34-item constructed specifically to assess the perceived impact of IBS on QOL in 8 domains (dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual dysfunction, and relationships). Each item is scored on a 5-point scale (1 not at all, 5 a great deal). The individual responses to the 34 items were summed and averaged for a total score and then transformed to a 0-100 scale for ease of

interpretation with higher scores indicated better quality of life. Overall total score of IBS-related QOL ranging from 0 (poor quality of life) to 100 (maximum quality of life). The transformation formula used for the IBS-QOL total and scale scores is: (The sum of the items - lowest possible score) / (Possible raw score range) * 100.

IBS-QOL-34 questionnaire has a satisfactory internal consistent reliability and test-retest reliability with a Cronbach's alpha and intraclass correlation coefficient of 0.93 and 0.88, respectively[15].

**Psychiatric assessment:**

**Structured Clinical Interview for DSM-IV Axis I &II [16]:**

It contains seven different diagnostic groups: mood, psychotic, substance abuse, anxiety, somatoform, eating, and adjustment disorders. The SCID-I interview begins with an overview section that obtains demographic information, work history, chief complaint, history of psychiatric illness, treatment history and assessment of current functioning with open ended questions to elicit responses in the subjects' own words.

The SCID-II is an efficient instrument that helps researchers and clinicians make standardized, reliable, and accurate diagnoses of personality disorders (paranoid, schizoid, schizotypal, histrionic, borderline, antisocial, narcissistic, obsessive compulsive, defendant, avoidant, passive aggressive, depressive, and personality disorder not otherwise specified.

Structured Clinical Interview for DSM-IV Axis I and II is considered the standard interview to verify diagnosis in clinical trials and is extensively used in other forms of psychiatric research.

**Montreal cognitive assessment function scale (MoCA) [17]:**

The MoCA assesses several cognitive domains as:Short-term memory recall task (5 points) involves two learning trials of five nouns and delayed recall after approximately five minutes, visuospatial abilities are assessed by clock-drawing task (3 points) and a three-dimensional

cube copy (1 point), multiple aspects of executive functions are assessed using an alternation task adapted from the trail-making B task (1 point), a phonemic fluency task (1 point), and a two-item verbal abstraction task (2 points), attention, concentration, and working memory are evaluated using a sustained attention task (target detection using tapping; 1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each), language is assessed using a three item confrontation naming task with low familiarity animals (lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points), and the aforementioned fluency task, abstract reasoning is assessed by describing the similarity task with 2 points being available, orientation to time and place is evaluated by asking the subject for the date and the city in which the test is occurring (6 points).

Visuospatial and executive functioning: 5 points, animal Naming: 3 points, attention: 6 points, language: 3 points, abstraction: 2 points, delayed recall (short-term memory): 5 points, orientation: 6 points

**Hamilton Rating scale for depression (HRSD) [18]:**

The HRSD is a checklist of items (mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms) which are ranked on a scale of 0-4 or 0-2. Items with quantifiable severity are scored 0-4; 4 indicate the greatest severity. Although the original scale had 21 items, Hamilton suggested scoring only the initial 17 items because the last 4 items either occurred infrequently (e.g.,depersonalisation) or described other aspects of the illness rather than severity (e.g. diurnal variation). Hamilton believed some symptoms were more difficult to quantify reliably and these have a range of 0-2.very severe >23; severe 19-22; moderate 14-18; mild 8-13; normal <7. Similar thresholds have been reported by others.

The following norms were used:0- 6 (Normal), 7 – 17 (mild), 18-24 (moderate), >24 (severe)

**Immunological assessment**

**Serum Interleukin-6 using ELISA [19]:**

The microtiter plate provided in this kit is pre-coated with a monoclonal antibody specific to IL-6 (1st antibody). Samples were then added to the appropriate microtiter plate wells and incubated after washing a biotin-conjugated polyclonal antibody preparation (2nd antibody) specific for IL-6 was added and incubated.

The standard density taken for the horizontal and OD value taken for the vertical, the standard curve on graph paper was drawn, the corresponding density found out according to the sample OD value by the sample curve (the result is the sample density). Normal range: undetected or below 1 pg/mL

**Statistical analysis**

Statistical analysis was done by SPSS v20 (SPSS Inc., Chicago, IL). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%).Student-t- test used to compare between two independent means. Chi-square (X2): used to test the significance of the difference between the frequencies of the different observations i.e., qualitative data. Spearman Correlation Test (r) used when studying the relationship of quantitative variables simultaneously.A two tailed P value < 0.05 was considered significant.

## Results:

There was a statistically significant difference between patients with irritable bowel syndrome and healthy control groupand between male and female patients also between young and old age group of patients. Table 1

**Table (1): Comparison between patients with irritable bowel syndrome and healthy control group, male and female, young and old age patients with irritable bowel syndrome regarding Hamilton Rating scale of Depression**

| Hamilton Rating scale of Depression | | t | P |
|---|---|---|---|
| **Patients (60)** | 12.96 ± 4.69 | 7.92 | 0** |
| **Control (20)** | 4.55 ± 0.99 | | |
| **Male (31)** | 10.54 ± 3.47 | 4.85 | 0** |

| | | | |
|---|---|---|---|
| **Female (29)** | 15.55 ± 4.47 | | |
| **(18-40 years) (36)** | 10.69 ± 4.32 | 5.68 | 0** |
| **(41-65 years) (24)** | 16.37 ± 2.77 | | |

Data are presented as mean± SD

52% (31/60) of patients have psychiatric comorbidities while healthy control group have only 10% (2/20) psychiatric comorbidities with a statistically significant difference between them.Table 2

**Table (2): Comparison between patients with irritable bowel syndrome and healthy control group regarding Structured Clinical Interview for DSM-IV Axis I & II Disorders**

| **SCID** | **Patient (60)** | | **Control (20)** | | |
|---|---|---|---|---|---|
| **SCID I** | **N** | **%** | **N** | **%** | **P** |
| **Obsessive personality disorder** | 2 | 3 | 0 | 0 | 0.2 |
| **Histrionic Personality disorder** | 1 | 2 | 1 | 0 | 0.4 |
| **SCID II** | **N** | **%** | **N** | **%** | **P** |
| **Somatoform disorder** | 9 | 15 | 0 | 0 | 0.02* |
| **Generalized Anxiety Disorder** | 7 | 12 | 0 | 5 | 0.04* |
| **Major Depressive Disorder** | 6 | 10 | 1 | 5 | 0.5 |
| **Panic disorder** | 4 | 7 | 0 | 0 | 0.1 |
| **Social Phobia** | 2 | 3 | 0 | 0 | 0.2 |
| **Total comorbidity** | **31** | **52** | **2** | **10** | **0.02*** |

Data are presented as frequency (%) ***Significant (P≤0.05)**

Patients with irritable bowel syndrome not associated with psychiatric comorbidity showed higher quality of life than patients with psychiatric comorbidity with a statistically significant difference in overall score and domains of dysphoria, interference with activity, health worry and relationships.Table 3, Figure 1

**Table (3): Comparison between patients with irritable bowel syndrome comorbid with psychiatric disorders and patients without psychiatric comorbidity regarding the Quality of life**

| **Patients with IBS** | **Comorbidity (31)** | **No comorbidity (29)** | **t** | **P** |
|---|---|---|---|---|
| **Overall score** | 54.22± 6.84 | 59.65± 8.62 | -2.68 | **0.01 *** |
| **Dysphoria** | 50.48 ± 9.40 | 56.37± 9.39 | -2.42 | **0.01*** |
| **Body Image** | 62.25 ± 7.72 | 64.13± 11.02 | -0.76 | 0.4 |
| **Food Avoidance** | 49.45± 12.50 | 52.18± 11.55 | -0.87 | 0.3 |
| **Sexual conern** | 74.83± 11.21 | 78.27± 14.89 | -1.1 | 0.3 |
| **Interference with Activity** | 50.59 ± 8.08 | 56.43 ± 9.78 | -2.51 | **0.01*** |
| **Health worry** | 50.13± 10.72 | 56.48± 12.35 | -2.12 | **0.03*** |
| **Social Reaction** | 54.73± 9.63 | 58.33± 9.85 | -1.43 | 0.1 |
| **Relationships** | 56.12 ± 10.99 | 66.89± 9.16 | -4.13 | **0.0002*** |

Data are presented as mean± SD*Significant (P≤0.05)

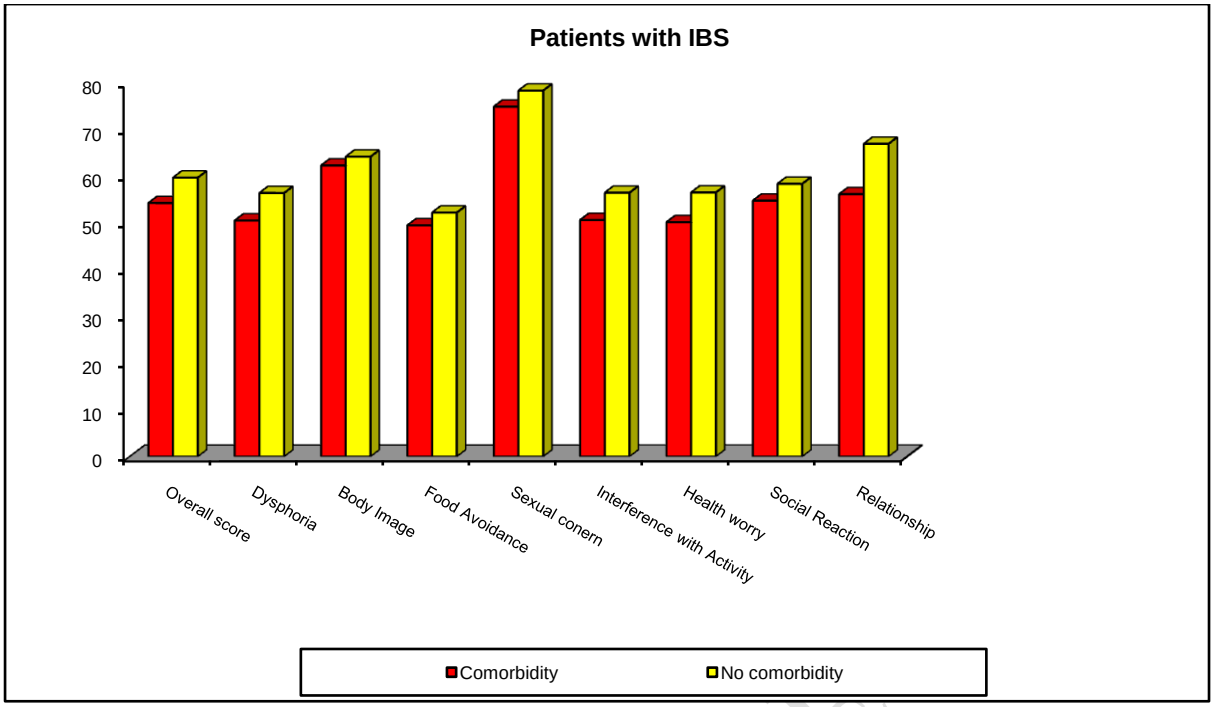


**Figure 1: Comparison between patients with irritable bowel syndrome comorbid with psychiatric disorders and patients without psychiatric comorbidity regarding the Quality of life**

Patients with irritable bowel syndrome have a higher serum level of interlukin-6 than healthy control group with a statistically significant difference between them. Patients with irritable bowel syndrome associated with psychiatric disorders have a higher level of serum interlukin-6 than patients without psychiatric comorbidity with a statistically significant difference between them. Table 4

**Table (4): Comparison between patients with irritable bowel syndrome and healthy control group regarding serum level of Inerlukin-6**

| Interlukin-6 | | | t | P |
|---|---|---|---|---|
| **Interlukin-6** | **Patients (60)** | **4.01 ± 3.84** | **7.42** | **0**** |
| | **Control (20)** | **0.31 ± 0.20** | | |
| **Patients with IBS** | **Comorbidity (31)** | **7.22± 2.61** | **14.1** | **0**** |
| | **No comorbidity (29)** | **0.57± 0.24** | | |

Data are presented as mean± SD

There was a positive correlation with no statistically significant value between Hamilton Rating scale of Depression and serum Interlukin-6 in patients with irritable bowel syndrome. Figure 2

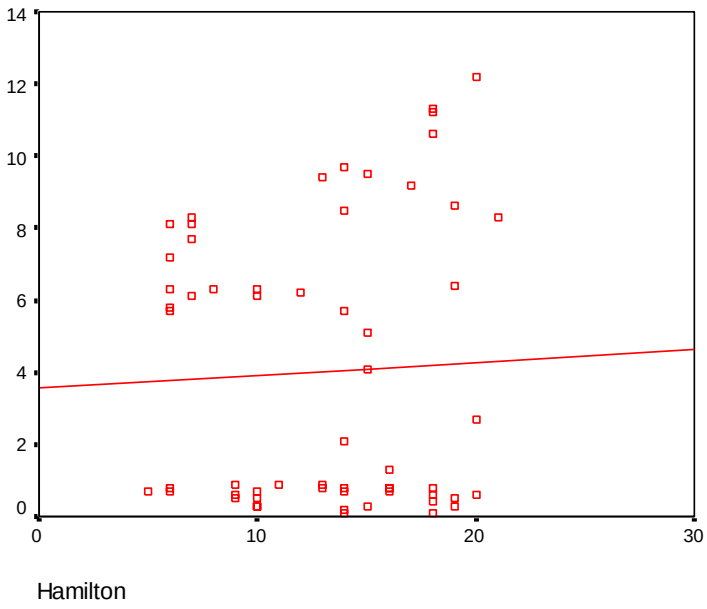


**Figure 2: Correlation between Hamilton Rating scale of Depression and serum Interlukin-6 in patients with irritable bowel syndrome**

## Discussion

Our study found that 80% of patients with irritable bowel syndrome have depressive symptoms through using Hamilton Rating Scale of Depression. Our results were consistent with a study by Tosic-Golubovic et al, [20]who reported that prevalence of depression in patients with irritable bowel syndrome was approximately 83.33%.

Our results found that Hamilton Rating Scale of Depression scores were significantly higher in patients than in control. Moreover, itwas significantly higher in female patients than in male patients. Our results were consistent with Zhang et al, [21]who demonstrated that patients with irritable bowel syndrome had more frequent and severe depressive symptoms than healthy controls, particularly females.

Our results were inconsistent with previous study that showed no significant association between irritable bowel syndrome and severity of depressive symptoms[22].

Our results found a significant difference between young and old age groups which were significantly higher in older age groups than in younger age groups. Our results were

consistent with a study by Modabbernia et al, [23] which found that older age patients (>40 years) suffered from more depressive symptoms and severer type of irritable bowel syndrome than younger age (21-39 years). Our results were inconsistent with a study by Lovell and Ford, [24]which found that depressive symptoms are severer in younger patients than in older patients.

Our results found that the overall score of quality of life in patients with irritable bowel syndrome was negatively correlated with Hamilton depression scale regarding age and sex groups. Our results were consistent with a study by Zhu et al, [25]which found that quality of life in patients with irritable bowel syndrome was negatively correlated with depression.

Our results found comorbid psychiatric disorders were statistically significant difference between both groups. Our results were consistent with western studies where the percentage of psychiatric disorders ranged from 40–60% in patients with irritable bowel syndrome[26].

Our results were consistent with a study by Singh et al in which comorbid psychiatric disorders were statistically significant difference between both groups [27].

Our results found that patients with psychiatric comorbidity have a lower overall quality of life score than patients without psychiatric comorbidity with a statistically significant difference between them. We also found that patients with psychiatric comorbidity have lower quality of life domains than patients without psychiatric comorbidity with a statistically significant difference between them in domains of dysphoria, activity, health worry, and relationship. Our results were consistent with a study by Cho et al, [28]which found that quality of life and its domains is negatively affected not only by severity of gastrointestinal symptoms but also with comorbid psychiatric disorders such as anxiety and depression .

The major psychiatric disorders found in our cases according to Structured Clinical Interview I and II were; somatoform disorders (15%), generalized anxiety disorders (12%), major depressive disorders (10%), panic disorder (7%), social phobia (3%), obsessive personality

disorders (3%), and histrionic personality disorder (2%) in comparable to results of control which were generalized anxiety disorders (5%), major depressive disorders (5%). Our results were consistent with a study by Wouters and Boeckxstaens,[29]which found that prevalence rates of somatoform disorders among patients with irritable bowel syndrome vary from 15-48%.However, our results were inconsistent with a study by Kawoos et al, [30]which showed more prevalence of anxiety and depression in patients with irritable bowel syndrome.Michael et al, [31]reported that the most frequent comorbidity was neurotic and behavioral syndromes (53.3%) followed by psychotic and affective syndromes (32%), then organic mental and substance use syndrome (8%), and lastly, personality disorders (4%).Cho et al, [28]reported elevated levels of anxiety and depression in patients than in healthy controls. However, a study by Banerjee et al, [32]found no such association between them.

Our results found a low percentage of personality disorders (5%) including obsessive and histrionic personality disorders. Tosic-Golubovic et al, [20]revealed that neuroticism is one of the few personality traits that had been consistently found to be increased in patients with irritable bowel syndrome.

Our results found no cases of bipolar disorder or schizophrenia in subjects. Our results were consistent with Mykletun et al, [33]which found that there were no cases of schizophrenia or bipolar disorders reported in patients with irritable bowel syndrome. On the contrary, a cohort study explored the association between irritable bowel syndrome and the development of bipolar disorder and suggested that irritable bowel syndrome might increases the risk of developing subsequent bipolar disorder [34].

Our study doesn't exclude the presence of bipolar disorder, this was supported with a Canadian study by O'Donovan & Alda, [35]which found that most people with bipolar disorder are initially misdiagnosed with another mental health disorder, most commonly unipolar depression with the majority of them remain misdiagnosed for years.

Garakaniet al,[36] reported that patients with schizophrenia rarely complain about symptoms of irritable bowel syndrome unless specifically asked. In addition, the difficulties in their assessment might be secondary to psychotic symptomatology, stigma, and financial problems.

Our results found a significant difference in serum Interlukin-6 between patients with irritable bowel syndrome and healthy control group. In addition, there was a significant difference in serum Interlukin-6 between patients with irritable bowel syndrome comorbid with psychiatric disorders and patients without psychiatric comorbidity. Moreover, there was a positive correlation with no significant value between Hamilton rating depression score and serum Interlukin-6. Our results were consistent with a study by Nishuty et al [37]which found that serum Interlukin-6 was elevated in patients with depressive symptoms than in control with a significant difference between both groups.

Our results were inconsistent with a study by Patel et al, [38]who found that the mean levels of Interlukin-2, Interlukin-6, and Interluki-8 were increased in patients as compared to controls, whereas, the mean level of Interlukin-10 was reduced in patients as compared to controls.

Our results were consistent with a study by Liebregts et al,[39]whichresults suggested that patients display enhanced proinflammatory cytokine release, particularly in comorbid anxiety and depressive disorders.

Limitations: The sample size was relatively small. Self-reported measures didn't distinguish between different severities of symptoms. Referral filter bias may affect the representativeness of our sample as patients were recruited from outpatient clinic of gastroenterology department.Studies on comorbidity of psychiatric disorders and irritable bowel syndrome are few in numbers, with heterogeneous designs secondary to cultural and socioeconomic differences and lower number of subjects seeking medical help. We didn't include the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Studies on

irritable bowel syndrome didn't have much collaborative research with (DSM-5). Although, there is no demand for a lack of medical explanation of symptoms anymore after (DSM-5).The Rome classification of irritable bowel syndrome could define the uncomplicated prototype of complaints.

**Conclusions:**

Psychiatric symptoms may be present and even started earlier than irritable bowel syndrome in Egyptian culture. A higher percentage of psychiatric disorders are presented with severer forms of irritable bowel syndrome. Stigmatization of psychiatric illness in Egypt culture has an impact on the prognosis of irritable bowel syndrome and subsequently the quality of life and health costs.

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