



## Cognitive Functions and Depression in Patients with Irritable Bowel Syndrome in Riyadh Region, Saudi Arabia

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### ABSTRACT

**Objective:** Irritable bowel syndrome (IBS) is associated with alterations in the gut-brain axis which influences various gastrointestinal and psychological functions. The cognitive performance and frequency of depression have not been previously assessed among Saudi patients with IBS so the primary aim was to study cognitive functions and depression in patients with IBS. **Methods:** This cross-sectional study enrolled Saudi males and females of more than 18 years of age living in Riyadh and Kharj cities, Central Region, Kingdom of Saudi Arabia. Participants were invited to complete 2 self-administered validated questionnaires. One questionnaire focused on Rome III criteria which classify functional GI disorders (FGIDs) in addition to the Patient Health Questionnaire (PHQ-9) which includes a set of 3 self-report scales designed to measure the major depressive disorder. Individuals who did not show IBS criteria have been enrolled as control subjects. **Results:** The overall prevalence of IBS among the enrolled subjects was 17.3% of whom women constituted (73.4%). Among subjects with IBS, 71.3% had mixed (constipation and diarrhea) type, 5.3% had diarrhea predominant type and 23.4% had constipation predominant IBS. Depression was significantly higher in IBS patients compared to control subjects. Among IBS cases, 20.2% had minimal depressive symptoms and 20.2% had major depression, mild severity. Major depression with moderate severity was found in 18.1% and major depression with severe severity was found in 28.7%. Depression was associated with impaired cognitive function in 25% of IBS patients. **Conclusion:** IBS was associated with depression and mild impairment of cognitive functions. The frequency of depression in IBS subjects suggests the importance of the psychological assessment of these patients and the integration of cognitive therapy with pharmacologic IBS therapy.

**Keywords:** Anxiety, Depression, Cognitive defects, Irritable bowel syndrome, Psychiatric problem

### INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by abdominal pain and altered bowel habits in the absence of a specific and unique organic pathology, although microscopic inflammation has been documented in some patients [1]. Population-based studies estimate the prevalence of irritable bowel syndrome at 10%-20% according to the studied cohorts. The incidence of IBS ranges between 1% and 2% per year [2].

The accurate case definition is hard to achieve IBS due to the high overlap of its symptoms with other gastrointestinal symptoms. Furthermore, the variations in diagnostic criteria along with the lack of specific histopathological changes, and the lack of a definitive point of onset make it difficult to accurately discriminate the syndrome. IBS is characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology. Patients with IBS may complain of a variety of intestinal symptoms such as abdominal pain, disturbed defecation (urgency, straining, incomplete evacuation, altered stool form, and frequency), bloating, and extra intestinal symptoms such as frequency, the urgency of micturition, incomplete bladder emptying, and back pain [3,4].

Despite the high prevalence of IBS in the general population along with the personal and economic costs, its etiology remains unknown; however, various studies have shown that several factors including abnormal motility of intestine, visceral hypersensitivity, inflammation, neurotransmitter imbalance, disturbance of brain-gut interaction, abnormal central processing, autonomic and hormonal events, and genetic, environmental, and psychosocial factors may contribute to incidence of IBS [5,6].

The pathophysiology of IBS has not been fully understood, however, it is probably disorder caused by dysregulation of the complex interactions along the brain-gut axis and interactions with gut microbiota [7-9]. Such interactions may result in psychiatric disorders such as neurosis, anxiety, depression and dysfunctional cognition are more prevalent in patients with IBS. Few studies assessed depression and cognitive performance in IBS [10-12].

In a large randomized controlled trial found that 44% of IBS patients had psychiatric co-morbidity which depressive and anxiety disorders were the most common conditions [13]. Depression in patients with IBS is more severe and prevalent than in healthy individuals [14]. In a study conducted in KSA, to determine the prevalence of IBS among educated and working women, it was found that the overall prevalence of IBS was 35.7% [15].

To date, no studies have been conducted to assess the relation between IBS and depression or cognitive status in KSA. Therefore, the current study was designed to investigate the relation of IBS to depressive symptoms and cognitive performance.

### MATERIALS AND METHODS

This cross-sectional study was conducted on Riyadh general population during the 2016-2017 years. The study included Saudi citizen's age above 18 years of age; those who are under 18 years of age were excluded.

The sample size was calculated using the sample size equation:  $n = z^2 p (1-p) / e^2$ , considering the target population more than 1000, and study power 95%. Systematic random sampling technique was followed. After identifying the first house randomly in the selected area, every 9<sup>th</sup> house was visited to include all the adult subjects residing in those selected houses till the required sample is covered.

Data were collected through personal interviews with the sampled population and filling the questionnaires. Two self-administered and validated questionnaires were used. The first questionnaire is the Rome III criteria, a system developed to classify functional GI disorders (FGIDs), which are disorders of the digestive system for which clinical symptoms cannot be explained by the presence of structural or tissue abnormalities [15]. The second questionnaire was the Patient Health Questionnaire (PHQ-9) [16], a set of 3 self-report scales designed to measure the major depressive disorder.

Cognitive assessment was conducted in a subset of patients with IBS using tests from the CANTAB<sup>®</sup> battery (Cambridge Cognition, Ltd, UK; Robbins and Sahakian,) and a computerized Stroop word-colour interference test (Stroop; Xavier Educational Software Ltd, UK) as previously described. The cognitive assessment lasted approximately 45 min with each participant first completing the big/little circle as a short familiarization task, followed by the IED, PAL and SWM tests from the CANTAB, and finally the Stroop test [17,18].

### Statistical Analysis

We utilized the statistical package for social sciences, version 16 (SPSS Inc., Chicago, Illinois, USA) to analyze the study data. The results were displayed as counts and percentages. The X<sup>2</sup> test was used as a test of significance, and differences were considered significant at  $p > 0.05$ .

### RESULTS

The prevalence of IBS in the study cohort was 17.3%. Concerning the types of IBS, 71.3% of cases had mixed (constipation and diarrhea) type, 5.3% had diarrhea predominant type and 23.4% had constipation predominant IBS (Table 1).

**Table 1 Sex, age, a region of the studied population, prevalence, and types of irritable bowel syndrome in the Riyadh region, KSA, 2018 (N=548)**

Sex	Frequency	Percent
Female	369	67.3%
Male	179	32.7%
Age (Years)		
<15	11	2.0%
15-30	288	52.6%
31-40	128	23.4%

41-50	88	16.1%
51+	3	0.5%
<b>Region</b>		
South	44	8.0%
East	65	11.9%
North	14	2.6%
West	99	18.1%
Middle	326	59.5%
<b>Irritable Bowel Syndrome</b>		
Positive	94	17.2%
Negative	212	38.7%
Suspicious	242	44.2%
<b>Type of Irritable Bowel Syndrome (N=94)</b>		
Constipation predominant	22	23.4%
Diarrhea predominant	5	5.3%
Mixed diarrhea and constipation	67	71.3%

Table 2 illustrates the relation between IBS and sex, age, region of the studied population. Most (73.4%) of the IBS cases were females, 48.9% of cases aged 15 to 30 years and 55.3% from the middle region.

**Table 2 Relation between IBS and sex, age, a region of the studied population, Riyadh, 2018**

Variable	IBS		Total (n=548)	p-value
	Yes (n=94)	No (n=454)		
<b>Sex</b>				
Female	69 (73.4%)	300 (66.1%)	369 (67.3%)	0.103
Male	25 (26.6%)	154 (33.9%)	179 (32.7%)	
<b>Age</b>				
<15	1 (1.1%)	10 (2.2%)	11 (2%)	0.013
15-30	46 (48.9%)	242 (53.3%)	288 (52.6%)	
31-40	33 (35.1%)	95 (20.9%)	128 (23.4%)	
41-50	14 (14.9%)	74 (16.3%)	88 (16.1%)	
51+	0 (0%)	3 (0.7%)	3 (0.5%)	
<b>Region</b>				
South	11 (11.7%)	33 (7.3%)	44 (8%)	0.664
East	11 (11.7%)	54 (11.9%)	65 (11.9%)	
North	2 (2.1%)	12 (2.6%)	14 (2.6%)	
West	18 (19.1%)	81 (17.8%)	99 (18.1%)	
Middle	52 (55.3%)	274 (60.4%)	326 (59.5%)	

Table 3 shows the relation between IBS and depressive symptoms. We found that, among IBS cases, 20.2% had minimal depressive symptoms, 20.2% had major depression, mild severity. Major depression with moderate severity was observed in 18.1% and major depression with severe severity was found in 28.7%. We found that 66.0% of IBS cases receive medications, compared to 41.3% of the normal population.

**Table 3 Relation between IBS and depressive symptoms of the studied population, Riyadh, 2018**

Depressive Symptoms	IBS		Total (n=548)	p-value
	Yes (n=94)	No (n=454)		
Normal	12 (12.8%)	173 (38.1%)	185 (33.8%)	0.000
Minimal depressive symptoms	19 (20.2%)	107 (23.6%)	126 (23%)	
Major depressive mild severity	19 (20.2%)	96 (21.1%)	115 (21%)	
Major depression, moderate severity	17 (18.1%)	42 (9.3%)	59 (10.8%)	
Major depression, severe severity	27 (28.7%)	36 (7.9%)	63 (11.5%)	

The family history of Crohn's disease was found in 92.6% of IBS cases and in 93.4% of the normal population. The family history of milk allergy, coeliac disease, and stomach cancer was found in 16.0%, 1.1% and 17.0% of IBS cases

respectively, while they were found in 11.9%, 0.7% and 7.5% of the normal population respectively. In comparing the family history of stomach cancer among IBS cases and normal population p-value was significant (0.005) (Tables 4 and 5).

**Table 4 Relation between IBS and taking medications, family history of Crohn's disease, milk allergy, coeliac disease and stomach cancer among the studied population, Riyadh, 2018**

Variables	IBS		Total (n=548)	p-value
	Yes (n=94)	No (n=454)		
<b>Taking medications</b>				
Yes	62 (66%)	187 (41.2%)	249 (45.4%)	0
No	32 (34%)	267 (58.8%)	299 (54.6%)	
<b>Family history of Crohn's disease</b>				
Yes	87 (92.6%)	424 (93.4%)	511 (93.2%)	0.455
No	7 (7.4%)	30 (6.6%)	37 (6.8%)	
<b>Family history of milk allergy</b>				
Yes	15 (16%)	54 (11.9%)	69 (12.6%)	0.18
No	79 (84%)	400 (88.1%)	479 (87.4%)	
<b>Family history of coeliac disease</b>				
Yes	1 (1.1%)	3 (0.7%)	4 (0.7%)	0.53
No	93 (98.9%)	451 (99.3%)	544 (99.3%)	
<b>Family history of stomach cancer</b>				
Yes	16 (17%)	34 (7.5%)	50 (9.1%)	0.005
No	78 (83%)	420 (92.5%)	498 (90.9%)	

**Table 5 Summary of mean test scores for assessment of depression and cognitive function**

Cognitive test	Control	IBS	p-value
WAIS-R full-scale IQ (NART conversion)	109.43 ± 1.38	101.28 ± 1.08	0.070
PHQ-9	2.13 ± 0.34	6.50 ± 0.97	<0.001
Stroop effect (ms)	264.32 ± 25.26	332.27 ± 35.46	0.047
Stages complete	8.50 ± 0.17	8.90 ± 0.11	0.940
Total errors (adjusted)	23.27 ± 4.17	25.24 ± 3.17	0.740
Reversal learning (errors)	4.95 ± 0.64	6.46 ± 0.83	0.043
Attentional flexibility (errors)	12.75 ± 1.27	10.86 ± 1.33	0.050
Total between errors	14.37 ± 2.47	24.63 ± 2.75	0.002
Total errors	18.27 ± 3.15	25.26 ± 2.34	0.034
Strategy score	29.16 ± 1.12	31.50 ± 0.89	0.073

HADS-A/D: Hospital anxiety and depression scale-anxiety/depression; PHQ-9: Nine-item patient health questionnaire, IED: Intra-extra dimensional set shift; SWM: Spatial working memory; IBS: Irritable bowel syndrome

## DISCUSSION

The relationship between psychiatric disorders and GI disorders such as IBS is well established. IBS patients typically suffer from anxiety and depression, which can aggravate their IBS symptoms [3]. This was a cross-sectional study, conducted on the Riyadh general population to quantify the prevalence of IBS and its association with depressive symptoms.

In this study, the prevalence of IBS was 17.2% which is in line with the finding of a study which conducted an international study among 41,984 individuals across 8 European countries and found that the prevalence of IBS was 11.5% [19].

The prevalence of IBS was higher compared to the findings of a cross-sectional study conducted in Suez governorate, Egypt, and found that the prevalence of IBS among the studied population was 34.2% and the results of a study were carried out in Karachi, Pakistan where the prevalence of IBS was 28.3% [20,21]. The present results revealed that 71.3% of the diseased participants had a mixed IBS type, 5.3% had diarrhea IBS type and 23.4% had constipation predominant IBS which is inconsistent with the findings of a study done among Japanese University students who showed that the constipation predominant type was more prevalent (47.8%) [22]. However, the conclusion of the

present study is in agreement that the most common type was the mixed IBS type followed by constipation predominant IBS type in a study conducted to students and interns at King Abdulaziz University, Jeddah, Saudi Arabia [13]. The type of IBS was constipation type in 22% of our participants, diarrhea type in 5% and mixed in 67%. In this study, IBS cases were 73.4% females and 26.6% males but there was no significant difference between males and females ( $p=0.103$ ). Our results agreed with the study conducted in Korea [23].

Also in another study done on medical students at King Saud bin Abdulaziz University for health sciences in Riyadh; their results demonstrated that IBS was more prevalent among females [24].

In the present study, we found a significant correlation between age and IBS ( $p=0.013$ ). Also, the results indicated a highly significant correlation between depressive symptoms and IBS ( $p=0.000$ ).

A high number of our positive IBS participants (46 over 94 participants) were in the age between 15 to 30 years and the number gets lesser with advanced age. This inverse relationship between age and IBS was also reported in the study done in Korea [23]. The majority of positive IBS participants in our study were having depressive symptoms varying between mild to severe. In the study carried at King Abdulaziz University, Jeddah, they found that participants with morbid depression had a higher prevalence (41.9%) of IBS compared to those with borderline depression (29.5%) or normal participants (31.5%) [13]. Another study done in Japan showed that individuals with IBS had higher scores on the Hospital Anxiety and Depression Scale (HADS) compared to control subjects [25]. Also, a study reported that 24.4% of students complaining of IBS have depression symptoms [26]. The logistic regression analysis the general population in Colombia also showed an association with depressive symptoms and female sex independently of age and depression and anxiety symptoms [27]. The association between psychological disorders (including depression) and functional bowel disorders is well established.

## CONCLUSION

The high prevalence of depression symptoms observed in our subjects emphasizes the importance of the psychological evaluation of the patients with IBS, in order to better manage and deal with the patients which could help in minimizing the burden of health care costs.

## DECLARATIONS

### Ethical Considerations

Data collector gave a brief introduction to the participants by explaining the aims and benefits of the study. Informed written consent was obtained from all participants. Anonymity and confidentiality of data were maintained throughout the study. There was no conflict of interest, financially or otherwise.

### Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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