



Evaluation of the use of Probiotics in Patients with Irritable Bowel Syndrome

A Thesis

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By

Omar Ahmed Mohamed Abdel-Samie

M.B.B.Ch

Under supervision of

Prof. Dr. Eman Mohamed ElGindy

*Professor of Tropical Medicine
Faculty of Medicine - Ain Shams University*

Assist. Prof. Dr. Iman Mohamed Fawzy

*Assistant Professor of Tropical Medicine
Faculty of Medicine - Ain Shams University*

Dr. Heba Ismail Saad

*Lecturer of Tropical Medicine
Faculty of Medicine- Ain Shams University*

*Faculty of Medicine
Ain Shams University*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
<i>5-HT</i>	<i>5-hydroxytryptamine</i>
<i>A.muciniphila</i>	<i>Akkermansia muciniphila</i>
<i>ACG</i>	<i>American college of gastroenterology</i>
<i>AMPs</i>	<i>Antimicrobial proteins</i>
<i>Anti-PD1</i>	<i>Anti-programmed cell death protein 1</i>
<i>B. Fragilis</i>	<i>Bacillus Fragilis</i>
<i>BDA</i>	<i>British diabetic association</i>
<i>CD</i>	<i>Celiac disease</i>
<i>CCK</i>	<i>Cholecystokinin</i>
<i>CBC</i>	<i>Complete Blood Count</i>
<i>CRP</i>	<i>C-Reactive protein</i>
<i>CD</i>	<i>Crohn's disease</i>
<i>DNA</i>	<i>Deoxyribonucleic acid</i>
<i>ENS</i>	<i>Enteric nervous system</i>
<i>ESR</i>	<i>Erythrocyte sedimentation rate</i>
<i>EcN</i>	<i>Escherichia coli Nissle</i>
<i>ESPCG</i>	<i>European Society for Primary Care Gastroenterology</i>
<i>F. Prausnitzii</i>	<i>Faecalibacterium prausnitzii</i>
<i>FMT</i>	<i>Fecal microbial transplantation</i>
<i>FODMAPs</i>	<i>Fermentable oligosaccharides, Disaccharides, Monosaccharides and polyols</i>
<i>FD</i>	<i>Functional dyspepsia</i>
<i>FGIDs</i>	<i>Functional gastrointestinal disorders</i>
<i>SpaCBA</i>	<i>functional mucus binding pili</i>
<i>GABA</i>	<i>Gamma-aminobutyric acid</i>
<i>GI</i>	<i>Gastrointestinal</i>
<i>HFD</i>	<i>High fat diet</i>
<i>HPA axis</i>	<i>Hypothalamic- pituitary- adrenal axis</i>
<i>IG</i>	<i>Immunoglobulin</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>IBD</i>	<i>Inflammatory bowel disease</i>
<i>IL</i>	<i>Interleukin</i>
<i>IBS</i>	<i>Irritable bowel syndrome</i>
<i>IBS-QOL</i>	<i>Irritable Bowel Syndrome – Quality of Life</i>
<i>IBS-SSSS</i>	<i>Irritable Bowel Syndrome – Symptom Severity Scale</i>
<i>IBS-M</i>	<i>Irritable bowel syndrome mixed</i>
<i>IBS-C</i>	<i>Irritable bowel syndrome predominant constipation</i>
<i>IBD-D</i>	<i>Irritable bowel syndrome predominant diarrhea</i>
<i>IBS-U</i>	<i>Irritable bowel syndrome unsubtyped</i>
<i>L. Acidophilus</i>	<i>Lactobacillus Acidophilus</i>
<i>L. Casei</i>	<i>Lactobacillus Casei</i>
<i>L. Reuteri</i>	<i>Lactobacillus Reuteri</i>
<i>L. Rhamnosus</i>	<i>Lactobacillus Rhamnosus</i>
<i>LPS</i>	<i>Lipopolysaccharide</i>
<i>MACs</i>	<i>Microbiota-accessible carbohydrates</i>
<i>MS</i>	<i>Multiple sclerosis</i>
<i>NES</i>	<i>Neuro-endocrine system</i>
<i>RA</i>	<i>Rheumatoid arthritis</i>
<i>SIgA</i>	<i>Secretory IgA</i>
<i>SSRIs</i>	<i>Selective serotonin reuptake inhibitors</i>
<i>SCFAs</i>	<i>Short chain fatty acids</i>
<i>SCFA</i>	<i>Short-chain fatty acid</i>
<i>SIBO</i>	<i>Small intestinal bacterial overgrowth</i>
<i>SCN5A</i>	<i>Sodium channel, voltage gated, type V alpha subunit</i>
<i>SFB</i>	<i>Spore forming bacteria</i>
<i>TOT-BI</i>	<i>Total- Body Image</i>
<i>TOT-DY</i>	<i>Total- Dysphoria</i>
<i>TOT-FA</i>	<i>Total- Food Avoidance</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>TOT-HW</i>	<i>Total- Health Worry</i>
<i>TOT-IN</i>	<i>Total- Interference with Activity</i>
<i>TOT-RL</i>	<i>Total- Relationship</i>
<i>TOT-SX</i>	<i>Total- Sexual</i>
<i>TOT-SR</i>	<i>Total- Social Reaction</i>
<i>TOT-OV</i>	<i>Total-Overall</i>
<i>TMA</i>	<i>Trimethylamine</i>
<i>T2DM</i>	<i>Type 2 Diabetes Mellitus</i>
<i>NICE</i>	<i>UK's National Institute of Health and Care Excellence</i>
<i>UC</i>	<i>Ulcerative colitis</i>
<i>VAS score</i>	<i>visual analog scale score</i>
<i>VDRs</i>	<i>Vitamin D receptors</i>

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INTRODUCTION

Irritable bowel syndrome (IBS) is one of the most prevalent functional gastrointestinal disorders (FGIDs), afflicting around 11% of the adult population worldwide. Due to the lack of specific and sensitive diagnostic biomarkers, IBS is still diagnosed by symptomatic criteria, namely the Rome criteria (Rome IV in its current version) (*Drossman and Hasler, 2016*).

The Rome Foundation, an independent body dedicated to assisting in the diagnosis and treatment of functional gastrointestinal disorders “FGIDs”, published the “Rome IV criteria” for the diagnosis of IBS in May 2016 (*Ford et al., 2017*).

IBS threatens the quality of life of millions and poses a substantial financial burden on healthcare systems around the world (*Kennedy et al., 2014*). IBS accounts for up to 50% of visits to general practitioners for gastrointestinal (GI) complaints (*Hillilä et al., 2010*).

Despite the availability of a great variety of therapeutic options, treatment satisfaction is suboptimal for both the patient and the doctor (*Lacy, 2016*). A relevant implication of treatment dissatisfaction is a marked reduction in quality of life and growing social, sanitary and economic burden worldwide (*Buono et al., 2017*).

There is strong evidence supporting the role of bacterial, viral and parasitic infections in triggering IBS (**Klem et al., 2017**). Some IBS patients respond well to certain non-absorbable antibiotics and prebiotic/probiotic administration (**Moraes-Filho and Quigley, 2015**), some of them show improvement after fecal transplantation. Therefore, the role of the intestinal microbiota emerges as an essential feature in developing future therapeutic approaches in IBS (**Johnsen et al., 2017**).

A growing body of evidence indicates dysbiosis as a hallmark of IBS. Despite divergences between studies, there is good evidence that the microbiota is a -predominant factor in the IBS pathophysiology. In general, data suggest that there is a relative abundance of proinflammatory bacterial species including Enterobacteriaceae, with a corresponding reduction in Lactobacillus and Bifidobacterium (**Zhuang et al., 2017**).

Probiotics may influence the IBS symptoms including abdominal pain, bloating, distension, flatulence and altered bowel movements (**Dai et al., 2013**). A 2015 meta-analysis of 24 human clinical trials concluded that probiotics, overall, were more beneficial than placebo in reducing pain and symptom severity scores (**Didari, 2015**).

Studies of selected probiotic species have suggested potential efficacy in several gastrointestinal illnesses, the best studied of which are the inflammatory bowel diseases (particularly pouchitis) (**Singh et al., 2015**). Therapeutic benefit has also been

suggested in several other disorders, including antibiotic-related diarrhea, *Clostridioides* (formerly *Clostridium*) *difficile* toxin-induced colitis, infectious diarrhea, hepatic encephalopathy, irritable bowel syndrome, and allergy (***Parker et al., 2018***).

We try in current study to evaluate the role of probiotics in the improvement of irritable bowel syndrome symptoms.

AIM OF THE WORK

The aim of the current study is to evaluate the role of probiotics in the:

- Improvement of IBS symptoms via Irritable Bowel Syndrome – Symptom Severity Scale (IBS-SSSS) (Arabic version licensed by Rome Foundation).
- Improvement of quality of life via Irritable Bowel Syndrome – Quality of Life survey (IBS-QOL) (Arabic version licensed by Rome Foundation).

Chapter 1**IRRITABLE BOWEL SYNDROME “IBS”****Introduction:**

IBS is a functional bowel disorder and one of the most commonly diagnosed gastrointestinal illnesses. It is a symptom-based condition characterized by abdominal pain or discomfort, with altered bowel habits, in the absence of any other disease to cause these sorts of symptoms (*Ford et al., 2014c*).

The first description of the condition was in 1820 while the current term "irritable bowel syndrome" came into use in 1944 (*Tamparo, 2011*).

IBS was first documented more than 100 years ago. A functional bowel disorder is defined as changes in intestinal motility, intestinal nerve sensitivity, and the way the brain controls the normal function of the gut (*Occhipinti and Smith, 2012*).

The term ‘irritable colon syndrome’ (subsequently changed to irritable bowel syndrome) is attributed to Walter C. Alvarez in 1915. He considered factors such as differences in rhythm and irritability to share in altering the gradient of forces through the intestinal tract (*Alvarez, 1915*).

Alvarez continued to study the gradient of ‘irritability’ of small intestinal muscle, reflecting the frequency and amplitude of contraction. Mucous colitis or the syndrome of the sore bowel or the spastic colon are not accurate terms because the trouble is not limited to the colon (**Alvarez and Hosoi, 1929**).

Manning and colleagues (**Manning et al. 1978**) recommending the positive symptom-based diagnosis of IBS that coincided with the study held by Kruis and colleagues (**Kruis et al. 1984**), in which simple screening tests such as hemoglobin level and erythrocyte sedimentation rate were part of a screen for alarm features, consensus criteria were developed to codify the diagnosis based on symptom (**Manning et al., 1978**).

The Rome classification system was introduced by an international group of gastrointestinal experts at the University of Rome, Italy, and is used in daily practice for patients with gastrointestinal complaints (**Drossman, 2016**). The Rome IV criteria were introduced in May 2016 and are currently used to diagnose IBS by healthcare providers in daily practice today (**Simren et al., 2017**).

IBS symptoms occur over a long time, often years. It has been classified into four main types depending on whether diarrhea is common, constipation is common, both are common, or neither occurs very often (IBS-D, IBS-C, IBS-M, or IBS-U respectively) (**Levy et al., 2014**).