An-Najah National University

Faculty of Graduate Studies

EVALUATION OF SAFETY AND EFFICACY OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENTS USED BY IRRITABLE BOWEL SYNDROME PATIENTS

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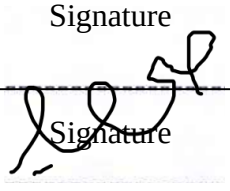
Dr. Suhaib Hattab	
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Dedication

First, I dedicate this project to God Almighty, my creator, my strong pillar, and my source of inspiration.

I dedicate this to my parents, who gave me the gift of dreams and the ability to realize them. To my husband, my greatest supporter and best friend,

Mohammad

To my child, who fills my heart with joy and whose laughter is favorite sound, Khalid

To my whole family, thank you all.

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Declaration

I, the undersigned, declare that I submitted the thesis entitled:

EVALUATION OF SAFETY AND EFFICACY OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENTS USED BY IRRITABLE BOWEL SYNDROME PATIENTS

Unless otherwise referenced, I declare that the work provided in this thesis is the researcher's work and has not been submitted elsewhere for any other degree or qualification.

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EVALUATION OF SAFETY AND EFFICACY OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENTS USED BY IRRITABLE BOWEL SYNDROME PATIENTS

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Abstract

Background: Many people in Palestine suffer from irritable bowel syndrome (IBS). Some people deal with the disease using medications, while others prefer non-pharmacological treatments and avoid food that aggravate the symptoms.

Objectives: The study aims to assess the severity of IBS, the lifestyle the patients live and evaluate the safety and efficacy of pharmacological and non-pharmacological modalities to treat irritable bowel syndrome among Palestinian patients.

Methodology: This was a cross-sectional study using a data collection form to collect data from patients by a face-to-face interview. Patients were met from gastroenterology outpatient clinics, community pharmacies and hospital pharmacies in Bethlehem. The Statistical Package for Social Sciences was performed using statistical analysis (SPSS version 21).

Results: A total of 407 patients with irritable bowel syndrome in Bethlehem and surrounding areas participated in this study. The mean age was 36.87±13.8 years old. Among them, 253(62.2%) were females, 263(64.6%) were married and 201(49.4%) were living in the city. Regarding clinical and disease characteristics, 258(63.4%) did not have a family history of IBS, 201(49.4%) had alternate diarrhea and constipation, 229(56.3%) had mixture of solid and watery stool, 310(76.2%) had abdominal pain, 352(86.5%) had abdominal bloating, 350(86%) had abdominal gases, and 69(17.0%) had a bloody stool. Furthermore, the disease affected patients' life by different ways; 248(60.9%) became nervous, 129(31.7%) couldn't sleep well. Regarding non-pharmacologic treatments, 206(75.2%) used herbs to sooth IBS symptoms, and 234(57.5%) avoided food that irritates colon. It was found that using herbs that sooth the IBS, increasing liquids, avoiding food that irritates the colon and having exercise

were all significantly associated with improvement in IBS symptoms; P-values were <0.001, 0.032, 0.001 and 0.029 respectively. About pharmacologic treatments, 188(46.2%) had taken chlordiazepoxide and clinidium bromide, and 143(35.1%) had taken probiotics to treat IBS symptoms. 148(36,4%) patients told that they had full improvement from pharmacological treatments. Use of probiotics, synthetic fibers, (chlordiazepoxide & clinidium bromide) and hyoscain significantly associated with improvement in symptoms, P-values were <0.001, <0.001, <0.001 and 0.030 respectively

Conclusion: Irritable bowel syndrome is a bothering problem that affects daily life, many patients try non-pharmacological treatments with accepted efficacy. Even with pharmacological treatments many patients could not attain satisfactory improvement.

Keywords: Irritable bowel disease, constipation, diarrhea, non-pharmacological, pharmacological, Palestine.

Chapter One

Introduction and Theoretical Background

1.1 Introduction

Irritable bowel syndrome (IBS), earlier termed functional gastrointestinal disorders, represents one of the most widespread disorders of gut-brain interactions which affects one of ten people in the world. This is characterized by a specific group of signs the patient experiences such as abdominal pain that occurs with defecation or a change in bowel behavior (either constipation, diarrhea, or a mix of the two) (1). IBS impacts between 196 and 260 people per 100,000 people every year, and it is more widespread among women than in males. Patients under 50 are also more likely to be assigned IBS (2).

Its incidence rate ranges from 10% to 20%, while there are some regional variations; for instance, its frequency is 21% in South America and 7% in Southeast Asia (3).

Among the common inflammatory bowel diseases (IBDs) are ulcerative colitis (UC) and Crohn's disease (CD). Unlike UC, which is distinguished by rectal urgency and bloody diarrhea, CD is characterized by weight loss, abdominal pain, and chronic or nocturnal diarrhea. While IBD and IBS can be distinguished from one other using various biomarkers, they also share a number of signs. Patients with overlapping IBD and IBS frequently have diarrhea and excruciating stomach pain. A 2020 meta-analysis study found that 32.5% of IBD patients had a pooled prevalence of symptoms similar to IBS. The intestinal barrier and microbiota are the two factors that connect gut infections to IBS-D. Therefore, following a prolonged infection, patients with chronic diarrhea are often diagnosed with IBS-D. IBD and IBS may have different stages of the same condition. Therefore, it's crucial to take into account the overlapping between IBD and IBS when a patient has a history of intestinal infection. Preventing IBS is crucial when diagnosing IBD (4).

IBS is subdivided into three types according to the Rome III criteria, IBS with constipation (IBS-C), IBS with diarrhea (IBS-D) and IBS mixed between (IBS-M). The pathophysiology of IBS is thought to be multifactorial; it could be due to:

1.1.1 Infection and immune activation

Post-infection, IBS can develop as a result of viral, bacterial, or protozoal infections. Giardia lamblia and other protozoan agents have frequently been linked to the development of post infection IBS. Multiple risk variables raise the likelihood of post infection IBS following acute gastroenteritis; A family history of functional digestive disorders, female sex, younger age, smoking, anxiety, depression, recent unfavorable life events, bad mental beliefs, history of stress, and insomnia, and severity of the acute gastroenteritis (abdominal pain, bleeding per rectum, antibiotic therapy) are among the risk factors. Another significant component in the development of post infection IBS is dysbiosis of the gut. Regarding treatment, a Chinese randomized controlled trial demonstrated the advantages of dietary glutamine. Tri-cyclic antidepressants and 5-amino salicylic acid were also beneficial (5).

Numerous researches substantiate the immune system's function. Before acquiring IBS, 10% of patients thought they had an infectious disease. Intestinal infections account for 3% to 36% of cases with persistent new symptoms of IBS, depending on the specific organism causing the infection, according to prospective research. Viral gastroenteritis tends to produce only transient symptoms, in contrast to persistent post infection IBS that follows bacterial enteritis, protozoan, and helminth infections (6).

1.1.2 Genetic disposition

Based on the information that is currently accessible, altered brain-gut axis is the primary mechanism linked to autonomic dysfunction, disturbed motility, and visceral hypersensitivity. Numerous neurotransmitters are involved; substances P, CCK, and serotonin (5-hydroxytryptamine, or 5-HT). Furthermore, current studies have demonstrated that the corticotropin- releasing hormone (CRH) could contribute to the pathogenesis of intestinal mucosal inflammation in addition to IBS pathophysiology associated with stress. Every one of these systems, influencing the core and peripheral connections between the brain and the gut, and could be impacted by hereditary variables. Some authors have established the presence of certain substances and genes associated with the brain gut axis which could be the key to treating IBS (7).

Thirty-three (33%) of patients have a family history of IBS that is significant. Many studies have looked into the potential significance of gene polymorphisms encoding for serotonin (SERT), cholecystokinin (CCK), alpha 2 adrenergic receptors, and anti-inflammatory and pro-inflammatory interleukins. The intensity of IBS symptoms is strongly linked with SERT polymorphisms (8).

Several studies have demonstrated that childhood abuse and stressful life have a big effect on gastro-intestinal symptomatology, make IBS symptoms worse and psychiatric therapy has a good impact. The existing data provide novel information indicating the strong connection between genetic history, specific interleukins, IL receptors, central nervous system mechanisms, and IBS physiopathology (9).

1.1.3 Traumatic stress

A vital contributing element to IBS is stress. For instance, IBS is more likely to develop in people with Post Traumatic Stress Disorder (PTSD), A meta-analysis research states that, PTSD was a significant risk factor for IBS, $P < 0.001$).(10).

Several environmental variables, such as food, gastrointestinal infections, and persistent stress in childhood and/or adulthood, are linked to irritable bowel syndrome (IBS). Chronic stress can make someone more susceptible to getting IBS and/or can aggravate or cause the symptoms of IBS to worsen. When the body response is disrupted by an external or biological stimulation, the body replies by producing stress. It has an impact on gut physiology, resulting in modifications to mucosal transport, intestinal motility, and gut barrier function, which alter permeability and visceral perception. The physiological impacts of stress are controlled by a combination of the sympathetic nervous system and the corticotropin releasing factor (CRF)/HPA axis pathways.

Glucocorticoids, important HPA axis mediator chemicals, connect to intracellular receptors and control the body's stress-related responses.Glucocorticoids, such as cortisol/corticosterone, bind to glucocorticoid receptors (GR) and mineralocorticoid receptors (MR) in the hippocampus, anterior pituitary gland, and paraventricular nucleus (PVN) of the brain to activate negative feedback regulation (11).

1.1.4 Serotonin dysregulation

Changes in serotonin (5-HT) signaling have been linked to functional dyspepsia, IBS, chronic constipation, diarrhea, and other gastrointestinal illnesses in recent investigations. According to certain research, one pathophysiologic mechanism causing the symptoms of D-IBS, including visceral hypersensitivity, aberrant secretomotor function, and gastrointestinal dysmotility, may be changed enterochromaffin (EC) cells. There is growing evidence connecting dysregulated 5-HT signaling to the pathophysiology of IBS-related constipation and diarrhea as well as slow-transit constipation. It has been observed that people with functional constipation have less EC cells.

Other research, however, has found equal changes in EC and 5-HT cells in people suffering from diarrhea and constipation. Colonic mucosal specimens from endoscopic biopsies in healthy individuals, IBS patients with diarrhea as their predominant bowel complaint, and IBS patients with constipation were recently assessed. IBS patients with constipation compared with normal controls and IBS patients with diarrhea compared were found to have significantly higher mucosal 5-HT concentrations. The observation of elevated vesicular 5-HT concentrations in patients with C-IBS may suggest normal synthesis (12).

The primary neural signaling transmitter, serotonin (5-HT), offers perspective on the intricate relationships between the gut, brain, and microbiome axis. Meanwhile, it has been noted that IBS patients' blood contains more 5-HT than usual. Tryptophan and 5-HT are converted into one another in two steps. The rate-limiting enzyme tryptophan hydroxylase (TPH) comes in two isoforms: TPH1 and TPH2. The transcription of Tph1 and Tph2, and the subsequent synthesis of 5-HT, may be induced by the gut microbiota, according to studies. Twenty percent of the microbial genome may be able to synthesize 5-HT utilizing a framework based on metabolites. The gut epithelium's enterochromaffin cells are the primary site of Tph1 expression, whereas the central and enteric nervous systems' serotonergic neurons are the primary source of Tph2 (13).

Although the bacteria in the stomach can produce 5-HT, the microbes there can is far exceeded by biosynthesis in enterochromaffin (EC) Cells. Researchers found that a decrease in the production of intestinal serotonin leads to the weakening of the intestinal lining, which inevitably results in clogging or constipation. In patients with IBS, SERT expression tends to be low. However, the injection of SSRIs enhances colonic motility, and stomach cramps in high degree. Mice treated with the serotonin reuptake inhibitor (SSRI) paroxetine over a long duration of time showed delayed upper GI motility and decreased stool production. These results suggest that altered mucosal 5-HT signaling may play a role in IBS symptoms (14).

1.2 Diagnosis

A complete history and physical examination are part of the evaluation process for suspected IBS, even if the results of the examination are typically normal. The criteria must have been satisfied for the preceding three months, with the onset of symptoms occurring at least six months prior to diagnosis. These criteria include improvement in pain during defecation, onset associated with a change in the frequency of stools, and onset associated with a change in the form (appearance) of stools. A systematic evaluation involving over 4,000 patients found that 4% of those with IBS presenting with diarrhea mostly or in a mixed manner had celiac disease confirmed by biopsy. For this reason, doctors should think about doing routine celiac disease testing on patients who have mixed or diarrhea-predominant IBS presentations (15).

The diagnosis of IBS and the etiology is multi-factorial. IBS patients are divided into distinct subgroups that correspond to their current bowel habits since this allows treatment to focus on the dominant. The four subtypes of IBS include IBS with a predominant of constipation (IBS-C), IBS with a predominance of diarrhea (IBS-D), IBS with mixed bowel habits (IBS-M), and IBS without subtypes. Also, The Bristol Stool Form (BSF) Scale is used to confirm the diagnosis, it is subdivided into 7 types ranging from (hard, lumpy stool: type 1, type 2 to loose and watery stool: type 6 and type7).

In order to determine if a patient has IBS, the Bristol Scale Form Scale (BSFS) test should be done on days free of treatments, decision is based on Rome IV criteria:

- If bowel movements >25 % with BSF 1 or 2 or with BSFS 6 or 7 occurring less than 25%, its IBS-C.
- If bowel movements >25% with BSF 6 or 7 or with less than 25% of bowel movements with BSFS 1 or 2, its IBS-D.
- If bowel movements >25% with BSFS 1 or 2 and >25% of bowel movements associated with BSFS 6 or 7, its IBS-M.
- If it cannot be defined, its IBS-U (16).

A precise diagnosis is important to rule out any familiar gastrointestinal disease like celiac disease, lactose allergy and gluten sensitivity. The presence of biomarkers is a crucial part in the diagnosis of IBS. IBS-D and inflammatory bowel disease (IBD) can be hard to distinguish from one another; symptoms alone may not always be able to do.

The two serologic tests that are most frequently used to rule out IBD in patients with IBS-D are the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).Colonoscopy has been suggested for patients with IBS symptoms and without warning signs because it has been presumed that pain during colonoscopy could be a possible link with the diagnosis of IBS (17).

1.3 Therapeutic approach.

The treatment plan for IBS should be focused on the most common signs and symptoms and may include both non-pharmacological therapies and medication.

1.3.1 Non-pharmacological treatments

Many non-pharmacological treatments to decrease IBS symptoms have been studied, examples include:

1.3.1.1 Vinegar and gut health

Many gastrointestinal tract issues can be treated with vinegar, especially apple cider vinegar, as the acetic acid contained in it can reduce inflammation and constipation

while also preventing the growth of harmful bacteria. As per a 2020 study, vinegar was found to be effective in treating constipation in obese persons. Additionally, vinegar works by blocking the enzymes that break down carbohydrates, allowing gut flora to proliferate (18).

1.3.1.2 Low FODMAP diet

IBS patients have noticed good results with the removal of dietary fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs). FODMAPs encourage the creation of short-chain fatty acids and gases in the colon and increase GI water secretion, which can trigger lumen dilatation and the development of meal-related symptoms in IBS patients (19).

In about 70% of IBS patients, reducing down high-FODMAP food results in significant improvement in symptoms, according to several clinical studies. A low-FODMAP diet, as in a standard IBS diet, produced a significant reduction in diarrhea, bloating, and stomach pain, according to the meta-analysis (20).

1.3.1.3 Increased dietary fiber

Dietary fiber influences bowel habits by stimulating the colonic mucosa mechanically and increasing the amount of the stool. Additional advantages of dietary fiber include improved glycemic control, body weight management, and a reduction in blood cholesterol. Dietary fiber comes in a variety of forms, even though not all of them are good for people with IBS due to their distinct physical and chemical characteristics. Due to the benefits of soluble fibers, they are commonly recommended. For example, they are helpful with diarrhea by making the stool harder in contrast to insoluble fibers which are nor preferred in this type of IBS (21). Long-chain, intermediate viscosity, soluble, and moderately fermentable—like psyllium—has been shown to help control IBS and can help patients with their overall symptoms. Patients with IBS-C should consider getting psyllium fiber supplements as they have stool-softening effect There may be a short period of discomfort, abnormal bowel habits, and abdominal bloating/distension after starting a fiber supplementation plan. For this reason, fiber

supplementation should be start gradually and increased by no more than 5 g/day every week (22).

A trial assessing the use of fiber in 275 individuals with IBS performed in a primary care setting. Patients were assigned to 12 weeks of treatment with soluble fiber (psyllium), insoluble bran fiber, or placebo. When compared to a placebo at 12 weeks, psyllium reduced the IBS symptom severity score (IBS-SSS), whereas bran had no benefit. A systematic analysis found that only psyllium had a positive impact on IBS symptoms, with only a moderate overall improvement (23).

1.3.1.4 Turmeric (Curcuma longa)

In a randomized pilot research, patients with IBS received two doses of turmeric extract over the course of eight weeks to see how it affected their symptoms. Approximately 75% of the participants said that their symptoms were getting better after receiving treatment. Curcumin possesses antioxidant and anti-inflammatory properties. Scientists provided the rationale for the medical application of turmeric in gastrointestinal illnesses, including IBS, in a different review. Based on these studies, it was shown that the main mechanism by which turmeric extract (curcumin) inhibits hyperactive states of the gut and airways is by blocking calcium channels. It's possible that curcuma's antibacterial, anti-inflammatory, and spasmolytic qualities account for its efficacy in treating IBS (24).

1.3.1.5 Fennel

The broad-spectrum antibacterial properties of foeniculum vulgare, also known as sweet or common fennel, may help maintain digestive health. Two trials using oral fennel essential oil treatment for IBS patients demonstrated significant statistical and clinical improvements, including a pain reduction of more than 50% (25).

Herbal medicines are becoming increasingly popular across patients, because of their laxative, anti-inflammatory, and antispasmodic features (26). According to some studies, herbal remedies are thought to have fewer adverse effects than chemical ones, and fennel appears to help with flatulence by encouraging bowel movements. Trans-anethole is fennel's primary constituent. Anethole relaxes the smooth muscles of the

intestines and shares chemical similarities with dopamine. Furthermore, fennel essential oil helps enhance the quality of life and symptoms of irritable bowel syndrome (IBS) in individuals (27).

Fennel oil combined with curcumin demonstrated encouraging outcomes for the symptoms and quality of life in an IBS research involving adult patients (28).

1.3.1.6 Lifestyle modification

Exercise is crucial for supporting both physical and mental health; it helps speed up gastrointestinal transit, promote gas clearance in bloated individuals, and may even boost gut microbial diversity via the gut-brain axis. So, it makes sense to anticipate that patients with IBS will benefit from exercise. In a randomized clinical trial, researchers noticed substantial improvements in constipation, compared with patients allocated to usual care, comparing 12 weeks of an exercise intervention with usual care, but no notable changes in other IBS symptoms or quality of life.

Also, stress is more prevalent in IBS patients than in healthy people. There is a clear justification for encouraging relaxation and having some leisure time in IBS patients, which may be advantageous to certain people (29).

1.3.2 Pharmacological treatments

1.3.2.1 Probiotics, Prebiotics, and Synbiotics

Live bacteria called probiotics are present in our bodies and can be used to modify the microbial makeup of dental plaque or to specifically suppress oral infections. Prebiotics are dietary supplements that are not digested. Prebiotics are intended to enhance health by increasing the quantity and activity of probiotics such as Lactobacilli and Bifidobacteria. Escherichia, Enterococcus, Bacillus, Saccharomyces, Streptococcus, and Propionibacterium are other probiotics. One of the negative effects of taking a probiotic pill is gas and bloating.

It has been demonstrated that prebiotics can help treat dental disorders in addition to probiotics. Their role is to suppress the growth and activity of potentially hazardous bacteria while simultaneously promoting the growth of probiotics and helpful species.

Synbiotics are dietary supplements that combine probiotics and prebiotics, which are believed to work in tandem. Since real probiotics cannot thrive in the digestive tract without their prebiotic diet, using a synbiotic is essentially advised. The probiotic will be less vulnerable to temperature, low pH, and oxygen when there isn't a critical food source present. Prebiotics provide probiotics with a great growing environment (30).

The use of probiotics in IBS treatment is still in need of investigation and standardization, but some studies such as Net-work Meta -Analysis suggest that Bacillus coagulans (B. coagulans), Clostridium butyricum (C. butyricum) and Bifidobacterium longum ranked as the top three interventions in improving the global symptom scores of patients with IBS (abdominal pain, bloating, and straining scores),while Lactobacillus plantarum (L. plantarum) ranked last. Additionally, compared to patients receiving various treatments, L. acidophilus patients with IBS experienced less side effects.(31). Some randomized trials investigated the efficacy of bifidobacterium for global symptom scores or stomach pain scores. It also has a positive impact on IBS through a variety of mechanisms, including a decrease in limited inflammation, control of gut motility, modifications to the metabolism of bile salts, and a decrease in the number of competing microbes through the formation of antimicrobial substances and disruption of intestinal mucosal adhesion (32).

1.3.2.2 Peppermint oil capsules

More research appears to support the effectiveness of Mentha piperita essential oil (peppermint oil) in treating IBS than other herbal remedies. Enteric-coated peppermint oil capsules were assessed in a prospective, placebo-controlled study involving outpatients with IBS. Improvements in the severity of abdominal pain were noted in 79% of patients taking Mentha capsules, along with reduced abdominal distension, fewer diarrhea episodes, and less flatulence in 83% of patients. The Mentha tablet significantly reduced symptoms as compared to a placebo. The Mentha group didn't suffer any serious side effects, and the peppermint oil tasted good. Research has shown that mentha possesses antimicrobial, antispasmodic, and inhibits the motility of the stomach (33).

based on a comprehensive analysis of 10 RCTs with 1030 patients. For all IBS symptoms, peppermint oil was better than a placebo; 95% CI 0.43–0.98, number required to treat [NNT] = 4; 95% CI 2.5–71. Peppermint oil significantly increased the rate of adverse events (RR of any adverse event = 1.57; 95% CI 1.04–2.37). Accordingly, peppermint oil was more effective than a placebo at treating IBS, although side effects were prevalent (34).

1.3.2.3 Chlordiazepoxide

Chlordiazepoxide belongs to benzodiazepine family which has sedative, anxiolytic, anticonvulsant, muscle relaxant properties. Chlordiazepoxide is especially helpful in treating anxiety disorders and alcohol withdrawal. Furthermore, it is used in concert with mebeverine hydrochloride to treat irritable bowel syndrome as a medication that eases intestinal tension and anxiety (35).

1.3.2.4 Simethicone

Simethicone has been used for more than 50 years. Simethicone's primary characteristics include its ability to deform surface tension and decrease surface viscosity and hydrophobicity, which allows it to spread readily across surfaces. This silicone derivative works by dispersing trapped gas pockets in the GI tract to reduce flatulence by its deforming action. It modifies the gas bubbles' surface tension, which promotes their coalescence (36).

Simethicone, a well-tolerated medication, it has been used since the 1960s to improve the quality of the stomach and colonic mucosal vision during endoscopy by reducing gas retention and bubble formation. Simethicone generally used in combination with other drugs to get result. One combination is GASTRAP® DIRECT, which combined simethicone and chitin -glucan in one device, Chitin-glucan, non-digestible dietary compound, slowly fermented in all colon without gas production. According to a prospective, open-label, multicenter study, 100 patients were introduced and took GASTRAP® DIRECT three times a day for 4 weeks, and the outcome was an improvement in abdominal pain, bloating, stool consistency in most patients (37).

Another combination is alverin citrate, it is an antispasmodic drug that relaxes smooth muscles of stomach. In a in a double-blind, placebo-controlled, randomized trial conducted in 17 sites in Hungary and Poland, they gave 412 IBS patients combination drug of 60 mg alverin citrate and 300mg simethicone three times a day for a month, and the patients ended with a high reduction in abdominal pain and discomfort which suggested a synergistic action (38).

1.3.2.5 5HT3 Antagonist Agents

The selective serotonin 5HT3 antagonist block serotonergic afferent neural signals and reduces GI motility, agents that antagonistically block 5-Hydroxytryptamine-3 receptors (5-HT3RAs) for treating IBS-D includes ondansetron, cilasetron, aleosetron, and ramosetron. Although ramosetron is exclusively available in Asia, cialansetron was never commercialized despite having shown efficacy. Despite being used extensively for 30 years to treat nausea, ondansetron has never been linked to ischemic colitis. While generic ondansetron is cheap, its current licensing is limited to treating nausea and vomiting brought on by radiotherapy, cytotoxic chemotherapy, or post-anesthesia. In a double-blind meta-analysis research, ondansetron was found to be beneficial for treating diarrhea-associated irritable bowel syndrome. Over the course of 12 weeks, ondansetron considerably improved stool consistency when compared to a placebo (adjusted mean (SE) difference −0.7 (0.19); 95% CI −1.0 to −0.3, p = 0.0013) (39).

A network meta-analysis conducted in 2021 found that all 5-HT3 receptor antagonists performed better than control groups. Alosetron was the most effective for overall symptom relief, whereas cilansetron was the most effective for abdominal discomfort or pain. Ondansetron was the best option for enhancing bowel habits and consistency, even when compared to other 5-HT3 antagonists and the least successful control regimens (mebeverine and placebo). As a result, this family of medications may be crucial in easing the incapacitating symptoms of diarrhea in patients with IBS (40).

1.3.2.6 Linaclotide

Linacelotide, a minimally absorbed guanylate cyclase-C agonist that reduces abdominal symptoms, is an effective treatment for irritable bowel syndrome with constipation (IBS-C). The body creates more cyclic guanosine monophosphate (cGMP) when linaclotide binds to the GC-C receptors on the intestinal mucosa. This increases the amount of fluid discharged into the colon, which in turn improves gastrointestinal motility and reduces constipation.

Diarrhea was the most frequent side effect of linaclotide. The National Medical Products Administration of China approved linaclotide (290 μg once daily) in January 2019 for the treatment of IBS-C, making it the sole medication prescribed for the condition in that country. Treatment with linaclotide improved symptoms beginning two weeks after the commencement of treatment and continued to improve at the 12-week mark (41).

1.3.2.7 Loperamide

Loperamide is a known agonist of the peripheral μ-opioid receptor (MOR) with antisecretory effects. Because of its ability to reduce gastrointestinal motility and secretion, it has been used for more than thirty years to treat both acute and chronic diarrhea. By inhibiting gastrointestinal motility and prolong enteral transit, loperamide activates MOR, promoting fluid absorption and decreasing the frequency of stools (42).

The bulk of research found that loperamide was effective in reducing stomach pain, which is a frequent IBS symptom. However, there are a few negative effects, including oral blisters, swollen fingers, difficulty sleeping, and constipation. Due to a lack of high-quality evidence, the American College of Gastroenterology does not currently suggest the dose of 2 mg to 8 mg per day, but it may be helpful in certain people with IBS-D (43).

1.3.2.8 ELuxadoline

The US FDA and EMA both approved the oral medication Eluxadoline, which has mixed opioid effects, for the treatment of IBS-D in May 2015 and July 2016, respectively. It influences both directions of brain-gut transmission through the enteric opioid system. The enteric opioid receptors ε, κ, and δ control gut motility, secretion, and feeling. The primary mechanism by which loperamide functions is via activating ε-opioid receptors, which inhibits secretion and motility.

The IBS element that causes stomach discomfort may be connected to persistent visceral hypersensitivity, which is characterized by raised κ-opioid receptor expression.The effects of μ- and κ-opioid receptor-mediated effects on visceral feeling are enhanced by antagonistic interactions with the δ receptor, which also opposes the constipating effects of μ-opioid activation caused by increased sphincter tone and suppression of gastrointestinal peristalsis. In order to treat the diarrhea and stomach pain associated with IBS-D, eluxadoline, a δ- and κ- opioid receptor antagonist and μ- and κ-opioid receptor agonist, was created with the objective of developing the use of this mixed opioid profile (44).

1.3.2.9 Dicyclomine

Dicyclomine hydrochloride is used as an anti-cholinergic and anti-spasmodic medication in the management of irritable bowel syndrome. It is a BCS class I medication, with a peak plasma concentration is reached 60–90 minutes after oral treatment and has about 4–6 hours half-life in plasma. Typically, it is used in the management of irritable bowel syndrome and further aids in the treatment of intestinal, bladder, and stomach pains. Dicyclomine HCl would be advantageous as a colon-targeted medication delivery method primarily because decrease in these systemic adverse effects, improving patient adherence by lowering the frequency of dosage and enhancing therapeutic effects by localizing its effects on the colon, which is the main site of action for treating irritable bowel syndrome symptoms (45).

1.3.2.10 Hyoscaine butyl bromide

Hyoscine butylbromide (HBB) is one of the most used anticholinergic and antispasmodic drugs on the market (46). Hyoscine-N-butyl bromide has a significant anticholinergic effect on the human duodenum of smooth muscle by inhibiting the muscarinic receptors M2 and M3, especially in cholinergic spasticity and reduce intestinal spasms, or abdominal pain (47).

1.3.2.11 Mebeverine

Mebeverine is a direct antispasmodic that acts on smooth muscles in the intestines. It may also have mild atropine-like effects and a local anesthetic effect. According to current guidelines, the drug of choice for IBS patients with a predominance of pain is an antispasmodic. A systematic review of 26 randomized clinical trials (RCTs) involving 2811 IBS patients and 13 different antispasmodics revealed that antispasmodic medication significantly reduced IBS symptoms when compared to placebo. Nowadays, drotaverine and hyoscine are preferred over other antispasmodic medications for the treatment of IBS (48).

Treatment for IBS-C involves bulking medications and osmotic laxatives (polyethylene glycol). Patients with IBS-C have been reported to benefit from soluble fibers like psyllium and ispaghula, whereas insoluble fibers like bran are ineffective. On the other hand, it might make flatulence and discomfort worse. Second line treatments include prokinetic substances like 5-HT4 serotonin agonists increase intestinal motility. Prucalopride works well for laxative insufficiency and persistent idiopathic constipation, however it has negative effects on the heart. A prostaglandin derivative called lubiprostone (Type 2 chloride-channel activator) promotes intestinal fluid output, relieving constipation and other general IBS symptoms. According to a recent review, linaclotide was the most effective medication for treating the stomach flatulence that IBS-C patients frequently experience (49).

1.3.2.12 Anti-Depressants

Patients with IBS may benefit from antidepressants because they may target peripheral effects such pain perception, motility, and visceral hypersensitivity. Antidepressants have the ability to modify a patient's perception of pain by inhibiting incoming pain impulses and altering visceral afferents through anticholinergic actions. It is unclear how exactly these medications work to treat IBS and other types of stomach pain. Their positive impact on GI motility may stem from their effects on the levels of the antidepressant classes most frequently used to treat IBS: tricyclic antidepressants (TCAs), which slow down GI transit, and selective serotonin reuptake inhibitors (SSRIs), which speed up transit. This explains why TCAs are commonly supplied to IBS-D patients, while SSRIs are usually given to IBS-C patients or to IBS patients with significant psychiatric comorbidities (50).

1.3.2.13 Rifaximin

Rifaximin is nonsystemic antibiotic with low oral bioavailability, and thought to work by regulating the intestinal microbiota, suppressing inflammation, restoring visceral hypersensitivity, and lowering intestinal absorption (51).

1.3.2.14 Fecal microbiota transplantation (FMT)

Fecal microbiota transplantation, or FMT, was first utilized in the fourth century by the Chinese physician Ge Hong to treat severe diarrhea and malaria.When selecting a super donar, stability of the donor's gut bacterial makeup over time is an important factor. The criteria to apply when selecting an effective (superdonor) for FMT remain unclear, as do the optimal dose, fresh or frozen stool FMT, administration route, and frequency of treatment, single or mixed donor sample, IBS criteria (Rome III or Rome IV), IBS subtype and severity, and FMT delivery techniques (Colonoscopy, gastroscope, or naso-jejunal probe to the duodenum). FMT is now an effective treatment for infections caused by Clostridium difficile (52).

The therapeutic effect of FMT depends on the fecal transplant dose; amounts less than 30 g have no influence.

It is effective to administer the fecal transplant to the large or small intestine (53).

IBS patients may benefit from FMT at 12 weeks when given by colonoscopy or gastroscope, but not by oral capsules, according to a meta-analysis published in 2022. The capsule is the most often used and well-tolerated choice among participants, while the colonoscopy requires bowel lavage and takes a long time. For the treatment of recurrent Clostridium difficile infection, frozen stool FMT is just as effective as fresh stool FMT. While FMT is generally safe when used for IBS, further research is advised before extending its use (54).

FMT screened stool from a healthy donor is transferred to a recipient with the aim of changing the variety of the gut microbiota. FMT capsules or enema or tubes are one of the future treatments for IBS because the method of administration is colonscopy which is far less demanding than endoscopy. It is believed to be successful for managing inflammatory bowel disease and IBS, and it is suggested as a treatment strategy for Clostridium difficile infections (55).

1.3.2.15 Neurotransmitters

Chemical messengers called neurotransmitters (NTs) are responsible for signal transmission between neurons. There will be antidepressant effects if neurotransmitters such as norepinephrine (NE), dopamine, and serotonin (5-HT) are restored. Other neurotransmitter signals may also alter during depression, according to another research. For instance, whilst GABA neurotransmitter levels are lower, glutamate and acetylcholine neurotransmitter levels are higher. Both human behavior and the functioning of the neurological system are impacted. Anxiety disorders, sadness, and mood disorders are closely associated with abnormalities in neurotransmitters. Dopamine, 5-HT, and norepinephrine (NE) are associated with happiness, joy, and other positive emotions, but insufficient neurotransmitter levels would result in depressive symptoms, according to the monoaminergic neurotransmitter insufficiency theory. Because the intestinal flora also produces NTs, gut microorganisms also have an impact on the central nervous system (CNS) via the microbiota-gut-brain axis. According to a new study, modifications to the gut microbiota may influence how the brain and the

intestine communicate with one another and alter the cortical response by stimulating the neuroendocrine-immune system.

For instance, it is thought that the pathophysiology of depression may be associated with gut microorganisms, which are essential for the metabolism of short-chain fatty acids (SCFAs) and are critical for controlling neurotransmitters in the central nervous system (CNS), particularly in the hypothalamus. Anxiety, depression, visceral sensory abnormalities, irregular gastrointestinal motility, and central sensory abnormalities are among the physiological signs of IBS that are closely linked to neurotransmitters. The aberrant neurotransmitter expression in the system is linked to changes in microbial composition and metabolomics, which may also have an impact on the intestinal neural circuits that regulate gut sensory function. In addition to controlling blood flow, these neurotransmitters also affect the microbiota, natural immunity of the gastrointestinal tract, intestinal motility, and nutritional absorption (56).

1.3.2.16 Promising drugs for IBS

Mesalamine is a common anti-inflammatory medication used to treat inflammatory bowel disease. It is also known by the name 5-aminosalicylic acid. Mesalamine is recommended for IBS patients for the reason to the low-grade inflammation and mucosal immune activation associated with the condition. According to reports, mesalamine decreased fecal bacteria numbers in a different studies including 12 IBS-D patients and improved overall symptoms in a small trial involving 20 IBS patients.

The mast cell stabilizer, ketotifen offers a novel approach to treating IBS by targeting the GI tract's immune system. Cholecystokinin (CCK) has been proven to activate mucosal mast cells, although ketotifen can stop this from happening. A clinical investigation with 60 IBS patients supports the effectiveness of ketotifen as a treatment for IBS. Patients with IBS experienced a substantial decrease in stomach pain when using ketotifen, as seen by a boosted discomfort threshold to rectal balloon distension. Furthermore, IBS patients using ketotifen had fewer mast cells in their rectal biopsies and spontaneous tryptase release. As for the side effects, sedation and sleepiness were mild and well tolerated (57).

1.3.3 Psychological treatment

Many psychological interventions were found to be more beneficial than a control intervention, according to a thorough evaluation. These included group Cognitive Behavioral Treatment (CBT), gut-directed hypnosis, face-to-face multi-component psychological therapy, stress management, self-administered or minimal contact CBT, and contingency management. But no psychological treatment outperformed any of the other active therapies in a discernible way (58).

The most comprehensive research relates to CBT, which modifies behavior and alters maladaptive thought processes to affect mood and physical symptoms. It consists of cognitive restructuring (recognizing and correcting cognitive distortions to produce more accurate and balanced perspectives about stress and symptoms), psycho-education, and relaxation techniques (such as breathing exercises) (59).

1.4 Literature review

This part includes some previous studies that have evaluated types, symptoms and treatment of IBS.

A postal survey in north and west Birmingham calculated the incidence of IBS using gender, age and symptoms done on 8646 patients over 18 years and found that main symptoms were diarrhea (25.4%), constipation (24.1%) and alternating symptoms (46.7%). Also, quality of life was affected by IBS patients (60).

Another observational population-based study done on Lebanese adults found that 20.1% of the study population had IBS, as determined by Rome III criteria. IBS was 1.67 times more common in women than in men (P 0.05). Participants under the age of 30 had a higher risk of developing IBS (P = 0.01). People who smoked waterpipe were 1063 times more likely to have IBS (P 0.05) than those who did not and IBS prevalence was higher in alcohol drinkers (P = 0.01) (61).

A study in 2020 found that IBS affects the quality of life of patients, and it puts a heavy burden on healthcare resources. Treating a patient for one year costs around $355-3,344 (62).

Family cluster research conducted in the United States with 643 participants found a significant correlation between presenting with IBS and having a first-degree relative with bowel issues (odds ratio, 2.3; 95% confidence interval (CI), 1.3-3.9) (63).

According to a Japanese study, there was a higher likelihood of positive family history in IBS patients and patients who denied ever having seen a physician about these symptoms (IBS non-consulters) compared to controls (33.9% vs. 12.6%, $P < 0.001$, for patients; 26.1% vs. 12.6%, $P < 0.01$, for nonconsulters). Clinical manifestations such as anxiety, diarrhea, constipation, and dyspepsia were found to be significantly influenced by the parental background. And the conclusion was that having gastrointestinal issues in one's parents increases the chance of developing IBS (64).

A fixed dosage combination (FDC) of 135 mg of mebeverine hydrochloride and 5 mg of chlordiazepoxide was used in an observational research conducted in India to treat IBS. The FDC was well accepted, had a good safety profile, and was useful in managing IBS symptoms in Indian patients (65).

The safety of herbal drugs is a major problem. According to a systematic evaluation of 22 RCTs using herbal remedies for IBS symptoms, 2.97 percent of patients experienced adverse effects. (9.50% CI 2.04% to 3.90%), so it is important to consider safety and efficacy of herbal medications if they are used for IBS patients (66).

The IBS Symptom Severity Score (IBS-SSS) was used in a randomized controlled study (RCT) to assess the effectiveness of FMT. The researcher looked at the percentages of patients with moderate and severe symptom severity at various points following FMT. Over 20% of patients receiving FMT experienced side effects like diarrhea, constipation, cramps, discomfort, or abdominal pain, compared to 2% of patients getting a placebo. The fact that these side effects occurred in the first two days after FMT and were minor and self-limiting is noteworthy (67).

In 2012, a double-blind, placebo-controlled trial was conducted to assess the effectiveness and safety of Linaclotide. The results showed that taking 290 μg of the medication once day considerably reduced symptoms related to the abdomen and colon, as well as discomfort, fullness, cramping, and bloating. Similar to stomach discomfort,

benefits started to show up within the first week of treatment and reached their peak by the 12th week. Regarding safety, during the experiment, more than half of the participants experienced mild diarrhea (68).

Eluxadoline was well tolerated in the Phase 2, 3, and 4 clinical trials of IBS-D. Constipation, discomfort in the abdomen, and nausea were the three adverse events (AEs) that occurred most frequently. In the pooled Phase 2 and 3 trials, pancreatitis was the most commonly reported serious adverse event (SAE) among patients receiving eluxadoline; nevertheless, the incidence was generally quite low. Every occurrence was deemed moderate. Patients without a gallbladder or those who drink more than three glasses of alcohol a day should not use eluxadoline because of the higher risk of pancreatitis (69).

In 2014, A cross-sectional study in Palestine was randomly done to see how residential area affected the incidence of IBS and the results were that IBS was more prevalent in refugee camps (34%) and in villages (34%). IBS-M being the most predominant category of IBS (55%). Middle-aged and elderly Palestinians suffered from IBS at high rates. IBS was more common among residents of rural areas and refugee camps than in urban regions (70).

Low fermentable, oligosaccharide-, disaccharide-, monosaccharide-, and polyol (FODMAP) diet (LFD) has long been a mainstay treatment for IBS. However, statistics continue to point to a 30% not responding rate for this management strategy. The results of the investigation show uniformity in the proof that each IBS subtype can enhance general symptoms and bowel function with the LFD (71).

The COVID19 epidemic has caused a rise in concern among female IBS sufferers in Egypt. Anxiety and symptoms of irritable bowel syndrome were found to be related in a cross-sectional study conducted in Egypt. The study used questionaries to collect data, and the symptoms were assessed according to the Rome IV criteria. During the pandemic, anxiety levels rose in both the IBS and non-IBS groups, with no discernible difference between them (P value =.657). Additionally, the study showed a strong correlation between severe anxiety and higher levels of education (P value =.031).

Furthermore, compared to rural home, living in an urban area was substantially related with 13.5 times higher odds of having elevated IBS symptoms (P value <.001). Additionally, patients who experienced job loss during the pandemic had a 12.9-fold higher likelihood of experiencing worsening symptoms (P value = 0.01). Anxiety levels rising are linked to an increase in IBS symptoms (72).

A double-blind clinical study was conducted on patients with IBS and SIBO to study the influence of the probiotic Mutaflor on SIBO relapse in IBS patients. It was found that this probiotic might effectively cure SIBO patients by alterin g the usual microbiota in their guts. 159 of the 172 IBS and SIBO patients who had antibiotic treatment and negative breath results were included in the research. The demographic characteristics of both groups were equivalent, including age, sex, type of IBS, and use of PPIs.

Frequency of SIBO recurrence were significantly lower in the probiotic group than the placebo group (P=0.033). Frequency rate of constipation and mixed type of IBS were almost similar in both groups (P>0.05) (73).

Rifaximin has been shown in several randomized, placebo-controlled trials made in 2020 to reduce overall symptoms in IBS-D patients. In both the US and Canada, rifaximin is currently licensed for the treatment of people with IBS-D. Adults with IBS-D who take short (2-week) regimens of the non-systemic (poorly absorbed) antibiotic rifaximin exhibit improved IBS symptoms that are well tolerated. Rifaximin's mechanisms of action remain incompletely understood, however there is indirect evidence that the medication reduces mucosal inflammation, stabilizes the microbiota, and helps SIBO (74).

1.5 Problem statement

In our country, data about IBS patients is very limited. Patients with this disease suffer a lot, most of them try many treatments and in many times, they still have some symptoms. In general, limited studies have been established to provide sufficient information about the efficacy of pharmacological and non-pharmacological treatments used by IBS patients and their effect on quality of life.

1.6 Significance of the study

Studies about IBS in our country are very limited. This study will give baseline data about patients with IBS, the lifestyle the patients live, the treatments used among them and the differences between them. The results may help in recommending the best treatment according to the case, and providing suitable counseling, this may improve treatment outcomes and quality of life of these Palestinian patients.

1.7 Objectives

1.7.1 General objective

The overall aim of this study is to assess the severity of IBS, the lifestyle the patients live and pharmacologic and non-pharmacologic treatments used by Palestinian patients.

1.7.2 Specific objectives

1. Evaluate the presentation and severity of symptoms of patients with irritable bowel syndrome (IBS).
2. Evaluate the types of IBS (constipation mainly, diarrhea mainly or mixed) among patients.
3. Describe the management of irritable bowel syndrome (IBS) used by patients.
4. Evaluate patients' compliance with treatment and lifestyle modifications.
5. Find any possible association between treatments and outcomes.

Chapter Two

Methodology

2.1 Study design and setting

This was a cross-sectional study using data collection form to collect data from patients by a face-to-face interview. Patients were met from gastroenterology outpatient clinics, community pharmacies and hospital pharmacies in Bethlehem. It was conducted between February and June 2024.

2.2 Population

Patients from Bethlehem city and surrounding areas diagnosed with irritable bowel syndrome undergoing medical treatment for any stage of the disease.

2.3 Inclusion criteria and exclusion criteria:

2.3.1 Inclusions criteria was as follows:

1. Male and female patients
2. Confirmed diagnosis of irritable bowel syndrome
3. Patients who received treatment

2.3.2 Exclusion criteria was as follows:

1. Pregnant women
2. Patients who did not have confirmed diagnosis of irritable bowel syndrome
3. Patients who did not receive treatment

2.4 Sample size

The number of IBS population in our country is not known, so we assumed they are more than 20000 patients. By assuming a response distribution to be 50%, and allowing 5% margin of error at 95% confidence interval, the required sample size for the study was determined using Raosoft sample size calculator (http://www.raosoft.com/samplesize.html) and the recommended sample size is 377. Convenient sampling method was used to collect the sample.

2.5 Data Collection

Given the significance of data standardization for a study's internal validity, data collection was standardized by employing a Data Collection Form to collect information from the patients (Appendix B). The information covers gender, age, education, living place, the severity of symptoms, the type of their IBS, the non-pharmacological treatments they tried as herbs or exercise in addition to their pharmacological treatments (medications used, their doses, any side effects reported due to them) and the outcomes of treatment (the degree of symptoms control, their severity and frequency).

A pilot study which was conducted in 20 patients to find if the data collection form is clear and if any modifications are needed, these patients were not included in the final analysis.

2.6 Ethical considerations

The study protocol was authorized by An-Najah National University Institutional Review Board (IRB) before the initiation of this study (Appendix A).

Patients' written consent was obtained before the interview. All information obtained from the questionnaire was kept confidential and only summarized data was presented in reports or publications.

Maintenance of high-level objectivity in discussion and analysis throughout the research was assured.

2.7 Statistical Analysis Methods

The Statistical Package for Social Sciences was used for statistical analysis (SPSS version 21). For continuous data, the mean ± standard deviation was determined. For categorical variables, frequencies and percentages were computed. Categorical variables were compared using the Chi square test or the Fisher test, depending on the situation. For all analyses, a p-value of less than 0.05 was considered statistically significant.

Chapter Three

Results

3.1 Sociodemographic data

Our study was a cross-sectional study that was conducted on 407 patients of irritable bowel syndrome from different areas in West Bank in Palestine, to evaluate the safety and efficacy of pharmacological and non-pharmacological treatments used by irritable bowel syndrome patients. Table 1 shows that more than half of the patients were females 253 (62.2%) as in figure 1, with amean age of 36.87±13.8 years old. As for the educational status, the largest group of the patients were under graduates 203 (49.9%), those with secondary education were 95 (23.3%), preparatory school 42 (10.3%), post-graduates 30 (7.4%), uneducated 23 (5.7%) and elementary school 14 (3.4%) as in figure 2. Regarding income, 225 (55.3%) had a moderate income123 (30.2%) had a low, and 59 (14.5%) had a high income as in figure 3. The table also shows that 263 (64.6%) of them were married, and the rest were single 123 (30.2%), divorced 11 (2.7%) or widowed 10 (2.5%) as in figure 4. Regarding employment status, 229 (56.3%) were employed and the rest 178 (43.7%) were unemployed as in figure 5. According to the locality, 201 (49.4%) of the patients were living in city, 164 (40.3%) in village, and 42 (10.3%) in camps as in figure 6. Table 1 also shows that 247 (60.7%) had health insurance, and 160 (39.3%) had no insurance. As for chronic diseases, 307 (75.4%) of the participants hadn’t a chronic disease, and the rest 100 (24.6%) had a chronic disease.

Table 1

Socio-demographic and clinical characteristics of the study sample

Socio-demographic Variables		Frequency (%) N=407
Gender	Male	154(37.8)
	Female	253(62.2)
Educational status	Uneducated	23(5.7)
	Elementary school	14(3.4)
	Preparatory school	42(10.3)
	Secondary school	95(23.3)
	Under graduated	203(49.9)
	Post graduated	30(7.4)
Social status	Single	123(30.2)
	Married	263(64.6)
	Divorced	11(2.7)
	Widower	10(2.5)
Income/month (Shekel)	less than 2000	123(30.2)
	2000-5000	225(55.3)
	more than 5000	59(14.5)
Employment status	Employed	229(56.3)
	Unemployed	178(43.7)
Locality	City	201(49.4)
	Village	164(40.3)
	Camp	42(10.3)
Health insurance	Don’t have insurance	160(39.3)
	Have insurance	247(60.7)
Chronic disease	Yes	100(24.6)
	No	307(75.4)

Figure 1

Male and female percentages

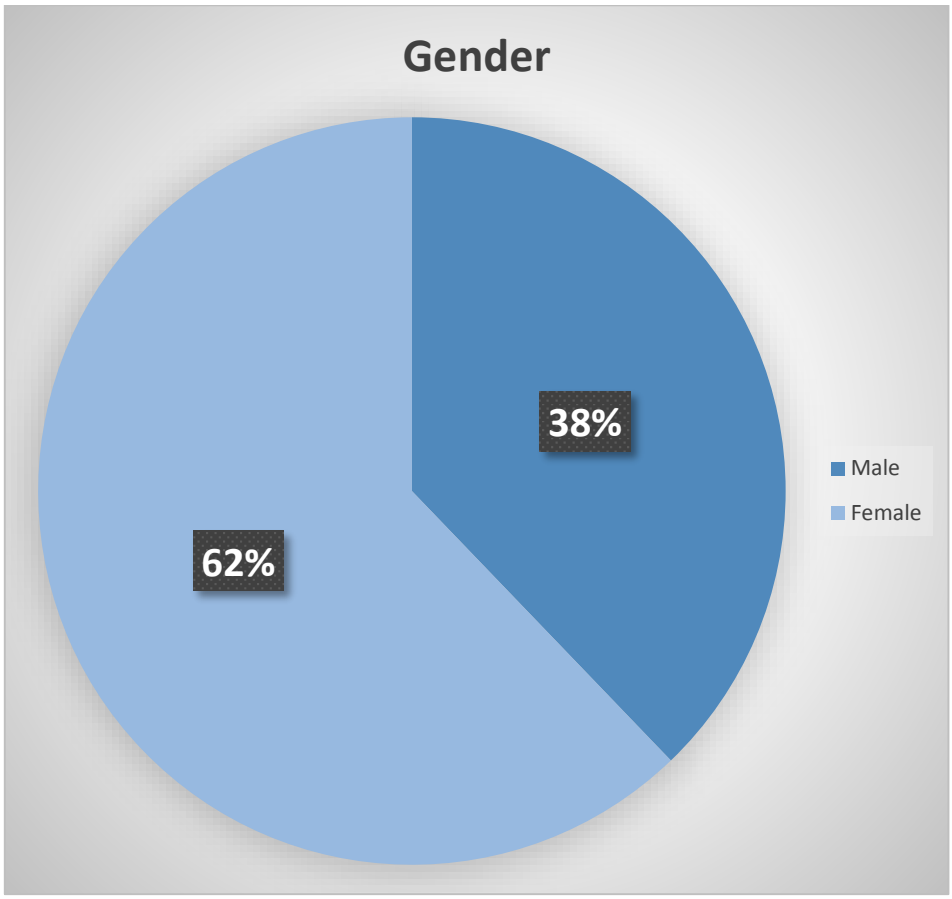


Figure 2

Educational level percentages

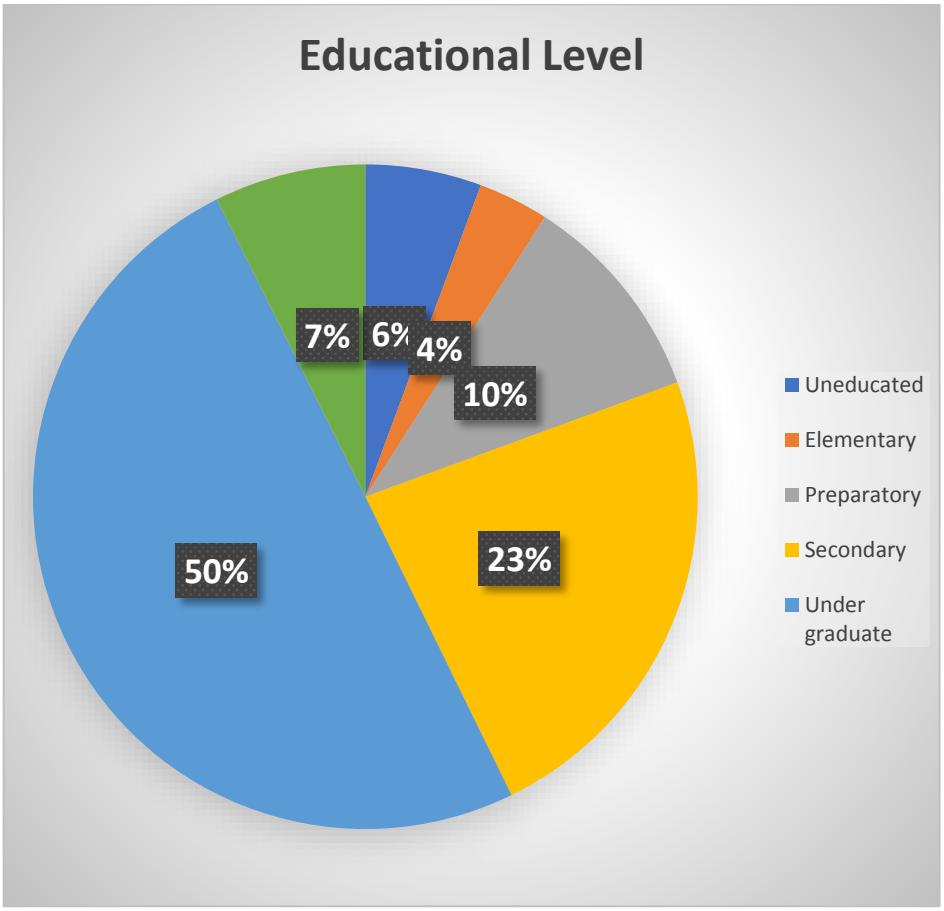


Figure 3

Monthly income percentages

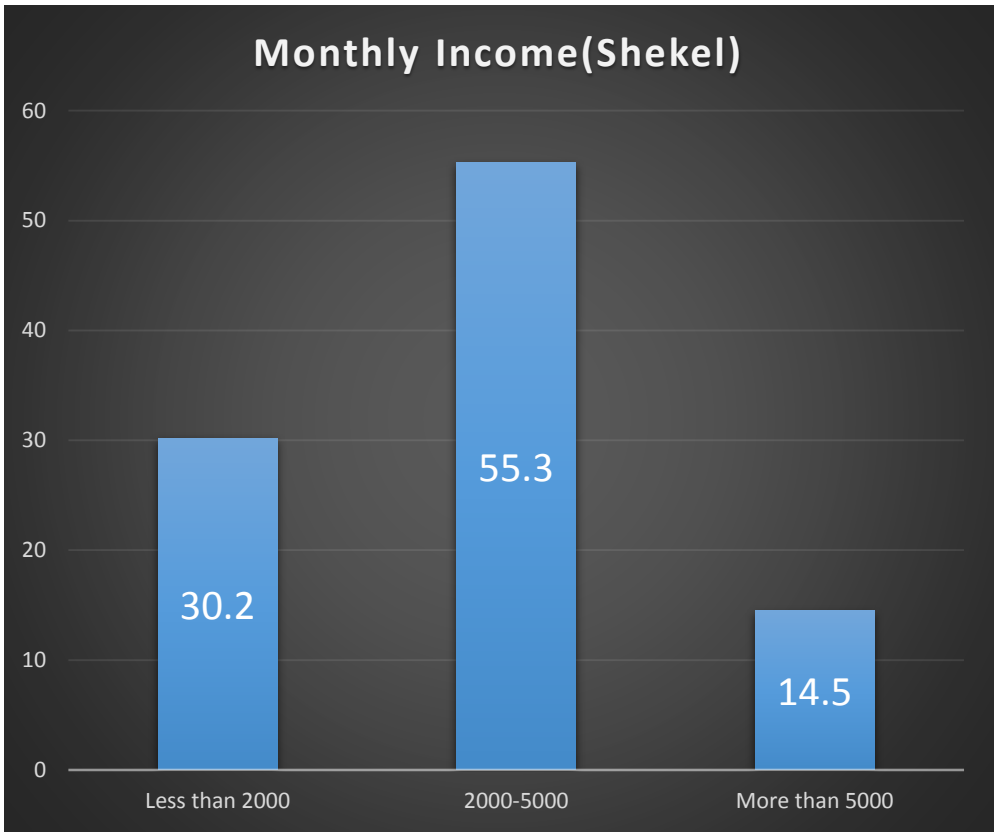


Figure 4

Marital status percentages

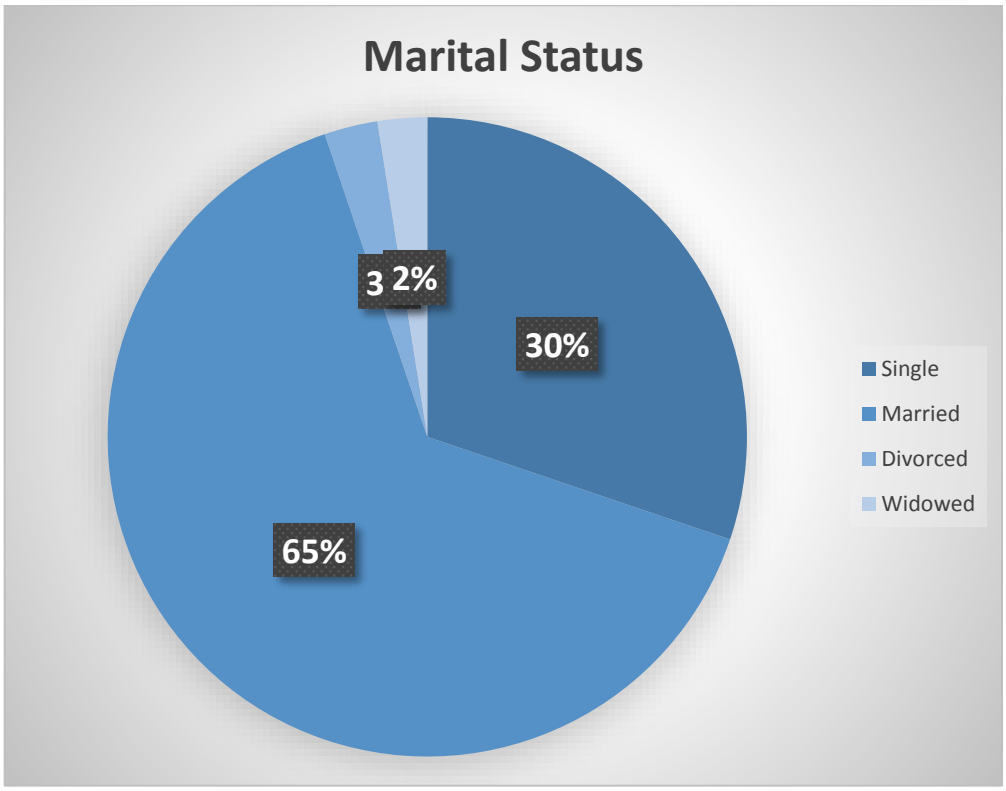


Figure 5

Employment status percentages

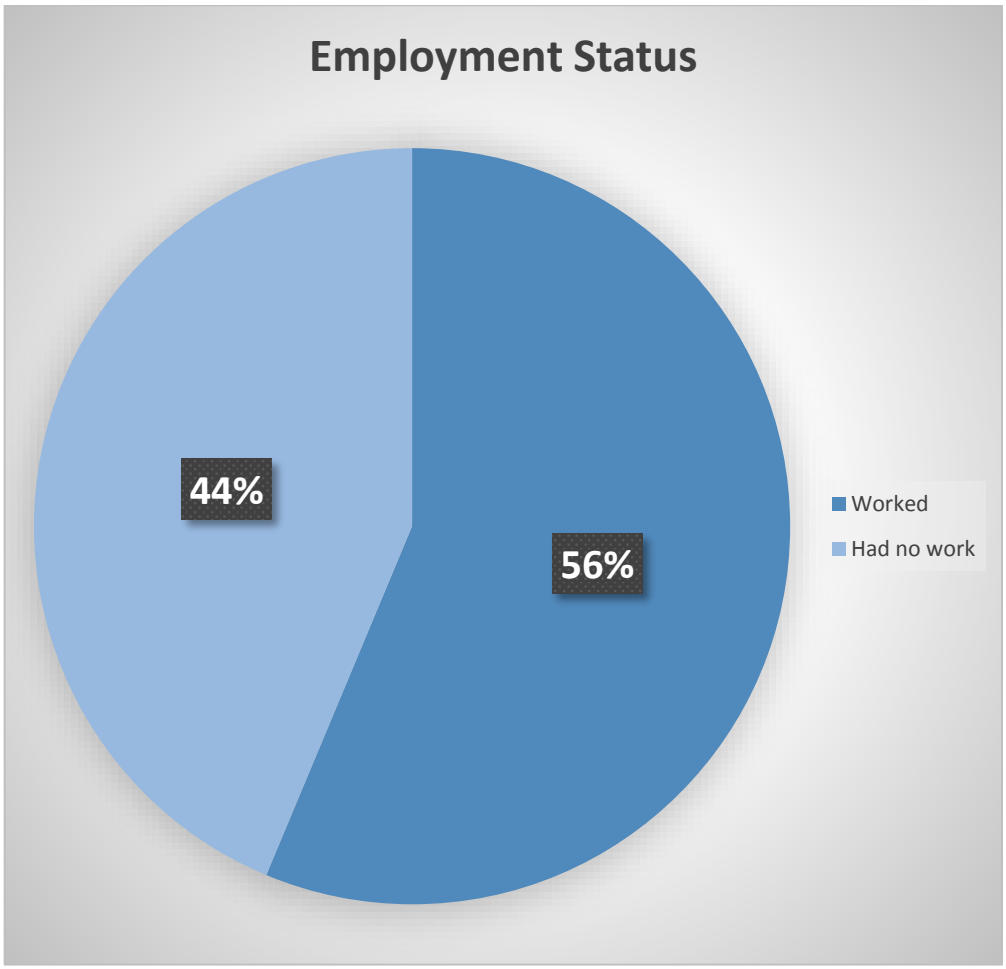
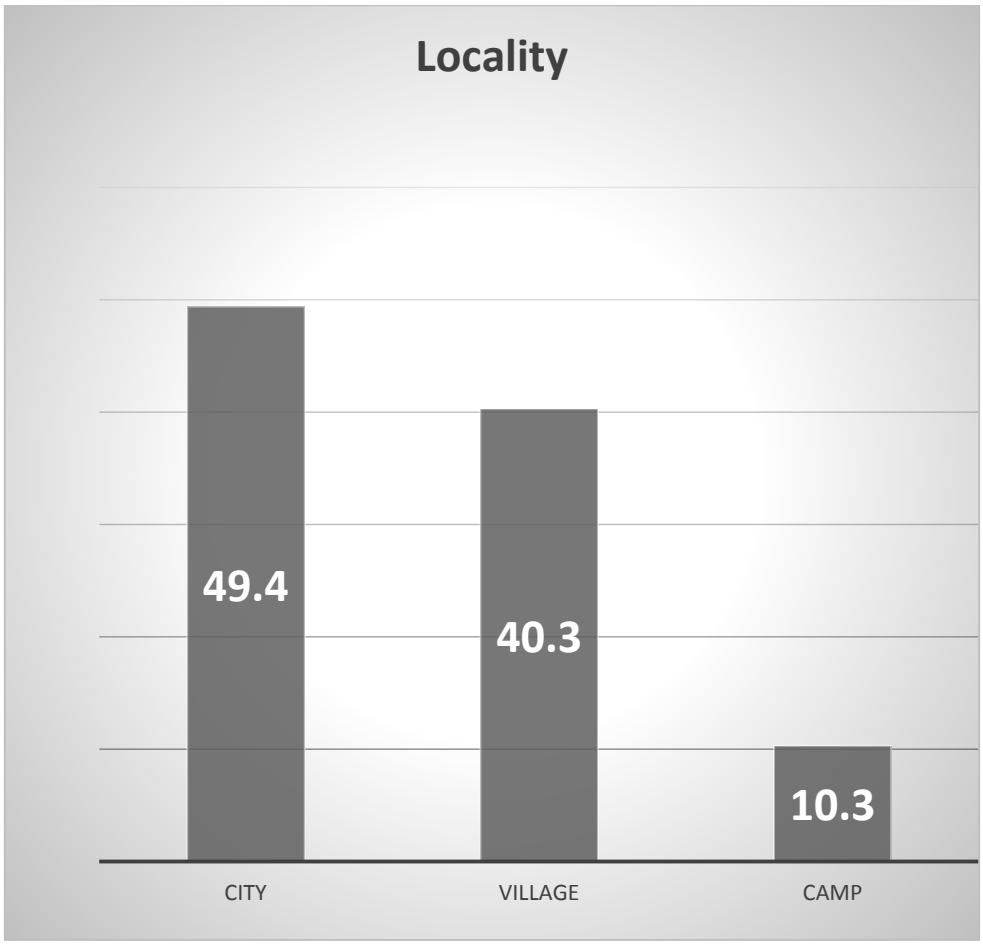


Figure 6

Place of living percentages



3.2 Clinical and Disease Characteristics of irritable bowel syndrome patients

This study described clinical and disease characteristics for 407 patients. Among them, 63.4% of patients didn't have a family history of irritable bowel disease, and the rest 36.6% told that they had a family history of disease.

As for the type of irritable bowel syndrome (IBS), nearly the half had alternate diarrhea and constipation (49.4%) while 36.9% had mainly constipation, and 13.8% had mainly diarrhea as in figure 7. Females were more likely to have mixed type (67.7% vs 32.3%) and constipation type (61.3% vs 38.7%) while males were more likely to have diarrhea type (55.4% vs 44.6%); p-value = 0.007.

Figure 8 described stool type for irritable bowel syndrome patients, 31.2% had a solid or lumpy stool 12.5% had a watery stool, and 56.3% had a mixture of two.

Concerning the number of defecations per day, almost half of patients had 1-2 defecation per day (50.1%), 31.7% of patients had less than three times per day, and 18.2% had more than three times a day.

With regard to clinical characteristics of the disease showed in Table 2, 76.2% of patients had abdominal pain, 86.5% had abdominal bloating, 86% had abdominal gases, and 17% had bloody stool. As for the age when diagnosed with the disease, it was between (15-70) years, with a mean of 29.3±10.3 years.

Figure 7

Irritable Bowel Syndrome types among patients

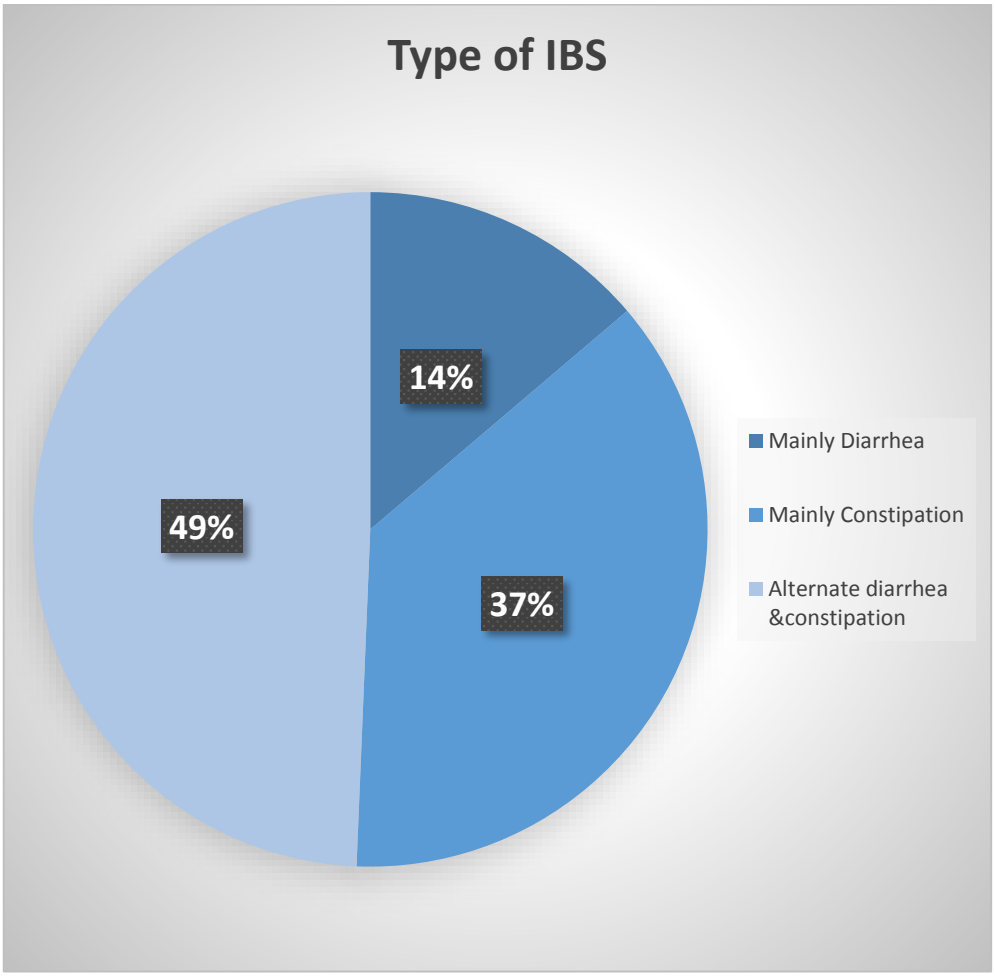


Figure 8

Stool types among patients

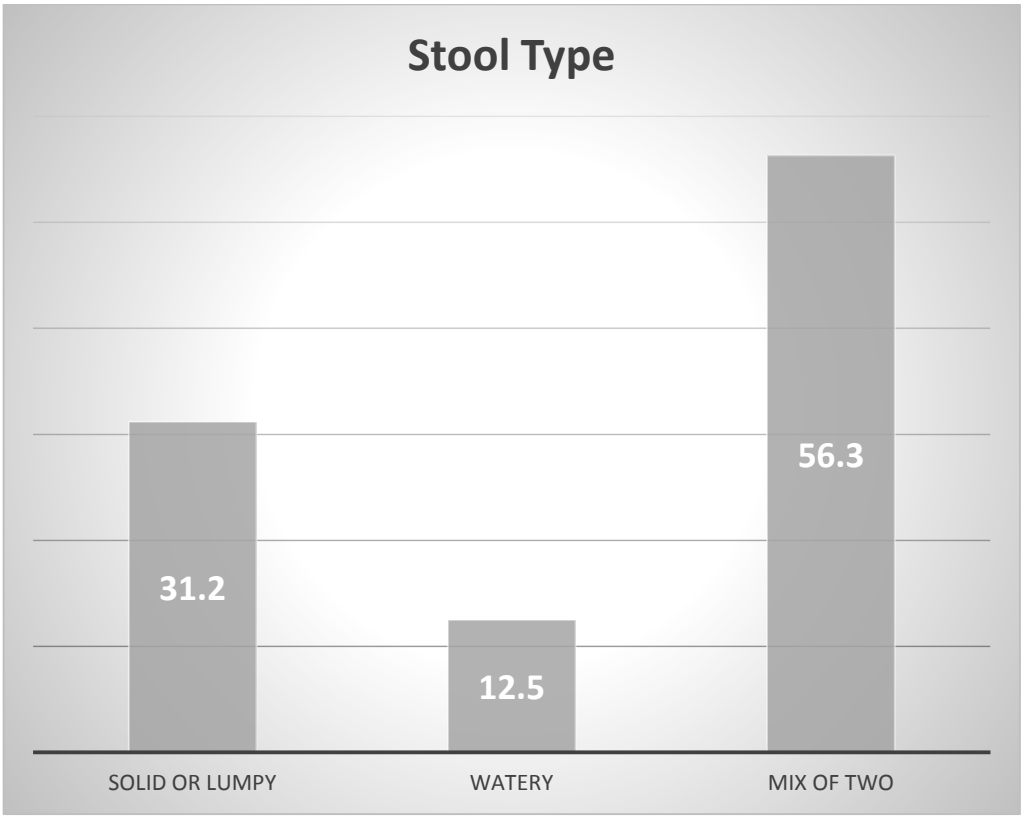


Table 2

Some of clinical characteristics of disease

Clinical characteristics	Number of patients(frequency)
Abdominal bloating	352(86.5%)
Abdominal gases	350(86%)
Abdominal pain	310(76.2%)
Bloody stool	69(17%)

3.3 Effect of disease on daily life of the patients

Table 3 and Figure 9 described how the disease affected patients' life by different ways, 248(60.9%) became nervous, 129(31.7%) couldn't sleep well, 69(83%) had nausea and fainted, 128(31.4%) rushed to bathroom, and 187(45.9%) embarrassed from gases.

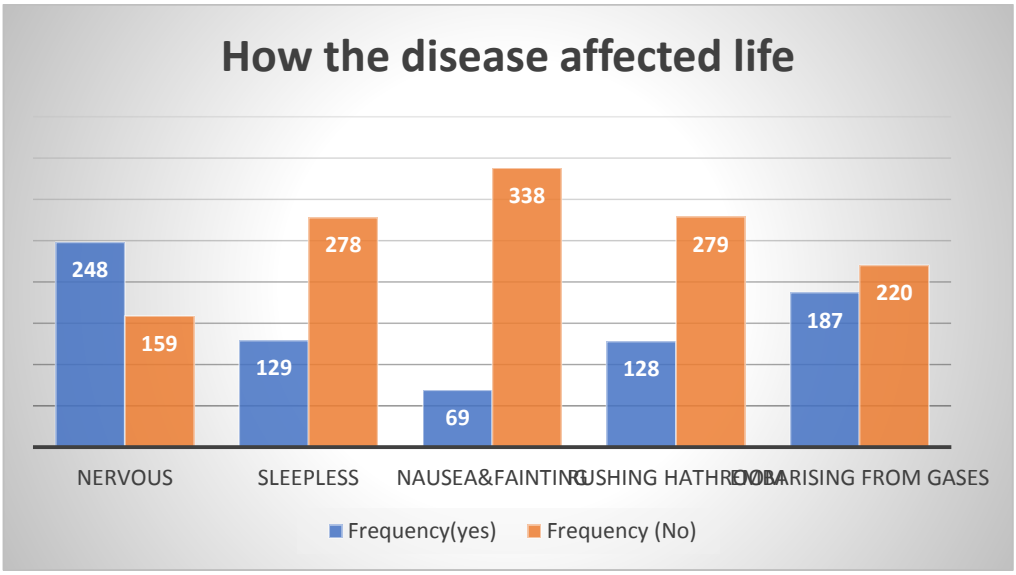
Table 3

How the disease affected patients' life

Symptoms	Frequency(yes)
Nervous	248
Embarrassing from gases	187
Sleepless	129
Rushing bathroom	128
Nausea and Fainting	69

Figure 9

Frequency of symptoms affected the patient's life.



3.4 Effect of some types of food on irritable bowel syndrome patients

In Table 4, we had summarized the food that may affect the patients' symptoms, we found that fries increase the symptoms of disease in 279(68.6%) of patients, spices in 209(51.4%), soda in193(47.4%), coffee in 142(34.9%), onion in 159(39.1%), cabbage in 261(64%), and beans in 228(56%) of patients.

Table 4

Effect of some types of food on patients

How the food affected IBS patients	Frequency (%) (Yes)
Fries	279(68.60%)
Hot spices	209(51.40%)
Soda	193(47.40%)
Coffee	142(34.90%)
Onion	159(39.10%)
Cabbage	261(64.10%)
Bean	228(56.0%)

3.5 Non-pharmacological treatments among patients

Concerning what the patients did to treat the disease non-pharmacologically, 206 (75.2%) of patients used herbs to sooth IBS, 123 (30.2%) of patients increased the amount of fibers, 33 (8.1%) decreased amount of fibers, 168 (41.3%) increased liquids, 234 (57.5%) avoided food which irritated colon, 113 (27.8%) did exercise, and 103 (25.3%) went to doctor as in table 5. Regarding the efficacy of these non-pharmacological treatments, 160 (39.3%) of patients said that they had improved completely by these treatments, 154 (37.8%) of patients answered that they had partially improved from non-pharmacological treatments as in figure 10. It was found that using herbs that sooth the IBS, increasing liquids, avoiding food that irritates the colon and having exercise were all significantly associated with improvement in IBS symptoms; P-values were <0.001, 0.032, 0.001 and 0.029 respectively as shown in table 6. Regarding the safety none of the patients reported possible side effects due to these non-pharmacological modalities.

Table 5

Non-pharmacological treatments used by patients

What the patient did to treat the disease	Frequency (%) (Yes)
Use herbs to sooth IBS (e.g mint, anise, fennel)	306(75.20%)
Avoided food that irritates colon	234(57.5%)
Increased liquids	168(41.3%)
Increased fibers	123(30.2%)
Had exercise	113(27.8%)
Decreased fibers	33(8.1%)

Figure 10

Improvement from non-pharmacological treatments

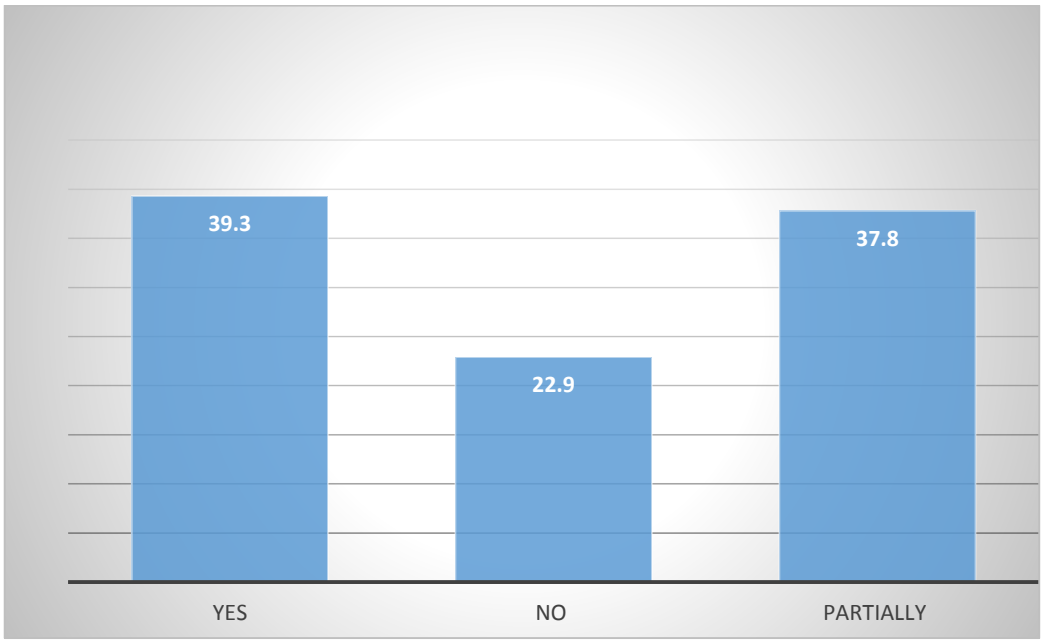


Table 6

Association between non-pharmacological treatments and improvement

Non-pharmacological treatment	Full improvement	No improvement	Partially improvement	P-value
Herbs soothes colon				<0.001
Yes	136(44.4%)	46(15%)	124(40.5%)	
No	24(23.8%)	47(46.5%)	30(29.7%)	
Increase fibers				0.094
Yes	55(44.7%)	20(16.3%)	48(39%)	
No	105(37.0%)	73(25.7%)	106937.3%)	
Reduce fibers				0.0797
Yes	14(42.4%)	6(18.2%)	13(39.4%)	
No	146(39%)	87(23.3%)	141(37.7%)	
Increase liquids				0.032
Yes	75(44.6%)	28(16.7%)	65(38.7%)	
No	85(35.6%)	65(27.2%)	89(37.2%)	
Avoids food that irritates colon				0.001
Yes	108(46.2%)	40(17.1%)	86(36.8%)	
No	52(30.1%)	53(30.6%)	68(39.3%)	
Have exercise				0.029
Yes	54(47.8%)	17(15%)	42(37.2%)	
No	106(36.1%)	76(25.9%)	112(38.1%)	

3.6 Pharmacological treatments among patients

Regarding pharmacological medications used by patients to treat IBS, the largest group of patients used chlodiazepoxide & clinidium bromide 188(46.2%) and probiotics 143(35.1%), and the lowest were anti- diarrheal 33(8.1%) and rifaximin 19(4.7%) as in Table 7, when the patients were asked about possible side effects due to these

medications, 64(16%) of patients told that they suffered from symptoms that they think they were due to the use of medications, unfortunately, none of them mentioned what these side effects were. When the patients were asked about the efficacy of these treatments in relieving IBS symptoms, 148(36,4%) patients told that they had full improvement from pharmacological treatments. Use of probiotics, synthetic fibers, chlordiazepoxide & clinidium bromide and hyoscain significantly associated with improvement in symptoms, P-values were <0.001, <0.001, <0.001 and 0.030 respectively (Table 8).

Table 7

Pharmacological medications used by patients to treat IBS

What drugs did the patients used to treat the disease	Frequency (%) (yes)
Chlodiazepoxide &Clinidium bromide	188(46.2%)
Probiotics	143(35.1%)
Synthetic fibers (Psyllium)	77(18.9%)
Hyoscain	59(14.5%)
Mebeverene	37(9.1%)
Loperamide	33(8.1%)
Rifixamin	19(4.7%)

Table 8

Association between pharmacological treatments and improvement

Treatments	Full improvement	No improvement	Partially improvement	P-value
Probiotics				<0.001
Yes	63(44.1%)	25(17.5%)	55(38.5%)	
No	85(32.2%)	114(43.2%)	65(24.6%)	
Synthetic Fibers (Psyllium)				<0.001
Yes	30(39%)	13(16.9%)	34(44.2%)	
No	118(35.8%)	126(38.2%)	86(26.1%)	
Chlordiazepoxide & clinidium				<0.001
Yes	88(46.8%)	31(16.5%)	69(36.7%)	
No	60(27.5%)	10749.1%)	51(23.4%)	
Mebeverine				0.443
Yes	17(45.9%)	11(29.7%)	9(24.3%)	
No	131(35.4%)	128(34.6%)	111(30.0%)	
Loperamide				0.946
Yes	12(36.4%)	12(36.4%)	9(27.3%)	
No	136(36.4%)	127(34%)	111(29.7%)	
Rivixamin				0.252
Yes	10(52.6%)	6(31.6%)	3(15.8%)	
No	138(35.6%)	133(34.3%)	117(30.2%)	
Hyoscaine				0.030
Yes	29(49.2%)	12(20.3%)	18(30.5%)	
No	119(34.2%)	127(36.5%)	102(29.3%)	

Chapter Four

Discussion and Conclusion

4.1 Discussion

This was the first study in Palestine to evaluate the safety and efficacy of pharmacological and non-pharmacological treatments used by irritable bowel syndrome patients. Most of the participants were females, married, educated, had moderate income, employed, living in cities, and had health insurance. Furthermore, many of them did not have chronic diseases.

This syndrome affects many people all over the world, some studies showed that up to 10% of the worldwide population suffers from this disease. While according to other sources, the prevalence may possibly be higher and reaches 45%. Males tends to have diarrheal type of IBS, women are 1.5–3 times more likely than males to suffer from it, and women are twice as likely to experience symptoms related with constipation (75). In this study, around half of the patients had alternate diarrhea and constipation (49.4%) while 36.9% had mainly constipation, and 13.8% had mainly diarrhea. This is similar to a previous study from the West Bank where the Mixed IBS (IBS-M) was the most common of IBS subtypes (55%, n=244) (70). Females were more likely to have mixed type (67.7% vs 32.3%) and constipation type (61.3% vs 38.7%) while males were more likely to have diarrhea type (55.4% vs 44.6%); p-value = 0.007.

A major complaint among patients with IBS is that their symptoms exacerbate followin g eating, and with regard to clinical characteristics, the majority of participants in this study had abdominal pain, abdominal bloating and gases, and a few of them had bloody stool. these symptoms affected the patients' daily life and caused many of them to became nervous, angry, couldn't sleep well, had nausea and fainted, rushed to bathroom, and were embarrassed from gases. A previous study revealed that psychological abnormalities, such anxiety, are common in those seeking heath care for gastrointestinal diseases, and anxiety becomes more common as GI symptoms worsen. In Sweden, a major survey of individuals with IBS revealed between 26% and 45% of the participants had sadness and anxiety levels that were higher than typical. Fatigue

and visceral hypersensitivity were more common in those experiencing psychological distress (76).

Furthermore, the study showed some options that may reduce severity of symptoms of disease. About half of patients used herbs to sooth colon, most of them avoided food which irritates colon, the rest played sport or went to doctor. Randomized double-blinded clinical trial reveled reduction in daily abdominal pain and bloating after the intervention in the herbal medicine group, and increase in stool frequency and stool consistency in IBS-C patients after the treatment with herbs (77). The findings of this study also confirm efficacy of non-pharmacological treatments in relieving symptoms as 160(39.3%) of patients said that they had improved completely by these treatments and 154(37.8%) of patients answered that they had partially improved. It was found that using herbs that sooth the IBS, increasing liquids, avoiding food that irritates the colon and having exercise were all significantly associated with improvement in IBS symptoms; P-values were <0.001, 0.032, 0.001 and 0.029 respectively. So, in treating IBS patients, non-pharmacological treatments and avoidance of certain types of food are highly recommended.

Polyphenols from brewer's yeast, soy, anise oil, fennel, aloe, curcumin, and peppermint oil have been linked to reduced symptoms of IBS, according to several studies. It has also been demonstrated that minerals including selenium, zinc, and magnesium may be beneficial for IBS. Because of their anti-inflammatory and antioxidant qualities, polyphenols have shown promise in relieving IBS-related digestive problems and suppressing inflammation (78). These choices were not used by patients, so further education and trials may be recommended.

IBS Treatment with Randomized Controlled Trials (RCTs) of Psychological Therapies in 2014 demonstrated that psychological therapy had a statistically significant effect on the severity of IBS symptoms, with improvements in the IBS-QOL (SMD 0.604; 95% CI: 0.440 to 0.768), SMD −0.618; 95% CI: −0.853 to −0.383), and SMD −0.282; 95% CI: −0.562 to −0.001). Conversely, though. The frequencies of diarrhea and constipation did not differ in a way that was statistically significant (79). This confirms

that treatment of IBS should not include pharmacological treatment only, treatment plan should include counseling about all factors and foods that may worsen the condition.

Research has indicated that engaging in aerobic exercise can enhance the diversity of gut microbiota, hence fostering the growth of advantageous bacteria like Lactobacillus and Bifidobacterium. Frequent exercise also improves gut motility, which is essential for maintain the ideal transit time for food to pass through the digestive system. Ensuring proper absorption of nutrients and efficient excretion of waste materials is contingent upon an ideal transit time. This procedure helps IBS patients maintain a balanced gut microbiota by preventing the proliferation of harmful bacteria, which can flourish in stagnant conditions (80). The findings of this study confirm the benefits of exercise also, so patients are recommended to maintain healthy life style including suitable exercise.

Regarding pharmacological medications used by patients to treat IBS, the largest group of patients used chlordiazepoxide & clinidium bromide 188 (46.2%) and probiotics 143 (35.1%), and the lowest were anti- diarrheal (loperamide) 33 (8.1%) and rifaximin 19 (4.7%). When the patients were asked about possible side effects due to these medications, 64 (16%) of patients told that they suffered from symptoms that they think they were due to the use of medications, when the patients were asked about the efficacy of these treatments in relieving IBS symptoms, 148 (36,4%) patients told that they had full improvement from pharmacological treatments. Use of probiotics, synthetic fibers, chlordiazepoxide & clinidium bromide and hyoscain significantly associated with improvement in symptoms, P-values were <0.001, <0.001, <0.001 and 0.030 respectively. The last ten years have seen a significant increase in the use of probiotics due to increased public knowledge of "good bacteria". Probiotic strains such as *Lactobacillus rhamnosus*, *Bifidobacterium animalis* and *Lactobacillus* acidophilus are beneficial in the alleviation of inflammatory diseases that are persistent and difficult, such IBS, which is characterized by complicated symptoms in the gastrointestinal tract symptoms. In a study done in 2022, probiotics demonstrated efficacy in alleviating the symptoms representing 67% of the clinical trials analyzed (81) In this study,

143(35.1%) of patients used probiotics to treat their IBS symptoms and their use was significantly associated with improvement in symptoms, P-values <0.001.

According to a 2024 meta-analysis study, probiotics are a useful treatment for IBS. In particular, a combination of Lactobacillus and Bifidobacterium has superior IBS treatment effects. According to additional research, Bifidobacterium is thought to be a useful strain for treating IBS.

However, a network meta-analysis has shown that Bacillus coagulans is a very successful treatment for people with IBS. Combinations of probiotics have been demonstrated to dramatically lower IBS-QoL scores, abdominal pain, and symptoms of the illness. The predominant strains found in these probiotic blends are Lactobacillus and Bifidobacterium (82).

Also regarding pharmacological treatments, many of the approved treatments were not used, for example, when compared to a placebo, linaclotide showed to be a safe and efficient treatment for CC and IBS-C (83), but no one used this medication here. Other examples include anti-depressants, eluxadoline, dicyclomine, fecal microbiota transplantation, so some pharmacological treatments are not widely used and they may be recommended for cases who continue to suffer from symptoms even with medications prescribed.

4.2 Strengths and limitations

4.2.1 Strength

To the best of our knowledge, this study was one of few studies to evaluate safety and efficacy of pharmacological and non-pharmacological treatments used by irritable bowel syndrome patients in general and the first in Palestine.

4.2.2 Limitations

Since this is a cross-sectional study, it is challenging to establish causal links between the factors that are related to the questions that have been used and those factors. Due to the fact that the information was acquired via in-person interviews, interviewer bias

could have been present. Furthermore, because only one city was included in the study, the conclusions cannot be applied to other cities.

4.3 Conclusion and Recommendations

4.3.1 Conclusion

Irritable bowel syndrome is a bothering problem that affects daily life, many patients try non-pharmacological treatments with accepted efficacy. Even with pharmacological treatments many patients could not reach full improvement.

4.3.2 Recommendations

Non-pharmacological treatments are recommended for IBS patients, so we recommend IBS patients to change their lifestyle, such as using herbs that sooth the IBS, increasing liquids, avoiding food that irritates the colon, increasing their physical activity, having enough sleep, and reducing stress

Pharmacological treatments could be useful if non-pharmacological measures are not enough, so we recommend IBS patients with constipation to take fibers and laxatives and patients with abdominal pain to take antispasmodics, antidepressants, and peppermint oil capsules. Probiotics may be added to relief IBS symptoms. It is highly recommended to avoid foods that may worsen the patients' symptoms, as fries, seasoning, soda, coffee, onion, cabbage, and beans.

Healthcare providers as doctors and pharmacists are recommended to give suitable counselling to IBS patients that includes pharmacological and non-pharmacological treatments, in addition to foods to avoid having the required treatment outcomes and improvement. Other studies about IBS are highly recommended to improve quality of care and decrease patients' suffering because the symptoms of this disease may affect all aspects of patient's life.

List of Abbreviations

Abbreviation	Definition
ACG	American Collage Gastroenterology
BSFS	Bristol Stool Form Scale
CBT	Cognitive Behavioral therapy
CCK	Cholecystokinin
CDI	Clostridium Difficili Infections
CNS	Central Nervous System
CRF	Corticotropin Releasing Hormone
EC	Enterochromaffin
FMT	Fecal Microbiota Transplantation
FODMAP	Fermentable,Oligosaccharides, Disaccharides, Monosaccharides and Polyols
GR	Glucocorticoid Receptor
IBS	Irritable Bowel Syndrome
IBS-C	Irritable Bowel Syndrome with constipation
IBS-D	Irritable Bowel Syndrome with diarrhea
IBS-M	Irritable Bowel Syndrome constipation and diarrhea
IBS-U	Irritable Bowel Syndrome un-sup typed
IRB	Institutional Review Board
MR	Mineralocorticoid Receptor
NMA	Net Work Meta Analysis
PVN	Paraventricular nucleus
RCT	Randomized Controlled Trials
SCFA	Short Chain Fatty Acid
SERT	Serotonin
SSRI	Selective Serotonin Reuptake Inhibitors

TCA	Tri Cyclic Antidepressant
TPH	Tryptophan Hydroxylase
LIN	Linaclotide
FDC	Fixed dose combination
NE	Norepinephrine
FGIDs	Functional gastrointestinal disorders
AGE	Acute gastroenteritis
CC	Chronic constipation
MOR	μ-opioid receptor

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Appendices

Appendix A

IRB approval

An-Najah National University
Faculty of Medicine & Health Sciences
Institutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref : Mas. June. 2023/4

IRB Approval Letter

Title of Research:

Evaluation of Safety and Efficacy of Pharmacological and Non-pharmacological Treatments Used by Irritable Bowel Syndrome Patients

Submitted by:
Reem Sarhan

Supervisor:
Rowa Alramahi

Approved:
6th June. 2023

Your Study Title **"Evaluation of Safety and Efficacy of Pharmacological and Non-pharmacological Treatments Used by Irritable Bowel Syndrome Patients."** reviewed by An-Najah National University IRB committee and was approved on 6th , June . 2023

Hasan Fitian, MD

IRB Committee Chairman

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910| E-mail : IRB@najah.edu

Appendix B

Questionair

استمارة جمع البيانات

هذا الاستبيان مطلوب لاتمام رسالة الماجستير ويهدف الى تقييم سلامة وفعالية العلاجات الدوائية وغير الدوائية المستخدمة من قبل مرضى متلازمة القولون العصبي. علما بان المعلومات ستعامل بسرية تامة ولن يتم التعرض لخصوصيات المشترك وستستخدم لأغراض البحث العلمي فقط. المشاركة في هذه الدراسة اختيارية و تطوعية.

هل توافق على المشاركة؟ _____

في حال موافقتكم الكريمة نرجو من حضرتكم التكرم بالإجابة عن جميع الأسئلة التالية بدقة شاكرين لكم حســن تعاونكم

الخصائص الديموغرافية للمرضى

1. عمر المريض:_____

2. جنس المريض

( ) ذكر ( ) أنثى

3. المستوى التعليمي

( ) غير متعلم ( ) ابتدائي ( ) اعدادي

( ) ثانوي ( ) جامعي ( ) دراسات عليا

4. الدخل الشهري للاسرة (بالشيكل)

( ) اقل من 2000 ( ) 2000-5000 ( ) اعلى من 5000

5. الحالة الاجتماعية

( ) اعزب\اعزباء ( ) متزوج\ة

( ) مطلق\ة ( ) ارمل\ة

6. مكان السكن

( ) مدينة ( ) قرية ( ) مخيم

7. التأمين الصحي

( ) يوجد ( ) لا يوجد

8. الحالة الوظيفية

( ) يعمل ( ) لا يعمل

9. هل يوجد امراض مزمنة،اذكرها اذا كانت الاجابة نعم

( ) نعم ( ) لا

10. هل يوجد تاريخ في العائلة و اقارب مصابون بهذا المرض؟

( ) نعم ( ) لا

نوع المرض و اعراضه

نوع متلازمة القولون العصبي

( ) اساسه اسهال ( ) اساسه امساك ( ) اسهال و امساك بالتناوب

العمر وقت تشخيص المرض:_____

كيف هو براز المريض؟

( ) صلبة او متكتلة ( ) مائي ( ) مزيج من النوعين

كم مرة تذهب الى الحمام من أجل البراز؟

( ) مرة الى ثلاث مرات في اليوم ( ) كثر من ثلاث مرات في اليوم

( ) أقل من ثلاث مرات في الأسبوع

هل تعاني من ألم في البطن؟

( ) نعم ( ) لا

هل تعاني من انتفاخ في البطن؟

( ) نعم ( ) لا

هل يوجد غازات عند المريض؟

( ) نعم ( ) لا

هل يوجد دم في البراز؟

( ) نعم ( ) لا

كيف كان تأثير المرض على حياتك؟

( ) يجعلك متوتر طوال الوقت ( ) يجعلك غاضبا طوال الوقت

( ) يسبب نقص في النوم ( ) يسبب الغثيان والاغماء

( ) الاستعجال لدخول الحمام ( ) الاحراج من التحرك بسبب الاغازات

اي من الاطعمة التالية تزيد من شدة الاعراض؟ (يمكن اختيار اكثر من اجابة)

( ) المقالي ( ) البهارات ( ) المشروبات الغازية

( ) القهوة ( ) البصل ( ) الملفوف

( ) الفول ( ) غيرها؟ اذكرها_____

العلاجات الدوائية وغير الدوائية لمتلازمة القولون العصبي

ماذا تفعل لعلاج هذا المرض و تقليل الاعراض؟ (يمكن اختيار اكثر من اجابة)

( ) استخدام الاعشاب التي تهدى القولون ( ) زيادة كمية الالياف في الطعام

( ) تقليل كمية الالياف في الطعام ( ) زيادة تناول السوائل في حياتك اليومية

( ) تجنب الاطعمة التي تسبب لك تهيج القولون ( ) ممارسة الرياضة

( ) الذهاب الى الطبيب لاخذ العلاج ( ) لم افعل شيء

( ) غيرها مثل_____

اذا كنت تستخدم اعشاب معينة اذكرها:_____

هل تحسنت على العلاجات الغير دوائية و تعديل نمط الحياة؟

( ) نعم ( ) لا ( ) تحسنت بشكل جزئي

6. ماذا وصف لك الطبيب من الأدوية؟

( ) Probiotics (Bioflora,Acidophilus) البكتيريا النافعة

( ) (Normalax,Relax powder,Hydralax,) الألياف الصناعية

( ) Modex

( ) Meberene,Modulon,Colotal

( ) Lopiramide(Diacare)

( ) Rifaximin(Lormyx)

( ) Hyoscine(Scobutyl)

( ) غيرها اذكرها_____

هل تحسنت على العلاجات الدوائية؟

( ) نعم ( ) لا ( ) تحسنت بشكل جزئي

هل عانيت اي اعراض جانبية من الادوية التي استخدمتها؟

( ) نعم ( ) لا

اذا كان الجواب نعم الرجاء ذكر الدواء و ما هو العرض الجانبية الذي عانيت منه

تشكر لكم وقتكم و تعاونكم

جامعة النجاح الوطنية
كلية الدراسات العليا

تقييم سلامة وفعالية العلاجات الدوائية وغير الدوائية المستخدمة من قبل مرضي متلازمة القولون العصبي

إعداد
ريم عماد صالح سرحان

إشراف
أ. د. رواء الرمحي

قدمت هذه الرسالة استكمالا لمتطلبات الحصول على درجة الماجستير في علم الأدوية،
من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس –فلسطين.

2024

تقييم سلامة وفعالية العلاجات الدوائية وغير الدوائية المستخدمة من قبل مرضي متلازمة القولون العصبي

إعداد

ريم عماد صالح سرحان

إشراف

أ. د. رواء الرمحي

الملخص

خلفية: يعاني العديد من الناس في فلسطين من متلازمة القولون العصبي. يتعامل بعض الأشخاص مع المرض باستخدام الأدوية، بينما يفضل آخرون العلاجات غير الدوائية ويتجنبون الأطعمة التي تفاقم الأعراض. الأهداف: تهدف الدراسة إلى تقييم شدة متلازمة القولون العصبي، ونمط الحياة الذي يعيش فيه المرضى، وتقييم سلامة وفعالية الوسائل الدوائية وغير الدوائية لعلاج متلازمة القولون العصبي بين المرضى الفلسطينيين. المنهجية: كانت هذه دراسة مقطعية تستخدم نموذج جمع البيانات لجمع المعلومات من المرضى من خلال مقابلة وجهًا لوجه. تم لقاء المرضى من عيادات الجهاز الهضمي الخارجية، والصيدليات المجتمعية، وصيدليات المستشفيات في بيت لحم. تم إجراء التحليل الإحصائي باستخدام حزمة البرامج الإحصائية للعلوم الاجتماعية SPSS (الإصدار 21).

النتائج: شارك في هذه الدراسة 407 مرضى يعانون من متلازمة القولون العصبي في بيت لحم والمناطق المحيطة. كان متوسط العمر 36.87±13.8 سنة. من بينهم، كانت 253 (62.2%) إناث، و263 (64.6%) متزوجين، و201 (49.4%) يعيشون في المدينة. فيما يتعلق بالخصائص السريرية والمرضية، لم يكن لدى 258 (63.4%) تاريخ عائلي لمتلازمة القولون العصبي، و201 (49.4%) كانوا يعانون من إسهال متناوب وإمساك، و229 (56.3%) كانوا يعانون من مزيج من البراز الصلب والسائل، و310 (76.2%) كانوا يعانون من آلام في البطن، و352 (86.5%) كانوا يعانون من انتفاخ في البطن، و350 (86%) كانوا يعانون من غازات في البطن، و69 (17.0%) كانوا يعانون من براز دموي. علاوة على ذلك، أثرت المرض على حياة المرضى بطرق مختلفة؛ أصبح 248 (60.9%) منهم عصبيين، و129 (31.7%) لم يتمكنوا من النوم بشكل جيد. فيما

يتعلق بالعلاجات غير الدوائية، استخدم 206 (75.2%) الأعشاب المهدئة لأعراض متلازمة القولون العصبي، وتجنب 234 (57.5%) الأطعمة التي تهيج القولون. وُجد أن استخدام الأعشاب المهدئة لأعراض متلازمة القولون العصبي، وزيادة السوائل، وتجنب الأطعمة التي تهيج القولون، وممارسة الرياضة كانت جميعها مرتبطة بشكل كبير بتحسن في أعراض متلازمة القولون العصبي؛ كانت قيم$P < 0.001$ ، 0.032، 0.001 و0.029 على التوالي. حول العلاجات الدوائية، تناول 188 (46.2%) كلورديازيبوكسيد وبروميد كلينيديوم، وتناول 143 (35.1%) بروبيوتيك لعلاج أعراض متلازمة القولون العصبي. قال 148 (36.4%) من المرضى إنهم شهدوا تحسناً كاملاً من العلاجات الدوائية. كان استخدام البروبيوتيك، والألياف الاصطناعية، (كلورديازيبوكسيد وبروميد كلينيديوم) وهايوسين مرتبطًا بشكل كبير بتحسن الأعراض.

الخاتمة: متلازمة القولون العصبي هي مشكلة مزعجة تؤثر على الحياة اليومية، حيث يحاول العديد من المرضى العلاجات غير الدوائية التي تُظهر فعالية مقبولة. وحتى مع العلاجات الدوائية، لم يتمكن العديد من المرضى من تحقيق تحسن مُرضٍ.

الكلمات المفتاحية: متلازمة القولون العصبي، الإمساك، الإسهال، غير الدوائي، الدوائي، فلسطين.