Impact evaluation of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life

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B.Sc.(Hons) NUTRITION AND DIETETICS

Impact evaluation of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life

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CERTIFICATE

This is to certifY that the dissertation entitled "Impact evaluation of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life" is the bona fide research work carried out by Ms. SHARON JACOB student of M.Sc., at The Maharaja Sayajirao University of Baroda, faculty of Family and Community Science, department of Foods and Nutrition during the year 2019-2021, in partial fulfilment of the requirements for the award of the Degree of Masters in Foods and Nutrition and that the dissertation has not formed the basis for the award previously of any degree, diploma, associate ship, fellowship or any other similar title.

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-Sharon Jacob

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ABSTRACT

Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract, also referred to as spastic, nervous, or irritable colon, and is characterized by abdominal pain and alterations in bowel habits in the absence of specific organic pathology. Though the causes of IBS have not to date been fully elucidated, it's believed that symptoms occur as a result of a combination of factors which includes visceral hypersensitivity, altered bowel motility, neurotransmitters imbalance, infection, and psychosocial factors. The treatment includes an array of self-care and lifestyle therapies like dietary modifications, physical activity, medications (antidiarrhoeal, antispasmodic, laxatives, painkillers, dietary supplements, etc) sometimes, psychotic drugs, and probiotics. Amongst these the lesser-explored treatment option is probiotic, it's an upcoming treatment with several health benefitting properties. It can be incorporated into the daily diet which could influence the functioning of gut microbiota by improving gut dysbiosis, thus aiding in better management of Irritable bowel syndrome.

Hence, the present study was designed with the major objective to determine the impact of consumption of probiotics on IBS patients in the DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life.

The population was screened and 47 subjects who reported that they have recurrent abdominal pain with onset more than 6 months ago, occurring on an average at least 1 day per week for the last 3 months (both males and females) of the age group 15-70 yrs were included from Delhi NCR. Based on the results of the preliminary assessment and willingness of the subjects to further participate in the intervention phase of the study, subjects were asked to give consent to purchase and drink the proposed probiotic for a period of 6 weeks. Anthropometric measurements, dietary intake, physical activity, depression status, the severity of symptoms, and IBS specific quality of life using global physical activity questionnaire, beck depression inventory, IBS- the quality of life questionnaire were determined before and after the intervention.

On supplementation of the IBS subjects with probiotics resulted in a decrease ($p<0.001$) in depression scores and the number of symptoms by 18.41% and 33.85% respectively. Post-intervention there was a small reduction in the number of impaired domains of quality of life but was not statistically significant.

CHAPTER-1

INTRODUCTION

Irritable bowel syndrome is a functional gastrointestinal disorder characterized by abdominal pain and altered bowel habits in the absence of specific organic pathology. It is often referred to the as spastic, nervous, or irritable colon. The general understanding developed is abdominal pain or discomfort associated with a disorder related to defecation and often associated with relief of pain with defecation. Various symptoms of IBS may include abdominal pain, distention, bloating, and indigestion. Although all causes of IBS have not to date been fully elucidated, it is believed that symptoms can occur as a result of a combination of factors, including visceral hypersensitivity, altered bowel motility, neurotransmitters imbalance, infection, and psychosocial factors. IBS can be classified into three subcategories,(1) IBS with constipation (IBS-C), (2) IBS with diarrhea (IBS-D), and (3) mixed IBS (IBS-M), which is according to the principal symptoms. (Rajesh Upadhyay, Aesha Singh, Gastroenterology chapter 56 irritable bowel syndrome: the Indian scenario).

The incidence rate of IBS is not usually calculated, and prevalence estimates fluctuate internationally, both between and within countries, and also depend on the diagnostic criteria used (Canavan, West & Card, 2014). Such disparities have been attributed to the heterogeneity of prevalence investigations:- including variations in the use of methods, instruments, diagnostic criteria, populations, and cultures assessed (Sperber *et al*, 2017).

Irritable bowel syndrome (IBS) is a common health problem affecting a substantial proportion of the population; point prevalence estimates usually range from 12-30% and the incidence of IBS at 1−2% per year. The prevalence of IBS in the general population of India is 15% (Y. Endo *et al*, 2015). As the Indian bowel pattern differs from that of the Westerners. In India, 99% of normal subjects have a stool frequency of at least 1 or more per day in contrast to a normal stool frequency of three times per week to three times per day in the West. Hence the Asian Neuro-gastroenterologist and Motility Association suggest the use of a broader definition of irritable bowel syndrome. They define irritable bowel syndrome as "a condition characterized by abdominal pain, bloating or discomfort occurring in association with disturbed bowel pattern in the absence of organic causes that can be detected by routine medical tests".

Although traditional therapies for IBS (e.g., laxatives, antidepressants, antispasmodics, and bulking agents) are useful for some patients in relieving a single IBS symptom, patients are generally dissatisfied with their overall efficacy. Many of these agents have not been proven in randomized or controlled clinical trials to be more effective than placebo in providing a relief of the multiple symptoms of IBS. For more than past 2 decades, advancements in the diagnosis and management of IBS have provided optimism about the future, including research in understanding the underlying pathophysiology of IBS (Hulisz Darrell, 2004).

Countless investigations have established there is a dissipated utilization of health care resources by patients with IBS, which has a negative impact of IBS on patient's quality of life (Agarwal & Spiegel, 2011).There is also an additional burden of IBS that falls on those who live with or care for people with the disorder; studies have reported an adverse effect on the quality of life of partners of IBS patients (Canavan, West & Card, 2014).

It is not surprising that, IBS has been shown to negatively impact patient's quality of life, and also adversely affect society's financial resources. The development of IBS symptoms have been acknowledged as multifactorial in nature, making the treatment of the syndrome a complicated, clinical endearing task. There is only a suboptimal relief by pharmacological management as the approaches are based on the reduction of the patient symptoms (Grundmann & Yoon, 2014).

It is well known that dysfunction of the immune and neuroendocrine systems, in addition to neuroplasticity, is among the pathways that underlie irritable bowel syndrome (IBS) and depression. From as early as the 1950s, the association of IBS with psychiatric disease was postulated; however, the exact mechanism remains unknown. In a meta-analysis showed depression and anxiety levels to be higher in IBS patients than in healthy controls, regardless of IBS-subtype (A .Tatenda, Mudyanadzo *et al,* 2018).

In a cohort study on Korean population for the coexistence of depression and insomnia revealed that there was a higher BDI score or the presence of insomnia and is significantly associated with irritable bowel syndrome (Seung Ku Lee et al, 2017).

Exercise can help maintain gastrointestinal function and reduce stress, which can help relief some of the IBS symptoms. Certain Studies of IBS indicates a positive relationship between physical activity

and relief of symptoms. A study by E. Johannesson *et al*, 2015 stated that an increase in physical activity for 12 weeks has been shown to improve irritable bowel syndrome (IBS) symptoms. Another follow-up study found that the patients included in an intervention to increase physical activity show improvements in IBS symptoms, as well as different aspects of the disease specific quality of life, fatigue, depression and anxiety on the long term (D. Schumann , J. Langhorst *et al*, 2018).

Yoga as an exercise regimen has been identified that helps in increasing sympathetic tone, which is decreased in IBS-D Patients. In a two-month study, intervention group practiced yoga twice daily, while the conventional treatment group received 2-6 mg loperamide daily. Results indicated that yoga as exercise regime improves the IBS symptoms equivalent to conventional treatment (I.Taneja *et al*, 2004).

Several studies have reported some efficacy of diets low FODMAPs in Irritable Bowel Syndrome (IBS) but there is no evidence of its superiority compared to gluten-free and balanced diets in improving IBS patient's quality of life (QoL).(S. S. C. Rao et al ,2015; D. Paduano et al, 2019 ; N. Pedersen et al, 2014).

Probiotics are defined as "live microorganisms that, when administered in adequate amounts confer a health benefit on the host". Probiotics are bacterial cultures or live microorganisms which when used as supplements exhibits beneficial effect on intestinal and oral microbial balance of the host (FAO/WHO 2002).The concept of probiotics was, for the first time, suggested in 1908 by Elie Metchinko, a Russian Noble Laureate who observed that consumption of fermented foods containing lactic acid bacteria had a beneficial effect on human health and based on his own theory that lactic acid could prolong life, he consumed sour milk every day, and named it yoghurt.

Since then, the effects of probiotics have been widely investigated for a broad spectrum of diseases and are currently suggested as a possible treatment or prevention in several gastrointestinal disorders (Hanna Fjeldheim Dale *et al*, 2019).

Many studies show that small intestinal bacterial overgrowth (SIBO) is prevalent in IBS, it remains unclear whether SIBO causes or is the effect of IBS (Spiegel BM. 2011). About 84% patients with IBS have been found to have small intestinal bacterial overgrowth (SIBO). Some studies suggest the

prevalence of SIBO to be 11% in India. However, tropical enteropathy with bacterial overgrowth is also common in India.

The proposed mechanism action of probiotics in IBS is undefined but is thought to include inhibition of colonization of pathogens, support of intestinal barrier integrity and function, production of beneficial micronutrients, activation and augmentation of the enteric nervous system. The benefits of probiotics however depend on strain, delivery of sufficient amount of active cells and duration of therapy (Ratna Sudha Madempudi, Jayesh J. Ahire *et al*, 2019).

A systematic review in 2019 was undertaken to assess the most recent randomized controlled trials (RCTs) evaluating the effect of probiotic supplementation on symptoms in IBS patients, indicated that identification of specific bacterial strains or probiotic supplements with beneficial effects on IBS symptoms may lead to more effective therapy strategies. The theory that probiotic supplements improve IBS symptoms through modulation of the gut microbiota or its metabolic pathways needs further mechanistic evidence (Hanna Fjeldheim Dale *et al*, 2019).

Another systematic review in 2013 and Delphi consensus outlined that specific probiotics can benefit adult patients with irritable bowel syndrome (IBS) and other gastrointestinal (GI) problems. Consensus statements with 100% agreement and "high" evidence level indicating that specific probiotics help reduce overall symptom burden and abdominal pain in few patients with IBS also reduced duration and intensity of diarrhoea in patients prescribed antibiotics or H. pylori eradication therapy, and have commendatory safety (A.P. S. Hungin *et al*, 2018).

In a study to determine whether Lactobacillus casei strain Shirota (Yakult®) can alter small intestinal bacterial overgrowth (SIBO), as tested by the lactulose breath test, and whether this can be associated with changes in symptoms in irritable bowel syndrome (IBS). It was found that Yakult is effective in altering fermentation patterns in the small bowel, consistent with reducing SIBO. The loss of an early rise in breath hydrogen with lactulose (ERBHAL) was associated with reduced symptoms (Jacqueline S Barrett *et al*, 2008).

Although various combinations of symbiotic supplements are readily available in the market, their efficacy is limited and there is an ever increasing global prevalence of IBS that can be attributed to lifestyle changes, decreased physical activity and other internal and external factors. Also IBS affect patients in terms of quality of life, work potential, mental and physical health etc.

The small intestinal bacterial overgrowth (SIBO) being a common feature of irritable bowel syndrome (IBS) is considered to be directly related to the genesis of IBS symptoms. Since, the use of antibiotics and elemental diets has been shown to be effective in treating SIBO, but studies for the efficacy in terms of dosage and duration of probiotics are limited. Thus a thorough study and implementation based on strong scientific evidences that come from research is required. Hence the present study is undertaken to determine the impact of consumption of probiotics on IBS patients in DELHI NCR population and it's effectiveness in terms of relief of symptoms and improvement in IBS quality of life.

CHAPTER 2

REVIEW OF LITERATURE

Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract, mostly characterized by abdominal pain and alterations in bowel habits in the absence of specific organic pathology (C.Canavan, J.West & T.Card, 2014). It is often referred as spastic, nervous or irritable colon. The symptoms of IBS may include abdominal pain, distention, bloating, indigestion and various symptoms of defecation. Although the causes of IBS have not to date been fully elucidated, it is believed that symptoms can occur as a result of a combination of factors, including visceral hypersensitivity, altered bowel motility, neurotransmitters imbalance, infection and psychosocial factors. There are three subcategories of IBS: - IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and mixed IBS (IBS-M), according to the principal symptoms. These are pain associated with diarrhea; pain associated with constipation; and pain and diarrhea alternating with constipation.

Risk factors include consumption of NSAID's, enteritis, other infections, dysbiosis, faulty dietary habits, gluten and lactose intolerance etc. Diagnosis is based on various lab tests like blood tests, tests for allergies/ gluten intolerance and imaging techniques like colonoscopy, sigmoidoscopy, x-ray, CT-scan etc. Treatments include an array of self care and lifestyle therapies like dietary modifications, physical activity, medications (antidiarrhoeal, antispasmodic, laxatives, painkillers, dietary supplements etc..) sometimes, psychotic drugs can also be used for relieving psychological symptoms such as anxiety and depression and probiotics. Application of probiotics as biotherapeutics is a new emerging area in developing dietary strategies which may have a concrete role in reducing the burden of Irritable Bowel Syndrome.

Bearing this in mind the present study was designed under the title, **"The impact of consumption of probiotics on IBS patients in DELHI NCR population and it's effectiveness in terms of relief of symptoms and improvement in IBS quality of life."** This chapter compiles the available literature for the study into following sections:

2.1 Global and Indian prevalence of Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is the most common disorders of gut−brain interaction, estimated to affect around 1 in 10 people globally. Prevalence rates appear to differ from country to country, but the enormity of the effect of IBS, in terms of quality of life is comparable around the world. The pathophysiology of IBS is complex and the role of risk factors such as genetics, diet and the microbiome operates differently and is thought to be dependent on geography. As developing countries are adopting a Western diet and lifestyle, we can see a corresponding increase in IBS prevalence rates, it in turn might also reflect on increasing awareness of the condition. (C.J Black *et al*, 2020).

In recent years, it was reported that approximately 10-20% of adults in western countries have IBS symptoms and an analogous prevalence has been reported in Asia. A meta-analysis of studies on the epidemiology of IBS by Lovell and Ford estimated a global prevalence of 11.2%, it was concluded that the rate has not changed in the last 30 years (R.Lovell *et al*, 2012). They also found that the odds ratio of women has only slightly increased in comparison with men and that socioeconomic status does not show any effect on prevalence, though there are some conflicting results. Global trends show that Southeast Asians have lowest prevalence of IBS (7.0%) and South Americans have the highest (21.0%) prevalence (Y.Endo *et al*, 2015). Such studies are needed in the countries that lack precise epidemiological data. It is well known that criteria used to define IBS greatly influence prevalence estimates. Even if prevalence rates remain unchanged, projections of global population growth alone indicate that there will be many more people living with IBS worldwide.

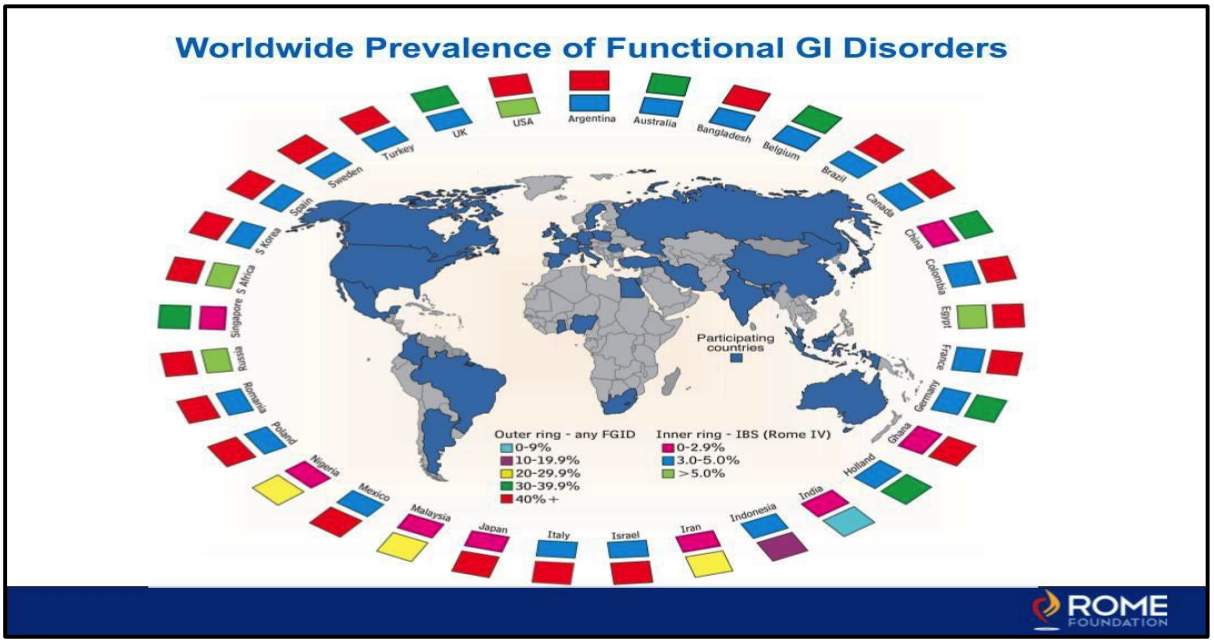

Figure: 2.1 Global prevalence of IBS (Copyright Rome Foundation, 2020www.ibspatient.org)

The bowel pattern of Indians is different from that of the Westerners. In India, 99% of normal subjects have a stool frequency of at least 1 or more per day. This is in contrast to a normal stool frequency of three times per week to three times per day in the West. The Asian Neurogastroenterologist and Motility Association suggest the use of a broader definition of irritable bowel syndrome rather than the use of Rome criteria. They define IBS as "a condition characterized by abdominal pain, bloating or discomfort occurring in association with disturbed bowel pattern in the absence of organic causes that can be detected by routine medical tests" (gastroenterology chapter 56 irritable bowel syndrome: the Indian scenario).Another notable difference reported is the increasing prevalence of IBS with advancing age, with the maximum in the 50-60 age groups, but across Asia, it has been noted that the prevalence of IBS is higher in the younger age group (A. S Chua, 2011)

The prevalence of IBS in Indian community according to studies varies from 10% to 20%. Most of the patients approach the general practitioner and only 30%–50% of the workload at gastroenterology outpatient clinics which is just a tip of an iceberg (S.N. Nagaonkar *et al,* 2018). In a clinico-epidemiological single visit study that was conducted across 20 centres in India from November 2014 to March 2015, it reported that there is a high frequency and severity of constipation-related symptoms in Indian population (R.Rooprai *et al*, 2018).A unique observation was reported by Ghosal that there is the much higher incidence of diarrhea predominant IBS (1.5%) compared to IBS constipation (0.3%) (Ghosal *et al,* 2008).

Table 2.1 Prevalence of IBS in India (M.M. Rahman *et al*, 2018)

Reference	Study site	Sample size	Study type	Criteria	Prevalence	Male to female ratio
Shah *et al*	Urban Mumbai	2549	Community	Manning	7.5%	1/0.87
Ghosal *et al*	Multiple site	4500	Community	Clinical	4.2%	1/0.93
Makharia *et al*	Haryana	4767	Community	Rome III	4%	1/1.5
Ghosal *et al*	Uttar Pradesh	2867	Community	Rome III	6.8%	1/1.09

A 2013 study the prevalence of depression and anxiety was evaluated to be 37.1% and 31.4% respectively. In same study patients with IBS the Odds ratio for depression was 6.3 (95% CI 1.6-24.74, P=0.009) and the Odds ratio for anxiety disorder was 7.56 (95% CI 1.53-37.29, P=0.01) despite strong evidence of high prevalence of depression and anxiety in IBS there is very limited research on this in India (N. Kabira et al, 2013). Well-designed and adequately funded research, which is multi-cultural and encourages global collaboration, is needed to further advance our understanding of IBS and promote optimized patient care.

2.2 Types of IBS

According to WHO DMS-IV code classification for IBS and its subcategories, IBS can be classified as either diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), or with alternating stool pattern (IBS-A) or pain-predominant. In some individuals, IBS may have an acute onset and develop after an infectious illness characterized by two or more of the following: fever, vomiting, diarrhea, or positive stool culture. This post-infective syndrome has consequently been termed "post-infectious IBS" (IBS-PI) (K.B. Holten *et al*, 2003).

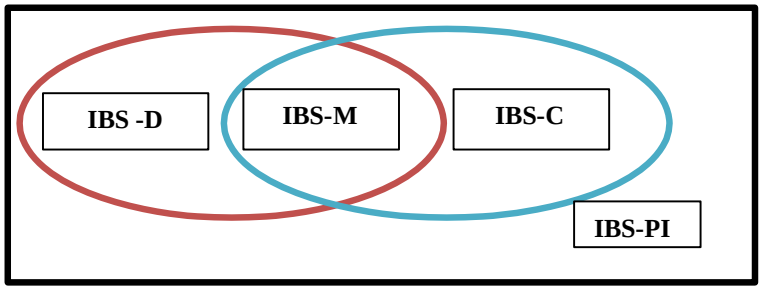

Figure: 2.2 Types of IBS

2.3 Pathophysiology of IBS

IBS is considered to be disorder of dysregulation of brain-gut axis, involving abnormal function in the enteric, autonomic and/or central nervous system (CNS). Conventionally, IBS has been conceptualized as a condition of gastrointestinal motor disturbances (leading to diarrhea or constipation) and visceral hypersensitivity (leading to abdominal discomfort or pain).

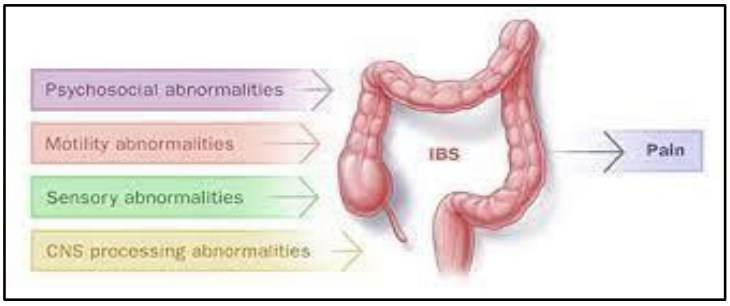

Figure: 2.3 Biopsychosocial model of IBS.(Irritable Bowel Syndrome: Introduction, 2013)

2.3.1 Infection and Immune Activation: Increasing evidence showing the role of immune activation in the etiology of IBS, which has mainly been shown in studies investigating mechanisms of IBS-PI (Post Infectious). Approximately 1 in ten patients with IBS believe their IBS began with an infectious illness. Studies have shown that 3%-36% of enteric infections lead to persistent new IBS symptoms (J.Matricon, M. Meleine, *et al*. 2012).

Exposure to intestinal infection induces persistent low-grade systemic and mucosal inflammation, which is characterized by an altered population of circulating cells, mucosal infiltration of immune cells and increased production of various cytokines in IBS patients. Some studies indicate an increased innate immune response in patients by evaluating expression and activation of Toll-like receptors (L.Belmonte, *et al*.2012). These findings suggest that immune activation may plays a crucial role in the pathogenesis of IBS. Additional, psychological stress has been reported to be one of the factors that induce immune activation. However, it remains unknown whether immune activation in IBS patients is largely dependent on infectious gastroenteritis and/or psychological stress.

2.3.2 Serotonin Dysregulation: A fundamental feature of IBS is change in bowel pattern which is due to abnormality of gut motility. Sympathetic and parasympathetic nerves control the function of enteric nervous system via a variety of mediators and receptors such as serotonin, especially activation of 5-HT3 and 5-HT4 receptors enhances gut motility while inhibition of 5-HT3 delays transit time. It is observed that plasma 5-HT concentrations are reduced in IBS patients with constipation, but raised in those with diarrhea (L.Saha, 2014).

2.3.3 Small Intestine Bacterial Overgrowth: The dysbiosis of microflora in IBS has been recognized by the Rome Foundation Working Team as a plausible contributing factor to this condition (M.Simren et al, 2013). Many studies show that small intestinal bacterial overgrowth (SIBO) is prevalent in IBS, it remains unclear whether SIBO causes or is the effect of IBS (B.M Spiegel, 2011). About 84% patients with IBS have been found to have small intestinal bacterial overgrowth (SIBO). Some studies suggest the prevalence of SIBO to be 11% in India. However, tropical enteropathy with bacterial overgrowth is also common in India.

2.3.4 Central Dysregulation and Brain-Gut Interaction: Psychosocial factors appear to be important in irritable bowel syndrome, although whether these factors directly alter gastrointestinal functioning remains uncertain. Anxiety and depression are common in IBS patients. Signals from the gut, are involved in regulating reflexes. Events in the gut involve activation of afferent pathways, with information being modulated at different levels, both at peripheral and central. Advances in understanding of brain gut interaction and its alteration in IBS happened with the introduction of functional magnetic resonance imaging (L. Saha, 2014).In an independent study of psychiatric disorders and IBS, the use of structured interviews delineated that 40% of patients had a mood disorder and 23% of patients had anxiety developed after the onset of IBS (Holtmann *et al*, 2016).

2.3.5 Genetics: There is some evidence to suggest a genetic factor in causation of IBS. One of study found that 33% of patients with IBS had a positive family history. Some studies have reported that IBS aggregates in families, and studies of IBS in twins have shown higher concurrence in monozygotic twins than in dizygotic twins, suggesting that genetic factors might play a role in IBS (Holtmann, J.Gerald *et al*, 2016).

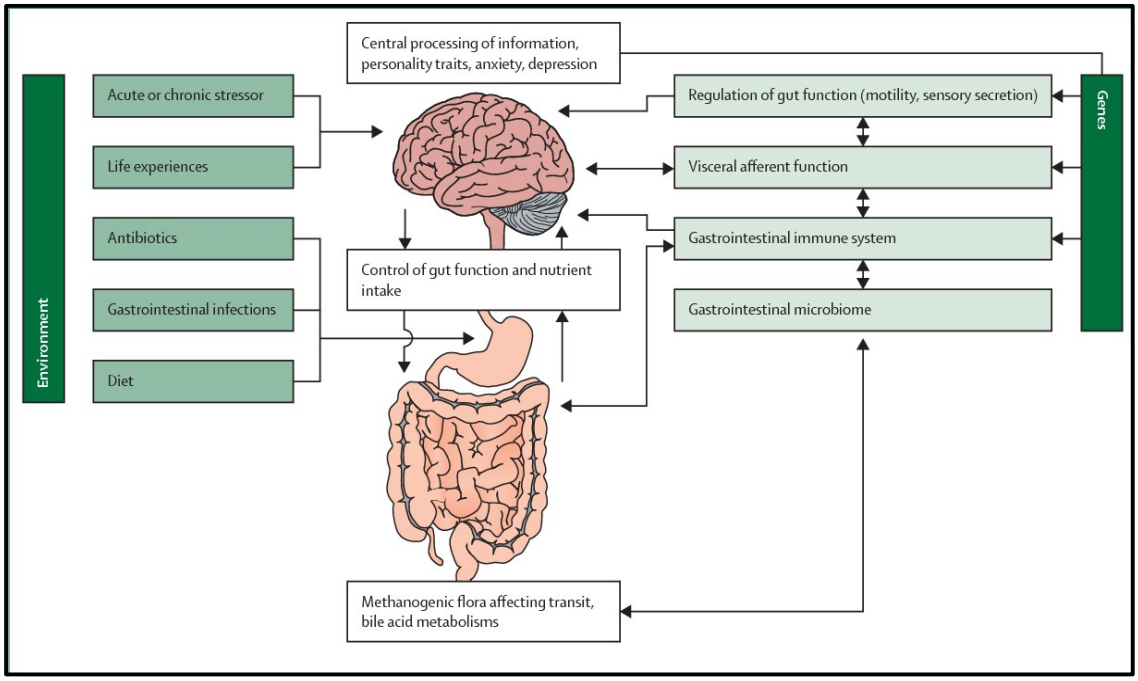

Figure: 2.4 Aetiology of Irritable Bowel Syndrome (The Lancet Gastroenterology & Hepatology, Volume 1, Issue 2)

2.4 Symptoms

The cardinal symptom of IBS is abdominal pain or discomfort associated with either a change in bowel habits or disordered defecation. The pain or discomfort associated with IBS is often poorly localized and at times is migratory or variable. It can occur after meals, during stress or at the time of menses (Weaver *et al*, 2017).

In addition to pain and discomfort, altered bowel habits are common, including diarrhoea, constipation, and diarrhoea alternating with constipation. Patients also complain of bloating, abdominal distension, mucous in the stool, urgency, and a feeling of incomplete evacuation. Some describe frequent episodes, whereas other patients describe long symptom-free periods. Patients with irritable bowel frequently report symptoms of other functional gastrointestinal disorders also, including chest pain, heartburn, nausea or dyspepsia, difficulty swallowing.

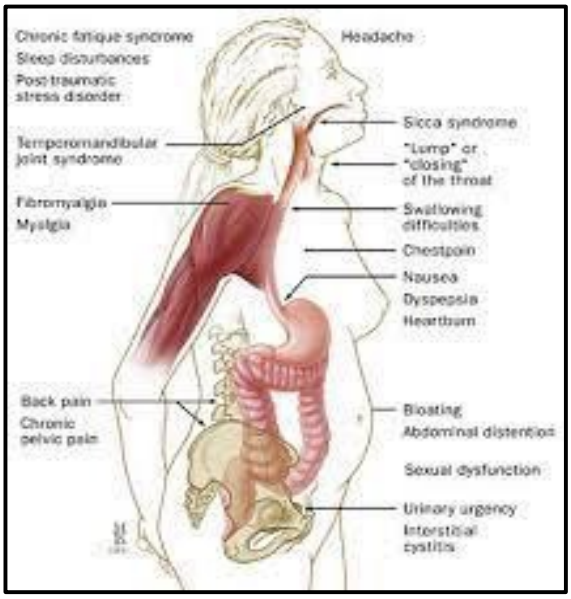

Figure: 2.5 Symptoms of IBS

2.5 Diagnosis of IBS

IBS is the gastrointestinal disorder that is most commonly diagnosed; the diagnosis is made from the presence of certain symptoms in the absence of organic disease (Chey, Kurlander & Eswaran, 2015). Definitive diagnosis of irritable bowel syndrome has proven to be difficult because of number of factors. Traditionally in the absence of definitive biological markers or diagnostic physical findings, the diagnosis of IBS rests on physician's recognition of classic clinical symptoms and the exclusion of other diseases. The presence of abdominal pain or discomfort is essential to the diagnosis of IBS. Effective diagnosis of IBS commence with a

careful history collection and physical examination. The presence of alarm symptoms or red flags suggests more extensive evaluation for organic causes (H .Vahedi *et al*, 2010).

The initial evaluation should include: a complete blood count, chemistry panel, and erythrocyte sedimentation rate, and a stool test for faecal occult blood (P.Enck *et al*, 2016). A colonoscopy should be performed in patients 50 years of age or older and may detect organic disease in 1-2% of patients. The prevalence of lactose intolerance in patients with IBS is about 25%, which is not significantly higher than that in the general population. Further evaluation depends on the predominant clinical symptom—pain, constipation or diarrhoea. Lactose malabsorption, celiac disease and other malabsorptive disorders should be considered in suspected IBS patients (B.E.Lacy, 2003).

Diagnostic criterion has evolved since 1979 when Manning *et al* first published their criteria. The changes have included the Rome I, II, III and now to the most recent Rome IV criteria to allow for ease of diagnosis.

Table: 2.2 Diagnostic criteria for Irritable bowel syndrome

Diagnostic criteria	**Symptoms, signs, and laboratory investigations included in criteria**
Manning (1978)	IBS was defined as the symptoms given below with no duration of symptoms described. The number of symptoms that need to be present to diagnose IBS is not reported in the paper, but a threshold of three positive is the most commonly used: 1. Abdominal pain relieved by defecation 2. More frequent stools with onset of pain 3. Looser stools with onset of pain 4. Mucus per rectum 5. Feeling of incomplete emptying 6. Patient-reported visible abdominal distension
Kruis (1984)	IBS is defined by a logistic regression model that describes the probability of IBS. Symptoms need to be present for more than two years. Symptoms: 1. Abdominal pain, flatulence, or bowel irregularity 2. Description of character and severity of abdominal pain 3. Alternating constipation and diarrhea 4. Signs that exclude IBS (each determined by the physician): 5. Abnormal physical findings and/or

	history pathognomonic for any diagnosis other than IBS 6. Erythrocyte sedimentation rate > 20 mm/2 h 7. Leukocytosis> 10000/cc 8. Anemia (Hemoglobin< 12 for women or < 14 for men) 9. Impression by the physician that the patient has rectal bleeding
Rome Ⅰ(1990)	Abdominal pain or discomfort relieved with defecation, or associated with a change in stool frequency or consistency, PLUS two or more of the following on at least 25% of occasions or days for 3 months: 1. Altered stool frequency 2. Altered stool form 3. Altered stool passage 4. Passage of mucus 5. Bloating or distension
Rome Ⅱ(1999)	Abdominal discomfort or pain that has two of three features for 12 week (need not be consecutive) in the last one year: 1. Relieved with defecation 2. Onset associated with a change in frequency of stool 3. Onset associated with a change in form of stool
Rome Ⅲ(2006)	Recurrent abdominal pain or discomfort three days per month in the last 3 months associated with two or more of: 1. Improvement with defecation 2. Onset associated with a change in frequency of stool 3. Onset associated with a change in form of stool
Rome IV(2016)	Recurrent abdominal pain with onset more than 6 months ago, occurring on an average at least 1 day per week for last 3 months associated with one or more of the following criteria:- 1. Related to defecation 2. Associated with change in frequency of stool 3. Associated with the change in the form (appearance) of the stool.

2.6 Treatment and Management of IBS

The heterogeneity of IBS complicates the development of a single method to all patients, even within individual IBS subtypes. Management of Irritable Bowel Syndrome is based on a positive diagnosis of the syndrome, with exclusion of organic disorders, and specific therapies. Treatment for IBS should address the main pathophysiological factors—psychosocial disturbances, visceral hypersensitivity, and dysmotility. IBS management enwraps an integrated approach that includes establishment of an effective patient-caregiver relationship, education and reassurance, nutritional interventions, drug therapy and psychological therapy (A.I Ferreira *et al,* 2020).
Treatment should be patient oriented and geared towards relief of symptoms. The majority of conventional IBS treatments currently used is experimental and has not been formally reviewed and approved. Therapies may include fibre consumption for constipation, anti-diarrheal, smooth muscle relaxants and psychotropic agents for pain, diarrhoea and depression.

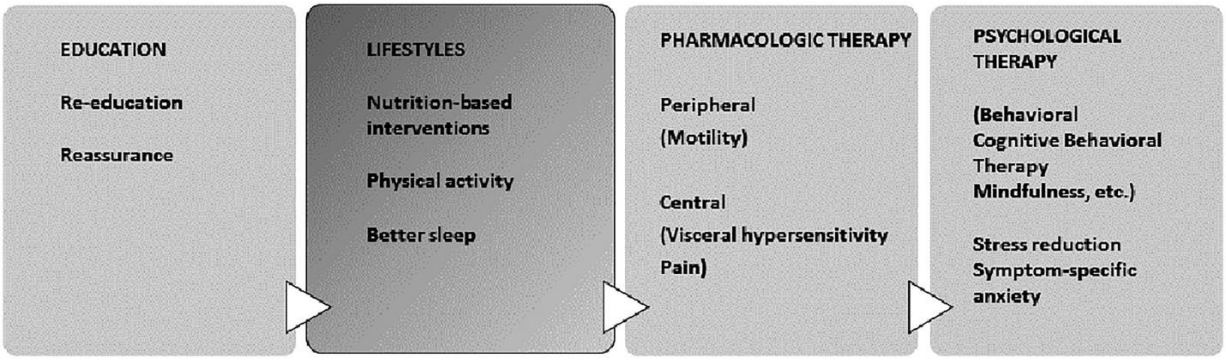

Figure: 2.6 General therapeutic approaches in irritable bowel syndrome (IBS) patients(*Gastroenterol Rep (Oxf)*, Volume 5, Issue 1, February 2017, Pages 11–19, https://doi.org/10.1093/gastro/gow047)

2.6.1 Dietary Management: Although the data from various clinical trials may in some cases not provide strong evidence for benefits of dietary modification, it remains the primary non-pharmacological clinical intervention for IBS patients; exclusion diets are successfully used by many clinication (I.Posserud *et al*, 2013). Food intolerances or allergies are considered to the exacerbation of IBS symptoms.

For around 60–70% of patients certain foods aggravate the symptoms. The response rate of various exclusion diets varies from 12.5% to 67%. Data show benefit of soluble fibres in relief of symptoms and some benefit for treatment of constipation. Insoluble fibres are not beneficial and may even worsen IBS. Lactose and fructose intolerance should be considered in IBS-D and excluded from the diet as and when required (Gastroenterology chapter 56 irritable bowel syndrome: the Indian scenario,Rajesh Upadhyay, Aesha Singh).

A diet low in fermentable oligosaccharides, disaccharides, monosaccharide and polyol (FODMAPs) which are slowly absorbed or indigestible short-chain carbohydrates is considered as one of the major option for the treatment of IBS, with a symptomatic improvement in about 70% of the patients (S. Khan *et al*, 2010).

Effect of Low FODMAP and other diets

Diet low in fermentable oligosaccharides,disaccharides, monosaccharides, and polyols (FODMAPs) are often used to manage functional gastrointestinal symptoms in patients with irritable bowel syndrome (IBS), yet there is limited evidence of its efficacy in comparison with a normal diet (P.R.Gibson *et al, 2010*).Although all of these sugars individually have shown to contribute to IBS symptoms the concept of limiting their usage as a treatment for IBS is relatively new (P.R.Gibson *et al,* 2005).

In a systematic review to evaluate dietary fibre and FODMAP- restricted diet in the management irritable bowel syndrome. From the 550 potentially eligible clinical trials on fiber and FODMAP restricted diet it was concluded that fibre rich diet and supplementation is beneficial in mild to moderate constipation predominant IBS, although more rigorous and long-term clinical trials are required and the FODMAP-restricted diet may be effective for short term management of selective patients with IBS (S.S.C.Rao *et al,* 2015).

In another study by Suma Magge, and Anthony Lembo, it stated that although there are few effective medical therapies currently available but recently there is an increasing interest in diet therapies for IBS, particularly a diet low in fermentable oligosaccharides, disaccharides, monosaccharides,and polyols (FODMAPs).Despite limited data available low-FODMAP diet implementation should be considered in patients with IBS, especially those subjects in whom food is a trigger for symptoms (S.Magge *et al,* 2012).

A clinical study delineated that there is outpouring of data supporting use of low FODMAP diet in IBS patients. In comparison to most dietary manipulations tried in the past to alleviate symptoms of IBS, most studies on low FODMAP diet have frequently shown symptomatic benefits in the majority of patients. However, adherence to diet by the patients and clear dietary intervention by dietitians appear to be vital (W.S.Nanayakkara *et al,* 2016).

In a study to investigate the long-term effect of dietary education on a low fermentable oligosaccharide, disaccharide and polyol (FODMAP) diet on irritable bowel syndrome and selectively reintroduction of FODMAP foods in diet reported that a low FODMAP diet education was able to reduce severity of the symptom and improve quality of life in IBS patients, which was sustained for around a six months. But the reintroduction of FODMAP foods this improvement is hardly maintained (R.M. Harvie *et al*, 2017).

Natalia Pedersen *et al* in a study on Danish population reported that both low FODMAP and Lactobacillus rhamnosus GG are effective when treating IBS patients, chiefly in the IBS-D and IBS-A subtypes (N. Pedersen *et al,* 2014).

So far several studies have reported some form of efficacy of diets low in Fermentable Oligo-, Di-, Monosaccharides and Polyols (FODMAPs) in Irritable Bowel Syndrome (IBS). However there is no evidence of its supremacy in comparison to gluten-free and balanced diets in improving IBS patient's quality of life. In a study Forty-two patients with IBS, according to Rome IV criteria, were enrolled. Low-FODMAP, gluten-free and balanced diets were proposed to be followed for 4weeks each. Analyses were done using the Bristol Stool Scale, the Visual Analogue Scale (VAS) for bloating and abdominal pain, and the SF12 questionnaire for health-related quality of life. All the three diets significantly reduced symptom severity and improved quality of life. However only 3% of patients expressed a preference for the low-FODMAP diet, while 11% preferred gluten-free and majority of them opted (86%) for balanced diet (D. Paduano *et al,* 2019).

2.6.2 Physical Activity: Exercise can help maintain gastrointestinal function and reduce stress, which can help relieve some IBS symptoms. Certain Studies of IBS indicates a positive relationship between physical activity and relief of symptoms.

Yoga has been identified as an exercise regimen that increases sympathetic tone, which is decreased in IBS-D Patients (I.Taneja et al. 2004). In a two-month study, a yoga intervention group practiced twice daily, while the conventional treatment group received 2-6 mg loperamide daily. Results indicated that yoga demonstrated improvement of IBS symptoms equivalent to conventional treatment (L.Saha, 2014).

Effect of Physical activity on IBS

Various studies involving healthy adults indicate that exercise helps in improving the symptoms of fatigue, bloating and constipation (SN. Sullian *et al,* 1994). Hence, it seemed appealing to promote regular exercise in the management of IBS. While many of IBS management programmes have often suggested that exercise might have positive impact on health promoting activity, but there is limited to no randomized controlled trials (RCT) that have evaluated the effects of an exercise intervention in patients experiencing IBS.

According to E. Johannesson *et al,* a quantitative analysis conducted on 15 subjects aged 31-78 years 10 women and 5 men, it showed that it is equally important to take into consideration the patients experiences of the effect of physical activity when we are to recommend them being physically active. Thus implying that the treatment method should be individual centered (E. Johannesson *et al,* 2018).

In another study by E. Johannesson *et al,* 2011 the primary aim of the study was to assess the change in IBS Severity Scoring System (IBS-SSS).and it was reported that there was a significant difference in improvement in IBS-SSS between physical activity group and control group. The proportion of subjects in the control group with increased symptom score during the study was significantly larger than the physical activity group. Thus, suggesting that physical activity should be used as a primary treatment module in treating IBS patients (E. Johannesson *et al,* 2011).

In an intervention study to increase the physical activity to show a long term positive effect on IBS patients, a total of seventy six patients from a previous randomized clinical trial were requested to participate in a long term study to assess their IBS- SSS before and after a exercise intervention. It revealed that that a moderate increase of physical activity could be included in the initial management of patients with IBS. In the present work it showed 54% of the subjects had a clinically significant improvement of the IBS symptoms comparing to the previous study after a 12 wk intervention that have 43% of improvement in symptoms (E. Johannesson *et al,* 2015).

A study on Iranian adults to find the relation between physical activity and IBS a cross sectional study design was imployed and it was reported that in comparison to physically active subjects (>1 hr/week) those with sedentary physical activity (<1hr/wk) had 1.27 times

higher probability of suffering from IBS. When the analysis was additionally adjusting the diet-related practices and body mass index (BMI), it showed a non-significant association between sedentary physical activity and IBS. It was concluded that a significant positive association between sedentary physical activity and IBS, particularly among women and individuals of normal weight (M .Sadeghian *et al*, 2018).

Jin choi *et al* studied the relationship between IBS and physical activity in women nurses the study was conducted on 706 nurses working at university affiliated tertiary hospitals various parameters studies like depression, anxiety and health behavior. It was concluded that in Korean working women IBS was not associated with Physical activity level but the higher levels of anxiety and stress and dysmenorrhea were independently associated with increased risk of IBS among them (Jin choi *et al*, 2010).

In a randomized controlled trail to assess the effect of exercise upon symptoms and IBS quality of life it was reported that there was no change observed in IBS specific quality of life after 12 weeks of exercise intervention but had an impact on symptoms and it had significantly improved. This study has demonstrated a low cost exercise consultation can be delivered to IBS patients within a hospital setting (A. J. Daley *et al,* 2008).

For another randomized clinical trial by D. Schumann *et al*, 2011 to assess the effect of yoga based intervention versus low FODMAP diet on patients with IBS for this a total of 59 patients were asked to enroll into a 12 weeks single blinded randomized trial involving yoga or low FODMAP diet. Outcomes of the study stated that there was no significant difference between the intervention groups in respect to IBS-SSS score at the end of either 12weeks or 24 weeks but within the group it showed a statistically significant effect for both Yoga and low FODMAP at 12 and 24 weeks (D. Schumann *et al*, 2018).

2.6.3 Probiotics: Probiotic bacteria have become popular in past two decades as a result of the continuously expanding scientific evidence pointing to their beneficial effects on human health. As a result they have been applied as various products with the food industry having been very active in studying and promoting them. They have been incorporated in various products, mainly fermented dairy foods (M.Kechagia *et al*, 2013).

The term probiotic was formulated from the Greek language meaning "for life" but now the definition of probiotics has evolved over time with the increasing interest in the use of viable

bacterial supplements and in relation to the progress made in understanding their mechanisms of action. It was originally used to describe substances produced by one microorganism that stimulated the growth of others and was later used to describe tissue extracts that stimulated microbial growth and animal feed supplements exerting a beneficial effect on animals by contributing to their intestinal flora balance (Fuller R, 1999).

Nutrition is only concerned the strains classified as lactic acid bacteria are of significance and from them the ones considered most important are those belonging to the genera Lactococcus and Bifidobacterium (W.H. Holzapfel *et al*, 2001). Lactic acid bacteria are Gram-positive, catalase-negative bacterial species that are capable to produce lactic acid the main end-product of carbohydrate fermentation.

The genus Bifidobacterium is rather traditionally than phylogenetically listed, as they use a separate metabolic pathway. Two other species that play an important role in the food industry in particular the dairy products, although not always considered as probiotics are Streptococcus thermophilus and Lactococcus lactis, two of the most commercially important lactic acid bacteria (G.E Felis *et al*, 2007).

Mechanism of action Probiotics:- The exact mechanisms of action by which probiotics accomplish their beneficial actions have not been well documented. However, there are several postulated mechanisms that explain some of their favorable effects. These mechanisms include:-

(1) Competition for dietary ingredients as growth substrates,

(2) Bioconversion of, for example, sugars into fermentation products with inhibitory properties,

(3) Production of growth substrates, for example, eps or vitamins, for other bacteria,

(4) Direct antagonism by bacteriocins,

(5) Competitive exclusion for binding sites,

(6) Improved barrier function,

(7) Reduction of inflammation, thus altering intestinal properties for colonization and persistence within, and

(8) Stimulation of innate immune response (by unknown mechanisms)(p.w. o'toole *et al,* 2008).

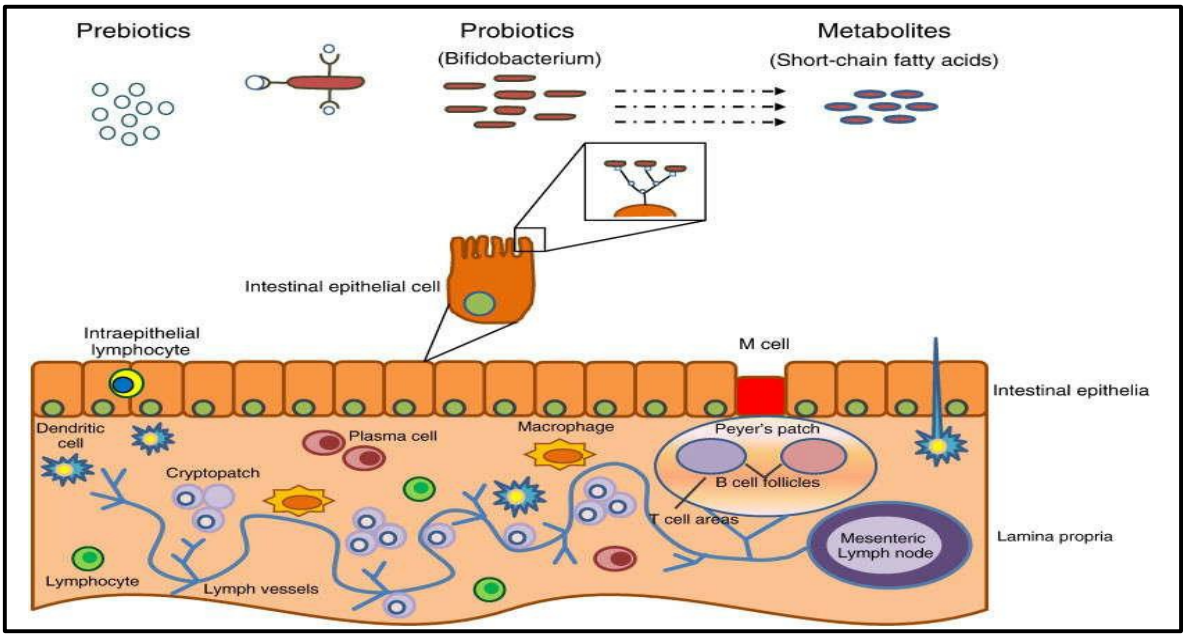

Figure: 2.7 Mechanism of action of probiotics (A.Abdulhussein *et al,* 2018)

Effect of probiotics on IBS

Patients with IBS have found to have altered microflora but not proved to have any role in pathogenesis. A recent systematic review of 2013 summarized data of probiotics in IBS and Delphi consensus reported that specific probiotics can benefit adult patients with irritable bowel syndrome (IBS) and other gastrointestinal (GI) problems. Consensus statements with 100% agreement and evidence level indicated that specific probiotics help reduce overall symptom burden and abdominal pain in some patients with IBS and duration/intensity of diarrhea in patients prescribed antibiotics or H. pylori eradication therapy, and have favorable safety.

Although there are some disparities in different studies, but there are enough evidence to suggest their efficacy in reducing IBS symptoms, such as bloating, abdominal pain and flatulence (T.Didari *et al*, 2015). Among all the strains of bacterias used as probiotics

Lactobacillus strain *Lactobacillus plantarum* had the most evidence of being beneficial for IBS (A.C. Ford *et al,* 2014).

In recent years the use of probiotics for the management of dysbiosis of the microbiota in IBS is gaining lot of interest (A. P. Hungin, *et al,* 2018). It is well known that the benefits of probiotics rely on strain, delivery of sufficient amount of active cells and duration of therapy (Y. Zhang *et al,* 2016).

In a randomized clinical trial was undertaken to evaluate the therapeutic efficacy of probiotic *Bacillus coagulans* Unique IS2 versus placebo on the management of irritable bowel syndrome symptoms in adults. B. coagulans Unique IS2 showed significant improvement in reducing abdominal discomfort/pain intensity and increased complete spontaneous bowel movements secondary endpoints of the study like serum cytokines also improved in comparison to placebo. B. coagulans was well tolerated with no severe adverse events. Hence, it was reported that B. coagulans Unique IS2 is potent in the management of IBS symptoms in 18−60 years (R.S. Madempudi *et al,* 2019).

The modification or alteration of gut microbiota in IBS patients by supplementing probiotics may be an alternative strategy to ameliorate or prevent depression to assess this Muhammed Majeed *et al*, did a study using Bacillus coagulans MTCC 5856 strain results showed that B. coagulans MTCC 5856 has a higher efficacy for the treatment of IBS patients having with major depressive disorder. The improvements shown by IBS patients were statistically significant and clinically meaningful for depression and IBS symptoms (M. Majeed *et al,* 2018).

In a study by Jacqueline S Barrett *et al,* for the effects of probiotic on intestinal fermentation patterns in patients with irritable bowel syndrome they used *Lactobacillus casei* strain Shirota (Yakult®) to assess it by the lactulose breath test. From the fourteen patients who completed the study, 9 (64%) had successfully reversal of early rise in breath hydrogen with lactulose (ERBHAL). Thus safely establishing that Yakult was efficacious in altering fermentation patterns and consistent in reducing small intestine bacterial overgrowth. The loss of ERBHAL was also associated with reduced symptoms (J.S.Barrett *et al,* 2008).

In a multi-strain probiotic versus placebo study that used Biokult contain 14 different strains. It was inferred that there was a significant improvement in symptoms in patients with diarrhea dominant IBS and is safe and superior to placebo in improving IBS symptoms in a duration of 4 months in patients with Diarrhea predominant IBS. Moreover, improvement in symptoms was assimilated by statistically significant benefits in all 8 measures of quality of life (S.M.Ishaque *et al*, 2018).

In a clinical study to assess the therapeutic effect of multistrain probiotic on diarrhea predominant irritable bowel syndrome using Rome III criteria. After probiotic intervention of 8 weeks the changes in gastrointestinal symptoms, fecal microbiome, and small intestine bacterial overgrowth was determined. Results indicated that there was an increase in beneficial bacteria and a decrease in harmful bacteria in the stool analysis. The SIBO prevalence was also decreased by the end of treatment (S.H.Lee *et al,* 2018).

A technical review article 2020, by the American Gastroenterological Association (AGA) for IBS they concluded that overall evidence across all critical outcomes for probiotics for the treatment of children and adults was Low (G.A.Preidis *et al*, 2020).

In a systematic review to assess the randomized controlled trials (RCTs) of past five years evaluated the effect of probiotic supplementation on symptoms in IBS patients. Of total 35 studies, only 11 fulfilled the inclusion criteria and were included in the review. Seven studies reported that supplementation with probiotics in IBS patients significantly improved symptoms in comparison to placebo, whereas the remaining four studies (36.4%) did not report any significant improvement in symptoms after probiotic supplementation.

Mainly the beneficial effects were more prominent when multi-strain supplements were used with an intervention of 8 weeks or more, indicating that multi-strain probiotics supplements over a longer duration of time have the potential to improve IBS symptoms (H.F. Dale *et al,* 2019).

In a cohort study evaluating the efficacy of homemade yogurt for the treatment of irritable bowel syndrome, the study confirmed that administering lactic acid bacteria (LAB) with

same characteristics over a long duration of time ranging from 180-400days had a replenishing effect the microbiota of the gut leading to remission IBS to a certain extent. Furthermore, homemade yogurt can be used as a probiotics to provide an easy, cost efficient and established medium with nutritional benefits for patients suffering from IBS (N.Ramachandran *et al,* 2020).

In 2013, a systematic review and Delphi consensus reported that specific probiotics can benefit adult patients with irritable bowel syndrome (IBS) and other gastrointestinal (GI) problems to evaluate the same another systematic review was undertaken they identified 70 studies published between January 2012 and June 2017. Thirty four IBS studies assessed 15 studies examined IBS symptoms as a primary outcome parameter, 8 reported significant effect of probiotics versus placebo. High level of evidence indicated that specific probiotics might help reduce overall symptom burden and abdominal pain in IBS patients (P. S. Hungin *et al,* 2018).

In another systematic review stated that IBS can be prime example of the limited clinical data; though many studies have been published only few of them have actually achieved standards appropriate for clinical trials in humans. Moreover taking into consideration the variability in number, characteristics and properties of microorganisms that have been studied, it might be disproportionate to combine the results of various trials (J.Prado*et al,* 2015).

A randomized trail assessing the efficacy of supplementation with two multispecies probiotic formulations on subjects diagnosed with IBS-C. They used faecal microbiological analyses by species-specific qPCR to assess the different amount of probiotics. It was reported that clinical improvement might be associated with the maintenance stability of the gut microbiota from probiotics consumption (V.Mezzasalma *et al,* 2016).

2.6.4 Pharmaceutical: The pharmacologic treatment remains mainly symptom directed and in patients with mixed type of IBS combination of treatments may be needed (B.E.Lacy *et al*, 2015). The American Gastroenterological Association (AGA) gave guidelines on the management of IBS pharmacological. These guidelines range in the level of

recommendation from weak to strong, and are based on the level of the evidence being very low, low, moderate, and high (D.S Weinberg *et al*, 2014).Various methods used for management of symptoms in IBS include anticholinergics, antidiarrheals, tricyclic anti-depressants (TCAs), prokinetics, bulk-forming laxatives, serotonin receptor antagonists, chloride channel activators and guanylate cyclase C (GC-C) agonists.

2.6.4.1 Antispasmodics: antispasmodic are known to provide relief of abdominal pain and discomfort but systematic reviews and data on long-term efficacy does not exist. Commonly used antispasmodics are nonselective anticholinergics. In double blinded study in 3 hospitals in China reported that pinaverium has a better effect on improving IBS abdominal pain and stool frequency and can be considered a first-line treatment for IBS (L. Zheng *et al*, 2015). In a systematic review it was found that several antispasmodics, including peppermint oil, pinaverium, trimebutine and cimetropium/dicyclomine, have a significant effect and are better than placebo for improving IBS symptoms.

2.6.4.2 Antidiarrheals: Loperamide is μ-opioid receptor agonist that acts on myenteric plexus of the large intestine and is known to increases the stool transit time, colonic movement and suppresses the gastrocolic reflex. Clinical trials have shown reduction in the stool frequency and improved consistency in patient with diarrhea dominant IBS (B.Lavo *et al,* 1987) (P.S Efskind *et al*, 1996).

2.6.4.3 Laxatives: In a study, patients with constipation simple laxatives were found to be more suitable therapeutic option due to their relative safety, low cost and availability but more research are needed, no trials have evaluated their roles (KA Jadallah *et al,* 2014).

2.6.4.4 Antibiotics: Use of antibiotics for the treatment of IBS has been extensively evaluated. Commonly used antibiotics are rifaximin, neomycin and clarithromycin. The studies show that there is a statistically significant improvement in symptoms and bloating as compared to placebo. In a 2012 meta-analysis of 5 studies which incorporating about 1,803 patients determined that antibiotics (rifaximin) is more effective that placebo for relief in symptom and bloating.

2.6.4.5 5-HT3 Receptor Antagonist: 5-HT3 receptor antagonists have shown to be effective in patients with IBS-D in both slowing colonic transit through the inhibition of peristaltic reflex

(P. Clave, 2011) and modulating visceral nociception (C. Stasi *et al*, 2014). Alosetron has been approved by Food and Drug Administration (FDA) for female patients with severe, chronic IBS-D who failed conventional therapy.

2.6.4.6 5-HT4 Receptor Agonist: Tegaserod is a relatively specific 5-HT4 partial agonist but may also facilitate enteric cholinergic transmission. In a short study tegaserod accelerates orocaecal transit in female patients with constipation predominant IBS without altering gastric emptying (CM. Prather *et al,* 2000). It was found to be more effective than placebo for treating global IBS symptoms, abdominal discomforts, satisfaction with bowel habits and bloating. This drug has now been withdrawn from many countries because of rise in heart attack and stroke.

2.6.4.7 C2 Chloride Channel Activators: Lubiprostone is the only used selective C2 chloride channel activator; it is incompletely absorbed and works nominally in intestinal tract. Studies have shown that it helps to improve global symptoms in IBS-C and abdominal pain/discomfort, stool consistency, straining and constipation severity (L.I. Brandt *et al,* 2009).

2.6.4.8 Antidepressants: Antidepressants and antipsychotic drugs are used as treatment option for IBS. Several of the studies have illustrated that some of these medications, like duloxetine, have shown a positive effect on patients with generalized anxiety disorder (GAD) along with IBS (A kalpan *et al,* 2014). Also some studies have reported that tianeptine and amitriptyline have a positive impact on irritable bowel syndrome with diarrhea (IBS-D) (W. Sohn *et al,* 2012). Both TCA and selective serotonin reuptake inhibitor (SSRI) have been extensively studied with numerous trials, but with inconclusive results.

2.6.5 Other Therapies

2.6.5.1Herbal Therapies and Acupuncture: In a randomizied controlled study by MacPherson it stated that acupuncture with usual care can be used in controlling IBS symptoms and also illustrated that acupuncture has better results and should be a treatment option for IBS (H. MacPherson *et al,* 2012). Research is needed before these therapies can be recommended.

2.6.5.2Psychological: Hypnotherapy, cognitive behavior therapy, interpersonal psychotherapy and relaxation therapies have been tried but there is limited data to support or invalidate its efficacy. In a study it showed that patients who do not respond to pharmacological therapy after 12 months should be referred to cognitive behavioural therapy or other psychological therapies (P. Enck *et al,* 2016). Gut directed hypnotherapy seems to be a durable in reducing IBS symptoms (C.Xie *et al,* 2015).

2.7 Impact of age and gender on IBS

There is a significant gender discrepancy that has been observed in individuals with irritable bowel syndrome; studies have revealed that IBS is more common in women than men. As for its subtype, IBS with constipation is significantly prevalent among women than in men. Hence it is contemplated that sex hormones and gender differences may play a role in the pathophysiology of IBS. However, its pathophysiological mechanism still remains unknown, and its therapeutic implications are limited. Moreover, female IBS subjects have reported to feel more fatigue, depression, anxiety, and lower quality of life than their male counterparts. In addition to this, there has been evidence of differences in the treatment efficacy in men and women, although relatively only few men are enrolled in most relevant clinical trials (Y.S. kim *et al,* 2018).

In a comparative study by S.J Anbaradan *et al* it stated that the IBS is more widespread among women. They conducted a gender difference analysis by comparing the different findings and reported that among 144 patients 100 were women aged 37-50 years. The commonest subtype of IBS in men was diarrhea dominated while constipation dominated IBS was more frequent in female subjects (S.J Anbaradan *et al,* 2012).

According to epidemiological studies women are twice more likely to be affected by IBS in western countries in comparison to men furthermore studies have came to conclusion that there is a role of sex hormones in sensorimotor dysfunctions and to addressed it to the possible interplay of sex hormones with common risk factors associated with IBS (M.Meleine *et al,* 2014).

In a Meta analysis to evaluate the difference in IBS symptoms in men and women the relationship between IBS symptoms and its relation to menstrual cycle phase and menopause.

This study had four main findings: female subjects experienced a greater prevalence of IBS symptoms than males, particularly constipation related symptoms; they appeared to have more frequent and severe IBS symptoms during menstruation compared to other phases of the menstrual cycle; the effectiveness of hormonal therapy on IBS symptoms cannot be determined based on limited data available; and there are insufficient studies comparing IBS symptoms in pre and postmenopausal women (M. A. Adeyemo *et al,* 2010).

In another systemic review and meta analysis that assessed the effect of gender on prevalence of IBS in community it was reported that out 390 paper under evaluation the Odds Ratio for women compared to men in all studies was 1.67, the prevalence was not found to be higher among women in South Asian, South American or African studies. But the subtypes definitely varied in accordance with gender (R.M. Lovell *et al,* 2012).

In a prospective study to evaluate the difference across the severity of constipation and diarrhea in IBS subjects it was observed that there is positive association of constipation and gender. It also indicated that the female to male ratio significantly increase in accordance with the severity of constipation. The prevalence of diarrhea was similar between the genders (J Herman *et al,* 2010).

As reported by a study that investigated the relationship between gender and symptomatology in IBS quality of life enrolling 4015 subjects 452 subjects aged 14-79 years had IBS and male to female ratio was about 1:1.3. It also reported that gender composition between the types of IBS differs significantly but not in frequency of attack and also in comparison to men women had a higher depression and anxiety scores. Hence, there is a significant gender differences in the IBS symptoms, psychological rating, and QOL scores. Symptoms, anxiety, and depression all known to contribute to the negatively impact the IBS-QoL. Their findings suggested that gender differences should be recognized in IBS treatment (Y.R. Tang *et al,* 2012).

In a cross-sectional multi-center study that was conducted to assess the impact of gender on adverse childhood experiences and illness anxiety in irritable bowel syndrome comparing IBS patients with Healthy Controls revealed that female IBS subjects show a higher correlation to level of illness anxiety and ACE than males. However, after controlling depression and anxiety, this correlation disappeared. It was concluded that a possible gender-specific association of ACE with

illness anxiety in IBS patients can be linked to increased levels of depression and anxiety (S. Berens *et al,* 2020).

2.8 Effect of depression and anxiety on IBS

In recent years studies have shown that subjects with Irritable bowel syndrome have higher levels of depression and anxiety as compared to health individuals (N.A. Koloski *et al, 2002*) (G.R. Locke *et al,* 2004). Various studies have also shown that 30-40% of IBS patient have co-morbid depression or anxiety disorder (R.B.Lydiard *et al,* 1999). It has been reported that patients who come to medical attention tend to have a greater number of symptoms and are found to be much more anxious and depressed.

In review by R. Bruce he examined and observed that there is a higher prevalence of psychiatric disorder in patients with IBS and in all the published literature it indicated the fewer individuals with IBS seek treatment for psychiatric disorders (R.B.Lydiard *et al,* 1999).

In a study in an African population assess the brain-gut interaction and the effects on behavioral or psychiatric conditions in irritable bowel syndrome (IBS). They used the Rome Ⅱ diagnostic criteria. Depression was assessed using the symptom-check list from the Research Diagnostic Criteria (DSM-Ⅳ) of the American Psychiatric Association. About 56.8% of the total 132 IBS patients were depressed whereas only 20.1% of the 268 healthy subjects were depressed. There was a significant relationship between depression and IBS. It was concluded that IBS is significantly associated with major depression but not with gender and IBS subtypes (N.G.Ladep *et al,* 2006).

A cohort study using the General Practice Research Database reported that antidepressant drugs were prescribed from 2 years before the date of diagnosis, more irritable bowel syndrome patients (13%) than controls (5%). The prescription rates for anxiety were higher even before diagnosis, and both anxiety and depression remained prevalent up to 6 years after diagnosis (R.Jones *et al,* 2006).

In another systematic review which included 10 studies for analysis, IBS subjects had significantly higher anxiety and depression levels than controls group (SMD = 0.76, and SMD = 0.80 respectively). This significant difference was confirmed for patients with constipation dominant and Diarrhea dominant subtypes for anxiety, and only in diarrhea predominant subjects for depression (G. Fond *et al,* 2014).

An animal model study results showed that any form of early life stress can result in an altered brain-gut axis and therefore can be an important model for investigating potential perfunctory into stress-related disorders including irritable bowel syndrome (M.Siobhain *et al*, 2009).

In a review article by Tatenda A. Mudyanadzo *et al,* analyzed that the pathophysiology associates both conditions: - depression and IBS. It explored the bidirectional intereaction between the brain and the gastrointestinal tract, and the ways these influenced the endocrine and immune systems. It was summarized that there is a positive association between depression and IBS. But, this association is multifaceted, and there is a need for more research to further elucidate the association and to propose therapeutic approach (T.A. Mudyanadzo *et al,* 2018).

Since there have been fewer studies in Asian countries in relation with Anxiety and depression and their association to IBS, Hyun sun cho *et al* studied and evaluated frequency of anxiety and depression in Korea. For this they enrolled 124 and 91 IBS and health subjects respectively and anxiety and depression were observed in 38.6% and 38.6% IBS subjects respectively and 24.2% and 16.5% in healthy subjects. Thus it was concluded that both anxiety and depression is more frequent in subjects with IBS (H.S.Cho e*t al,* 2011).

In a cohort study that explored the relation between IBS and the coexistence of depression and insomnia in Korean population. A total of 3429 individuals who were enrolled in the Korean Genome and Epidemiology Study were analyzed. Of the participants, 374 were diagnosed with IBS using the Rome II criteria of diagnosis. For depressive symptoms, participants were sub-divided into three groups on the basis of Beck Depression Inventory (BDI) score. The odds ratio of participant with IBS increased proportionally as depressive symptoms worsened and participants of IBS with insomnia showed a higher OR than those without insomnia. It was concluded that the presence of both depression and insomnia is significantly associated with IBS (S.K. Lee *et al,* 2017).

In a Indian study to assess the prevalence of anxiety and depression in IBS using Hamilton anxiety and Hamilton depression rating scales. It was observed presence of anxiety and depression was 31.4%and 37.1% respectively and the odds ratio of depression came out to be 6.3 whereas odds ratio of anxiety was 7.56. Therefore it was deduced that screening of anxiety and depression in IBS should be mandatory to provide appropriate interventions and care (N. Kabra *et al,* 2013).

2.9 Effect of IBS on Quality of life

Irritable Bowel Syndrome (IBS) has a considerable impact on quality of life (QoL) but high quality data using the IBS−Quality of Life (IBS-QOL) measure are limited. It has been documented that Quality of Life in IBS patients is even lower than Quality of Life of patients with diabetes mellitus, dialysis dependent end-stage renal disease or gastroesophageal reflux (I.M.Gralnek *et al,* 2000).

The IBS-QOL measure is a specific tool developed to assess and validated impairment of quality of life in IBS patients (D.L.Patrick *et al,* 1998). This measure has eight IBS-QOL subscales: dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual concerns and relationships (D.A. Drossman *et al,* 2007).

In a study to evaluate sex-related differences in clinical symptoms and quality of life it was observed that female IBS subjects reported a greater severity of IBS symptoms, increased inflammatory cytokines, and had an impaired quality of life compared with male (R.Choghakhori *et al*, 2017).

In a cross sectional study to analysis the influence of weight on IBS quality of life. The overall inference of the study was that the individuals with IBS reported to have a lower QOL scores across all QOL-subscales compared to healthy individuals. The greatest QOL impairment was observed in Normal weight women and overweight men with IBS. Body fat percent could be a confounding factor on the relation between IBS and QOL. This disparity between QOL scores in IBS participants by both gender and weight groups reflects different social pressures perceived by normal and overweight women and men (L.B.Sherwin *et al,* 2017).

A population based study that assess quality of life in older people versus younger people with IBS reported that in the older group there was a higher prevalence of IBS among divorced subjects and similar higher prevalence was observed in below poverty level of income younger subjects. Utilization of Health care between the two IBS groups in terms of number of visits to physician, use of prescription and alternative medications was similar. They reported to have found no difference in the overall QOL score means or in its general health and physical functioning components. However, older IBS patients had better social functioning compared to younger IBS patients (A.Minocha *et al,* 2006).

A study by Hubert Mönnikes reported that there was no major difference in HR-QoL based on IBS subtypes but, the patients with worse bowel symptoms have a greater diminished QoL compared with patients with milder symptoms. Thus the severity of IBS symptoms could be associated with impact on health related quality of life. Evidence also indicated that HRQoL in patients with IBS is affected by gender and psychological conditions (H. Mönnikes *et al,* 2011). Prashant singh *et al* in their study to determine effect of irritable bowel syndrome (IBS) subtype on IBS-specific quality of life (QOL) and its subscales it was reported that diarrhea predominant and mixed subtype of IBS patients had an overall lower IBS-QOL than IBS-C patients. Therefore it is necessary to pay special attention to patient reporting food avoidance, interference with daily activities, social reactions and problems with relationships, which are known to be more prominent in IBS-D and IBS-M than other subtypes (P.Singh *et al*, 2015).

The impact of irritable bowel syndrome (IBS) on health related quality of life (HR-QOL) has been widely studied in the Western countries there are only limited data from Asian countries. Therefore a study was undertaken in Korea to assess the health-related quality of life (HRQOL) of patients suffering from IBS. They reported that of the 932 subjects with abdominal pain and bowel symptoms, 664 subjects fulfilling the Rome II criteria were analyzed. HRQOL of IBS patients was significantly worse than the general population. The mean of scores for the IBS-QOL was 74.2. The health concern domain was most affected having mean score 64.2, and the sexual domain had mean score 86.7 was least affected in the IBS-QOL (J.M.Park *et al,* 2009).

In a prospective, cohort study the patients with Irritable Bowel Syndrome (IBS) were diagnosed using the Rome III criteria in four countries to assess the quality of life using quality of life measures at the end of 4 and 8 weeks of treatment with mebeverine hydrochloride or pinaverium bromide. The results indicated that of the total 607 patients who were enrolled. IBS-QOL at the baseline were 52.0 in Poland, 48.9 in Egypt, 51.9 in Mexico, 76.4 in China. There was a statistically significant increase in IBS-QOL total scores at Weeks 4 and 8.Improvements were reported in all IBS-QOL subscales (X.Hou *et al,* 2014).

CHAPTER 3

SCOPE OF INVESTIGATION

Based on the literature reviewed, the present study was undertaken titled **"Impact evaluation of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life"** following research hypothesis has been formulated:

Research Hypothesis: Consumption of probiotic drink for 6 weeks positively impacts the depression score, IBS quality of life and provides relief in symptoms in irritable bowel syndrome subjects.

To authenticate the above mentioned hypothesis present study was undertaken with following as specific objectives:-

- Screening the population using Rome IV criteria.
- Enrolling subjects reporting positive for Rome IV criteria.
- To determine relation of Medical history in IBS patients.
- To determine impact of socio-economic status in IBS subjects.
- To find the degree of depression in IBS subjects.
- To study the Physical activity pattern in IBS subjects.
- To assess the dietary intake of high FODMAP foods in IBS subjects.
- To study the impact of consumption of probiotics for the period of 6 weeks on IBS quality of life and relief from symptoms.
- To distribute compliance sheet for determining the intake of probiotics.

CHAPTER 4

MATERIALS AND METHODS

The study was conducted with the primary objective to determine the impact of consumption of probiotics on IBS patients in Delhi NCR population and its effectiveness in terms of relief in symptoms and improvement in IBS quality of life**.** In order to arrive at the results various methods and materials used are described under the following headings. The experimental design of the study is designed in figure 4.1.

4.1 Location of the study.

4.2 Selection of the subjects.

4.3 Screening of the population

4.3.1 Rome IV criteria.

4.4 Collection of baseline information.

4.4.1 General information.

4.4.2 Dietary intake.

4.4.3 Anthropometric measurements

4.4.4 Physical activity level.

4.4.5 Depression status.

4.4.6 IBS Quality of life.

4.5 Nutrition Intervention.

4.5.1 Study protocol.

4.6 Ethical committee approval.

4.7 Statistical analysis.

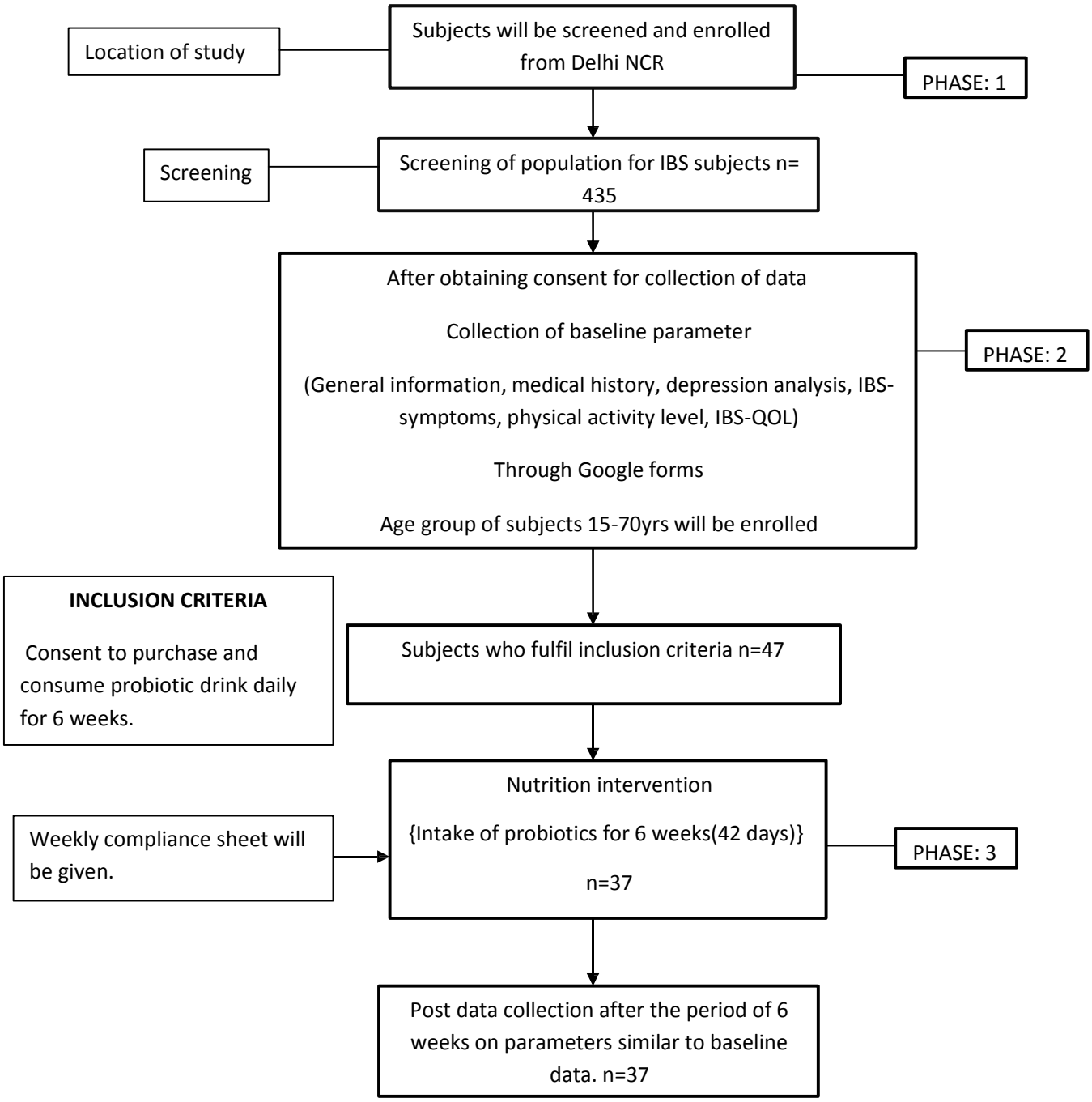

Figure 4.1 Experimental design of the study

4.1 Location of the study:

The subjects for the study were conveniently selected to conduct the research study from the free living population of Delhi North Central Region (NCR).

4.2 Selection of subjects:

The subjects were selected randomly through different directories using Rome IV criteria (based on frequency of abdominal pain over the past 3 months, changes in stool patterns and frequency. Age group of selected was 15-70yrs.

4.3 Screening of the population:

The subjects were screened for irritable bowel syndrome randomly using Rome IV criteria (based on frequency of abdominal pain over the past 3 months, changes in stool patterns and frequency. Out of 435 screened 61 subjects reporting positively for having abdominal pain related to defecation were enrolled into the study. The willingness of the subjects was considered for participate through informed consent letter (Appendix I).

4.3.1 Rome IV criteria:

Table: 4.1 Rome IV criteria

ROME IV DIAGNOSTIC CRITERIA FOR IRRITABL BOWEL SYNDROME
Recurrent abdominal pain with onset more than 6 months ago, occurring on an average at least 1 day per week for last 3 months associated with one or more of the following criteria:- 1. Related to defecation 2. Associated with change in frequency of stool 3. Associated with the change in the form (appearance) of the stool. ***Criteria fulfilled for the last 3 months with symptoms onset at least 6 months prior to diagnosis*.**

4.4 Collection of the baseline information:

Baseline data was collected for all 47 subjects on dietary information, anthropometric measurements, physical activity status, depression status, IBS related symptoms and IBS- quality of life were assessed using food frequency questionnaire, global physical activity questionnaire, becks depression inventory and IBS- quality of life questionnaire respectively (Appendix II).

4.4.1 General information

General information with reference to age, gender, type of family, educational level, personal habits, family and personal medical and medication history were assessed using structured questionnaire.

4.4.2 Dietary intake

On the basis of the data obtained through the food frequency questionnaire, the subjects consumption of high FODMAP was obtained as per daily, weekly, fortnightly, monthly or never. For the purpose of determining the frequency of consumption of high FODMAP food items, the data on food frequency was grouped into three categories. The food that were consumed daily, 2-3 times a week and weekly were clubbed as more frequently, the foods that were consumed fortnightly and monthly were grouped as frequently and occasional and seasonally consumed were grouped as less frequently.

4.4.3 Anthropometric measurements

Anthropometric measurements are a series of quantitative measurements of the muscle, bone, and adipose tissue used to assess the composition of the body. The core elements of anthropometry are height, weight, body mass index (BMI), body circumferences (waist, hip, and limbs), and skinfold thickness (Casadei, K.,Kiel, J. 2020).

4.4.3.1 Weight: It is the most widely used and simplest reproducible anthropometric measurement. It indicates the body mass and is a composite of all body constituents like water, mineral, fat, protein, bone etc (Robinson *et al,* 1988)

4.4.3.2 Height: It is a linear measurement made up of the sum of four components that is legs, pelvis, spine and skull (Jellife, 1966).

4.4.3.3 Body Mass Index: The BMI is a convenient and valid measure of adiposity.

It is computed as: -

$$BMI\ (kg/m^2) = \frac{Weight\ (kg)}{Height\ (m^2)}$$

Table 4.2 BMI cut-offs

Nutritional status based on the WHO and "Asian criteria" values		
Nutritional Status	**WHO criteria BMI cut-off**	**"Asian criteria"BMI cut-off**
Underweight	<18.5	<18.5
Normal	18.5 - 24.9	18.5 - 22.9
Overweight	25 - 29.9	23 - 24.9
Pre-Obese	-	25 - 29.9
Obese	≥ 30	≥ 30
Obese Type 1 (obese)	30 - 40	30 - 40
Obese Type Type 2 (morbid obese)	40.1 - 50	40.1 - 50
Obese type 3 (super obese)	>50	>50

the WHO Asia Pacific classification 2004

4.4.4 Physical activity level

WHO defines physical activity as any bodily movement produced by skeletal muscles that requires energy expenditure. Physical activity refers to all movement including during leisure time, for transport to get to and from places, or as part of a person's work. Both moderate- and vigorous-intensity physical activity improve health. In the present study global physical activity questionnaire was used to assess the physical activity level of subjects.

4.4.4.1 Global Physical Activity Questionnaire: The Global Physical Activity Questionnaire was developed by WHO for physical activity surveillance in countries. It collects information on physical activity participation in three settings (or domains) as well as sedentary behaviour, comprising 16 questions. The domains are:

1. Activity at work
2. Travel to and from places
3. Recreational activities

4.4.5 Depression status

The National Institute of Mental Health defines depression (major depressive disorder or clinical depression) as a common but serious mood disorder. It causes severe symptoms that affect how you feel, think, and handle daily activities, such as sleeping, eating, or working. To be diagnosed with depression, the symptoms must be present for at least two weeks. In this study we used Beck depression inventory as scale to assess depression status of IBS subjects.

4.4.5.1 Beck depression inventory: The Beck Depression Inventory (BDI) is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression (Beck, et al., 1961). The BDI has been developed in different forms, including several computerized forms, a card form (May, Urquhart, Tarran, 1969, cited in Groth-Marnat, 1990), the 13-item short form and the more recent BDI-II by Beck, Steer & Brown, 1996.

4.4.6 IBS- Quality of Life

The IBS-QOL is a self-report quality-of-life measure specific to Irritable Bowel Syndrome (IBS) that can be used to assess the impact of IBS and its treatment. The IBS-QOL was developed using a needs based model. The IBS-QOL was developed by a team of researchers from the University of Washington, Seattle under the direction of Dr. Donald L. Patrick and Dr. Douglas Drossman (Magdalena Kopczyńska,*et al.*2018).

4.5 Nutritional intervention:

The willingness of the subjects was considered through informed consent form (appendix III). Subjects were asked to purchase and drink the proposed probiotic supplement for a period of 6 weeks and also filling the compliance sheet (appendix IV). After 42 days of intervention post data was collected from the subjects on parameters similar to pre data (appendix V).

4.5.1 Study protocol

In the present study 435 subjects were screened and 47 subjects who reported that they have recurrent abdominal pain with onset more than 6 months ago, occurring on an average at least 1 day per week for last 3 months (both males and females) of the age group 15-70 yrs were included. Information regarding socio-demographic profile, general habits, dietary intake and clinical and medical history were collected (both individuals and family) using semi structured questionnaire. Subjects were also screened for various parameters in terms of anthropometric, dietary, physical activity, depression status, severity of symptoms and IBS-quality of life using global physical activity questionnaire, beck depression inventory, IBS-quality of life questionnaire etc.

Based on the results of the preliminary assessment and willingness of the subjects to further participate in the intervention phase of the study, subjects were asked to give consent to purchase and drink proposed probiotic for a period of 6 weeks. Subjects were advised to keep a compliance sheet for the period of intervention. Post intervention of 6 weeks the subjects were assessed on similar parameters of the pre data (depression status, severity of symptoms and IBS- quality of life).

4.6 Ethical Committee Approval

The study protocol was approved by the Medical Ethics Committee of the Foods and Nutrition Department, The Maharaja Sayajirao University of Baroda- "Institutional Ethical Committee for Human Research (IECHR)" in compliance with the guidelines issued by Indian Council of Medical Research with the medical ethics approval number IECHR/FCSC/2020/43.

All the subjects were informed and their consents were obtained to be enrolled into nutrition intervention. Consent form attached in appendix III

4.7 Statistical analysis

The data obtained were subjected to appropriate statistical analysis tools like chi square, paired T-test etc, to make the maximum use of the information gathered from the collected data.

4.7.1 Arithmetic Mean

For a data set, the arithmetic mean, also known as average or arithmetic average, is a central value of a finite set of numbers:- Specifically, the sum of the values divided by the number of values. The data set were based on a series of observations obtained by sampling from a statistical population; the arithmetic mean is the sample mean.

$$\overline{X} = \frac{\sum_{i=1}^{n} X_i}{n} = \frac{X_1 + X_2 + \lambda + X_n}{n}$$

4.7.2 Standard Deviation

In statistics, standard deviation is the measure of the amount of dispersion or variation in a set of values. A low standard deviation suggests that the values tend to be close to the mean (also called the expected value) of the set, while a high standard deviation indicates that the values are spread out over a wider range.

Standard deviation may be abbreviated SD, and is most commonly represented in mathematical texts and equations by the lower case Greek letter sigma σ, for the population standard deviation, or the Latin letter s, for the sample standard deviation.

$$\mathrm{SD} = \sqrt{\frac{\sum |x - \bar{x}|^2}{n}}$$

4.7.3 T- Test

The t-test is any statistical hypothesis test in which the test statistic follows a Student's t-distribution under the null hypothesis. A t-test is the most commonly applied when the test statistic would follow a normal distribution. The t-test can be used, to determine if the means of two sets of data are significantly different from each other. There are three main types of t-test:

1. An Independent Samples t-test compares the means for two groups.
2. A Paired sample t-test compares means from the same group at different times.
3. A One sample t-test tests the mean of a single group against a known mean.

CHAPTER-5

RESULT AND DISCUSSION

The present study was undertaken to ascertain the **"Impact of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life".** The results of the study are presented under following legends.

5.1 Identification & screening of IBS subjects

5.1.1 Screening of the population

5.1.2 Defecation profile of the screened IBS subjects

5.2 Baseline information of the subjects

5.2.1 Background information of the IBS subjects.

5.2.2 Body Mass Index of the subjects.

5.2.3 Medical history of the subjects.

5.2.4 Family history of co-morbidities in IBS subjects.

5.2.5 Personal Habits of the IBS subjects.

5.2.6 Dietary practices and information on intake of High FODMAP foods.

5.2.7Depression scores of the IBS subjects.

5.2.8 Symptoms related to IBS in Subjects

5.2.9 Impaired quality of life in IBS subjects.

5.2.10 Co- relation between various parameters.

5.3 Impact evaluation of Probiotics on IBS subjects

5.3.1 Effect on Depression scores.

5.3.2 Effect on symptoms related to IBS.

5.3.3 Effect on quality of life.

5.1 Identification & screening of IBS subjects

5.1.1 Screening of the population

Screening tool used was Google forms on Rome-IV criteria (based on frequency of abdominal pain over the past 3 months, changes in stool patterns and frequency.) administered to screen population for IBS after seeking their consent. The population was screened till n=435 was achieved, from the screened population number of subjects reporting for abdomen pain once a week for past 3 months were only 10.80% and around 89.19% reported negatively to the Rome IV criteria as shown in table 5.1.1.1 and figure 5.1.1.1.

Table: 5.1.1.1 Number of IBS subjects reporting for abdomen pain once a week for last 3 months (n=435)

	N	PERCENT (%)
YES	47	10.80
NO	388	89.19
TOTAL	435	

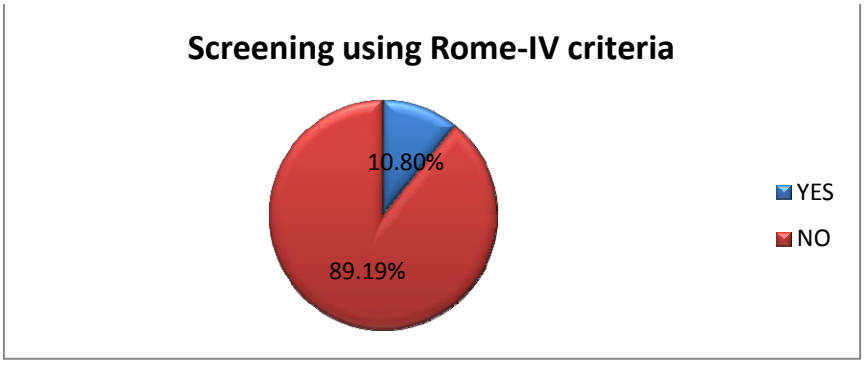

Figure: 5.1.1.1 Number of subjects reporting for abdomen pain once a week for past 3 months

5.1.2 Defecation profile of the screened IBS subjects

As seen in figure 5.1.2.1 the defecation profile in forty seven consenting IBS subjects 31.9% reported it to be pain related to defecation, 29.78% reported it to associate with change in frequency of stool and 8.51% reported it be associated with change appearance of stool and a combination of change in appearance of stool and frequency of defecation. While, 4.25% associate it with all three factors namely pain related defecation, change in frequency and change in form.

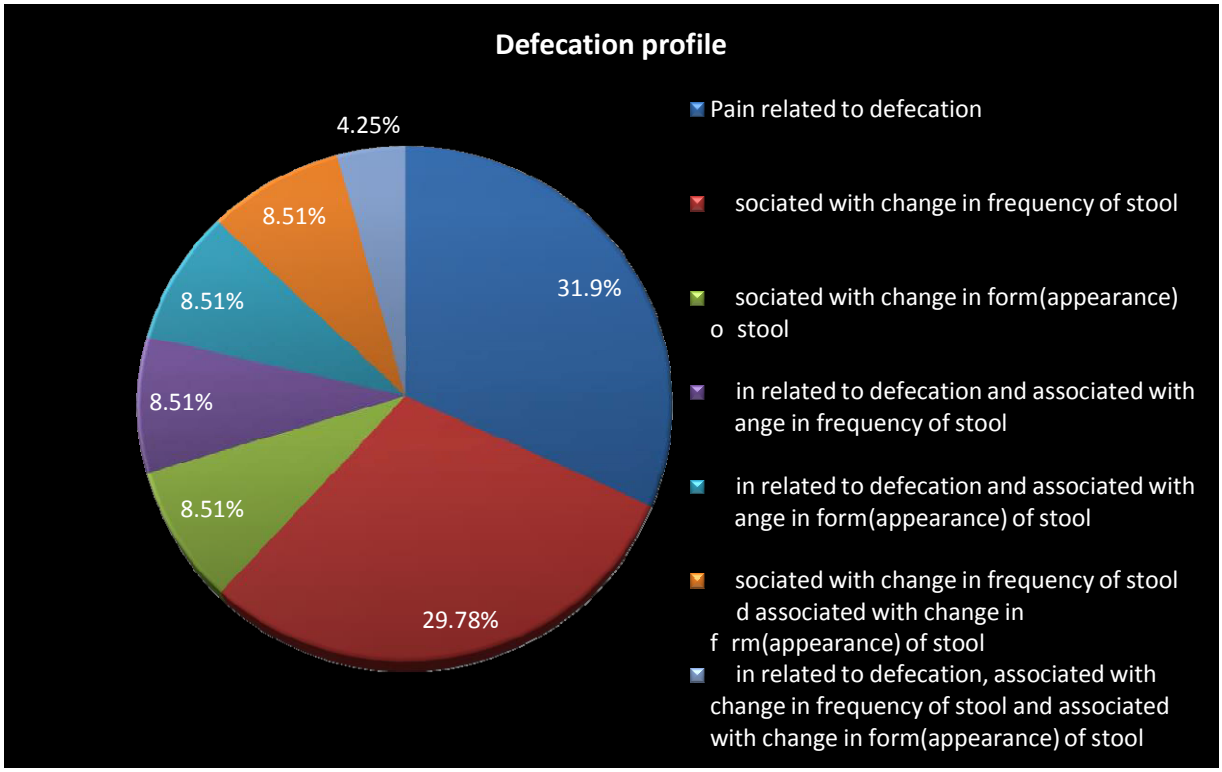

Figure: 5.1.2.1 Defecation Profiles of IBS Subjects

5.2 Baseline information of the subjects

5.2.1 Background information of the IBS subjects.

The IBS subjects involved in the study were in the age group of 15 years of age to 70 years with 54.05% females and 45.94% males. The education level of the IBS subjects 37.83% were graduates and 32.43% were in profession or honours followed by 24.32% who at least had completed diploma. For the occupation profile about 27.02% were working in private firms (figures: 5.2.1.1, 5.2.1.2, 5.2.1.3 and 5.2.1.4)

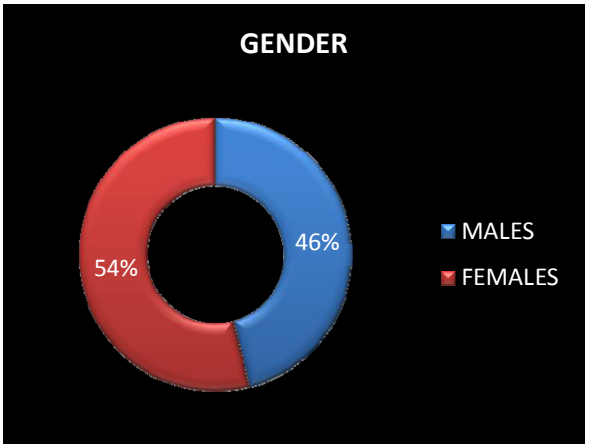

Figure: 5.2.1.1 Gender of the IBS subjects

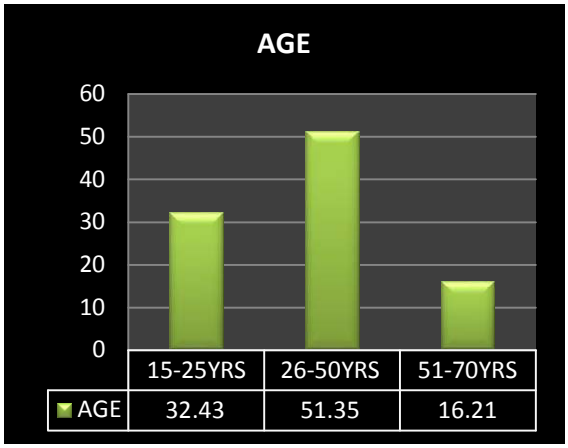

Figure: 5.2.1.2 Age of the IBS subjects

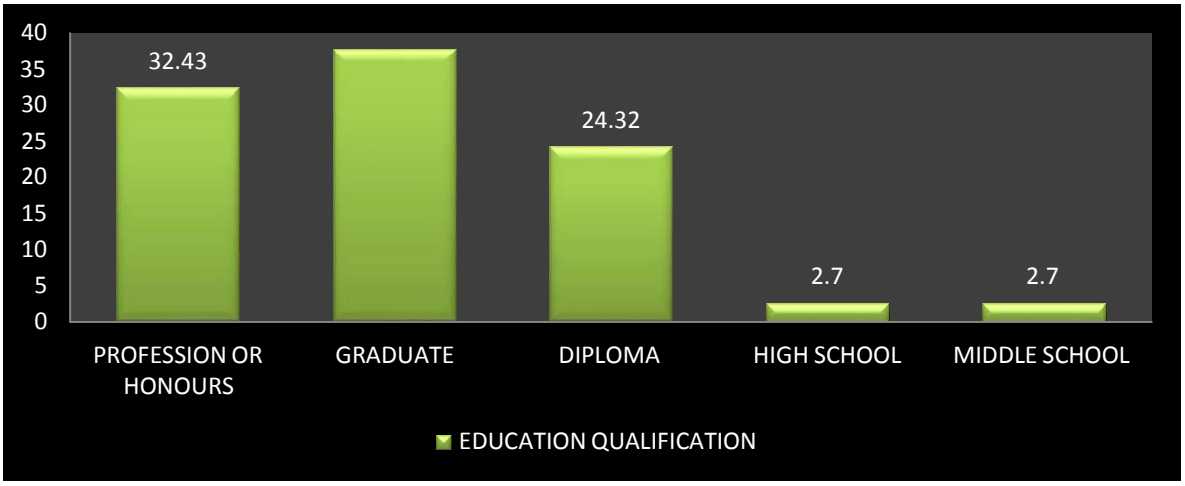

Figure: 5.2.1.3 Education Qualification of the IBS subjects

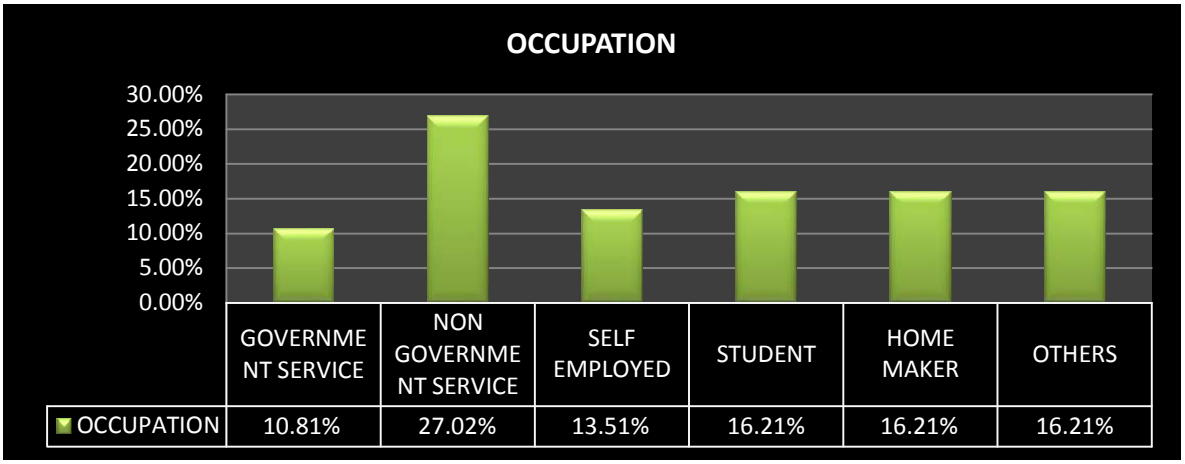

Figure: 5.2.1.4 Occupation of the IBS subjects

5.2.2 Body Mass Index of the subjects.

BMI of the IBS subjects 48.64% of them fall into obese category that is they have a BMI greater than of 25kg/m2 followed by 35.13% falling into normal category and 13.51% are overweight and 2.7% are underweight (figure:5.2.2.1).

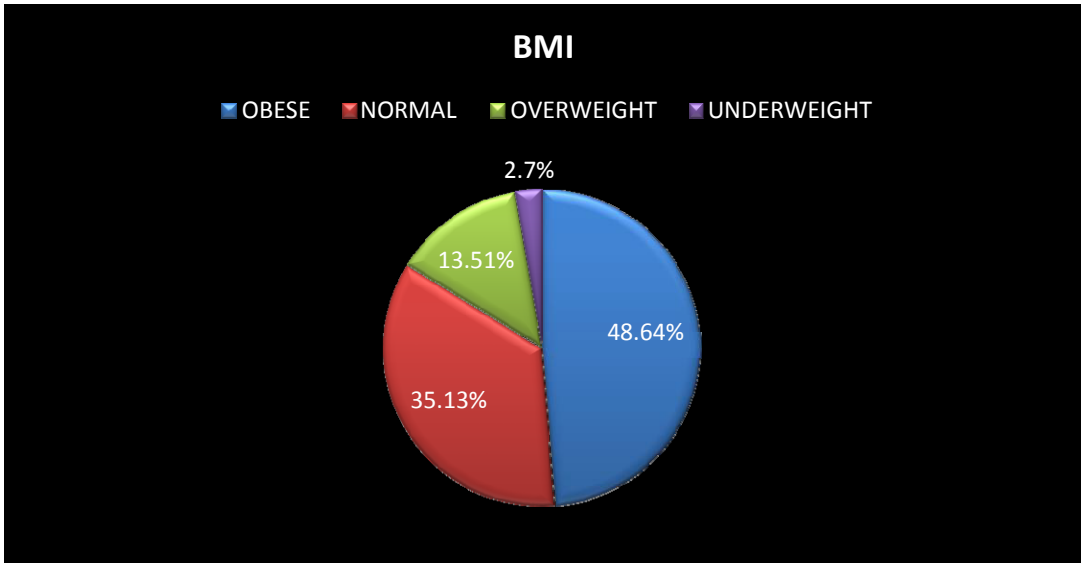

Figure: 5.2.2.1 BMI of IBS subjects*(*ranges of BMI: - Underweight- <18.5 kg/m^2, Normal- 18.5-22.9kg/m^2, Overweight- 23.0-24.9kg/m^2,Obese- >=25kg/m^2.)*

5.2.3 Medical history of the subjects.

A total of 15 of 37 IBS subjects had co-morbidities that are 40.54% of the sample. Almost 16.21% had diabetes followed by 10.81% having hypertension and diabetes, 5.40% had hypertension and 2.7% had cardiovascular diseases, combination of diabetes, hypertension and CVD. 40.54% of IBS subjects had a medication history also as represented in figure 5.2.3.1 and table 5.2.3.1 respectively.

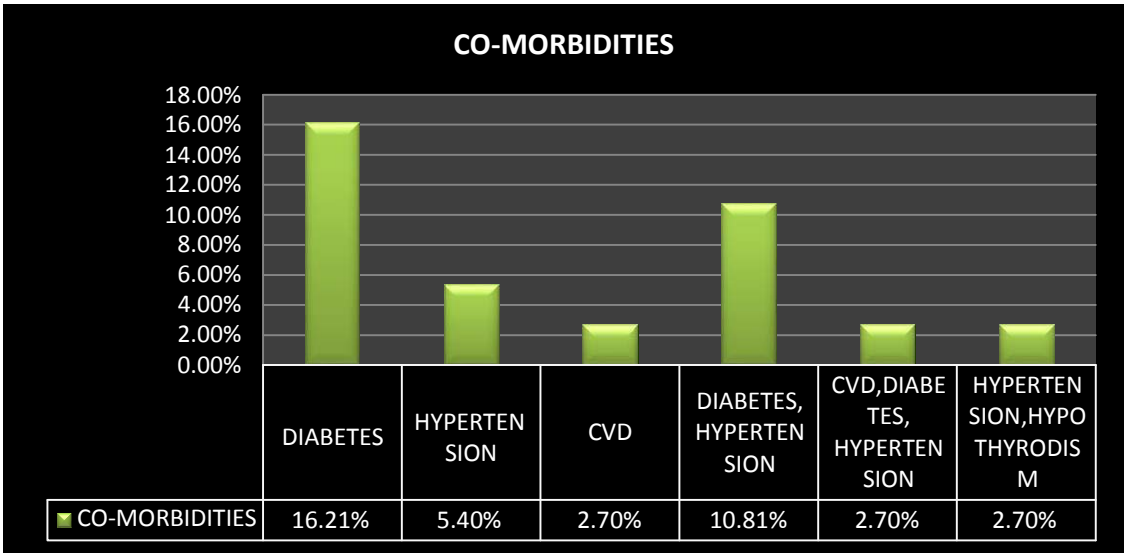

Figure: 5.2.3.1 Co-morbidities in IBS subjects

Table: 5.2.3.1 Number of IBS subjects with medication history

	N	PERCENT (%)
YES	15	40.54
NO	22	59.45

5.2.4 Family history of co-morbidities in IBS subjects.

Most the family members of the enrolled IBS subjects had history of co-morbidities (62.16%), with 51.35% having one type of Non communicable disease (NCD) and about 5.40% had the history of NCDs with GI cancer as can be seen in table 5.2.4.2 and figure 5.2.4.1.And Only 16.21% of the IBS subject had a history of any kind of surgery previously done and 83.78% responded negatively to having a history of surgery (table 5.2.4.2).

Table: 5.2.4.1 Number of IBS subjects having family history with co-morbidities.

	N	**PERCENT (%)**
NCDS	19	51.35
NCDS AND ASTHMA	1	2.70
NCDS AND ARTHRITIS	1	2.70
NCDS AND GI CANCER	2	5.40
TOTAL	23	62.16

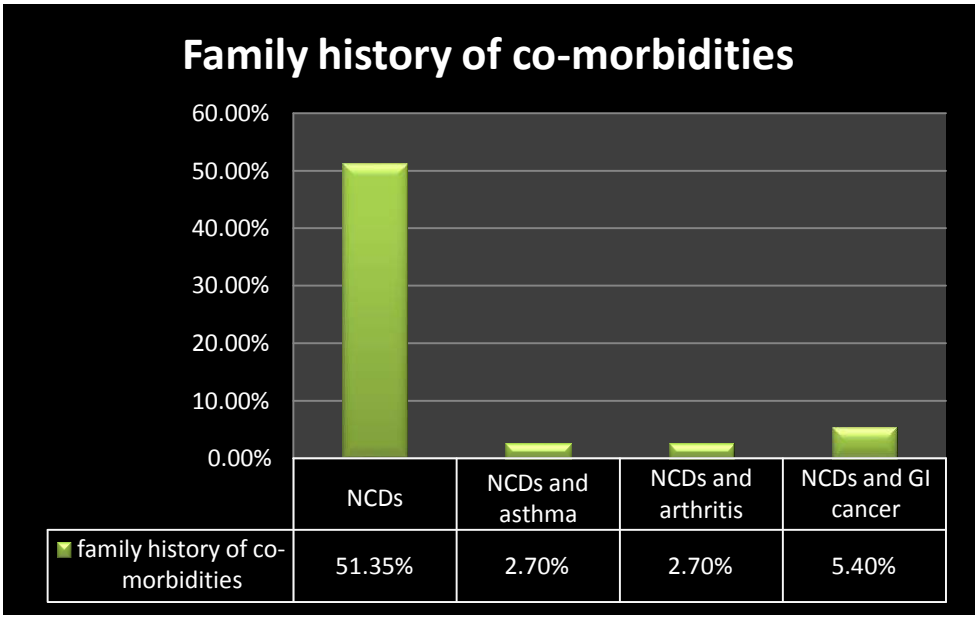

Figure: 5.2.4.1 IBS subjects having family history of co-morbidities

Table: 5.2.4.2 Number of IBS subjects with history of surgery

HISTORY OF SURGERY	**N**	**PERCENT (%)**
YES	6	16.21
NO	31	83.78

5.2.5 Personal Habits of the IBS subjects.

As seen in figure 5.2.5.1 the preponderance of consumption of tobacco and alcoholic products by the IBS subjects is 43.24% and 40.54% respectively. 100% of the IBS subjects were highly inactive and had a sedentary lifestyle (Table 5.2.5.1)

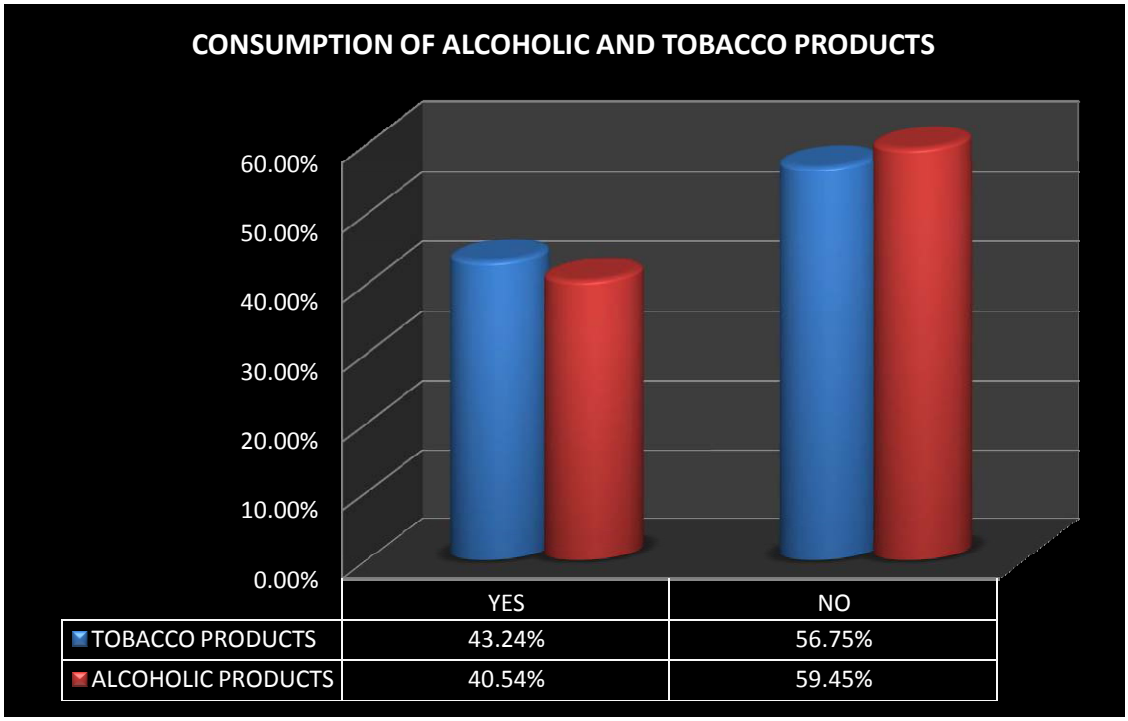

Figure: 5.2.5.1 Consumption of alcoholic and tobacco products by IBS subjects.

Table: 5.2.5.1 Physical active levels in IBS subjects

	N	**PERCENT (%)**
HIGHLY ACTIVE	-	-
MODERATELY ACTIVE	-	-
SEDENTARY	37	100

5.2.6 Dietary practices and information on intake of High FODMAP foods.

The information provided on the frequency in consumption of high FODMAP foods by the subjects revealed that 33% vegetables that were rarely and the most frequently consumed high FODMAP vegetable was onion and garlic which were consumed on a daily basis. Almost 62.5% fruits were consumed rarely because most of them are seasonally consumed. Consumption of wheat based products had the highest frequency because they were consumed multiple times on regular basis and in pulses and lentils kidney beans and moong dal were consumed more frequently. But nuts and oilseeds were mostly consumed occasionally. Among sweetners agave and polyols are rarely in Indian households and other sweetner were also used rarely. Around 72% high FODMAP beverages were rarely consumed and most frequently consumed high FODMAP drink is strongly flavoured teas which are more than once consumed in a day (Table 5.2.6.1).

Table: 5.2.6.1 Frequency of consumption of high FODMAP food group wise.

FOOD GROUP	MORE FREQUENTLY N (%)	FREQUENTLY N (%)	LESS FREQUENTLY N (%)	RARELY N (%)
Vegetable	22	22	22	33
Fruits	18.75	6.25	-	62.5
Cereals, pulses and nuts	12.5	12.5	18.75	43.75
Milk and its products and other alternatives	12.5	37.5	-	37.5
Sweetners and condiments	37.5	-	12.5	50
Beverages	14.28	-	14.28	71.42

5.2.7 Depression scores of the IBS subjects.

The Depression scores of IBS subjects was arrived at by using Becks depression inventory (BDI) it showed that majority of the subjects that is 87% were clinical depressed(Table 5.2.7.1 and figure 5.2.7.1). But the 100% IBS subject in the study reported that they were not undergoing any psychological treatments (Table 5.2.7.2).

Table: 5.2.7.1 Depression score of IBS subjects using Becks depression inventory

SCORE	N	PERCENT (%)
1-10 normal	0	0
11-16 mild mood disturbance	5	13.51
17-20 borderline clinical depression	14	37.83
21-30 moderate depression	18	48.64
31-40 severe depression	0	0
OVER 40 extreme depression	0	0

***range of depression scores:-**normal:1-10, mild mood disturbance:11-16, borderline clinical depression:17-21,moderate depression:21-30, severe depression:31-40.*

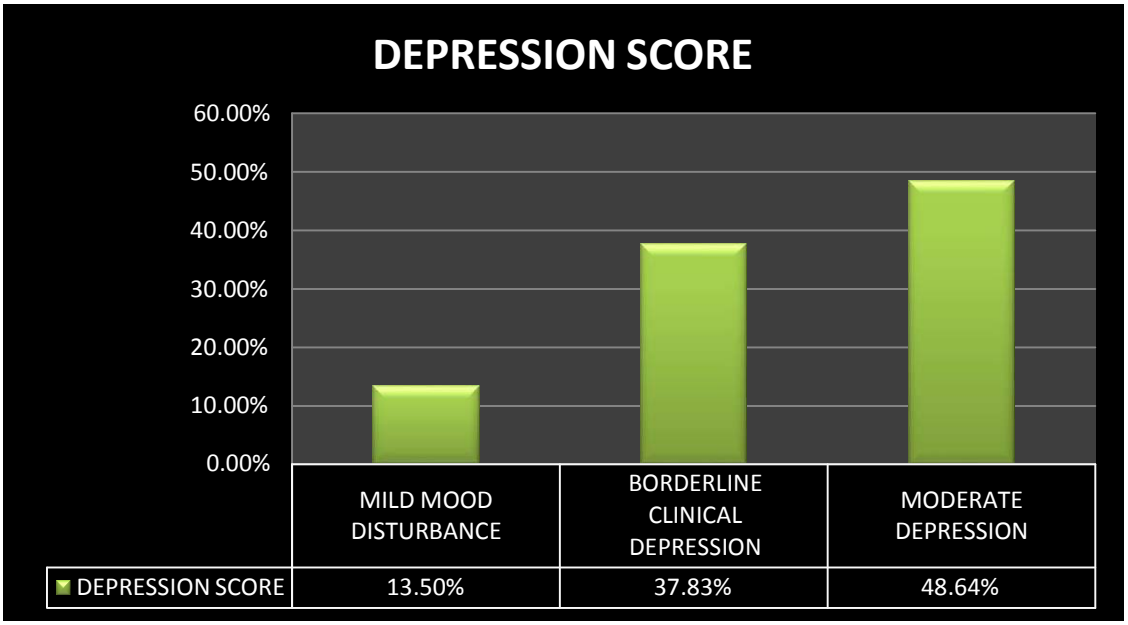

Figure: 5.2.7.1 Depression score of IBS subjects using Becks depression inventory

Table: 5.2.7.2 Number of IBS subjects undergoing psychological treatment

	N	PERCENT (%)
YES	0	0
NO	37	100

5.2.8 Symptoms related to IBS in Subjects

Among the IBS subject majority of them had 3-4 gastrointestinal symptoms related to IBS accounting to about 97.29% of the subjects and only 2.70% had 1-2 symptoms at a given time (Table 5.2.8.1 and figure 5.2.8.1).

Table: 5.2.8.1 Number of IBS subjects having symptoms related to IBS

NUMBER OF SYMPTOMS	N	PERCENT (%)
1-2	1	2.70
3-4	36	97.29
5-6	0	0

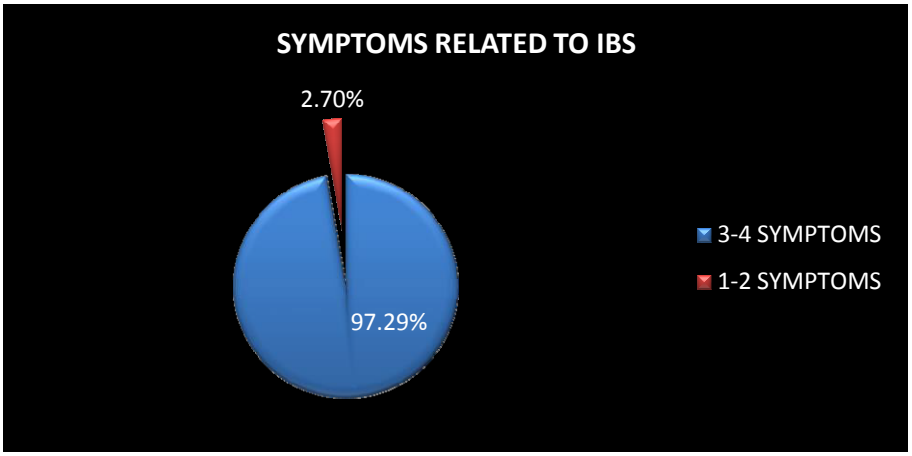

Figure: 5.2.8.1 IBS subjects having symptoms related to IBS

5.2.9 Impaired quality of life in IBS subjects.

Almost 73% of the IBS subjects in the study had reported to 3-4 domains impaired of quality of life among the six major domains of quality of life and only 19% subjects had 5-6 impaired domain of IBS quality of life.

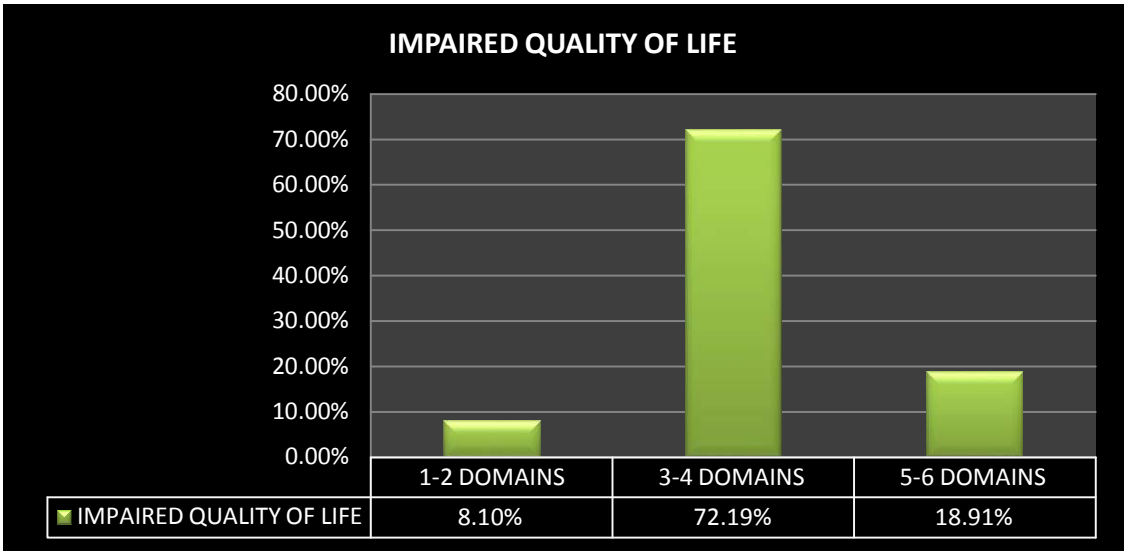

Figure: 5.2.9.1 IBS subjects having impaired domains of IBS quality of life

RESULT HIGHLIGHTS

- A total n= 435 were screened from population number of subjects for abdomen pain once a week for past 3 months and positive respondents were only 10.80% and around 89.19% reported not to have abdomen pain.
- Out of the 10.80% reporting positive for Rome IV criteria 31.9% reported it to be pain related to defecation, 29.78% reported it to associate with change in frequency of stool and 8.51% reported it be associated with change appearance of stool and a combination of change in appearance of stool and frequency of defecation.

- The IBS subjects involved in the study were in the age group of 15 years of age to 70 years with 54.05% females and 45.94% males. The education level of the IBS subjects 37.83% were graduates and 32.43% were in professional jobs followed by 24.32% who at least had completed diploma. For the occupation profile about 27.02% were working in private firms.
- BMI of the subjects 48.64% of them fall into obese category that is they have a BMI greater than of 25kg/m2.
- A total of 15 of 37 IBS subjects had co-morbidities that are 40.54% of the sample.
- Around 62.16% of the family members of the emolled IBS subjects had history of co-morbidities, and about 5.40% had the history ofNCDs with GI cancer.
- The preponderance of consumption of tobacco and alcoholic products by the subjects is 43.24% and 40.54% respectively and 100% of them were physically inactive.
- The frequency of certain high FODMAP foods like cereals and some vegetables were more frequent in comparison to sweetners or beverages.
- The Depression scores according to Beck depression inventory majority of the subjects were clinical depressed.
- Most of the subjects had multiple gastrointestinal symptoms related to IBS.
- Among the six major domains of quality of life most of the subject had atleast 3-4 impaired domains.

5.2.10 Co- relation between various parameters

Table 5.10 revealed that amongst the various baseline parameters age, BMI, and co-morbidities are positively co-related to number of IBS symptoms and negatively co-related to IBS specific quality of life and depression scores of subjects. Meanwhile, Gender and education qualification are positively co-related to IBS specific quality of life and depression scores and negatively co-related to number of symptoms. Occupation is negatively correlated to both quality of life and number of symptoms. Quality of life is positively co-related to depression score and negatively to number of symptoms. None of the parameters are significantly co-related to depression score, number of symptoms or quality of life at $p<0.05$.

Table: 5.2.10.1 Co-relation among various parameters observed in IBS subjects

	Gender	Age	Education qualification	Occupation	Co-morbidities	BMI	Depression score	Number of symptoms	Impaired quality of life
Gender	1	-.381*	-.052	-.566**	-.122	-.214	.200	-.283	.170
Age	-.381*	1	-.352*	.123	.754**	.374*	-.135	.317	-.032
Education qualification	-.052	-.352*	1	.306	-.183	-.043	.057	-.161	.009
Occupation	-.566**	.123	.306	1	.058	-.093	-.020	.070	-.042
Co-morbidities	-.122	.754**	-.183	.058	1	.316	-.178	.164	-.042
BMI	-.214	.374*	-.043	-.093	.316	1	-.182	.277	-.047
Depression score	.200	-.135	.057	-.020	-.178	-.182	1	-.041	.282
Number of symptoms	-.283	.317	-.161	.070	.164	.277	-.041	1	-.166
Impaired quality of life	.170	-.032	.009	-.042	-.042	-.047	.282	-.166	1

**. Correlation is significant at the 0.05 level (2-tailed).*

***. Correlation is significant at the 0.01 level (2-tailed).*

5.3 Impact evaluation of Probiotics on IBS subjects

Table 5.3.1 reveals that supplementing the IBS subjects with probiotic drink resulted in a significant reduction ($p<0.001$) in the depression score and number of symptoms by 18.41% and 33.85% and no significant improvement in IBS specific quality of life.

Table: 5.3.1 Effect of supplementation of Probiotic on depression score, number of symptoms and quality of life.

		Mean	difference	% difference	Standard deviation	Standard error	Paired T-test
Depression score	PRE	20.22	3.41	18.41	3.207	0.527	9.240**
	POST	16.81			2.355	0.387	
No. Of symptoms	PRE	3.35	0.157	33.85	0.588	0.097	6.184**
	POST	2.38			0.794	0.131	
Quality of life	PRE	2.65	0.230	8.66	0.978	0.161	0.941^{NS}
	POST	2.43			0.728	0.120	

***. Significant at the 0.001 level (2-tailed)*

^{NS}. Non -significant

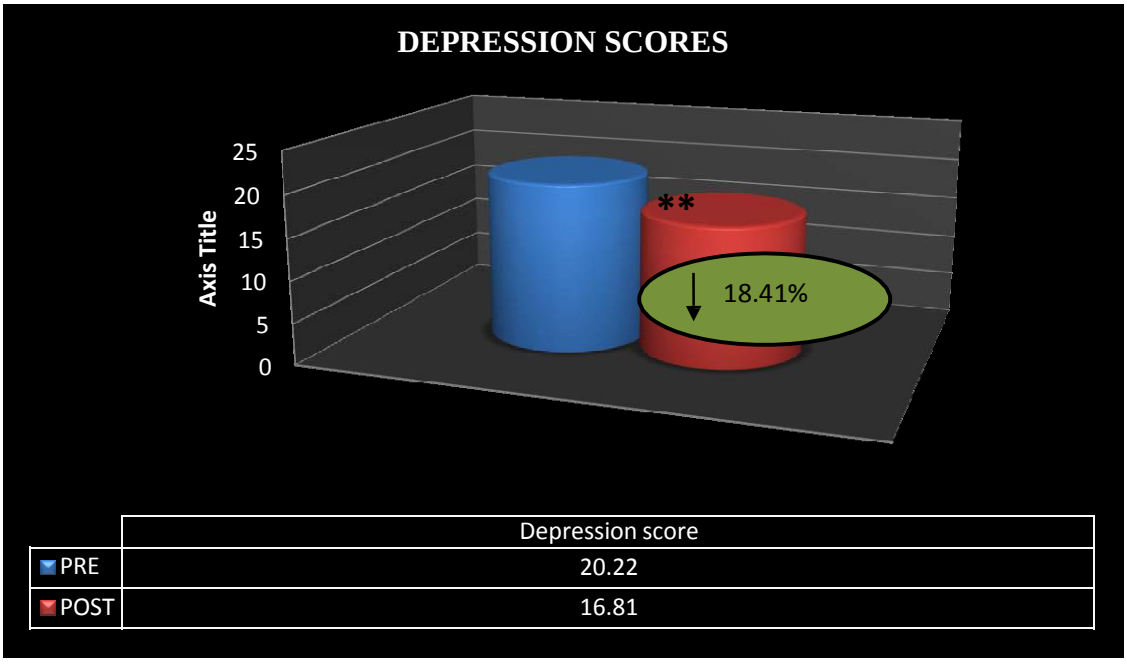

Figure: 5.3.1Depression scores of IBS subjects before and after probiotic supplementation.

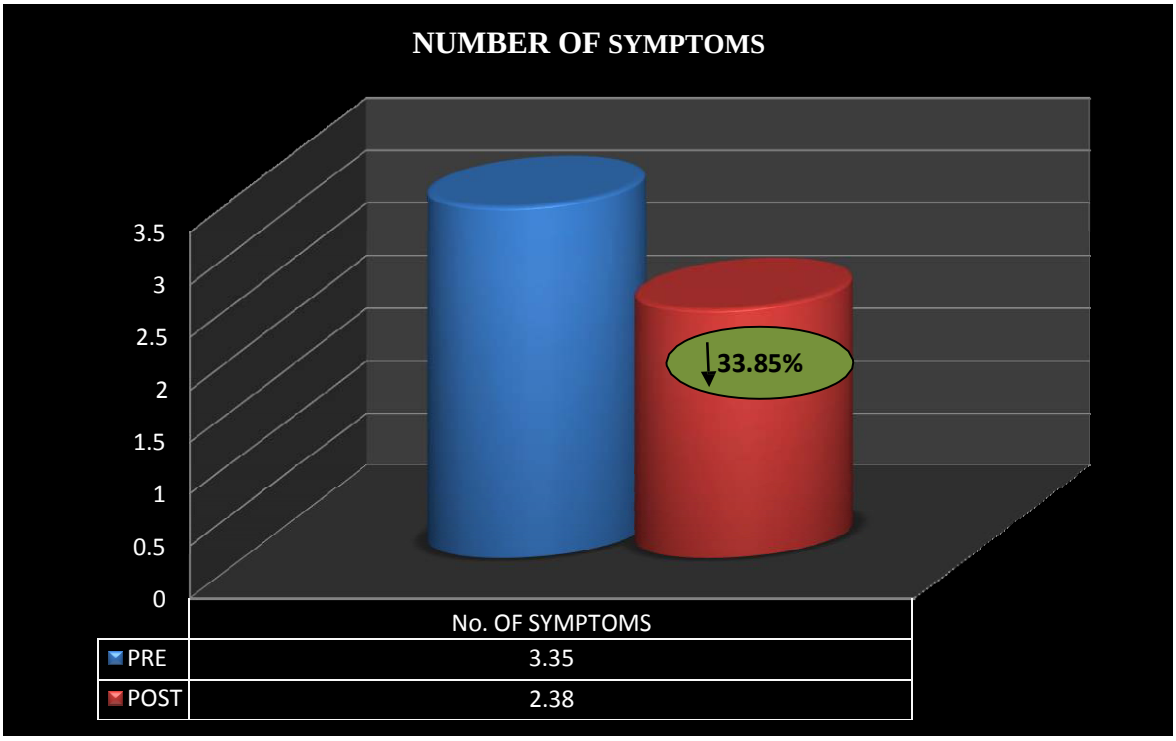

Figure: 5.3.2 Number of symptoms present before and after probiotic supplementation.

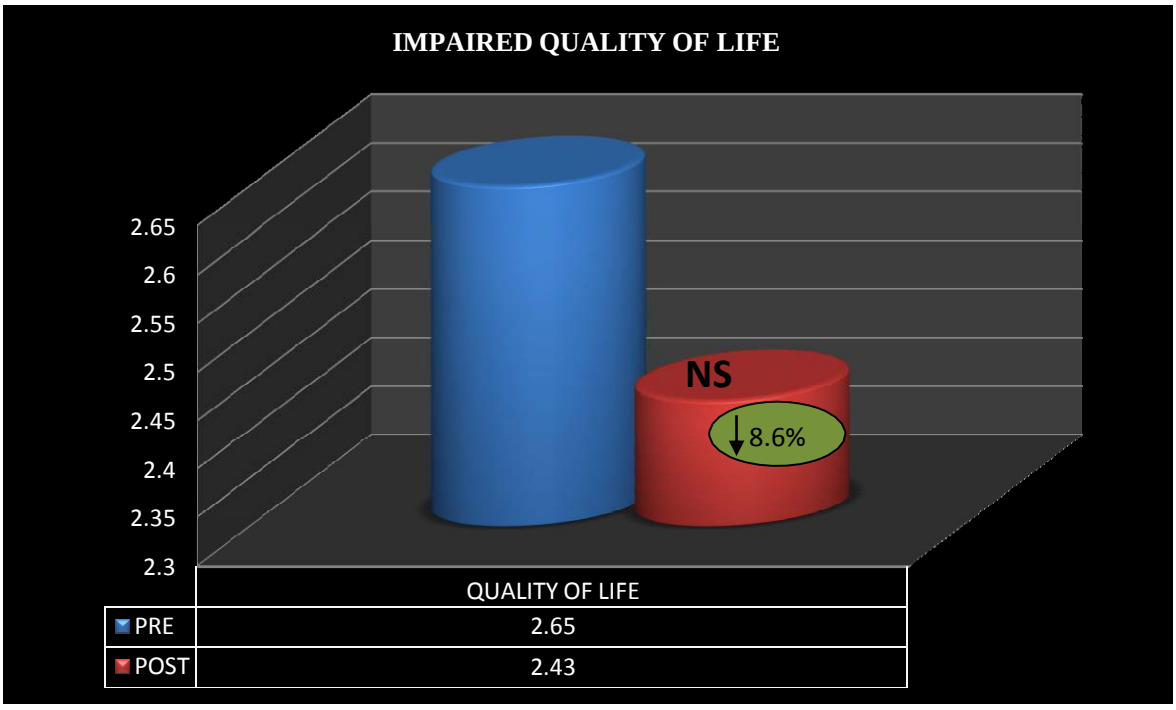

Figure: 5.3.3 Quality of life before and after probiotic supplementation

RESULT HIGHLIGHTS OF INTERVENTION

- Intervention with probiotic resulted in a significant decrease ($p<0.001$) in depression scores and number of symptoms by 18.41% and 33.85% respectively.
- Post intervention there was a small reduction in number of impaired domains of quality of life but was not statistically significant.

DISCUSSION

In the present study supplementation of probiotic drink for a period of six weeks to IBS subjects brought about a significant reduction in depression scores and presence of IBS specific symptoms along with a slight improvement in quality of life that was not statistically significant.

Previous studies have also shown that probiotic drinks to IBS subjects had a significant reduction depression, B. coagulans MTCC 5856 showed its efficacy in treatment of patients experiencing IBS symptoms with major depressive disorder. The improvement in depression and IBS symptoms was found to be statistically and clinically significant (M. Majeed, *et al*, 2018).

In a randomised trials patients (n = 136) were randomized (double blind) and were to receive either B.coagulans Unique IS2 (2 billion CFU) or placebo capsules daily for 8 weeks. It showed that there was a significant reduction of abdominal discomfort/pain intensity and increase in complete spontaneous bowel movements (R.S.Madempudi *et al*, 2019). In another study of 2008 using Lactobacillus casei strain Shirota (Yakult®)There was no significant improvement in the symptom score with probiotic therapy, except for wind (P = 0.04). Subjects with moderate symptoms and who

no longer had ERBHAL at the end of treatment, showed have a better improvement in the overall symptoms scores than those who had persisting ERBHAL (J.S. Barrett et al, 2008).

In randomised trial 152 patients who completed the study showed a statistically significant mean change in IBS-SSS 63.3 probiotic versus 28.3 placebo (G. Sisson et al, 2014). But they also reported that there was no significant improvement in the IBS-QOL. There are other studies reporting that there is a significant improvement in IBS- QoL when a probiotic drink was introduced versus placebo (C.C.Hwan et al, 2011).

The present study revealed that the various baseline parameters age, BMI, and co-morbidities are positively co-related to number of IBS symptoms and negatively co-related to IBS specific quality of life and depression scores of subjects. Meanwhile, Gender and education qualification are positively co-related to IBS specific quality of life and depression scores and negatively co-related to number of symptoms. Occupation is negatively correlated to both quality of life and number of symptoms. Quality of life is positively co-related to depression score and negatively to number of symptoms.

In previous study by Simrén et al they found that women with IBS reported lower QoL with higher levels of fatigue, depression, and anxiety; and less positive well-being and self-control than men with IBS (M.Simrén et al, 2001). In a systematic review that included 13 studies demonstrated that both IBS and healthy women reported increased IBS symptoms during menses vs. other phases. Hence suggesting that female sex hormones influence the severity of IBS symptoms, but more studies are needed (M. A. Adeyemo et al, 2010).Another study stated that IBS patients showed higher levels of anxiety and also reported higher prevalence for adverse childhood experiences(ACE) and it was correlated in female IBS patients, but not in males (S.Berens et al, 2020).

In the present study it was reported that out of 435 were screened from population number of subjects who fulfilled Rome −IV were only 10.80%. In previous studies on the epidemiology of IBS by Lovell and Ford estimated a global prevalence of 11.2%, it was concluded that the rate has not changed in the last 30 years (R.Lovell *et al,* 2012).

Present study stated that 48.64% of the subjects fall into obese category that is they have a BMI greater than of 25kg/m^2. In a systematic review including 11 studies (2 pediatric and 9 adult) investigated the relationship between obesity and IBS showed that the prevalence of obesity in children with IBS ranged from 24.8% to 42% and in adults, the prevalence of IBS in obese subjects varied from 11.6% to 24%, depending on the study population. The findings of this comprehensive review suggested that the frequency of IBS in obese children and adults are variable and depends on the study population (O. Pickett-Blakely, 2014).

Present study also reported that15 of 37 IBS subjects had co-morbidities that are 40.54% of the sample. Also around 62.16% of the family members of the enrolled IBS subjects had history of co-morbidities, and about 5.40% had the history of NCDs with GI cancer.

In a study 48 out of 51 symptom-based and 16 out of 25 biomarker-based diagnoses were found to be significantly more common in IBS than in controls. Bacterial, viral, and fungal infections and stroke were among diagnoses made more frequently in IBS. Greater somatic comorbidity was associated with concurrent psychiatric diagnosis. Only 16% of IBS patients had abnormally high numbers of comorbid diagnoses (E.W.Whitehead et al, 2007).

In the present study the preponderance of consumption of tobacco and alcoholic products by the subjects is 43.24% and 40.54% respectively and 100% of them were physically inactive. In a cross-sectional study that was conducted in a tertiary care hospital of Karachi it was reported that Smoking was significantly found to be associated with IBS (P=0.002). But the binary logistic regression analysis also indicated that non-smokers were more likely to have IBS (Crude OR: 3.00, 95% CI 1.23-7.30) than smokers (K. Mahmood et al, 2020).

A study reported that there is a strongest associations for IBS patients who tend to binge drinking have GI symptoms the next day (e.g., diarrhea , p=0.006; nausea, p=0.01; stomach pain, p=0.009; and indigestion, p=0.004), whereas it was reported that moderate and light drinking either were not associated or weakly associated with GI symptoms. Associations between alcohol intake and GI symptoms were stronger for women with IBS-diarrhea than for IBS-constipation or IBS-mixed (K.W.Reding et al, 2013).

Various studies involving healthy adults indicate that exercise helps in improving the symptoms of fatigue, bloating and constipation (SN. Sullian et al, 1994). Hence, it seemed appealing to promote regular exercise in the management of IBS. While many of IBS management programmes have

often suggested that exercise might have positive impact on health promoting activity, but there is limited to no randomized controlled trials (RCT) that have evaluated the effects of an exercise intervention in patients experiencing IBS.

In the present study the frequency of certain high FODMAP foods like cereals and some vegetables were more frequent in comparison to sweetners or beverages. For around 60−70% of patients certain foods aggravate the symptoms. The response rate of various exclusion diets varies from 12.5% to 67%.Although the data from various clinical trials may in some cases not provide strong evidence for benefits of dietary modification (I.Posserud *et al*, 2013).

A diet low in fermentable oligosaccharides, disaccharides, monosaccharide and polyol (FODMAPs) which are slowly absorbed or indigestible short-chain carbohydrates is considered as one of the major option for the treatment of IBS, with a symptomatic improvement in about 70% of the patients (S. Khan *et al*, 2010).

In recent years the use of probiotics for the management of dysbiosis of the microbiota in IBS has gained a lot of interest (A. P. Hungin, et al, 2018). The use probiotic cannot be the only method as all the probiotics are not effective in treatment of IBS as it is well known that the benefits of probiotics rely on strain, delivery of sufficient amount of active cells and duration of therapy (Y. Zhang et al, 2016).

CHAPTER-6

SUMMARY AND CONCLUSIONS

Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract, also referred as spastic, nervous or irritable colon and ischaracterized by abdominal pain and alterations in bowel habits in the absence of specific organic pathology (C.Canavan, J.West & T.Card, 2014). The symptoms of IBS may include abdominal pain, distention, bloating, indigestion and various symptoms of defecation. Though the causes of IBS have not to date been fully elucidated, it is believed that symptoms occur as a result of a combination of factors which includes visceral hypersensitivity, altered bowel motility, neurotransmitters imbalance, infection and psychosocial factors. The treatment includes an array of self care and lifestyle therapies like dietary modifications, physical activity, medications (antidiarrhoeal, antispasmodic, laxatives, painkillers, dietary supplements) sometimes, psychotic drugs are also used for relieving psychological symptoms such as anxiety and depression and probiotics. Application of probiotics as biotherapeutics is a new emerging area in developing dietary strategies which may have a concrete role in reducing the burden of Irritable Bowel Syndrome. Keeping same in mind the present study was designed under the title, **"The impact of consumption of probiotics on IBS patients in DELHI NCR population and it's effectiveness in terms of relief of symptoms and improvement in IBS quality of life."**The following specific objectives of the study included-

- Screening the population using Rome IV criteria.
- Enrolling subjects reporting positive for Rome IV criteria.
- To determine relation of Medical history in IBS patients.
- To determine impact of socio-economic status in IBS subjects.
- To find the degree of depression in IBS subjects.

- To study the Physical activity pattern in IBS subjects.
- To assess the dietary intake of high FODMAP foods in IBS subjects.
- To study the impact of consumption of probiotics for the period of 6 weeks on IBS quality of life and relief from symptoms.
- To distribute compliance sheet for determining the intake of probiotics.

Results on screening the population for IBS using Rome IV criteria

- A total four hundred and thirty five people were screened from population for abdomen pain once a week for past 3 months and positive respondents were only 10.80% and around 89.19% reported not to have abdomen pain.
- Out of the 10.80% reporting positive for Rome IV criteria 31.9% reported it to be pain related to defecation, 29.78% reported it to associate with change in frequency of stool and 8.51% reported it be associated with change appearance of stool and a combination of change in appearance of stool and frequency of defecation.

Results on baseline information of the IBS subjects (n=37)

- The IBS subjects involved in the study were in the age group of 15 years of age to 70 years with 54.05% females and 45.94% males.
- The education level of the IBS subjects 37.83% were graduates and 32.43% were in profession or honours followed by 24.32% who at least had completed diploma.
- For the occupation profile about 27.02% were working in private firms and around 17% were homemaker, students and other occupations each.
- Majority of the subjects that is 48.64% fall into obese category for the classification of BMI as given by WHO Asia Pacific 2004 that is they have a BMI greater than of 25kg/m2.
- A total of 15 of 37 IBS subjects had co-morbidities that are 40.54% of the sample. The most common co-morbidities were diabetes, hypertension and CVD.

- Around 62.16% of the family members of the enrolled IBS subjects had history of co-morbidities, and about 5.40% had the history of NCDs with GI cancer.
- The preponderance of consumption of tobacco and alcoholic products by the subjects is 43.24% and 40.54% respectively and 100% of them were physically inactive.
- The frequency of certain high FODMAP foods like cereals and some vegetables were more frequent in comparison to sweetners and other polyols.
- The information provided on the frequency in consumption of high FODMAP foods by the subjects revealed that 33% high FODMAP vegetables that were rarely and the most frequently consumed high FODMAP vegetable was onion and garlic which were consumed on a daily basis.
- Almost 62.5% high FODMAP fruits were consumed rarely because most of them are seasonally consumed.
- Consumption of wheat based products had the highest frequency because they were consumed multiple times on regular basis and in pulses and lentils kidney beans and moong dal were consumed more frequently. But nuts and oilseeds were mostly consumed occasionally.
- Among sweetners agave and polyols are rarely in Indian households and other sweetner were also used rarely. Around 72% high FODMAP beverages were rarely consumed and most frequently consumed high FODMAP drink is strongly flavoured teas which are more than once consumed in a day.
- The Depression scores of IBS subjects was arrived at by using Becks depression inventory (BDI) it showed that majority of the subjects that is 87% were clinical depressed. But the 100% IBS subject in the study reported that they were not undergoing any psychological treatment.
- Most of the subjects had multiple gastrointestinal symptoms related to IBS.Among the IBS subjects majority of them had 3-4 gastrointestinal symptoms related to IBS accounting to about 97.29% of the subjects and only 2.70% had 1-2 symptoms at a given time.
- Among the six major domains of quality of life most of the subject had atleast 3-4 impaired domains. Almost 73% of the IBS subjects in the study had reported to 3-4 domains impaired of quality of life among the six major domains of quality of life and only 19% subjects had 5-6 impaired domain of IBS quality of life.

- Amongst the various baseline parameters age, BMI, and co-morbidities are positively co-related to number of IBS symptoms and negatively co-related to IBS specific quality of life and depression scores of subjects.
- Meanwhile, Gender and education qualification are positively co-related to IBS specific quality of life and depression scores and negatively co-related to number of symptoms.
- Occupation is negatively correlated to both quality of life and number of symptoms. Quality of life is positively co-related to depression score and negatively to number of symptoms. None of the parameters are significantly co-related to depression score, number of symptoms or quality of life at $p<0.05$.

Salient features of the supplementation trial.

- Intervention with probiotic resulted in a significant decrease ($p<0.001$) in depression scores and number of symptoms by 18.41% and 33.85% respectively.
- Post intervention there was a small reduction (8.6%) in number of impaired domains of quality of life but was not statistically significant.

Hence, we can conclude that Irritable bowel syndrome subjects under the study had poor IBS specific quality of life. The Depression scores of IBS subjects, calculated using Becks depression inventory (BDI) it showed that majority of the subjects were clinical depressed marking a high prevalence of depression in IBS subjects. Therefore, supplementation of probiotics for six weeks is an attractive therapy for management of Irritable bowel syndrome which resulted in reduction of depression of scores and number of gastrointestinal symptoms and slight improvement in overall quality of life of the subjects. Hence, Probiotic drinks incorporation into daily diet of IBS patient can be recommended for better management.

CHAPTER-7

LIMITATIONS AND FUTURE SCOPE OF THE STUDY

- There is a vast future scope as due to present circumstances the study only undertook qualitative parameters and evaluated them. The finding of the study can be further validated using various quantitative analyses.
- Also the study was purely online based hence it did not include population who did not have access to internet facility a field based study can include all strata of the community.
- The study was also limited to Delhi NCR which does not give the actual prevalence of Irritable bowel syndrome in India.
- Moreover the present focuses only on commercially available probiotic drinks majority of them being single strained. Multi-strained probiotic drink can also be brought into the study.
- There was a time constrain in the study which could have result in less impact on improving quality, that can improved with a study of longer duration of supplementation of probiotics.
- In order to ensure maximum compliance to the intervention education about importance of other factors like FODMAP foods and physical activity was also provided hence, the changes brought about might not be only due to probiotic intervention.

CHAPTER-8

BIBLIOGRAPHY

1. Abdulhussein, A., Mtasher, A. & Mutlag, S. (2018). PROBIOTICS AND PREBIOTICS. International Journal of Current Research. 10. 75341-75352. 10.24941/ijcr.33164.11.2018.
2. Adeyemo, M. A., Spiegel, B. M., & Chang, L. (2010). Meta-analysis: do irritable bowel syndrome symptoms vary between men and women?. *Alimentary pharmacology & therapeutics*, *32*(6), 738–755. https://doi.org/10.1111/j.1365-2036.2010.04409.
3. Agarwal, N., & Spiegel, B. M. (2011). The effect of irritable bowel syndrome on health-related quality of life and health care expenditures. *Gastroenterology clinics of North America*, *40*(1), 11–19. https://doi.org/10.1016/j.gtc.2010.12.013
4. Anbardan, S. J., Daryani, N. E., Fereshtehnejad, S. M., Taba Taba Vakili, S., Keramati, M. R., & Ajdarkosh, H. (2012). Gender Role in Irritable Bowel Syndrome: A Comparison of Irritable Bowel Syndrome Module (ROME III) Between Male and Female Patients. *Journal of neurogastroenterology and motility*, *18*(1), 70–77. https://doi.org/10.5056/jnm.2012.18.1.70
5. BECK, A. T., WARD, C. H., MENDELSON, M., MOCK, J., & ERBAUGH, J. (1961). An inventory for measuring depression. *Archives of general psychiatry*, *4*, 561–571. https://doi.org/10.1001/archpsyc.1961.01710120031004
6. Black, C. J., & Ford, A. C. (2020). Global burden of irritable bowel syndrome: trends, predictions and risk factors. *Nature reviews. Gastroenterology & hepatology*, *17*(8), 473–486. https://doi.org/10.1038/s41575-020-0286-8
7. Barrett, J. S., Canale, K. E., Gearry, R. B., Irving, P. M., & Gibson, P. R. (2008). Probiotic effects on intestinal fermentation patterns in patients with irritable bowel syndrome. *World journal of gastroenterology*, *14*(32), 5020–5024. https://doi.org/10.3748/wjg.14.5020
8. Belmonte, L., Beutheu Youmba, S., Bertiaux-Vandaële, N., Antonietti, M., Lecleire, S., Zalar, A., Gourcerol, G., Leroi, A. M., Déchelotte, P., Coëffier, M., & Ducrotté, P. (2012). Role of toll like receptors in irritable bowel syndrome: differential mucosal immune activation according to the disease subtype. *PloS one*, *7*(8), e42777. https://doi.org/10.1371/journal.pone.0042777
9. Brandt, L. J., Chey, W. D., Foxx-Orenstein, A. E., Schiller, L. R., Schoenfeld, P. S., Spiegel, B. M., Talley, N. J., & Quigley, E. M. (2009). An evidence-based position statement on the

management of irritable bowel syndrome. *The American journal of gastroenterology*, *104 Suppl 1*, S1−S35. https://doi.org/10.1038/ajg.2008.122

10. Berens, S., Banzhaf, P., Baumeister, D., Gauss, A., Eich, W., Schaefert, R., & Tesarz, J. (2020). Relationship between adverse childhood experiences and illness anxiety in irritable bowel syndrome - The impact of gender. *Journal of psychosomatic research*, *128*, 109846. https://doi.org/10.1016/j.jpsychores.2019.109846
11. Chua A. S. (2011). Prevalence of irritable bowel syndrome in northern India. *Journal of neurogastroenterology and motility*, *17*(1), 6−8. https://doi.org/10.5056/jnm.2011.17.1.6
12. Canavan, C., West, J., & Card, T. (2014). The epidemiology of irritable bowel syndrome. *Clinical epidemiology*, *6*, 71−80. https://doi.org/10.2147/CLEP.S40245
13. Canavan, C., West, J., & Card, T. (2014). Review article: the economic impact of the irritable bowel syndrome. *Alimentary pharmacology & therapeutics*, *40*(9), 1023−1034. https://doi.org/10.1111/apt.12938
14. Casadei, K., & Kiel, J. (2021). Anthropometric Measurement. In *StatPearls*. StatPearls Publishing.
15. Choi, C. H., Jo, S. Y., Park, H. J., Chang, S. K., Byeon, J. S., & Myung, S. J. (2011). A randomized, double-blind, placebo-controlled multicenter trial of saccharomyces boulardii in irritable bowel syndrome: effect on quality of life. *Journal of clinical gastroenterology*, *45*(8), 679−683. https://doi.org/10.1097/MCG.0b013e318204593e
16. Cho, H. S., Park, J. M., Lim, C. H., Cho, Y. K., Lee, I. S., Kim, S. W., Choi, M. G., Chung, I. S., & Chung, Y. K. (2011). Anxiety, depression and quality of life in patients with irritable bowel syndrome. *Gut and liver*, *5*(1), 29−36. https://doi.org/10.5009/gnl.2011.5.1.29
17. Choi J, Song Y, Kim S, Park Y & Cho M (2010).A Relationship between Irritable Bowel Syndrome and Physical Activity in Women Nurses with Shift Work. Korean J Fam Med, 31:529-539 kjfm.2010.31.7.529.
18. Clavé P. (2011). Treatment of IBS-D with 5-HT3 receptor antagonists vs spasmolytic agents: similar therapeutical effects from heterogeneous pharmacological targets. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *23*(12), 1051−1055. https://doi.org/10.1111/j.1365-2982.2011.01808.x
19. Choghakhori, R., Abbasnezhad, A., Amani, R., & Alipour, M. (2017). Sex-Related Differences in Clinical Symptoms, Quality of Life, and Biochemical Factors in Irritable Bowel

Syndrome. *Digestive diseases and sciences*, *62*(6), 1550–1560. https://doi.org/10.1007/s10620-017-4554-6

20. Chey, W. D., Kurlander, J., & Eswaran, S. (2015). Irritable bowel syndrome: a clinical review. *JAMA*, *313*(9), 949–958. https://doi.org/10.1001/jama.2015.0954
21. Drossman, D., Morris, C. B., Hu, Y., Toner, B. B., Diamant, N., Whitehead, W. E., Dalton, C. B., Leserman, J., Patrick, D. L., & Bangdiwala, S. I. (2007). Characterization of health related quality of life (HRQOL) for patients with functional bowel disorder (FBD) and its response to treatment. *The American journal of gastroenterology*, *102*(7), 1442–1453. https://doi.org/10.1111/j.1572-0241.2007.01283.x
22. Daley, A. J., Grimmett, C., Roberts, L., Wilson, S., Fatek, M., Roalfe, A., & Singh, S. (2008). The effects of exercise upon symptoms and quality of life in patients diagnosed with irritable bowel syndrome: a randomised controlled trial. *International journal of sports medicine*, *29*(9), 778–782. https://doi.org/10.1055/s-2008-1038600
23. Dale, H. F., Rasmussen, S. H., Asiller, Ö. Ö., & Lied, G. A. (2019). Probiotics in Irritable Bowel Syndrome: An Up-to-Date Systematic Review. *Nutrients*, *11*(9), 2048. https://doi.org/10.3390/nu11092048
24. Dekel, R., Drossman, D. A., & Sperber, A. D. (2013). The use of psychotropic drugs in irritable bowel syndrome. *Expert opinion on investigational drugs*, *22*(3), 329–339. https://doi.org/10.1517/13543784.2013.761205
25. Didari, T., Mozaffari, S., Nikfar, S., & Abdollahi, M. (2015). Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis. *World journal of gastroenterology*, *21*(10), 3072–3084. https://doi.org/10.3748/wjg.v21.i10.3072
26. Enck, P., Aziz, Q., Barbara, G., Farmer, A. D., Fukudo, S., Mayer, E. A., Niesler, B., Quigley, E. M., Rajilić-Stojanović, M., Schemann, M., Schwille-Kiuntke, J., Simren, M., Zipfel, S., & Spiller, R. C. (2016). Irritable bowel syndrome. *Nature reviews. Disease primers*, *2*, 16014. https://doi.org/10.1038/nrdp.2016.14
27. Efskind, P. S., Bernklev, T., & Vatn, M. H. (1996). A double-blind placebo-controlled trial with loperamide in irritable bowel syndrome. *Scandinavian journal of gastroenterology*, *31*(5), 463–468. https://doi.org/10.3109/00365529609006766
28. Endo, Y., Shoji, T., & Fukudo, S. (2015). Epidemiology of irritable bowel syndrome. *Annals of gastroenterology*, *28*(2), 158–159.

29. Ford, A. C., Quigley, E. M., Lacy, B. E., Lembo, A. J., Saito, Y. A., Schiller, L. R., Soffer, E. E., Spiegel, B. M., & Moayyedi, P. (2014). Efficacy of prebiotics, probiotics, and synbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis. *The American journal of gastroenterology*, *109*(10), 1547–1562. https://doi.org/10.1038/ajg.2014.202
30. Ferreira, A. I., Garrido, M., & Castro-Poças, F. (2020). Irritable Bowel Syndrome: News from an Old Disorder. *GE Portuguese journal of gastroenterology*, *27*(4), 255–268. https://doi.org/10.1159/000503757
31. Fond, G., Loundou, A., Hamdani, N., Boukouaci, W., Dargel, A., Oliveira, J., Roger, M., Tamouza, R., Leboyer, M., & Boyer, L. (2014). Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. *European archives of psychiatry and clinical neuroscience*, *264*(8), 651–660. https://doi.org/10.1007/s00406-014-0502-z
32. Fuller R. Probiotics a Critical Review. Wymondham, UK: Horizon Scientific; 1999. Probiotics for farm animals; pp. 15–22.
33. Felis, G. E., & Dellaglio, F. (2007). Taxonomy of Lactobacilli and Bifidobacteria. *Current issues in intestinal microbiology*, *8*(2), 44–61.
34. Gibson, P. R., & Shepherd, S. J. (2005). Personal view: food for thought--western lifestyle and susceptibility to Crohn's disease. The FODMAP hypothesis. *Alimentary pharmacology & therapeutics*, *21*(12), 1399–1409. https://doi.org/10.1111/j.1365-2036.2005.02506.x
35. Gibson, P. R., & Shepherd, S. J. (2010). Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. *Journal of gastroenterology and hepatology*, *25*(2), 252–258. https://doi.org/10.1111/j.1440-1746.2009.06149.x
36. Gralnek, I. M., Hays, R. D., Kilbourne, A., Naliboff, B., & Mayer, E. A. (2000). The impact of irritable bowel syndrome on health-related quality of life. *Gastroenterology*, *119*(3), 654–660. https://doi.org/10.1053/gast.2000.16484
37. Grundmann, O., & Yoon, S. L. (2014). Complementary and alternative medicines in irritable bowel syndrome: an integrative view. *World journal of gastroenterology*, *20*(2), 346–362. https://doi.org/10.3748/wjg.v20.i2.346
38. Gendi, R., & Jahan, N. (2020). Pharmacological and Non-pharmacological Treatments of Irritable Bowel Syndrome and Their Impact on the Quality of Life: A Literature Review. *Cureus*, *12*(7), e9324. https://doi.org/10.7759/cureus.9324

39. Ghoshal, U. C., Abraham, P., Bhatt, C., Choudhuri, G., Bhatia, S. J., Shenoy, K. T., Banka, N. H., Bose, K., Bohidar, N. P., Chakravartty, K., Shekhar, N. C., Desai, N., Dutta, U., Das, G., Dutta, S., Dixit, V. K., Goswami, B. D., Jain, R. K., Jain, S., Jayanthi, V., ⋯ Vij, J. C. (2008). Epidemiological and clinical profile of irritable bowel syndrome in India: report of the Indian Society of Gastroenterology Task Force. *Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology*, *27*(1), 22–28.
40. Ghoshal, U. C., & Singh, R. (2017). Frequency and risk factors of functional gastro-intestinal disorders in a rural Indian population. *Journal of gastroenterology and hepatology*, *32*(2), 378–387. https://doi.org/10.1111/jgh.13465
41. Hulisz D. (2004). The burden of illness of irritable bowel syndrome: current challenges and hope for the future. *Journal of managed care pharmacy : JMCP*, *10*(4), 299–309. https://doi.org/10.18553/jmcp.2004.10.4.299
42. Herman, J., Pokkunuri, V., Braham, L., & Pimentel, M. (2010). Gender distribution in irritable bowel syndrome is proportional to the severity of constipation relative to diarrhea. *Gender medicine*, *7*(3), 240–246. https://doi.org/10.1016/j.genm.2010.06.007
43. Holtmann, G. J., Ford, A. C., & Talley, N. J. (2016). Pathophysiology of irritable bowel syndrome. *The lancet. Gastroenterology & hepatology*, *1*(2), 133–146. https://doi.org/10.1016/S2468-1253(16)30023-1
44. Holten, K. B., Wetherington, A., & Bankston, L. (2003). Diagnosing the patient with abdominal pain and altered bowel habits: is it irritable bowel syndrome?. *American family physician*, *67*(10), 2157–2162.
45. Holzapfel, W. H., Haberer, P., Geisen, R., Björkroth, J., & Schillinger, U. (2001). Taxonomy and important features of probiotic microorganisms in food and nutrition. *The American journal of clinical nutrition*, *73*(2 Suppl), 365S–373S. https://doi.org/10.1093/ajcn/73.2.365s
46. Hungin, A., Mitchell, C. R., Whorwell, P., Mulligan, C., Cole, O., Agréus, L., Fracasso, P., Lionis, C., Mendive, J., Philippart de Foy, J. M., Seifert, B., Wensaas, K. A., Winchester, C., de Wit, N., & European Society for Primary Care Gastroenterology (2018). Systematic review: probiotics in the management of lower gastrointestinal symptoms - an updated evidence-based international consensus. *Alimentary pharmacology & therapeutics*, *47*(8), 1054–1070. https://doi.org/10.1111/apt.14539
47. Harvie, R. M., Chisholm, A. W., Bisanz, J. E., Burton, J. P., Herbison, P., Schultz, K., & Schultz, M. (2017). Long-term irritable bowel syndrome symptom control with reintroduction

of selected FODMAPs. *World journal of gastroenterology*, *23*(25), 4632−4643. https://doi.org/10.3748/wjg.v23.i25.4632

48. Hou, X., Chen, S., Zhang, Y., Sha, W., Yu, X., Elsawah, H., Afifi, A. F., El-Khayat, H. R., Nouh, A., Hassan, M. F., Fatah, A. A., Rucker Joerg, I., Sánchez Núñez, J. M., Osthoff Rueda, R., Jurkowska, G., Walczak, M., Malecka-Panas, E., Linke, K., Hartleb, M., & Janssen-van Solingen, G. (2014). Quality of life in patients with Irritable Bowel Syndrome (IBS), assessed using the IBS-Quality of Life (IBS-QOL) measure after 4 and 8 weeks of treatment with mebeverine hydrochloride or pinaverium bromide: results of an international prospective observational cohort study in Poland, Egypt, Mexico and China. *Clinical drug investigation*, *34*(11), 783−793. https://doi.org/10.1007/s40261-014-0233-y
49. Ishaque, S. M., Khosruzzaman, S. M., Ahmed, D. S., & Sah, M. P. (2018). A randomized placebo-controlled clinical trial of a multi-strain probiotic formulation (Bio-Kult®) in the management of diarrhea-predominant irritable bowel syndrome. *BMC gastroenterology*, *18*(1), 71. https://doi.org/10.1186/s12876-018-0788-9
50. Johannesson, E., Simrén, M., Strid, H., Bajor, A., & Sadik, R. (2011). Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. *The American journal of gastroenterology*, *106*(5), 915−922. https://doi.org/10.1038/ajg.2010.480
51. Johannesson, E., Ringström, G., Abrahamsson, H., & Sadik, R. (2015). Intervention to increase physical activity in irritable bowel syndrome shows long-term positive effects. World journal of gastroenterology, 21(2), 600−608. https://doi.org/10.3748/wjg.v21.i2.600
52. Johannesson, E., Jakobsson Ung, E., Sadik, R., & Ringström, G. (2018). Experiences of the effects of physical activity in persons with irritable bowel syndrome (IBS): a qualitative content analysis. *Scandinavian journal of gastroenterology*, *53*(10-11), 1194−1200. https://doi.org/10.1080/00365521.2018.1519596
53. Jadallah, K. A., Kullab, S. M., & Sanders, D. S. (2014). Constipation-predominant irritable bowel syndrome: a review of current and emerging drug therapies. *World journal of gastroenterology*, *20*(27), 8898−8909. https://doi.org/10.3748/wjg.v20.i27.8898
54. Jones, R., Latinovic, R., Charlton, J., & Gulliford, M. (2006). Physical and psychological co-morbidity in irritable bowel syndrome: a matched cohort study using the General Practice Research Database. *Alimentary pharmacology & therapeutics*, *24*(5), 879−886. https://doi.org/10.1111/j.1365-2036.2006.03044.x

55. Kaplan, A., Franzen, M. D., Nickell, P. V., Ransom, D., & Lebovitz, P. J. (2014). An open-label trial of duloxetine in patients with irritable bowel syndrome and comorbid generalized anxiety disorder. *International journal of psychiatry in clinical practice*, *18*(1), 11−15. https://doi.org/10.3109/13651501.2013.838632
56. Kechagia, M., Basoulis, D., Konstantopoulou, S., Dimitriadi, D., Gyftopoulou, K., Skarmoutsou, N., &Fakiri, E. M. (2013). Health benefits of probiotics: a review. ISRN nutrition, 2013, 481651. https://doi.org/10.5402/2013/481651
57. Kabra, N., & Nadkarni, A. (2013). Prevalence of depression and anxiety in irritable bowel syndrome: A clinic based study from India. *Indian journal of psychiatry*, *55*(1), 77−80. https://doi.org/10.4103/0019-5545.105520
58. Koloski, N. A., Talley, N. J., & Boyce, P. M. (2002). Epidemiology and health care seeking in the functional GI disorders: a population-based study. *The American journal of gastroenterology*, *97*(9), 2290−2299. https://doi.org/10.1111/j.1572-0241.2002.05783.x
59. Lacy B. E. (2003). Irritable bowel syndrome: a primer on management. *Reviews in gastroenterological disorders*, *3 Suppl 3*, S32−S42.
60. Lacy, B. E., Chey, W. D., & Lembo, A. J. (2015). New and Emerging Treatment Options for Irritable Bowel Syndrome. *Gastroenterology & hepatology*, *11*(4 Suppl 2), 1−19.
61. Lavö, B., Stenstam, M., & Nielsen, A. L. (1987). Loperamide in treatment of irritable bowel syndrome--a double-blind placebo controlled study. *Scandinavian journal of gastroenterology. Supplement*, *130*, 77−80. https://doi.org/10.3109/00365528709091003
62. Locke, G. R., 3rd, Weaver, A. L., Melton, L. J., 3rd, & Talley, N. J. (2004). Psychosocial factors are linked to functional gastrointestinal disorders: a population based nested case-control study. *The American journal of gastroenterology*, *99*(2), 350−357. https://doi.org/10.1111/j.1572-0241.2004.04043.x
63. Ladep, N. G., Obindo, T. J., Audu, M. D., Okeke, E. N., & Malu, A. O. (2006). Depression in patients with irritable bowel syndrome in Jos, Nigeria. *World journal of gastroenterology*, *12*(48), 7844−7847. https://doi.org/10.3748/wjg.v12.i48.7844
64. Lee, S. H., Joo, N. S., Kim, K. M., & Kim, K. N. (2018). The Therapeutic Effect of a Multistrain Probiotic on Diarrhea-Predominant Irritable Bowel Syndrome: A Pilot Study. *Gastroenterology research and practice*, *2018*, 8791916. https://doi.org/10.1155/2018/8791916

65. Lydiard, R. B., & Falsetti, S. A. (1999). Experience with anxiety and depression treatment studies: implications for designing irritable bowel syndrome clinical trials. *The American journal of medicine*, *107*(5A), 65S−73S. https://doi.org/10.1016/s0002-9343(99)00082-0
66. Lovell, R. M., & Ford, A. C. (2012). Effect of gender on prevalence of irritable bowel syndrome in the community: systematic review and meta-analysis. *The American journal of gastroenterology*, *107*(7), 991−1000. https://doi.org/10.1038/ajg.2012.131
67. Lovell, R. M., & Ford, A. C. (2012). Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, *10*(7), 712−721.e4. https://doi.org/10.1016/j.cgh.2012.02.029
68. Lee, S. K., Yoon, D. W., Lee, S., Kim, J., Choi, K. M., & Shin, C. (2017). The association between irritable bowel syndrome and the coexistence of depression and insomnia. *Journal of psychosomatic research*, *93*, 1−5. https://doi.org/10.1016/j.jpsychores.2016.12.007
69. Manning, A. P., Thompson, W. G., Heaton, K. W., & Morris, A. F. (1978). Towards positive diagnosis of the irritable bowel. *British medical journal*, *2*(6138), 653−654. https://doi.org/10.1136/bmj.2.6138.653
70. Minocha, A., Johnson, W. D., Abell, T. L., & Wigington, W. C. (2006). Prevalence, sociodemography, and quality of life of older versus younger patients with irritable bowel syndrome: a population-based study. *Digestive diseases and sciences*, *51*(3), 446−453. https://doi.org/10.1007/s10620-006-3153-8
71. Makharia, G. K., Verma, A. K., Amarchand, R., Goswami, A., Singh, P., Agnihotri, A., Suhail, F., & Krishnan, A. (2011). Prevalence of irritable bowel syndrome: a community based study from northern India. *Journal of neurogastroenterology and motility*, *17*(1), 82−87. https://doi.org/10.5056/jnm.2011.17.1.82
72. MacPherson, H., Tilbrook, H., Bland, J. M., Bloor, K., Brabyn, S., Cox, H., Kang'ombe, A. R., Man, M. S., Stuardi, T., Torgerson, D., Watt, I., & Whorwell, P. (2012). Acupuncture for irritable bowel syndrome: primary care based pragmatic randomised controlled trial. *BMC gastroenterology*, *12*, 150. https://doi.org/10.1186/1471-230X-12-150
73. Matricon, J., Meleine, M., Gelot, A., Piche, T., Dapoigny, M., Muller, E., & Ardid, D. (2012). Review article: Associations between immune activation, intestinal permeability and the irritable bowel syndrome. *Alimentary pharmacology & therapeutics*, *36*(11-12), 1009−1031. https://doi.org/10.1111/apt.12080

74. Meleine, M., & Matricon, J. (2014). Gender-related differences in irritable bowel syndrome: potential mechanisms of sex hormones. *World journal of gastroenterology*, *20*(22), 6725–6743. https://doi.org/10.3748/wjg.v20.i22.6725

75. Mahmood, K., Riaz, R., Ul Haq, M. S., Hamid, K., & Jawed, H. (2020). Association of cigarette smoking with irritable bowel syndrome: A cross-sectional study. *Medical journal of the Islamic Republic of Iran*, *34*, 72. https://doi.org/10.34171/mjiri.34.72

76. Majeed, M., Nagabhushanam, K., Arumugam, S., Majeed, S., & Ali, F. (2018). *Bacillus coagulans* MTCC 5856 for the management of major depression with irritable bowel syndrome: a randomised, double-blind, placebo controlled, multi-centre, pilot clinical study. *Food & nutrition research*, *62*, 10.29219/fnr.v62.1218. https://doi.org/10.29219/fnr.v62.1218

77. Madempudi, R. S., Ahire, J. J., Neelamraju, J., Tripathi, A., & Nanal, S. (2019). Randomized clinical trial: the effect of probiotic Bacillus coagulans Unique IS2 vs. placebo on the symptoms management of irritable bowel syndrome in adults. *Scientific reports*, *9*(1), 12210. https://doi.org/10.1038/s41598-019-48554-x

78. Magge, S., & Lembo, A. (2012). Low-FODMAP Diet for Treatment of Irritable Bowel Syndrome. *Gastroenterology & hepatology*, *8*(11), 739–745.

79. Mearin, F., Lacy, B. E., Chang, L., Chey, W. D., Lembo, A. J., Simren, M., & Spiller, R. (2016). Bowel Disorders. *Gastroenterology*, S0016-5085(16)00222-5. Advance online publication. https://doi.org/10.1053/j.gastro.2016.02.031

80. Moraes-Filho, J. P., & Quigley, E. M. (2015). THE INTESTINAL MICROBIOTA AND THE ROLE OF PROBIOTICS IN IRRITABLE BOWEL SYNDROME: a review. *Arquivos de gastroenterologia*, *52*(4), 331–338. https://doi.org/10.1590/S0004-28032015000400015

81. Mudyanadzo, T. A., Hauzaree, C., Yerokhina, O., Architha, N. N., & Ashqar, H. M. (2018). Irritable Bowel Syndrome and Depression: A Shared Pathogenesis. *Cureus*, *10*(8), e3178. https://doi.org/10.7759/cureus.3178

82. Mezzasalma, V., Manfrini, E., Ferri, E., Sandionigi, A., La Ferla, B., Schiano, I., Michelotti, A., Nobile, V., Labra, M., & Di Gennaro, P. (2016). A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation. *BioMed research international*, *2016*, 4740907. https://doi.org/10.1155/2016/4740907

83. Nagaonkar S.N, Singh V.S, Kangule D.T &Sadhanala S (2018). A study of prevalence and determinants of irritable bowel syndrome in an urban slum community in Mumbai. J Datta MegheInst,Med Sci Univ,13:87-90.
84. Nanayakkara, W. S., Skidmore, P. M., O'Brien, L., Wilkinson, T. J., & Gearry, R. B. (2016). Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date. *Clinical and experimental gastroenterology*, *9*, 131–142. https://doi.org/10.2147/CEG.S86798
85. O'Mahony, S. M., Marchesi, J. R., Scully, P., Codling, C., Ceolho, A. M., Quigley, E. M., Cryan, J. F., & Dinan, T. G. (2009). Early life stress alters behavior, immunity, and microbiota in rats: implications for irritable bowel syndrome and psychiatric illnesses. *Biological psychiatry*, *65*(3), 263–267. https://doi.org/10.1016/j.biopsych.2008.06.026
86. O'Toole, P.W., Cooney, J.C. (2008). Probiotic bacteria influence the composition and function of the intestinal microbiota. Interdisciplinary Perspectives on Infectious Diseases, 10.1155/2008/175285. https://doi.org/10.1155/2008/175285
87. Prather, C. M., Camilleri, M., Zinsmeister, A. R., McKinzie, S., & Thomforde, G. (2000). Tegaserod accelerates orocecal transit in patients with constipation-predominant irritable bowel syndrome. *Gastroenterology*, *118*(3), 463–468. https://doi.org/10.1016/s0016-5085(00)70251-4
88. Paduano, D., Cingolani, A., Tanda, E., & Usai, P. (2019). Effect of Three Diets (Low-FODMAP, Gluten-free and Balanced) on Irritable Bowel Syndrome Symptoms and Health-Related Quality of Life. *Nutrients*, *11*(7), 1566. https://doi.org/10.3390/nu11071566
89. Patrick, D. L., Drossman, D. A., Frederick, I. O., DiCesare, J., & Puder, K. L. (1998). Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. *Digestive diseases and sciences*, *43*(2), 400–411. https://doi.org/10.1023/a:1018831127942
90. Posserud, I., Strid, H., Störsrud, S., Törnblom, H., Svensson, U., Tack, J., Van Oudenhove, L., & Simrén, M. (2013). Symptom pattern following a meal challenge test in patients with irritable bowel syndrome and healthy controls. *United European gastroenterology journal*, *1*(5), 358–367. https://doi.org/10.1177/2050640613501817
91. Park, J. M., Choi, M. G., Kim, Y. S., Choi, C. H., Choi, S. C., Hong, S. J., Jeong, J. J., Lee, D. H., Lee, J. S., Lee, K. J., Son, H. J., & Sung, I. K. (2009). Quality of life of patients with irritable bowel syndrome in Korea. *Quality of life research : an international journal of*

quality of life aspects of treatment, care and rehabilitation, *18*(4), 435–446. https://doi.org/10.1007/s11136-009-9461-7

92. Pedersen, N., Andersen, N. N., Végh, Z., Jensen, L., Ankersen, D. V., Felding, M., Simonsen, M. H., Burisch, J., & Munkholm, P. (2014). Ehealth: low FODMAP diet vs Lactobacillus rhamnosus GG in irritable bowel syndrome. *World journal of gastroenterology*, *20*(43), 16215–16226. https://doi.org/10.3748/wjg.v20.i43.16215
93. Preidis, G. A., Weizman, A. V., Kashyap, P. C., & Morgan, R. L. (2020). AGA Technical Review on the Role of Probiotics in the Management of Gastrointestinal Disorders. *Gastroenterology*, *159*(2), 708–738.e4. https://doi.org/10.1053/j.gastro.2020.05.060
94. Portincasa, P., Bonfrate, L., de Bari, O., Lembo, A., & Ballou, S. (2017). Irritable bowel syndrome and diet. *Gastroenterology report*, *5*(1), 11–19. https://doi.org/10.1093/gastro/gow047
95. Reding, K. W., Cain, K. C., Jarrett, M. E., Eugenio, M. D., & Heitkemper, M. M. (2013). Relationship between patterns of alcohol consumption and gastrointestinal symptoms among patients with irritable bowel syndrome. *The American journal of gastroenterology*, *108*(2), 270–276. https://doi.org/10.1038/ajg.2012.414
96. Rahman, M. M., Mahadeva, S., & Ghoshal, U. C. (2017). Epidemiological and clinical perspectives on irritable bowel syndrome in India, Bangladesh and Malaysia: A review. *World journal of gastroenterology*, *23*(37), 6788–6801. https://doi.org/10.3748/wjg.v23.i37.6788
97. Ramachandran, N. & Varghese, R. (2020). Cohort studies on potential use of homemade yogurt for systematic treatment of irritable bowel syndrome (IBS) for remission and cure. International Journal of Contemporary Medical Research, 7(2):B5-B10. 10.21276/ijcmr.2020.7.2.14
98. Rooprai, R., Bhat, N., Sainani, R. & Hegde, R. (2017). Epidemiology and clinical profiling of constipation predominant irritable bowel syndrome in India. International Journal of Medical and Health Research Volume 3; Issue 8; Page No. 28-33.
99. Rao, S. S., Yu, S., & Fedewa, A. (2015). Systematic review: dietary fibre and FODMAP-restricted diet in the management of constipation and irritable bowel syndrome. *Alimentary pharmacology & therapeutics*, *41*(12), 1256–1270. https://doi.org/10.1111/apt.13167
100. Spiegel B. M. (2011). Questioning the bacterial overgrowth hypothesis of irritable bowel syndrome: an epidemiologic and evolutionary perspective. *Clinical gastroenterology and*

hepatology : the official clinical practice journal of the American Gastroenterological Association, *9*(6), 461−e59. https://doi.org/10.1016/j.cgh.2011.02.030

101. Stasi, C., Bellini, M., Bassotti, G., Blandizzi, C., & Milani, S. (2014). Serotonin receptors and their role in the pathophysiology and therapy of irritable bowel syndrome. *Techniques in coloproctology*, *18*(7), 613−621. https://doi.org/10.1007/s10151-013-1106-8

102. Schumann, D., Langhorst, J., Dobos, G., & Cramer, H. (2018). Randomised clinical trial: yoga vs a low-FODMAP diet in patients with irritable bowel syndrome. *Alimentary pharmacology & therapeutics*, *47*(2), 203−211. https://doi.org/10.1111/apt.14400

103. Sisson, G., Ayis, S., Sherwood, R. A., & Bjarnason, I. (2014). Randomised clinical trial: A liquid multi-strain probiotic vs. placebo in the irritable bowel syndrome--a 12 week double-blind study. *Alimentary pharmacology & therapeutics*, *40*(1), 51−62. https://doi.org/10.1111/apt.12787

104. Sherwin, L. B., Ozoji, O. M., Boulineaux, C. M., Joseph, P. V., Fourie, N. H., Abey, S. K., Zhang, X., & Henderson, W. A. (2017). Gender and Weight Influence Quality of Life in Irritable Bowel Syndrome. *Journal of clinical medicine*, *6*(11), 103. https://doi.org/10.3390/jcm6110103

105. Sadeghian, M., Sadeghi, O., Hassanzadeh Keshteli, A., Daghaghzadeh, H., Esmaillzadeh, A., & Adibi, P. (2018). Physical activity in relation to irritable bowel syndrome among Iranian adults. *PloS one*, *13*(10), e0205806. https://doi.org/10.1371/journal.pone.0205806

106. Simrén, M., Abrahamsson, H., Svedlund, J., & Björnsson, E. S. (2001). Quality of life in patients with irritable bowel syndrome seen in referral centers versus primary care: the impact of gender and predominant bowel pattern. *Scandinavian journal of gastroenterology*, *36*(5), 545−552. https://doi.org/10.1080/003655201750153476

107. Simrén, M., Barbara, G., Flint, H. J., Spiegel, B. M., Spiller, R. C., Vanner, S., Verdu, E. F., Whorwell, P. J., Zoetendal, E. G., & Rome Foundation Committee (2013). Intestinal microbiota in functional bowel disorders: a Rome foundation report. *Gut*, *62*(1), 159−176. https://doi.org/10.1136/gutjnl-2012-302167

108. Sperber, A. D., Dumitrascu, D., Fukudo, S., Gerson, C., Ghoshal, U. C., Gwee, K. A., Hungin, A., Kang, J. Y., Minhu, C., Schmulson, M., Bolotin, A., Friger, M., Freud, T., & Whitehead, W. (2017). The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. *Gut*, *66*(6), 1075−1082. https://doi.org/10.1136/gutjnl-2015-311240

109. Sullivan, S. N., Wong, C., & Heidenheim, P. (1994). Does running cause gastrointestinal symptoms? A survey of 93 randomly selected runners compared with controls. *The New Zealand medical journal*, *107*(984), 328–331.

110. Shah, S. S., Bhatia, S. J., & Mistry, F. P. (2001). Epidemiology of dyspepsia in the general population in Mumbai. *Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology*, *20*(3), 103–106.

111. Sohn, W., Lee, O. Y., Kwon, J. G., Park, K. S., Lim, Y. J., Kim, T. H., Jung, S. W., & Kim, J. I. (2012). Tianeptine vs amitriptyline for the treatment of irritable bowel syndrome with diarrhea: a multicenter, open-label, non-inferiority, randomized controlled study. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *24*(9), 860–e398. https://doi.org/10.1111/j.1365-2982.2012.01945.x

112. Taneja, I., Deepak, K. K., Poojary, G., Acharya, I. N., Pandey, R. M., & Sharma, M. P. (2004). Yogic versus conventional treatment in diarrhea-predominant irritable bowel syndrome: a randomized control study. *Applied psychophysiology and biofeedback*, *29*(1), 19–33. https://doi.org/10.1023/b:apbi.0000017861.60439.95

113. Tang, Y. R., Yang, W. W., Wang, Y. L., & Lin, L. (2012). Sex differences in the symptoms and psychological factors that influence quality of life in patients with irritable bowel syndrome. *European journal of gastroenterology & hepatology*, *24*(6), 702–707. https://doi.org/10.1097/MEG.0b013e328351b2c2

114. Upadhyay, R., & Singh, A. Irritable Bowel Syndrome : The Indian Scenario. Corpus ID: 44010797

115. Vahedi, H., Ansari, R., Mir-Nasseri, M., & Jafari, E. (2010). Irritable bowel syndrome: a review article. *Middle East journal of digestive diseases*, *2*(2), 66–77.

116. Weaver, K. R., Melkus, G. D., & Henderson, W. A. (2017). Irritable Bowel Syndrome. *The American journal of nursing*, *117*(6), 48–55. https://doi.org/10.1097/01.NAJ.0000520253.57459.01

117. Weinberg, D. S., Smalley, W., Heidelbaugh, J. J., Sultan, S., & Amercian Gastroenterological Association (2014). American Gastroenterological Association Institute Guideline on the pharmacological management of irritable bowel syndrome. *Gastroenterology*, *147*(5), 1146–1148. https://doi.org/10.1053/j.gastro.2014.09.001

118. Whitehead, W. E., Palsson, O. S., Levy, R. R., Feld, A. D., Turner, M., & Von Korff, M. (2007). Comorbidity in irritable bowel syndrome. *The American journal of gastroenterology*, *102*(12), 2767−2776. https://doi.org/10.1111/j.1572-0241.2007.01540.x

119. Xie, C., Tang, Y., Wang, Y., Yu, T., Wang, Y., Jiang, L., & Lin, L. (2015). Efficacy and Safety of Antidepressants for the Treatment of Irritable Bowel Syndrome: A Meta-Analysis. *PloS one*, *10*(8), e0127815. https://doi.org/10.1371/journal.pone.0127815

120. Young, K.S., & Nayoung, K. (2018). Sex-Gender Differences in Irritable Bowel Syndrome J Neurogastroenterol Motil, Vol. 24 No. 4, pISSN: 2093-0879 eISSN: 2093-0887 https://doi.org/10.5056/jnm18082.

121. Zheng, L., Lai, Y., Lu, W., Li, B., Fan, H., Yan, Z., Gong, C., Wan, X., Wu, J., Huang, D., Wang, Y., Mei, Y., Li, Z., Jiang, Z., Liu, X., Ye, J., Yang, Y., Huang, H., & Xiao, J. (2015). Pinaverium Reduces Symptoms of Irritable Bowel Syndrome in a Multicenter, Randomized, Controlled Trial. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, *13*(7), 1285−1292.e1. https://doi.org/10.1016/j.cgh.2015.01.015

122. Zhang, Y., Li, L., Guo, C., Mu, D., Feng, B., Zuo, X., & Li, Y. (2016). Effects of probiotic type, dose and treatment duration on irritable bowel syndrome diagnosed by Rome III criteria: a meta-analysis. *BMC gastroenterology*, *16*(1), 62. https://doi.org/10.1186/s12876-016-0470-z

APPENDIX-I

SCREENING /SELECTION FORM

This form is intent for the use in study on "Impact evaluation of nutrition intervention on IBS patients and its effectiveness in terms of relief of symptoms and improvement in quality of life" using Rome IV criteria.

Name of the respondent*: _____

Age*: _____

Gender*:

1. Female
2. Male
3. Others: _____

Contact Number*: _____

I. Is there a recurrent abdominal pain on average at least 1day/week in last 3 months?
   A. Yes
   B. No

II. If yes , was the pain associated with any of the following (select multiple if present)

   A. Related to defecation

   B. Associated with a change in frequency of stool

   C. Associated with a change in form (appearance) of the stool

APPENDIX-II

QUESTIONNAIRE

PART-1

General Information

Name of respondent: _____
D.O.B. of respondent: _____
Age of respondent: _____ years
Number of members in household: _____
Occupation: _____
Contact no. :_____

PAST HISTORY:

History of DM/ HTN /TB/ BA/ IHD/ CVA/ EPILEPSY
History of similar illness in the past: _____
History of surgery: _____
Do you have any the following GI symptoms (select multiple if present):

1. Abdomen Pain
2. Cramps
3. Bloating
4. Flatulence
5. Irregular bowel movements
6. discomfort

Personal history:
History of alcohol intake: _____
History of smoking: _____
History of psychiatric illness: _____

Family history:
History of GI cancers/ inflammatory bowel disease/ celiac disease/ NCDs/others __

Other relevant history:
Relation to food: milk/ alcohol/ wheat etc.
Abnormal eating habits: _____

Medication history: _____
Anthropometric measurements:
Ht: _____
Wt: _____
BMI:_____

SOCIOECONOMIC STATUS

	Name	**Type of family**	**Gender (M/F)**	**Education**	**Occupation**
1.				1- Profession or Honours 2-Graduate 3- Intermediate or diploma 4-High school 5-Middle school 6- Primary school 7-Illiterate	1-Legislators, Senior Officials & Managers 2-Professionals 3- Technicians/Associate Professionals 4-Clerks 5-Skilled Workers, Shop/Market Sales Workers 6- Skilled Agricultural/Fishery Workers 7 Craft & Related Trade Workers 8-Plant/Machine Operators/Assemblers 9-Elementary Occupation 10- Unemployed

PART -2

Physical activity questionnaire

This questionnaire is to asses about the time you spend doing different types of physical activity in a typical week. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

* Required

Section1: Work

The time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment etc.

Question:1 Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like [carrying or lifting heavy loads, digging or construction work] for at least 10 minutes continuously? {if no go to question no.4}

A. Yes
B. No

Question:2 In a typical week, on how many days do you do vigorous intensity activities as part of your work?

_____

Question:3 How much time do you spend doing vigorous-intensity activities at work on a typical day?

_____

Question:4 Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking[or carrying light loads] for at least 10 minutes continuously?

A. Yes
B. No

Question:5 In a typical week, on how many days do you do moderate intensity activities as part of your work?

_____

Question: 6 How much time do you spend doing moderate-intensity activities at work on a typical day?

_____

Section 2: Travel to and from places

The next set of questions excludes the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship.

Question: 7 Do you walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places? {if no directly go to question no. 10}

A. Yes
B. No

Question:8 In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?

_____

Question:9 How much time do you spend walking or bicycling for travel on atypical day?

Section3: Recreational Activities

These questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure).

Question:10 Do you do any vigorous-intensity sports, fitness or recreational(leisure) activities that cause large increases in breathing or heart rate like [running or football] for at least 10 minutes continuously?{ if no go to question 13}

A. Yes
B. No

Question:11 In a typical week, on how many days do you do vigorous intensity sports, fitness or recreational (leisure) activities?

_____

Question:12 How much time do you spend doing vigorous-intensity sports,fitness or recreational activities on a typical day?

Question :13 Do you do any moderate-intensity sports, fitness or recreational(leisure) activities that cause a small increase in breathing or heart rate such as brisk walking, [cycling, swimming, volleyball]for at least 10 minutes continuously?

A. Yes
B. No

Question:14 In a typical week, on how many days do you do moderate intensity sports, fitness or recreational (leisure) activities?

_____

Question: 15 How much time do you spend doing moderate-intensity sports, fitness or recreational (leisure) activities on a typical day?

_____

Section4: sedentary behavior

The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, traveling in car, bus, train, reading, playing cards or watching television, but do not include time spent sleeping.

Question:16 How much time do you usually spend sitting or reclining on a typical day?

_____

PART -3

Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1. 0 I do not feel sad.
   1 I feel sad
   2 I am sad all the time and I can't snap out of it.
   3 I am so sad and unhappy that I can't stand it.
2. 0 I am not particularly discouraged about the future.
   1 I feel discouraged about the future.
   2 I feel I have nothing to look forward to.
   3 I feel the future is hopeless and that things cannot improve.
3. 0 I do not feel like a failure.
   1 I feel I have failed more than the average person.
   2 As I look back on my life, all I can see is a lot of failures.
   3 I feel I am a complete failure as a person.

4. 0 I get as much satisfaction out of things as I used to.
   1 I don't enjoy things the way I used to.
   2 I don't get real satisfaction out of anything anymore.
   3 I am dissatisfied or bored with everything.
5. 0 I don't feel particularly guilty
   1 I feel guilty a good part of the time.
   2 I feel quite guilty most of the time.
   3 I feel guilty all of the time.
6. 0 I don't feel I am being punished.
   1 I feel I may be punished.
   2 I expect to be punished.
   3 I feel I am being punished.
7. 0 I don't feel disappointed in myself.
   1 I am disappointed in myself.
   2 I am disgusted with myself.
   3 I hate myself.
8. 0 I don't feel I am any worse than anybody else.
   1 I am critical of myself for my weaknesses or mistakes.
   2 I blame myself all the time for my faults.
   3 I blame myself for everything bad that happens.
9. 0 I don't have any thoughts of killing myself.
   1 I have thoughts of killing myself, but I would not carry them out.
   2 I would like to kill myself.
   3 I would kill myself if I had the chance.
10. 0 I don't cry any more than usual.
   1 I cry more now than I used to.
   2 I cry all the time now.
   3 I used to be able to cry, but now I can't cry even though I want to.
11. 0 I am no more irritated by things than I ever was.
   1 I am slightly more irritated now than usual.
   2 I am quite annoyed or irritated a good deal of the time.
   3 I feel irritated all the time.
12. 0 I have not lost interest in other people.
   1 I am less interested in other people than I used to be.
   2 I have lost most of my interest in other people.
   3 I have lost all of my interest in other people.
13. 0 I make decisions about as well as I ever could.
   1 I put off making decisions more than I used to.
   2 I have greater difficulty in making decisions more than I used to.
   3 I can't make decisions at all anymore.
14. 0 I don't feel that I look any worse than I used to.
   1 I am worried that I am looking old or unattractive.
   2 I feel there are permanent changes in my appearance that make me look unattractive
   3 I believe that I look ugly.
15. 0 I can work about as well as before.
   1 It takes an extra effort to get started at doing something.

2 I have to push myself very hard to do anything.
3 I can't do any work at all.

16. 0 I can sleep as well as usual.
1 I don't sleep as well as I used to.
2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3 I wake up several hours earlier than I used to and cannot get back to sleep.
17. 0 I don't get more tired than usual.
1 I get tired more easily than I used to.
2 I get tired from doing almost anything.
3 I am too tired to do anything.
18. 0 My appetite is no worse than usual.
1 My appetite is not as good as it used to be.
2 My appetite is much worse now.
3 I have no appetite at all anymore.
19. 0 I haven't lost much weight, if any, lately.
1 I have lost more than five pounds.
2 I have lost more than ten pounds.
3 I have lost more than fifteen pounds.
20. 0 I am no more worried about my health than usual.
1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think of anything else.
21. 0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I have almost no interest in sex.
3 I have lost interest in sex completely.

PART -4

Food Frequency Questionnaire

For High FODMAP Foods

Sr. No.	Food groups and items	Daily	2-3 times a week	Weekly	Fortnightly	Monthly	Occasionally	Seasonally	Never
1.	**Grains, white roots and tubers and plantains**								

	Barley-based product								
	Freekeh								
	Laska noodles								
	Oat bread								
	Rye-based product								
	Sourdough, made with rye or kamut flour								
	Spelt, kernels/flakes								
	Whole wheat bread								
	Wheat-based products (bran, cereal, couscous, germ)								
	Inulin/Chicory root extract*								

2.	**PULSES**								
	Beans (adzuki, baked, black, borlotti, broad, fava, haricot, navy, red kidney, soya								
	Tofu, silken								
	Textured soy protein/TVP								
	Falafel								
	Split peas, boiled								
3.	**Nuts and Oilseeds**								
	Cashews								
	Pistachio								
4.	**Dairy &**								

	Alternatives								
	Buttermilk								
	Cream cheese								
	Cream,regular								
	Custard								
	Cow's and goat's milk								
	Ice cream								
	Kefir								
	Sour cream								
	Soy milk, made with soy beans								
	Yogurt								
5.	**vegetables**								
	Artichokes								
	Asparagus								
	Bittermelon/Karela								
	Cauliflower								
	Corn kernels, canned								
	Garlic								
	Green onion, white parts only								
	Leek bulbs								
	Lotus roots								
	Mushrooms								
	Onions								
	Onions, small pickled								
	Peas, green, thawed								
	Peas, sugar snap								
	Shallots								
	Tomato sauce with added garlic or onion								
6.	**fruits**								
	Apples								
	Apricots								
	Blackberries								
	Cherries								
	Other dried fruits								
	Figs								
	Guava, unripe								

	Lychee								
	Mango								
	Nectarines								
	Peaches								
	Pears (except prickly)								
	Plums								
	Watermelon								
7.	**sweeteners**								
	Agave								
	Apple syrup								
	Fructose								
	Fruit juice concentrates								
	High fructose corn syrup (called glucose-fructose in Canada)								
	Honey								
	Lactose								
	Polyols/sugar alcohols (sorbitol, mannitol, xylitol, maltitol, lactitol, and isomalt)								
8.	**Beverages**								
	Cordial (apple, orange, raspberry)								
	Juices made with high FODMAP fruits								
	Malted milk drink, original flavour								
	Rum								
	Certain teas (oolong, fennel, chamomile)								
	Certain teas, strongly infused (chai, dandelion,								

	and herbal containing chicory root)								
	Wine, only sticky/dessert type								

PART-5

Quality of life

Which of the following domains of IBS specific quality of life do you find impaired?

Quality of life domain	**Present**	**Absent**
Dysphoria (generalized dissatisfaction)		
Interference with activity		
Health worries		
Food avoidance		
Sexual issues		
Relationship issues		

APPENDIX-III

Department of Foods and Nutrition Faculty of Family and Community Sciences The Maharaja Sayajirao University of Baroda

CONSENT FORM

Research Topic: Impact evaluation of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life.

Primary Investigator: Prof.(Dr.) Mini Sheth

Student: Ms. Sharon Jacob

There is an increasing prevalence of irritable bowel syndrome (IBS) globally. It can be attributed to lifestyle changes, decreased physical activity and other internal and external factors. The disease may affect patients in terms of quality of life, work potential, mental and physical health etc. Accumulating evidence supports the view that an imbalance of gut bacteria contributes to IBS, and that increasing the mass of beneficial species of microbiota may reduce the numbers of pathogenic bacteria and help alleviate symptoms.

Hence keeping this in mind I am conducting my Master's research to assess impact of consumption of probiotics on IBS patients in DELHI NCR population and its effectiveness in terms of relief of symptoms and improvement in IBS quality of life.

For the same purpose, I require information about your general information, anthropometric data, medical and medication history (if any), socio-economic status and your willingness to purchase and consume probiotic drink for the period of 6 weeks. I will also require information post intervention it will take less than 15-30mins at a sitting. The information you have shared with me will remain confidential and shall be used only for research purpose.

If you have any further queries regarding this study, you can contact us.

Prof. (Dr.) Mini Sheth: 9879359229

Ms. Sharon Jacob: 8527602180

I _____ give my free and informed consent to participate in the study. I have been explained the purpose of the study and informed that I can quit the study at any point without giving any explanation.

Contact number: _____

Signature: _____

Department of Foods and Nutrition
Faculty of Family and Community Sciences
The Maharaja Sayajirao University of Baroda

सहमतिि

पत्र

अनसधा न ति षय : DELHI NCR की आबादी मेंं IBS रोगियो पर प्रोबायोगिक्स की खपत का प्रभाव मूल्ांकन और इसक लक्षणो को राहत और जीवन की IBS िुणवत्ता में सधार को सदभ मेंं इसकी प्रभावशीलता।

प्राथतमक जाचकिा: प्रो (डॉ।)
गमनी शठ

छात्: सशुी शरोन
जैकब

गवश्व स्तर पर गिइगिड़ा आत्र सडोम (IBS) का प्रिलन बढ़ रहा ह। इस जीवन शली मेंं बदलाव, शारीरक िगतगवध मेंं कमी और अन्य आतररक और बाह्य कारको को गलए गजम्मदार ठहराया जा सकता ह। रोिि जीवन की िुणवत्ता, काय क्षमता, मानगसक और शारीरक स्वास्थ्य आगद को सदभ मेंं रोगियो को प्रभागवत कर सकता ह। सगित प्रमाण इस दृगिकोण का समर्न करत हैं गक आत बक्टीरिया का असतलन IBS मेंं योिदान दता है, और इसस माइक्रोबायोिा की लाभकारी प्रजागतयो का द्रव्यमान बढ़न सके सख्या मेंं कमी हो सकती ह। रोिजनक बक्टीरिया और लक्षणो को कम करन मेंं मदद करता ह।

इसगलए मैंं इस ध्यान मेंं रखत हुए DELHI NCR की आबादी मेंं IBS रोगियो पर प्रोबायोगिक्स को प्रभाव और इसक लक्षणो को राहत और जीवन की IBS िुणवत्ता मेंं सधार केसदभ मेंं इसकी प्रभावशीलता का आकलन करन को गलए अपन मास्टर अनसधान का सिालन कर रहा ह।

इसी उद्देश्य को गलए, मझ आपकी सामान्य जानकारी, मानवशास्त्रीय डिा, गिगकत्सा और दवा को इगतहास (याद कोई हो), सामाजक-आर्ि क स्थर्ि गत और 6 सप्ताह की अवगध को गलए प्रोबायोगिक खरीदन और उपभोि करन की आपकी इच्छा को बार मेंं जानकारी की आवश्यकता ह। मझ सूिना पोस्ट हस्ताक्षप की भी आवश्यकता होिी,
यह एक बठक मेंं 15-30mins सके कम होिा। आपक द्वारा मर सार् साझा की िई जानकारी िोपनीय रहिी और इसका उपयोि कवल अनसधान प्रयोजन को गलए गकया जाएिा।

~~चगद आपक पास इस अध्ययन को ब मेंं कोई और प्न हैं, तो आप हमस सपक कर~~

सकत ह। प्रो। (डॉ।) गमनी शठ: 9879359229

सशुी शरोन जकब:
8527602180

मैंं _____अध्ययन मेंं भाि लन को गलए अपनी स्वत्र और सगित सहमगत दता ह। मझ अध्ययन का उद्देश्य समझाया िया है और बताया िया ह गक मैंं गकसी भी स्पिीकरण को गबना गकसी भी गबद पर अध्ययन छोड़ सकता ह।

सपक सख्या: _____

हस्ताक्षर: _____

APPENDIX-IV

COMPLIANCE SHEET

Name of respondent: _____
Age of respondent: _____ years
Contact no. : : _____

Tick days that you were able to consume probiotic drink.

week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week1							
Week2							
Week3							
Week4							
Week5							
Week6							

APPENDIX –V

POST INTERVENTION QUESTIONNAIRE

1. Email address*: _____
2. Name of the respondent*: _____
3. Gender*:
   - ○ Male
   - ○ Female
   - ○ Others:
4. AGE *: _____
5. Did you any health benefits on consumption of suggested probiotic drink?

○ Yes

○ No

6. Do you still have any the following GI symptoms (select multiple if present): Abdomen Pain
   Cramps
   Bloating
   Flatulence
   Irregular bowel movements
   Discomfort

PART -1

Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1. 0 I do not feel sad.
   1 I feel sad
   2 I am sad all the time and I can't snap out of it.
   3 I am so sad and unhappy that I can't stand it.
2. 0 I am not particularly discouraged about the future.

1 I feel discouraged about the future.
2 I feel I have nothing to look forward to.
3 I feel the future is hopeless and that things cannot improve.

3. 0 I do not feel like a failure.
1 I feel I have failed more than the average person.
2 As I look back on my life, all I can see is a lot of failures.
3 I feel I am a complete failure as a person.

4. 0 I get as much satisfaction out of things as I used to.
1 I don't enjoy things the way I used to.
2 I don't get real satisfaction out of anything anymore.
3 I am dissatisfied or bored with everything.

5. 0 I don't feel particularly guilty
1 I feel guilty a good part of the time.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. 0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. 0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

8. 0 I don't feel I am any worse than anybody else.
1 I am critical of myself for my weaknesses or mistakes.
2 I blame myself all the time for my faults.
3 I blame myself for everything bad that happens.

9. 0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. 0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry all the time now.
3 I used to be able to cry, but now I can't cry even though I want to.

11. 0 I am no more irritated by things than I ever was.
1 I am slightly more irritated now than usual.
2 I am quite annoyed or irritated a good deal of the time.
3 I feel irritated all the time.

12. 0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.

13. 0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions more than I used to.
3 I can't make decisions at all anymore.

14. 0 I don't feel that I look any worse than I used to.
    1 I am worried that I am looking old or unattractive.
    2 I feel there are permanent changes in my appearance that make me look unattractive
    3 I believe that I look ugly.
15. 0 I can work about as well as before.
    1 It takes an extra effort to get started at doing something.
    2 I have to push myself very hard to do anything.
    3 I can't do any work at all.
16. 0 I can sleep as well as usual.
    1 I don't sleep as well as I used to.
    2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
    3 I wake up several hours earlier than I used to and cannot get back to sleep.
17. 0 I don't get more tired than usual.
    1 I get tired more easily than I used to.
    2 I get tired from doing almost anything.
    3 I am too tired to do anything.
18. 0 My appetite is no worse than usual.
    1 My appetite is not as good as it used to be.
    2 My appetite is much worse now.
    3 I have no appetite at all anymore.
19. 0 I haven't lost much weight, if any, lately.
    1 I have lost more than five pounds.
    2 I have lost more than ten pounds.
    3 I have lost more than fifteen pounds.
20. 0 I am no more worried about my health than usual.
    1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
    2 I am very worried about physical problems and it's hard to think of much else.
    3 I am so worried about my physical problems that I cannot think of anything else.
21. 0 I have not noticed any recent change in my interest in sex.
    1 I am less interested in sex than I used to be.
    2 I have almost no interest in sex.
    3 I have lost interest in sex completely.

PART-2

Quality of life

Which of the following domains of IBS specific quality of life do you still find impaired?

Quality of life domain	Present	Absent
Dysphoria (generalized dissatisfaction)		
Interference with activity		
Health worries		
Food avoidance		
Sexual issues		
Relationship issues		