

A Salutogenic Approach To Treating Irritable Bowel Syndrome: A Narrative Review On The Efficacy Of The FODMAP-Diet To Manage IBS-Symptoms And Revive Quality Of Life

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Authors contributions

RV initiated the concept and design of the work and collected and analysed the secondary research data. RV, MV and JH conducted the analysis and interpretation of data. RV, MV and JH drafted the manuscript. MV and JH provided input and proof-read the manuscript. RV had primary responsibility for the final content. RV, MV and JH critically reviewed and approved the manuscript and agreed to be fully accountable for ensuring the integrity and accuracy of the work.

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1. Abstract

1.1. Introduction/Objective

The purpose of this review article is to critically evaluate the current studies that have investigated the efficacy of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) in gastrointestinal symptoms relief and QOL of patients with irritable bowel syndrome.

1.2. Methods

We systematically searched literature for studies that investigated the effect of the FODMAP-diet on IBS-symptoms and Food, IBS and Health-

related QoL of IBS-patients.

1.3. Results

A diet low in FODMAPs reduced IBS symptoms severity by a moderate-to-large extent as compared to a control diet. A diet low in FODMAPs also increases QoL scores, when compared with control diets and non-dietary interventions, such as probiotics, gut-directed hypnotherapy and yoga, across different studies.

1.4. Conclusion

A diet low in FODMAPs is an efficacious dietary therapy for reducing GI-symptoms and improving QOL in IBS-patients and these beneficial patient outcomes can be maintained on a personalised FODMAP-diet. This article contributes to the literature by proposing a Salutogenic approach to IBS, focusing on creating and sustaining QOL of IBS-patients through the FODMAP-diet as a personalized precision-nutrition therapy. Future research is warranted that utilizes precision microbiomics to design evidence-based effective precision diets for optimal health. Microbiomics and metabolomics can be used in identifying subsets of IBS-patients who exhibit a clinically meaningful response to the FODMAP-diet to personalize and tailor the diet to each individual IBS-patient, to alleviate patients' symptoms and improve their QOL.

Keywords:

Irritable Bowel Syndrome, FODMAP-diet, IBS-symptoms, Quality of Life, Salutogenesis Word count: 229

2. Introduction

IBS is a multifactorial, debilitating, complex, chronic, disorder of gut-brain interaction (DGBI) of heterogeneous pathogenesis, pathophysiology and clinical phenotype [1-11]. The initial diagnosis of IBS is based on symptomatology and diagnostic testing, in the absence of biomarkers to indicate organic causes of underlying IBS pathophysiology or detectable organic diseases [2,4,7,8,12,13]. The Rome IV criteria are used to diagnose IBS defining it as "recurrent abdominal pain present at least three days a week in the last 3 months, associated with at least two of the following criteria: 1) related to defecation, 2) associated with a change in frequency of stool, and 3) associated with a change in form/consistency of stool and irregular bowel habit (texture and frequency)"; symptoms should have persisted for at least six months prior to diagnosis [1,3, 6,9,14,15]. Based on the Rome IV criteria, four different subtypes of IBS are identified

according to the shape, consistency and pattern of stools, as per the Bristol Stool Scale (BSS): IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with mixed bowel habits (IBS-M), and unclassified IBS (IBS-U) [3, 7, 15-17].

IBS is one of the most common DGBIs globally, with prevalence rates between 5 and 25% worldwide, 10–16% in North America, 11.5% Europe, 7% in South Asia, 4-5% in India and China, 14% in Australasia, 17.5% in Latin America, 21% in South America and 5.8% in the Middle East and Africa [2,4,7,9,11, 18, 19]. IBS affects people of all ages, but is more likely to occur between 20 and 45 years of age [9]. Women are 1.5–3.0 times more likely to have IBS than men, reflecting a prevalence in women of 14% and in men of 8.9% [2, 4, 11, 13, 15,19] IBS leads to significant economic burdens and costs, including increased health care utilization and medical expenses, costing healthcare systems billions of dollars each year; absenteeism, presenteeism, reduced work functioning and productivity loss; impaired quality of life (QoL) [2,3, 4, 6-10, 12, 14, 15, 17-36]. The pathogenesis of IBS and its underlying molecular pathophysiology remain incompletely understood, but is suggested to involve visceral hypersensitivity, low-grade digestive tract inflammation, impaired gut barrier function, migrating motor complex and gut motility disturbances, altered gut microbiota composition, metabolomic profiles and microbial dysbiosis, and gut-brain axis [1-5, 7, 8, 9, 12, 14, 15, 20, 21, 23, 25, 31, 32, 38-47].

Diet plays a pivotal role in the pathophysiology of IBS. Approximately 60% to 89% of IBS patients have associated consumption of specific foods with GI-symptoms onset or exacerbation [3,14-17, 19, 21, 22, 24, 26, 38, 48, 50-53]. There fore, many IBS-patients have attempted dietary therapy for the treatment and control of their GI-symptoms and to enhance their QOL [7,10,36,37, 54-56]. The most evidence-supported dietary intervention for IBS is the FODMAP-diet, which is increasingly used as a first-line therapeutic dietary strategy [3, 8, 14, 26, 30, 36, 48, 50-53, 57-59]. FODMAP is an acronym that stands for Fermentable, Oligo-saccharides that comprise fructans (fructo-oligosaccharides or FOS), which are made up of short chains of fructose with a glucose on the end, and galacto-oligosaccharides (GOS), which are short chains of sucrose and galactose units, e.g. raffinose, stachyose, and verbascose; Di-saccharides (lactose); Mono-saccharides, e.g., fructose in excess of glucose; And Polyols, these are sugar alcohols, e.g., sorbitol, mannitol, maltitol, xylitol and isomalt [8, 14, 15, 17, 30, 36, 39, 43, 45, 50, 51, 58, 59- 61]. Three common functional properties of FODMAPs are the proposed mechanisms by which FODMAPs induce IBS-symptoms: a) limited absorption in the small intestine, resulting in increased luminal water content and subsequent distention of the small intestine; b) osmosis, which increases small bowel and lumen water content; and c) rapid fermentation of carbohydrates by gut microbes leading to gas production. These mechanisms, illustrated in, lead to symptoms of flatulence, abdominal bloating, luminal distension and pain associated with visceral hypersensitivity (abnormal pain signalling to chemical stimuli and/or mechanical distention and sensitized nociceptive and enteric neurons),

colonic hypermotility, and alteration of bowel habits due to abnormal motility responses [2, 7, 14, 15, 17, 18, 39,42, 43, 45, 47, 60-63]. The heterogeneity and instability of presenting GI-symptoms differ in extent and magnitude from patient to patient and symptoms fluctuates over time [25, 28,36, 50].

Abbreviations: FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; GI, gastrointestinal; SCFA, short-chain fatty acid. Adapted from ref. no. [34] The main proposed mechanisms of action of a diet low in FODMAPs are first, a reduction in small intestinal malabsorption of osmotically active short-chain carbohydrates, resulting in diminished intestinal water content and downstream effects on colonic fermentation and gas production; second, a decrease in visceral hypersensitivity via decreased LPS- a key component of gram-negative bacterial outer membrane-, which is associated with colonic barrier dysfunction and activation of mast cells and sensory neurons contributing to visceral hypersensitivity [14,31, 45-47, 60, 62]. Ultimately, FODMAP elimination or reduction results in a significant reduction in IBS-symptoms. Phase 1 of the diet entails the comprehensive restriction of FODMAPs to reduce GI-symptoms of pain, bloating, and improvement in both diarrhea and constipation and bowel habits. Phase 2 entails a re-challenge to assess FODMAP tolerance. This phase also entails a re-introduction of food constituents to assess response to FODMAPs to determine which FODMAP containing foods can be reintroduced into the diet. Phase 3 entails personalization of the diet to maintain symptoms control and enhance QOL [52, 62, 63].

There is a growing body of scientific evidence on the efficacy of the FODMAP-diet. Studies have shown that 50% to 86% of IBS-patients gain a clinically significant benefit from the LFD, i.e., elimination of FODMAPs from the diet is associated with beneficial patient outcomes [20, 23, 26, 29-31, 37, 38, 48, 49, 51, 52, 56, 58, 62, 64, 65, 66,67, 69]. There is a recognized need to better understand the efficacy of the FODMAP-diet in patient-reported outcomes. Two important and frequently assessed patient-reported outcomes are IBS-symptoms (type, severity and frequency) relief and QOL. QOL has gained prominence in medical and health research including studies on IBS, as well as in clinical care [46, 54,55]. Examining both IBS-symptoms and QOL as patient-reported outcomes is critical, because focusing on GI-symptoms only would present an incomplete measure of the patient's overall illness severity and fails to recognize the true impact of IBS on patients' QOL [46, 56,57]. The purpose of this review article is to critically evaluate the scientific evidence on the efficacy of the FODMAP-diet in IBS-symptoms and QOL as clinical endpoints.

3. Methods

3.1 Search strategy

We systematically searched the electronic databases Pub-Med/Medline, SCOPUS, and Web of Science. Titles, abstracts, and key words were searched for variations and combinations of the following terms: FODMAP

(s), saccharides, oligosaccharide, disaccharide, monosaccharide, galactooligosaccharides, fructan (s), fructose, galactans, lactose, polyol (s), sorbitol, mannitol, xylitol, maltitol, IBS, irritable bowel syndrome, and quality of life. Intervention and observational studies as well as systematic reviews and meta-analyses were included that examined the effect of the FODMAP-diet on IBS symptoms and quality of life in adult human subjects with IBS diagnosed according to the Rome III or IV criteria [1=Drossman, 2016, 26=Van Lanen et al., 2021]. Papers were excluded when they had been conducted in children, non-IBS patients or IBS patients with significant clinical co-morbidities. In the case of multiple papers referencing the same study, relevant data were extracted from both papers and included as a single study in the analysis. 6 observational studies were included in this review. The number of participants in the observational studies ranged from 52 to 234. 13 original studies, parallel or crossover trials, were included in this review. The number of participants in these trials ranged from 18 to 166. 4 systematic reviews and meta-analysis were included. All studies investigated the effect of a FODMAP-diet on GI-symptoms and QOL in IBS patients. The study duration ranged from 4 weeks to 44 months.

In terms of treatment type, studies were either controlled diet interventions or subjects in the studies received dietary education as an intervention. The control diets, provided or prescribed, comprised a traditional IBS diet, the subjects' habitual diet, typical diet for the country where the study was carried out, high-FODMAP diet, or a sham exclusion diet specifically designed for the study. Two studies administered the FODMAP-diet in combination with gut-directed hypnotherapy, probiotics and/or yoga.

3.2 Outcome assessment

The primary outcome of interest was IBS symptoms, measured by using one of the two following scales: first, the IBS-SSS [70], a self-reported questionnaire examining the severity and frequency of IBS-symptoms measured through stool frequency, stool consistency, abdominal pain, abdominal distension and bloating, intestinal transit, urgency, straining, a feeling of incomplete evacuation, frustration with bowel habits, and life interference of IBS. Improvements in overall IBS-symptoms are rated from 0 to 100 on a visual analogue scale (VAS), with a total score ranging from 0 to 500. Second, the disease-specific Birmingham IBS Symptom Questionnaire [71] that measures symptoms of abdominal pain, abdominal distension, malaise/nausea, constipation, diarrhea, heartburn, fatigue, depression, anxiety. The more frequent and severe the IBS symptoms are, the poorer the overall QOL tends to be.

The primary outcome of interest was QOL of IBS-patients measured with one or a combination of the following three instruments: First, health-related quality of life (HR-QOL), which refers to the holistic assessment of a patient's emotional, social and physical functioning in personal, work and social activities and close relationships, and wellbeing and illness experience [32]. HR-QOL reflects the physical, psychological and social impact of disease and treatment on daily functioning [32, 54, 55, 72]. The HR-QOL short form SF-36 [54] is an effective tool for the assessment

of disease (IBS) severity and treatment response (FODMAP-diet). The SF-36 evaluates limitations in usual role activities, social, physical and mental functioning (ability to work and engage in social and relationship activities), emotional problems (worry or feeling of loss or isolation due to having the disorder), bodily pain, general health perceptions, vitality and mental health [2, 54]. The advantage of such a general measure is that it can be applied to a wide variety of diseases and disorders. However, a problem with using general questionnaires is that they do not include questions about specific ways in which disorders can impact life and may, therefore miss unique and important aspects of how a particular illness affects a person's well-being and functioning. For this reason, disease-specific questionnaires are used to fully evaluate the QOL impact of a particular disease. The second instrument therefore is the IBS-QOL [73], a disease-specific questionnaire, made for the evaluation of one medical condition only, i.e., IBS. The IBS-QOL is the most extensively validated disease-specific QOL instrument to assess IBS disease impact and treatment response and has shown both accurate psychometric and methodological properties where a change of 10 to 14 points from baseline is clinically meaningful [54]. IBS-QOL assesses physical and psychosocial functioning of IBS-patients and consists of 8 subscales: dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual activity, and relationships [2, 3, 53, 73-75]. The third QOL instrument is the FR-QOL, which refers to the impact of diet, eating behaviours and relationship with food on a person's QOL. The FR-QOL questionnaire assesses the positive and negative aspects of eating and drinking, such as eating foods that triggers symptoms and not knowing which foods will affect symptoms [72, 76].

4. Results

4.1 Efficacy of the FODMAP diet in IBS-symptoms improvement and Quality of Life

Various retrospective, prospective, uncontrolled and controlled observational cohort studies and clinical trials from multiple centres around the world have assessed IBS-symptoms and QOL as primary and secondary patient outcomes to determine the efficacy of the FODMAP-diet. This review presents an overview of these studies. The two observational studies [29,77] that used the FR-QOL showed that GI-symptoms improvement and QOL can be maintained on a personalised FODMAP-diet (pFD) at 6 months from baseline. However, these two studies [29,77] also found that common difficulties participants noted with incorporating the LFD into their everyday lives were higher expense, eating out at friends' houses or restaurants, and traveling. The findings of these studies and other studies [14, 20, 38, 60, 69, 72] show that the dietary restrictions imposed on IBS-patient simple mentioning the FODMAP-diet affects socialization (given the social nature of eating), and it complicates eating away from home, thereby affecting patients' QOL. Furthermore, fear of aversive consequences of consuming high FODMAP foods (pain, urgency, diarrhoea or distension occurring during or immediately after a meal) has been found to result in excessive avoidance of activities or situations where patients expect GI symptoms to occur, such as social eating outside of one's home, resulting

in social isolation [2, 63, 78]. Social isolation and fear of symptoms occurrence (anticipatory food related anxiety) has been found to contribute profoundly to reduced QOL of IBS-patients [2]. This, in combination with the requirement of consistent monitoring of food intake can result in developing a negative relationship with food and research has shown that this is associated with poorer food-related QOL [2, 20, 53, 78, 79]. Never the less, despite the difficulties that patients encountered when adhering to the FODMAP-diet, findings of several studies [29, 57,79] contrast with the contention that the burden associated with applying the FODMAP-diet exerts an adverse impact on QOL of IBS-patients [36]. The inference is that although many IBS-patients do not find the LFD easy to incorporate into their lives due to its complex and restrictive nature, the perceived difficulties in FODMAP-diet implementation are outweighed by symptoms relief and enhanced QOL.

Various high-quality non-randomized and blinded RCTs that have been conducted to assess the effect of a LFD on GI-symptoms and QOL [33, 57, 66, 79-87] presented in. These trials consistently demonstrated that eliminating FODMAPs from the diet reduced IBS-symptoms. All trials reported superiority of the FODMAP-diet to other dietary regimens, including traditional dietary advice, habitual diets, sham dietary regimens, BDA (British Dietetic Association) and NICE (National Institute for Health and Care Excellence) dietary advice, which are not evidence-based and of ten times prove to be effective for IBS-patients. In these trials, a diet low in FODMAPs was more effective in reducing overall gastrointestinal symptoms and in improving QOL. Either gut-directed hypnotherapy, probiotics and/or yoga were found to be effective in conjunction with a LFD in improving IBS-symptoms and improving QOL as demonstrated by three comparative trials [41, 79,85]. One of the most promising findings from the observational studies and clinical trials is the lasting enhancement in QOL, long after the LFD treatment ends. Various observational studies and clinical trials showed significantly improved patients' symptoms relief and QOL long-term (after 6-12 months of treatment) compared to baseline [41, 56, 68, 81, 83, 88, 89].

The evidence from the reviews, systematic reviews and meta-analyses [20, 22, 26, 67] presented in, shows that an LFD can impart symptomatic relief and enhance QOL. Common findings of the studies were that greater adherence to the FODMAP-diet was significantly correlated with improved IBS-symptoms compared to a control diet, a high FODMAP-diet, sham-diet and non-dietary treatment and QOL improved when IBS-symptoms were reduced. This underscores the notion that impairment in QOL is, to a considerable extent, a consequence of IBS-symptoms frequency, type and severity. However, there were some discrepancies across studies, as most found improvements in QOL, whereas some did not find improvement in QOL after FODMAP diet implementation. The discrepancies in the findings can be attributed to substantial heterogeneity in methodology, including differences in the studied population (patients of all subtypes of IBS), differences in study design, such as a lack of randomization, blinding, heterogeneity between the clinical protocols, the choice of the placebo or the control group, assessment of adherence,

duration of intervention and sample size. Overall, the coherence between and consistency of findings across the studies evaluated in this review provide evidence of the efficacy of the FODMAP-diet in all IBS subtypes (IBS-D, IBS-C, IBS-M, IBS-U), although it must be noted that most studies have largely examined IBS-D patients. Of note, a lesser response of IBS-C patients has been reported in several, but not all studies [46, 82]. The explanation for these contrasting findings of less effectiveness of the LFD in IBS-C patients is the specific underlying pathophysiological mechanisms of FODMAPs [20, 42, 56]: The LFD decreases osmolarity and, thus, it decreases the water content in the intestinal lumen, which is advantageous in the management of IBS-D, as it reduces loose stools. However, it is disadvantageous in the management of IBS-C, as decreased osmolarity likely aggravates constipation. Taken together, the studies provide scientific evidence of the efficacy of the FODMAP-diet, which is important and clinically relevant in the treatment of IBS-symptoms and to enhance QOL.

5. Discussion

The studies reviewed in this article have provided significant scientific evidence of the efficacy of the FODMAP-diet in symptoms relief and enhancement of QOL of IBS-patients. However, to date, there is limited evidence from studies supporting the efficacy of the FODMAP diet long-term, as most of the studies examined FODMAP eliminations rather than provocations. Never the less, initial findings from studies that have examined the restriction, reintroduction and personalization phases hold promise, as these studies have shown that FODMAP reintroduction and personalization may normalize some of the effects of short-term FODMAP restriction. There is a need for further studies demonstrating the efficacy of the FODMAP-diet in the rechallenge/reintroduction phase and the personalization phase, investigating maintenance of symptom relief and improvement in QOL after FODMAP reintroduction with 1 or 2-year follow-up. Such studies will reassure the durability and long-term efficacy of the FODMAP-diet in symptoms improvement and enhancement of QOL of IBS-patient.

5.1 Salutogenic approach to the treatment of IBS

The FODMAP diet's effectiveness, customization, and flexibility make it a promising dietary therapy for IBS-patients, and we propose this dietary therapy as part of a Salutogenic approach to the treatment of IBS. 'Salutogenesis' means 'sources of health' from the Latin word 'salus', meaning 'health, and the Greek word 'genesis', meaning 'origin' [90, 91, 92]. A Salutogenic orientation to IBS focuses on improving patients' physical, mental and social functioning at work, at home and in society, and their QOL rather than the disease pathogenesis. A Salutogenic model of care encompasses treating IBS-patients from a holistic, integrative perspective, incorporating medical treatment regimens, lifestyle, personalized precision-nutrition, cognitive behavioural therapy/hypnotherapy and microbial therapies to reduce IBS-symptoms and enhance QOL. Salutogenic IBS-treatment requires synergy between gastroenterologists and allied healthcare professionals to deliver patient-

centred care to generate IBS-symptoms' relief and revive patients' QOL.

5.2 Potential potent alternative dietary treatments for IBS

An intriguing noveldietary intervention would be a comparison between the FODMAP-diet and two other potentially efficacious intervention diets. First, the Cedars-Sinai diet, also known as the 'Low Fermentation Eating' (LFE), originally developed by Dr. Pimentel and team, Cedars-Sinai Hospital, Los Angeles, California, USA [7]. This restrictive diet plan has two rules: 1) limiting fermentable carbohydrates, fibre and resistant starches in the diet that humans cannot digest and therefore become digested by fermenting bacteria and methanogenic archaea in the gut, resulting in gas and IBS-symptoms. Minimising the fermentation of undigested carbohydrates in the gut reduces the gases (carbon dioxide, hydrogen, hydrogen sulphide and methanogen) produced by gut microbes, thereby alleviating IBS-symptoms; 2) Meal spacing to keep the 'cleaning waves' in the GI-tract intact. This meal timing procedure will keep the small intestine clean of bacteria and residual foods, as well as residual enzymes that are secreted to move food through the GI-tract. This will reduce the likelihood of overgrowth of bacteria in the small intestine, especially in IBS-patients with impaired gut motility. Like the FODMAP-diet LFE eliminates the GOS in legumes and pulses, as well as the sugar alcohols (sweeteners). However, in contrast to the FODMAP-diet, LFE allows the Fructan vegetables and grains, as well as several sorbitol foods. Second, the Ketogenic diet, this restrictive diet is low in carbohydrates and therefore contains fewer fermentable foods. Hence, IBS-patients might feel better on this diet, because bacteria in the gut don't have enough nutrients to ferment. The Ketogenic diet, like the FODMAP-diet, excludes the fructans in grains foods, the GOS in legumes, and the fructose and sorbitol in several fruits. By contrast, the Keto-diet does include several polyol mannitol foods, the GOS in nuts, as well as some fructan vegetables.

A double-blind placebo-controlled cross-over trial in which IBS-patients in each trial arm receive the FODMAP-diet or Keto-diet or LFE for a period and then cross-over to the other dietary treatment would help to better identify food sensitivities and can demonstrate whether the FODMAP-diet, LFE and the Keto-diet are equally efficacious in managing IBS symptoms and enhancing QOL. Overall, the Keto-diet and LFE, in addition to the FODMAP-diet, open new avenues for investigating diet as a potential modulator of symptoms to enhance QOL of IBS-patients.

6. Conclusion

In conclusion, this comprehensive review article has elucidated the efficacy of the FODMAP-diet in IBS-symptoms management and enhancement of QOL of in IBS patients. Further research is required, firstly, to identify biomarkers associated with underlying biochemical and pathophysiologic mechanisms of IBS and its subtypes. Putative biomarkers, such as blood (serum), urine, saliva, fecal, immunological or tissue, micro RNAs [4,93] and their correlations with symptoms generation and severity in IBS will provide novel information regarding the pathophysiology of IBS.

Implementation of such biomarkers in clinical practice is critical for early diagnosis and treatment of IBS and to characterize improvements in QOL of IBS-patients. Second, research is warranted that investigates the predictive functional contribution of the gut microbiota to IBS and the crucial role of the gut microenvironment in shaping responses to dietary interventions. Of interest is precision microbiomics the use of the gut microbiome as a predictive biomarker of responsiveness to specific dietary constituents to design evidence-based effective precision diets for optimal health [40]. Precision microbiomics and metabolomics can be utilized to evaluate microbiome composition, richness and function, and microbiome-related metabolomic profiles (fecal metabolites and baseline fecal volatile organic compound) to identify individual microbial species in predicting responses to the LFD. The omics approaches can also be used in identifying subsets of IBS-patients who exhibit a clinically meaningful response to the LFD to determine in whom the FODMAP-diet is more efficacious. Elucidating the response of the gut microbiome to FODMAP elimination and reintroduction can shed light on the mechanisms through which an individual microbial ecosystem is affected by dietary components. The application of microbiomics and metabolomics and consequent manipulation of GI microbiota has promising potential in the treatment of IBS where the focus shifts from symptoms management towards disease modification. These are powerful tool for clinicians in the development of modulatory strategies to treat IBS, to personalize and tailor (dietary) therapy to each individual IBS-patient, to alleviate patients' symptoms and improve their QOL.

Word count: 3793 (excluding text, footnotes, literature citations, table, and legends). List of Abbreviations and terminology Dysbiosis Imbalance in intestinal microbiota (an increase in pathobionts and decrease in commensal) that alters the tight intercellular junctions (TJ) that allow access to pathogens and toxins (bacterial lipopolysaccharides, LPS). FODMAP Fermentable oligo-, di- and monosaccharides, and polyols Gut-brain axis The gut-brain axis comprises the enteric nervous system (ENS), the CNS, the gut wall in the periphery, and the hypothalamo-pituitary-adrenal (HPA) axis. The gut-brain axis serves as a key communication hub in the regulation of food intake, digestion and bowel movements. Gut microbiome the collective genomes of all the microbial organisms in the entire gut ecosystem. The gut microbiome is collectively the tens of trillions of microorganisms that live in interconnected populations on and in the body. The gut microbiome serves like a "physical barrier, preventing colonization by harmful pathogen. In the small intestine, distinct microbial populations also aid in digestion, metabolism and even immunity. Gut microbiota The gut microbiota are the collection of microorganisms (bacteria, viruses, fungi, and protozoa) present in the gut environment that play a crucial role in the maintenance of structural integrity of the gastrointestinal mucosal barrier, immunomodulation, metabolism of nutrients, and protection against pathogens and plays a crucial role in the maintenance of a healthy GI tract.

- IBS Irritable bowel syndrome
- IBS-C Irritable bowel syndrome with constipation

- IBS-D Irritable bowel syndrome with diarrhea
- IBS-M Irritable bowel syndrome with mixed stool pattern
- IBS-U Unspecified irritable bowel syndrome
- IBS-SSS Irritable bowel syndrome severity scoring
- LFD Low-FODMAP diet
- QoL Quality of life

7. Competing interests

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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9. Declaration of Generative AI and AI-assisted technologies

During the preparation of this work the author (s) used no AI tools in order to write this paper. The author (s) wrote, reviewed and edited the content as needed manually and take (s) full responsibility for the content of the publication.

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