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Review Article

The microbiota-gut-brain axis in irritable bowel syndrome: expert guidance on diagnosis and management

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ABSTRACT

Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal disorder marked by chronic abdominal pain, discomfort, and altered bowel habits, significantly affecting quality of life and healthcare costs. This review explores the role of the microbiota-gut-brain axis in IBS pathogenesis and discusses current and emerging management strategies. Dysbiosis, characterized by gut microbiota imbalance, contributes to inflammation, increased intestinal permeability, and disrupted gut-brain communication, exacerbating symptoms. Stress further impacts the gut microbiome, underscoring the psychological and gastrointestinal link in IBS. Diagnosis remains complex due to overlapping symptoms with other functional gastrointestinal disorders. The Rome IV criteria are standard for diagnosis, but Rome III may be more sensitive in India. Treatment is personalized, integrating dietary and lifestyle modifications with pharmacological options. Antispasmodics (e.g., mebeverine) provide pain relief, while rifaximin targets gut bacteria, and antidepressants address psychological factors and visceral hypersensitivity. Probiotics, especially Bifidobacterium and Lactobacillus strains, show promise in modulating gut microbiota and enhancing gut-brain signaling. Future IBS management aims to develop non-invasive biomarkers for improved diagnosis and identify novel therapeutic targets. Enhancing treatment accessibility and affordability, particularly in developing regions, remains critical. This review highlights the importance of understanding the microbiota-gut-brain axis to advance effective, individualized IBS treatments.

Keywords: Irritable bowel syndrome, Microbiota-gut-brain axis, Dysbiosis, Low-FODMAP diet, Antispasmodics, Functional gastrointestinal disorders

INTRODUCTION

Irritable bowel syndrome (IBS) is defined as a functional gastrointestinal disorder (FGID) characterized by chronic abdominal pain or discomfort, along with altered bowel habits. It is a common condition that affects a significant portion of the population, leading to substantial morbidity, work absenteeism, decreased productivity, and an economic burden on society. Consequently, IBS has a profound impact on the quality of life for affected individuals.[1,2] This disorder affects between 9% and 23% of people worldwide, with rates varying from 7% in South Asia to 21% in South America.[3] In India, primary care doctors frequently encounter IBS cases, while gastroenterologists typically manage 30% to 50% of patients. The most severe and complex cases are referred to specialists, highlighting the diverse range of IBS presentations.[4]

The diagnosis and management of IBS pose significant challenges due to the disorder's complex symptomatology and the intricacies involved in its treatment. Symptoms such as abdominal pain and bloating can vary widely among patients, making diagnosis difficult.[5] Additionally, cultural influences further complicate the diagnostic process, sometimes leading to misdiagnosis. The lack of specific biomarkers for IBS necessitates reliance on clinical criteria, such as the Rome IV, to establish a

diagnosis.[6] In terms of management, effective treatment requires a multifaceted approach that includes dietary modifications, medications, and psychological support, all of which can be difficult to implement consistently. The chronic nature of IBS also leads to frequent medical visits, placing an increased burden on healthcare systems. Despite these challenges, ongoing research continues to refine both diagnostic criteria and treatment strategies, underscoring the need for personalized management approaches.[5,6]

Meetings with Indian specialists were organized to gain deeper insights into the burden of IBS in India, including its diagnostic challenges, underlying pathophysiology, and management approaches. This review consolidates key literature and captures the perspectives of Indian experts on diagnosing and managing complex IBS cases, offering a comprehensive understanding of the disorder within the local context.

THE ROLE OF THE GUT MICROBIOME IN IRRITABLE BOWEL SYNDROME

The gut microbiome consists of various microbes, including bacteria, viruses, fungi, and protozoa, that contribute to vital functions such as nutrient metabolism, drug processing, maintaining the gut barrier, immune modulation, and protection against pathogens. Although only about one-third of bacterial species have been identified, the gastrointestinal tract is primarily dominated by Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria. An imbalance in gut flora, or dysbiosis, can result from the loss or overgrowth of specific organisms, reduced microbial diversity, or gene mutations. Evidence suggests that gut dysbiosis may play a role in the pathogenesis of IBS, as disturbances in the microbiome can lead to inflammatory changes, increased intestinal permeability, and oxidative stress. While studies have identified key differences in the gut microbiome of IBS patients, including higher levels of *Ruminococcus gnavus* and lower levels of beneficial bacteria like *Bifidobacterium* and *Lactobacillus*, a consistent microbiome signature for IBS remains elusive.

Meta-analyses have shown variations at different taxonomic levels, such as increased Firmicutes and decreased Bacteroidetes, but the methodologies and interpretations of these findings often vary. Additionally, recent research highlights the role of gut virome and its potential contribution to IBS. There is also growing interest in the connection between the gut microbiome and psychological conditions, as studies show links between gut microbial profiles in IBS patients and mental health conditions such as anxiety and depression.

Despite significant advancements, further research integrating metagenomics, metatranscriptomics, and metabolomics is necessary to fully understand the gut microbiome's role in IBS and related conditions.[7]

STRESS AND GUT MICROBIOME

Stress has a profound impact on gut microbiota, influencing both its composition and function. Various studies have shown that stress can lead to dysbiosis, an imbalance in the microbial community, which in turn affects gut health and immune responses. This interaction is largely mediated by the gut-brain axis, a bidirectional communication system between the gut and the brain, where stress alters gut microbiota, potentially impacting brain function and behavior. Moreover, stress can trigger the release of inflammatory mediators, altering microbial colonization patterns on the gut mucosal surface, which increases gut permeability. This allows harmful bacteria to enter the bloodstream, potentially exacerbating conditions like inflammatory bowel disease (IBD).[8] The complex relationship between stress and gut microbiota highlights the need for effective stress management strategies in treating conditions like IBS as further research is needed to better understand these interactions.[9]

MICROBIOTA-BRAIN-GUT AXIS IN IBS

The microbiota-brain-gut axis is a complex bidirectional communication network linking the central nervous system (CNS), autonomic nervous system (ANS), and enteric nervous system (ENS), and plays a key role in the pathophysiology of IBS. Normally, gut signals are relayed to the CNS autonomously, but in IBS, stress and other factors disrupt this communication, leading to symptoms like pain and discomfort. The vagus nerve, with its predominantly afferent fibers, serves as a critical pathway for interactions between gut microbiota and brain function. Dysbiosis, an imbalance in gut microbiota, is associated with IBS and affects neurotransmitter production, particularly serotonin (5-HT), which is essential for gut motility and sensitivity. Stress exacerbates IBS symptoms by altering gut motility and increasing intestinal permeability via the gut-brain axis. Probiotics have shown promise in modulating gut microbiota and improving gut-brain signaling, offering a potential therapeutic approach for managing IBS. Understanding the intricate microbiota-brain-gut axis is essential for developing effective treatments for IBS.

PATHOPHYSIOLOGY IN IBS

The pathogenesis of IBS is multifactorial, involving both host factors and environmental agents, although the precise mechanisms remain unclear. IBS is categorized as a brain-gut disorder, characterized by the interaction between the central nervous system and the myenteric plexus. This connection allows for the influence of emotions on intestinal motility and vice versa. Key factors traditionally associated with IBS include abnormalities in gut motility, altered visceral sensitivity, disrupted brain-gut communication, and psychosocial distress. Notably, patients with IBS often exhibit imbalances in neurotransmitters such as serotonin and dopamine, which can impact the clinical presentation of the disease. For

example, those with irritable bowel syndrome- diarrhea predominant (IBS-D) tend to have increased serotonin levels, while individuals with IBS-C generally display decreased levels. Recent insights highlight the role of intestinal sensitivity in IBS, with increased permeability and hypersensitivity to stimuli potentially leading to altered pain perception in some patients. The contribution of intestinal microbiota to IBS is an area of ongoing research, as these microorganisms may influence barrier function and mucosal inflammation, though findings in this domain are inconsistent. Psychosocial factors play a significant role in IBS, as psychological distress is commonly linked to symptom exacerbation, underscoring the importance of addressing mental health within treatment strategies. Furthermore, certain dietary components, particularly fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), have been identified as potential triggers for symptoms in sensitive individuals, indicating that diet is a crucial consideration in managing IBS.[10,11]

GASTROINTESTINAL AND EXTRA-INTESTINAL COMORBIDITIES

IBS is frequently associated with a range of gastrointestinal and extra-intestinal comorbidities, significantly affecting the quality of life of affected individuals. Research indicates a notable prevalence of psychiatric disorders, metabolic syndrome, and other systemic conditions among patients with IBS.

IBS commonly coexists with various gastrointestinal disorders, such as IBD. This overlap can exacerbate symptom severity and lead to increased healthcare utilization.[12] Additionally, patients with IBS may suffer from functional dyspepsia and gastroesophageal reflux disease (GERD), further complicating their clinical management.[13] A substantial proportion of IBS patients—approximately 80%—report psychiatric comorbidities, with anxiety and depression being the most prevalent.[14] Furthermore, conditions such as fibromyalgia and chronic fatigue syndrome are often observed in these patients, suggesting a potential central sensitization mechanism that may underlie IBS.[13] Additionally, metabolic syndrome, characterized by obesity and related disorders, has been associated with increased extra-intestinal manifestations in IBD, indicating that a similar trend may be present in IBS.[15] While IBS is primarily classified as a gastrointestinal disorder, its connection to various comorbidities emphasizes the necessity for a comprehensive treatment approach that addresses both physical and psychological health.

CHALLENGES IN DIAGNOSIS OF IBS

The diagnosis of IBS follows a stepwise approach, involving the exclusion of organic diseases and adherence to the Rome IV criteria. A thorough medical history and physical examination are essential, with close attention to alarming symptoms. Colonoscopy is recommended for patients with alarm symptoms or a family history of colorectal cancer. To rule out anemia or inflammation, a complete blood count, plasma C-reactive protein, and fecal calprotectin levels should be assessed. Identifying the IBS subtype is crucial for guiding treatment, which should be individualized and focused on the predominant symptoms.**Error! Bookmark not defined.**

The diagnosis of IBS is primarily clinical, relying on well-defined symptom-based criteria. Investigations are only recommended when specifically indicated, as the symptoms of IBS often overlap with other functional gastrointestinal disorders (FGIDs) and psychosocial factors, making accurate diagnosis challenging. Although no specific biomarker exists for IBS, the condition is diagnosed through a combination of symptoms without an identifiable organic cause.[2]

Various diagnostic criteria, such as Manning, Rome (I-IV), and Asian criteria, have been developed to aid in diagnosing IBS. A multicentric Indian study found the Manning criteria to be more sensitive than Rome I-III for diagnosing IBS in the Indian population. Although the Asian criteria proposed by the Asian Neurogastroenterology and Motility Association performed better than Rome criteria, they were still less effective than the Manning criteria. Studies consistently show that fulfilling the Rome criteria is associated with a positive IBS diagnosis, with less than 1% of patients meeting symptom-based criteria having an underlying organic disease.[2]

In a survey conducted in Bangladesh using the Asian Rome III questionnaire and endoscopy tests, 20.8% of patients with functional dyspepsia were found to have organic lesions explaining their symptoms. Given the similarities between the epidemiological profiles of Indian and Bangladeshi patients with FGIDs, it is reasonable to conclude that symptom-based Rome criteria may also be linked to organic diagnoses at similar rates in the Indian population.[2]

Diagnosis of IBS has evolved since its first discovery (Table 1), and today the Rome IV diagnostic criteria are used to diagnose IBS.[16]

ROME IV CRITERIA IN INDIA

An epidemiological study from northern India, involving 2774 subjects, reported that 14.9% had dyspepsia alone, 2.7% had IBS alone, and 4.1% exhibited dyspepsia-IBS overlap based on Rome III criteria. Another study using Rome IV criteria found a functional dyspepsia-IBS overlap in 4.4% of 1309 subjects from the same region. Additionally, a multicentric study noted that 3.2% of hospitalized COVID-19 patients developed IBS during a 12-month follow-up using the Rome IV criteria.[2]

A multinational survey revealed a lower global prevalence of IBS when diagnosed using Rome IV criteria compared

to Rome III. In internet surveys, the prevalence of IBS was 10.1% by Rome III criteria and 4.1% by Rome IV, while in household surveys, it was 3.5% and 1.5%, respectively.[2]

Indian IBS patients frequently report abdominal bloating and discomfort, symptoms that are not emphasized in the Rome IV criteria, while abdominal pain, a defining symptom in Rome IV, is less frequent and less severe in this population. The application of Rome IV criteria has also resulted in a shift within functional gastrointestinal disorder diagnoses, with higher rates of functional diarrhea and constipation compared to IBS.[2]

Given these observations, Rome III criteria may be more suitable for diagnosing IBS in India due to its higher sensitivity in capturing the symptom profile common among Indian patients.[2]

IBS includes subtypes such as IBS-D, constipation-predominant (IBS-C), mixed type (IBS-M), and undetermined IBS, with symptoms varying over time. Although IBS is not linked to severe diseases or higher mortality, its symptom overlap with organic conditions often leads to excessive invasive diagnostic procedures. This results in significant psychological, social, and economic burdens, including increased medication use, work absenteeism, reduced productivity, and frequent hospitalizations. The complex pathophysiology and diagnostic challenges emphasize the need for noninvasive biomarkers to improve diagnostic accuracy and cost-effectiveness in IBS management.[21]

For the evaluation of all IBS subtypes, a complete blood cell count and age-appropriate colorectal cancer screening are recommended. In patients with IBS with diarrhea, additional tests such as C-reactive protein or fecal calprotectin, IgA tissue transglutaminase (tTG) with or without quantitative IgA, and random biopsies during colonoscopy are advised. Where available, 75-selenium homocholic acid taurine (SeHCAT), fecal bile acids, or serum C4 levels may also be considered. For IBS with mixed bowel habits, similar testing with C-reactive protein or fecal calprotectin, as well as IgA tTG with or without quantitative IgA, is appropriate. A stool diary and abdominal radiography to assess stool accumulation should also be considered. In cases of IBS with constipation, particularly when severe or refractory to standard treatment, referral to a gastroenterology specialist for physiologic testing is warranted.[22]

MANAGEMENT OF IBS- DIET, LIFESTYLE AND STRESS MANAGEMENT

The management of IBS requires a personalized, holistic approach that integrates dietary, lifestyle, and stress management strategies, addressing the complex nature of IBS to improve patient outcomes. Tailored dietary interventions, such as the low FODMAP diet, have demonstrated significant efficacy in symptom management.[23,24] Research indicates that personalized dietary modifications can lead to substantial improvements in gastrointestinal symptoms.[25] Lifestyle modifications, such as regular physical activity and maintaining a consistent daily routine, contribute to symptom relief and overall well-being.[26] Additionally, stress management techniques, including mindfulness and cognitive behavioral therapy, play a vital role in addressing the psychological aspects of IBS.[26] While a holistic approach is beneficial, some suggest that the complexity of IBS may require more targeted pharmacological interventions alongside lifestyle changes, underscoring the need for continued research in this area.**Error! Bookmark not defined.**

Exercise plays a beneficial role in managing IBS by accelerating gastrointestinal transit, enhancing intestinal gas clearance in patients with bloating, and potentially increasing gut microbial diversity. These effects may positively influence symptoms via the gut-brain axis. In a randomized controlled trial involving 102 IBS patients, participation in a physical exercise program significantly improved IBS symptom severity scores compared to usual care ($p=0.003$), with benefits persisting for up to five years in some cases.[27]

Stress management is also crucial, as studies indicate that IBS patients experience higher stress levels compared to controls. The NICE guidelines for IBS treatment recommend encouraging patients to engage in leisure activities and incorporate more opportunities for relaxation to alleviate stress.[27]

PHARMACOLOGICAL MANAGEMENT OF IBS

The pharmacological management of IBS encompasses a variety of treatments, including antibiotics, antispasmodics, and psychiatric medications. Each of these plays a distinct role in addressing the multifaceted symptoms of IBS.

Antispasmodics, also known as spasmolytics, are a diverse group of medications that function through various mechanisms. Some agents, such as papaverine, mebeverine, and peppermint oil, work by directly relaxing smooth muscles. Others, like hyoscine butyl bromide, hyoscyamine, and pirenzepine, act by blocking cholinergic receptors, while another subset, including alverine citrate, pinaverium bromide, and otilonium bromide, inhibit calcium (Ca^{2+}) channels. Certain antispasmodics have mixed or poorly understood mechanisms of action. These medications primarily benefit patients with IBS-D by reducing colonic motility, improving stool form and frequency, and alleviating abdominal pain.[28]

Mebeverine is an antispasmodic medication indicated for alleviating abdominal pain associated with intestinal smooth muscle spasms and functional disorders related to IBS. It functions by relaxing intestinal muscles and regulating bowel activity. Research on mebeverine's efficacy in IBS began in the 1960s, prior to the introduction of the Rome I criteria for IBS diagnosis in

1992. A recently published systematic review concluded that mebeverine is an effective treatment for a diverse range of IBS patients experiencing abdominal pain, discomfort, distension, irregular bowel habits, bloating, constipation, and diarrhea, even if they do not fully meet the latest IBS criteria (Rome IV). The review also noted that mebeverine possesses a favorable safety profile, with a low incidence of adverse effects.[29]

Bacterial involvement in the pathogenesis of IBS has prompted the exploration of antibiotics as a treatment option. Research suggests that targeting specific gut bacteria, particularly with non-absorbable antibiotics like rifaximin, can alleviate IBS symptoms by reducing colonic bacterial overgrowth. While studies show rifaximin's efficacy in improving symptoms with minimal side effects, concerns remain about potential bacterial resistance and long-term safety. Further research is needed to confirm its optimal use and long-term benefits in managing IBS.[30]

Multiple studies suggest that probiotics may modulate gut microbiota, reduce pathogenic bacterial colonization, and moderately improve IBS symptoms. However, the findings are limited by the variety of strains and doses studied. Therefore, the systemic review and meta-analysis study conducted by Yang et al, aimed to evaluate the efficacy and safety of probiotics on overall IBS symptom improvement, individual symptom scores, and quality of life. The results showed that probiotics were more effective than placebo in improving overall IBS symptoms (RR=1.401, 95% CI 1.182–1.662, p<0.001) and quality of life (SMD=0.286, 95% CI 0.154–0.418, p<0.001). Shorter treatment durations (less than eight weeks) helped reduce distension (SMD=0.197, 95% CI 0.038–0.356, p=0.015), while high doses ($\geq 10^{10}$) and multiple probiotic strains benefited abdominal pain (SMD=0.412, p=0.007; SMD=0.590, p=0.032, respectively). However, no significant effect was seen on global symptom scores due to high inter-study heterogeneity, and there was no difference in adverse event frequency (RR=0.997, p=0.973). Authors concluded that, probiotics are an effective and tolerable treatment option for patients with IBS.[29]

The role of psychiatric medications, particularly antidepressants, in managing IBS is increasingly recognized due to the complex interplay between gastrointestinal and psychological factors. Antidepressants such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have shown efficacy in alleviating IBS symptoms by modulating the brain-gut axis and addressing both psychological and gastrointestinal components. TCAs are thought to improve symptoms through their analgesic properties, while SSRIs are particularly beneficial for patients with comorbid anxiety or depression, managing both emotional and gastrointestinal symptoms. Antidepressants may influence visceral pain perception and gut motility, but individual responses vary, necessitating further research to optimize treatment strategies and better understand the underlying mechanisms.[31-33] Pharmacological and non-pharmacological treatment approaches for various subtypes of IBS are mentioned in Table 2.

Table 1: Various criteria for diagnosis of IBS.

S. no.	Criteria
1	**The Manning criteria: 1987, Manning defined IBS as a collection of symptoms given below but did not describe their duration[17]**
	Onset of pain associated with more frequent bowel movements
	Onset of pain associated with more loose bowel movements
	Relief of pain with defecation
	Abdominal distension
	Sense of incomplete evacuation
	Passage of mucus
2	**Kruis criteria: 1984, symptoms need to be present >2 years, symptoms are as follows[18]**
	Flatulence, abdominal pain or bowel irregularity
	Description of character and severity of abdominal pain
	Alternating constipation and diarrhea
3	**Rome I: 1990, abdominal pain or discomfort relieved with defecation, or associated with a change in stool frequency or consistency + two or more of the following symptoms on at least 25% of occasions or days for three months**Error! Bookmark not defined.
	Altered stool form
	Altered stool frequency
	Altered stool passage
	Passage of mucus
	Bloating or distension
4	**Rome II: 1999, abdominal discomfort or pain that has two of three features for 12 weeks (need not be consecutive) in the last one year**Error! Bookmark not defined.

Continued.

S. no.	Criteria
	Onset associated with a change in frequency of stool
	Relieved with defecation
	Onset associated with a change in form of stool
5	**Rome III: 2006, IBS as recurrent abdominal pain or discomfort three days per month in the last three months associated with two or more of**Error! Bookmark not defined.
	Improvement with defecation
	Onset associated with a change in frequency of stool
	Onset associated with a change in form of stool
6	**Rome IV: 2016, patients have had recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with two or more of the following**[19]
	Defection
	A change in stool frequency
	A change in stool form or appearance
7	**Rome IV: 2021, IBS can be diagnosed if symptoms have lasted at least 8 weeks (therefore are chronic) and interfere with daily activities, cause worry, or interfere with quality of life**[20]
	Altered stool passage (straining and/or urgency)
	Nonbloody mucorrhea
	Abdominal bloating or subjective distention. This is common in IBS but is not required for diagnosis.

Table 2: Treatment of IBS based on the subtype (modified from Bonetto et al).[10]

Pharmacotherapy of diarrhea	Pharmacotherapy of constipation	Pharmacotherapy for abdominal pain	Non-pharmacological treatment
Loperamide	Psyllium	Dicyclomine	Dietary modification
Cholestyramine	Polyethylene glycol	Otilonium	Physical activity
Colestipol	Lubiprostone	Mebeverine	Stress reduction
Colesevelam	Linaclotide	Peppermint oil	Probiotics, prebiotics and synbiotics
Alosetron		Trimebutine	Acupuncture
Ondensetron		Desipramine	
Ondensetron		Amitriptyline	
Ramosetron		Paroxetine	
Eluxadoline		Sertraline	
Rifaximin			

For pain-predominant IBS, antispasmodics are the first-line treatment, with calcium channel blockers and NK2 receptor antagonists showing potential to replace anticholinergics in the future, particularly otilonium bromide, phloroglucinol, and mebeverine. For IBS with diarrhea (IBS-D), alosetron, eluxadoline, and rifaximin are FDA-approved, with eluxadoline also approved by the EMA. Alosetron has shown superior effectiveness compared to eluxadoline and rifaximin, though rifaximin remains the most tolerable short-term option due to minimal safety concerns, aside from potential antibiotic resistance. Linaclotide, approved by multiple regulatory bodies, is a preferred second-line treatment after laxatives/antispasmodics due to its efficacy, safety, and cost-effectiveness, outperforming other agents like lubiprostone, plecanatide, tegaserod, and tenapanor. While linaclotide is ranked highest for improving abdominal pain and complete spontaneous bowel movements (CSBM), tenapanor shows promise in reducing bloating and may become a second-line option. Gut-brain neuromodulators, such as TCAs, SSRIs, and SNRIs, may be used for severe pain or comorbid psychological disorders in moderate-to-severe IBS, although their safety and efficacy remain uncertain.[34]

PIPELINE THERAPIES IN IBS

Several new therapies are being explored to treat diarrhea-predominant IBS-D. These include ibudutant, blautix, BOS-589, solabegron, vibegron, olorinab, ebastine, and ORP-101, which target various mechanisms involved in IBS-D management (Table 3).[35]

The pharmacotherapy for IBS-C includes three FDA-approved medications: lubiprostone, linaclotide, and plecanatide. These agents alleviate constipation by increasing fluid secretion into the gastrointestinal (GI) tract, each utilizing distinct mechanisms of action targeting various receptors within the GI system. While traditional laxatives have shown limited benefit in IBS-C, emerging therapies like tenapanor, a sodium/hydrogen exchanger 3 inhibitor, offer promise but require further research. A patient-centric approach is essential, focusing on the primary symptoms of constipation, abdominal pain, and

bloating. Ongoing research may lead to novel therapies that better target specific symptoms, expanding the treatment landscape for IBS-C.[29]

Table 3: Pipeline therapies for IBS-D.[35]

Drug name (mechanism of action)	Clinical phase
Ibodutant (tachykinin NK2 receptors antagonist)	III
Solabegron (β3 adrenergic receptor agonist)	II
Ebastine (histamine -1 receptor antagonist)	II
Olorinab (cannabinoid CB2 receptor agonist)	II
Vibegron (β3 adrenergic receptor agonist)	II
Blautix (bacteria replacements; GI microbiome modulators)	II
ORP-101 (opioid kappa receptor antagonists)	II
BOS-589 (protein tyrosine kinase inhibitor)	II

In the past decade, there has been significant progress in exploring novel pathways and developing new treatments for both IBS-D and IBS-C. Promising agents for IBS-D include TPH1 inhibitors, bile acid binding resins, 5-HT3 receptor antagonists, opioid receptor antagonists, intestinal adsorbents, endocannabinoid receptor agonists, and local-acting antibiotics. For IBS-C, potential treatments involve GC-C activators, CIC-2 openers, NHE3 inhibitors, GLP-1 analogues, HMG-CoA reductase inhibitors, histamine H1 receptor antagonists, and IBAT antagonists.

However, challenges remain regarding the accessibility and affordability of these treatments, particularly in developing countries. Addressing this issue through comprehensive cost-effectiveness evaluations is crucial. Moreover, further studies are needed to better understand the pharmacokinetics and safety profiles of both approved and investigational treatments.[29]

EXPERTS' RECOMMENDATIONS

Pathophysiology

IBS is classified as a disorder of gut-brain interaction, with the gut microbiota playing a key role in symptom development.

Gut microbial dysbiosis is a potential target for therapeutic interventions in IBS management.

The relationship between gut microbiota, immune dysfunction, and low-grade inflammation is central to IBS pathophysiology.

Personalized treatment strategies based on the microbiota-gut-brain axis could improve patient outcomes.

Challenges and approach in diagnosis

IBS symptoms are non-specific, often overlapping with other FGIDs, and precise biomarkers are lacking in clinical practice.

Diagnosis is primarily clinical, based on well-defined symptom-based criteria, with Rome III criteria being preferred in India as Rome IV tends to underdiagnose IBS.

IBS is too heterogeneous to be captured by a single marker; therefore, a combination of biomarker profiling, clinical assessment, dietary factors, and microbial profiling may be necessary for accurate characterization.

Improved understanding of the pathophysiology and newer diagnostic paradigms can assist in more precise diagnosis.

Management approaches

Treatment can be either pathophysiology-guided or symptom-directed, with a combination of therapies tailored to individual patient needs.

A comprehensive management plan should include basic diet and lifestyle modifications, clear patient communication, realistic goal setting, and judicious use of cyclic therapy with prescription medications.

Antispasmodics such as mebeverine or otilonium are typically used for 6-8 weeks, especially for pain-predominant IBS.

Mebeverine is effective across all IBS subtypes (C/D/M) with a favorable safety profile, typically prescribed for 6-8 weeks based on symptom relief, though studies recommend 12 weeks.

Probiotics, particularly strains like Bifidobacterium and Lactobacillus, have shown the most benefit in managing IBS and should be included for at least two months.

CONCLUSION

IBS is a common functional gastrointestinal disorder. The microbiota-gut-brain axis plays a crucial role in IBS pathogenesis, with dysbiosis—an imbalance in gut microbiome—leading to inflammation, increased intestinal permeability, and disrupted gut-brain communication, all contributing to IBS symptoms. Diagnosing IBS is challenging, Rome III criteria may be more suitable in regions like India, as it captures local symptom profiles more effectively.

Holistic management approach is essential for IBS, incorporating dietary modifications such as the low

FODMAP diet, lifestyle changes that promote regular physical activity and stress management, and pharmacological interventions like antispasmodics, antibiotics, and antidepressants. Antispasmodics, which function through various mechanisms, benefit patients with IBS by alleviating abdominal pain, reducing colonic motility, improving stool form and frequency. Mebeverine is an effective treatment for a diverse range of IBS patients experiencing abdominal pain, discomfort, distension, irregular bowel habits, bloating, constipation, and diarrhea. Probiotics are an effective and tolerable treatment option for patients with IBS, particularly strains like Bifidobacterium and Lactobacillus.

Future research should focus on developing non-invasive biomarkers for improved diagnostic accuracy and exploring novel therapeutic targets.

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