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Review Article

Small Intestinal Bacterial Overgrowth in Irritable Bowel Syndrome: Consequences, Diagnosis and Treatment

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Abstract

Irritable Bowel Syndrome (IBS) is a multifactorial gastrointestinal disorder characterized by abdominal pain, bloating and altered bowel habits. Small intestinal bacterial overgrowth (SIBO) has emerged as a potential contributor to IBS pathophysiology. This review aims to elaborate the relationship between SIBO and IBS explaining the association, consequences, diagnostic approach and therapeutic strategies. Prevalence of SIBO in IBS shows a wide variation with higher estimates at 25 - 80%. Though symptoms of SIBO are classical, it is still sometimes difficult to diagnose. The gold standard test is jejunal aspirate and analysis of small bowel flora, but is cumbersome. Glucose hydrogen breath test (GHBT) and/or lactulose hydrogen breath test (LaHBT) can be screening tests and are practically easy to carry out. Treatment often includes antibiotics, probiotics and dietary intervention.

Keywords: IBS; SIBO; ROME IV; Dysbiosis; Rifaximin; Probiotics

Introduction

The GI tract is home to trillions of microorganisms including bacteria, viruses, and fungi. An individual is estimated to harbor more than 1000 microbial species-level phylotypes; Bacteroidetes and Firmicutes being the predominant bacterial phyla. The gut microbiome plays a role in human metabolism, nutrition, and immune function. The gut bacteria synthesize all essential and non-essential amino acids and various vitamins. They help in the metabolism of non-digestible carbohydrates and biotransformation of bile. They also prevent gut colonization by pathogens through barrier or competitive exclusion effects. Imbalance of the gut microbiome can lead to various diseases and functional abnormalities. Irritable bowel syndrome, inflammatory bowel disease, metabolic syndrome, Type 2 DM, atopy and several other disorders have been linked to alterations in the gut microbiome [1].

Irritable bowel syndrome

Irritable Bowel Syndrome (IBS) is a common functional gastrointestinal disorder that is characterized by recurrent abdominal pain and altered bowel habits, affecting 12% of the general population [2]. Prevalence in India seems a bit lower (Table 1) and it may vary with the population studied, whether rural or urban. The pathogenesis of IBS is multifactorial and it involves abnormal gut motility, visceral hypersensitivity, and dysregulation of the gut-brain axis. Recent research has implicated gut dysbiosis (an imbalance in gut bacteria) as a contributing factor to IBS development. 4% - 78% of patients with IBS and 1% - 40% of controls have small intestinal bacterial overgrowth (SIBO) [7]. Evidence suggests that dysbiosis can activate the gut immune system, leading to downstream effects on various factors of potential relevance to the pathophysiology of IBS [2].

The diagnosis of IBS is based on Rome IV criteria*[3]. which includes: Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with two or more of the following criteria:

- Related to defecation
- Associated with a change in the frequency of stool
- Associated with a change in form (appearance) of stool (*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.).

Author, year	Study setting	Diagnostic Criteria	Site	Total no. of subjects	Number (%) IBS	Male: female among IBS subjects	Number (%) IBS-C	Number (%) IBS-D	Number (%) IBS-M	Number (%) IBS-U
Sperber., *et al*. 2021	Community	ROME III	Southern India: TelanganaNorthern India: Uttar Pradesh	4592	18 (0.4)	Data not reported separately	Data not yet reported	Do	Do	Do
Ghoshal and Singh 2017	Community	ROME III	Jaunpur District Uttar Pradesh	2774	75(2.7)	45:30	5/75(6.6)	8/75 (10.6)	0	62/75 (82.6)
Makharia., *et al.* 2011	Community	ROME III	Ballavgarh Uttar Pradesh	4767	191 (4)	77:114	12/191 (6.3)	72/191 (37.7)	81/191 (42.4)	26/191 (13.6)
Ghoshal., *et al*. 2006	Community	Manning 3	Pan - India Study	4500	189 (4.2)	109:80	Not Reported	Not Reported	Not Reported	Not Reported

Table 1: Prevalence of irritable bowel syndrome in India according to the population-based studies [6].

Small intestinal bacterial overgrowth (SIBO)

The small intestine is a vital part of the digestive system, responsible for absorption of nutrients from food. In SIBO, the normal balance of gut bacteria is disrupted leading to an overgrowth of bacteria that can cause a range of symptoms. SIBO is defined as a bacterial load of ≥ 10^5 CFU/mL (colony-forming units per milliliter) or ≥ 103 CFU/mL (if coliforms are present) in a quantitative culture of upper gut aspirate. In contrast, healthy individuals typically have a much lower bacterial load than 103 CFU/Ml [4].

The most common species identified in SIBO are *Escherichia coli, Aeromonas,* and *Klebsiella* species.

Anaerobes cause direct epithelial injury and produce enterotoxins, whereas aerobes only produce enterotoxins, resulting in intestinal inflammation.

SIBO can elicit a spectrum of gastrointestinal (GI) symptoms, which classically include abdominal discomfort, bloating, flatulence, or chronic watery diarrhea. Steatorrhea and weight loss from fat malabsorption may also manifest, especially with altered gut anatomy (blind loop syndrome). There are several conditions that may predispose to SIBO.

Gastrointestinal (GI) Conditions	Non-GI Conditions	Medications
1. Irritable Bowel Syndrome	1. Systemic sclerosis	1. NSAIDS
2. Inflammatory Bowel Disease	2. Diabetes mellitus	2. Proton Pump Inhibitors
3. Tropical sprue	3. Hypothyroidism	
4. Celiac disease	4. Obesity	
5. Dyspepsia	5. Parkinson's disease	
6. SI diverticulosis/Stricture/Fistula	6. Multiple sclerosis	
7. Radiation enteropathy	7. Muscular dystrophy	
8. Pancreatitis	8. ESRD	
9. NAFLD	9. CAD	
10. Liver cirrhosis	10. Immunodeficiency	
11. Post-abdominal surgery	11. Chronic fatigue syndrome	
	12. Restless leg syndrome	
	13. Fibromyalgia	
	14. Rosacea	

Table 2: Conditions associated with SIBO [18].

Small intestinal bacterial overgrowth (SIBO) in irritable bowel syndrome (IBS) patients

The prevalence of SIBO among IBS patients varies widely, ranging from 4% to 78%; while in healthy individual, the prevalence ranged from 1% to 40% [7]. Case-control studies generally found that SIBO was more common in IBS patients than in controls, suggesting a potential link between the two conditions. Although breath testing can help identify SIBO, its sensitivity is relatively low (44%), while its specificity is higher (84%), meaning it is better at ruling out SIBO in healthy individuals than it is at correctly diagnosing SIBO in IBS patients [5,7].

The factors that help identify IBS patients at a higher risk of developing SIBO include: Female gender, older age, predominant symptoms of bloating and flatulence, diarrheal subtype of IBS (IBS-D) and PPI intake [9].

The symptoms of SIBO in IBS include bloating, abdominal pain, diarrhea, and food intolerance [8].

Diagnosis of SIBO in IBS

Accurate diagnosis and understanding of the IBS-SIBO relationship are crucial for the effective management of these conditions. A review of existing data reveals inconsistencies in SIBO frequency is due to the differences in using diagnostic methods.

Lactulose hydrogen breath test (LHBT)

The studies rely on early-peak criteria for diagnosing SIBO. LHBT has reported higher SIBO frequency but can be falsely positive. Procedure of LHBT involves administration of lactulose orally in a fasting state and obtaining the breath hydrogen (H_2). The test starts by estimation of baseline breath samples. 25 gms of lactulose mixed in 250 ml of lukewarm water is given orally and breath samples are obtained every 20 minutes for 2 hours and hydrogen in breath is estimated, by a hand held hydrogen breath analyser. The test is positive if there is a rise of hydrogen level by > 20 ppm above the baseline in 90-120 minutes of lactulose administration [10].

Glucose hydrogen breath test (GHBT)

Principle of the test is based on early production of H_2 after administration of oral glucose in subjects with SIBO. Glucose hydrogen breath testing (GHBT) has low sensitivity, potentially leading to underestimation of SIBO frequency especially in cases where bacterial overgrowth is distal within the small intestine. Procedure involves obtaining baseline breath samples and subsequently 50 gms of glucose mixed in 250 ml of water is given orally. Breath samples are obtained every 15 minutes for 2 hours and hydrogen in breath is estimated. The test is said to be positive, if there is a rise of hydrogen level by ≥ 20 ppm (parts per million) above the baseline within 90-120 minutes after glucose administration [16].

Jejunal aspirate culture

Jejunal aspirate culture is considered the gold standard but it is invasive and not patient-friendly. The procedure involves passage of a Nasoduodenal or nasojejunal tube through the nose, guided through the stomach, and positioned in the jejunum. Jejunal aspirate is collected in a tube and sent for microbiological analysis, including quantitative culture and bacterial identification. A bacterial count of ≥ 1000 colony forming units (CFU/ml) indicates SIBO.

Effect of SIBO on IBS

SIBO can have several consequences on IBS. Among gastrointestinal symptoms, there can be exaggerated bloating, increased gas production, abdominal pain and cramping. SIBO can disrupt the usual bowel movements leading to changes in stool frequency and consistency. In some cases nausea and/or vomiting can occur. There can be development of nutritional deficiencies due to impaired absorption of vitamins like ADEK and B12. Malabsorption can lead to weight loss and malnutrition. Some systemic manifestations like fatigue, cognitive impairment and mood changes like anxiety, depression and mood swings may be observed in patients with SIBO. Certain other rare consequences like increased risk of osteoporosis (malabsorption of calcium and vitamin D), impaired immune function and increased risk of IBD and GERD have been reported [17].

Treatment

Several treatment approaches are available for SIBO in IBS patients, including.

Antibiotics

These target and reduce pathogenic bacteria. Antibiotics, including rifaximin, metronidazole, neomycin, and ciprofloxacin, have shown to be more effective than placebo in normalizing breath tests in IBS patients with suspected SIBO [11]. In most recent studies rifaximin is the preferred antibiotic which works by inhibiting bacterial RNA synthesis. The TARGET studies have shown that rifaximin is very effective and well tolerated in patients with non-constipation IBS with a significant reduction in symptoms and improving QOL [12]. It has a low risk of inducing antibiotic resistance. The dose of Rifaximin used in the TARGET study was 550 mg three times daily for 14 days.

Probiotics

Probiotics are live microorganisms, which, when administered in sufficient quantities may alleviate symptoms of IBS [15]. They may work by suppressing pro-inflammatory cytokines, modulating gut microbiota and sustaining the intestinal epithelial integrity.

Certain probiotic strains have shown promise in reducing SIBO symptoms while others have shown variable or no benefit. Though probiotics hold promise, more large-scale, well-designed clinical trials, especially in diverse populations, are necessary before they can be universally recommended as a first-line therapy.

Prokinetics

Prokinetic drugs that increase gut motility are considered useful for patients with SIBO and IBS, both conditions linked to motility issues [14]. Improving small bowel motility can help prevent bacterial overgrowth. Pimentel., *et al.* found that IBS patients with SIBO had a lower frequency of the migratory motor complex (MMC), a key process for clearing bacteria from the small intestine [13].

Dietary manipulation

Therapy for both IBS and SIBO often includes dietary adjustments (like the Low FODMAP or SCD diet) alongside antibiotics or antimicrobials to reduce bacterial overgrowth. These have shown potential in alleviating SIBO symptoms.

Conclusion

The association between IBS and SIBO is well-established, but controversy surrounds whether patients with IBS and SIBO should be diagnosed as IBS or SIBO, given the similarity in symptoms. The current Rome Foundation diagnostic algorithm for IBS is symptom-based and does not require the exclusion of SIBO. An integrated approach combining symptom-based criteria with SIBO testing may improve diagnosis and treatment outcomes in patients with IBS and SIBO.

Study	Disease	N =	Dose	Duration	Response rate	
					Rifaximin	Placebo
TARGET 1	IBS-D	2579	550 TID	14 Days	40%	31%
TARGET 2	IBS-D	1046	550 TID	14 Days	36%	21%
Pimental., *et al.*	SIBO	111	400 TID	7 Days	62%	28%
Rezaie., *et al.*	SIBO	142	400 TID	14 Days	64%	20%

Table 3

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Conflict of Interest

We do not have any other conflict of interest.

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