Chapter 56
Irritable Bowel Syndrome: The Indian Scenario

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INTRODUCTION
The focus of clinicians has always been on “organic” diseases which have a clear etiology, defined clinicopathological features, specific diagnostic tests and effective treatment. However, since a long time physicians have been confronted with a constellation of abdominal symptoms without any structural basis or clear etiology, which have been labeled as “functional gastrointestinal disease” (FGID). FGID has a diagnostic problem without specific pathological or radiological markers and therapies targeted against them often being associated with poor efficacy and side effects.

Functional gastrointestinal disease has been defined into various subsets:
• Functional dyspepsia
• Epigastric pain syndrome
• Postprandial distress syndrome
• Cyclic vomiting syndrome
• Chronic idiopathic nausea
• Irritable bowel syndrome (IBS).

Irritable bowel syndrome is a functional GI disorder characterized by abdominal pain and altered bowel habits in the absence of specific organic pathology. The general understanding developed that IBS was lower abdominal pain or discomfort associated with disordered defecation and often associated with relief of pain with defecation.

Since 1960s, attempts were made to make a more positive diagnostic criteria for IBS without the risk of misdiagnosing an organic disease such as ulcerative colitis or colon cancer. A number of diagnostic criteria for IBS are available: the Manning criteria, the Kruis criteria, and the Rome I, II and III criteria. Rome III criterion is currently most widely accepted in clinical practice.

Diagnostic criteria for IBS according to Rome III are:
1. Recurrent abdominal pain or discomfort for at least 3 days a month in the last 3 months (with onset at least 6 months previously) associated with 2 or more of the following:
   1. Improvement with defecation.
   2. Onset associated with change in stool form.
   3. Onset associated with change in stool form (appearance of stool).

Four bowel patterns may be seen with irritable bowel syndrome:
1. IBS-D (diarrhea-predominant).
2. IBS-C (constipation-predominant).
3. IBS-M (mixed diarrhea and constipation).
4. IBS-A (alternating diarrhea and constipation).

The usefulness of these subtypes is debatable. Notable, within 1 year, 75% of patients change subtypes, and 29% switch between constipation-predominant IBS and diarrhea-predominant IBS.

INDIAN PERSPECTIVE
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.1

There are some key differences between IBS in India and the West and as such, the Asian Neurogastroenterologist and Motility Association suggest the use of a broader definition of IBS rather than the use of Rome criteria.2 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”. This definition avoids the description of lower abdominal pain, since upper abdominal pain has been found to be more common in Indian patients with IBS. In addition, the term bloating has been specifically included since it is a common symptom in Indians with IBS. Also, an assessment for exclusion of organic disease has also been advised.

The patient’s description of diarrhea or constipation can be fallacious because it is usually based on stool frequency. Many a times, patients with hard stools and feeling of incomplete defecation (with tachychezia) may describe it as diarrhea. Thus, the bowel pattern should not be assessed by stool frequency alone, but should include the stool type also. Patient should also be asked if their symptoms are relieved with defecation, if there is straining at stool, if there is feeling of incomplete evacuation, urgency, or an association with a change in stool frequency or consistency.

EPIDEMIOLOGY
Population-based studies estimate the prevalence of IBS at 10–20% and the incidence of IBS at 1–2% per year. Of people with IBS, approximately 10–20% seek medical care. An estimated 20–50% of gastroenterology referrals relate to this symptom complex. The prevalence, demography and clinical features are different among countries (Table 1).

ETIOLOGY
The etiology of IBS is uncertain but is likely to be multifactorial. IBS is a disorder of dysregulation of brain–gut axis, involving abnormal function in the enteric, autonomic and/or central nervous system (CNS).2 A number of mechanisms have been described in the etiology of IBS as summarized below.

Visceral Hypersensitivity
It is an important mechanism for abdominal pain in IBS. It is caused by heightened sensitivity of both peripheral and CNS due to inflammatory and noninflammatory agents.
### Abnormal Gut Motility

A cardinal 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. Activation of 5-HT3 and 5-HT4 receptors enhances gut motility while inhibition of 5-HT3 delays transit time. Gut motility is also regulated by psychogenic, somatic and immune stress.

### Autonomic Nervous System Dysfunction

There appears to be an imbalance resulting from increased sympathetic and decreased parasympathetic activity. Vagal and adrenergic dysfunctions are associated mainly with constipation and diarrhea, respectively.

### Small Intestine Bacterial Overgrowth

Up to 84% patients with IBS have been found to have small intestinal bacterial overgrowth (SIBO). Antibiotic treatment with nonabsorbable antibiotics, e.g. rifaximin leads to clinical improvement of IBS. Two studies suggest the prevalence of SIBO to be 11% in India. However, villous atrophy with bacterial overgrowth (tropical enteropathy) is also common in India. It is presently unclear whether SIBO is the cause or effect of IBS.

### Microscopic Inflammation

Microscopic inflammation has been documented in some patients. This concept is important because IBS has previously been considered to have no demonstrable pathologic alterations. Immunohistochemical studies reveal mucosal immune system activation in a subset of patients with diarrhea-predominant IBS.

### Postinfectious Irritable Bowel Syndrome

Postinfectious IBS affects 10% of IBS patients. This subtype is consequent to previous bacterial gastroenteritis and raises the importance of bacterial infections in causation of IBS. A longer duration of the diarrheal episode, younger age, female sex, bloody stools, depression, etc. increases the risk of development of IBS. Interestingly, some studies in India suggest a protective effect of previous exposure to amebic infection.

### Food Intolerance and Allergy

Hypersensitivity reactions lead to mast cell degranulation with production of local and systemic proinflammatory leukotrienes and histamine which act on smooth muscles. Sugar and gluten intolerance have also been implicated but seem to be unlikely cause of IBS although may contribute to bloating.

### Psychosocial Factors

Emotions affect gut motility and patients with history of physical or sexual abuse, loss and separation during childhood, and conflicting maternal relationship are all associated with development of IBS.

### Genetic Factors

There is some evidence to suggest a genetic factor in causation of IBS. One study found that 33% of patients with IBS had a positive family history. Also, first-degree relatives are twice likely to have IBS.

### Other Possible Mechanisms

There are also a number of other possible mechanisms which have been proposed which is beyond the scope of discussion in this chapter.

### Evaluation

A meticulous history is the key to establish a diagnosis of IBS. The Rome criteria provide the basis upon which questions are based. Physicians should be guided by diagnostic criteria rather than approaching IBS as a diagnosis of exclusion. A careful history taking, general examination and looking for alarm features (weight loss, rectal bleeding, nocturnal symptoms, anemia, family history of colorectal cancer, IBD) can help make the diagnosis. Patients suspected to have organic disease (Table 2) should undergo further evaluation as indicated.

Specific biomarkers for IBS do not exist. Current recommendations suggest sending complete blood count (CBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) initially. In India, stool should be sent for routine microscopic examination. Routine thyroid function test (TFT), colonoscopy and diagnostic imaging are not advised unless there are alarm features. Other problems to consider in differential diagnosis are:
- Inflammatory bowel disease
- Colorectal cancer
- Colonic tuberculosis
- Fructose intolerance
- Gastrinoma

### Table 1: The prevalence, demography and clinical features of irritable bowel syndrome in Western countries and India

<table>
<thead>
<tr>
<th></th>
<th>Western countries</th>
<th>India</th>
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<tbody>
<tr>
<td>Prevalence</td>
<td>10–20%</td>
<td>4.2–7.9%</td>
</tr>
<tr>
<td>Sex</td>
<td>Female &gt; male</td>
<td>Male &gt; female</td>
</tr>
<tr>
<td>Age</td>
<td>More common in young</td>
<td>More common in young</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>Inversely related</td>
<td>Inversely related</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Predominance of lower abdominal symptoms</td>
<td>Predominance of upper abdominal symptoms</td>
</tr>
</tbody>
</table>

### Table 2: Features suggestive of organic disease

<table>
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<tr>
<th>History</th>
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<tr>
<td>Age (&gt; 40 years) at onset of symptoms</td>
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<tr>
<td>Large-volume diarrhea or steatorrhea</td>
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<tr>
<td>Symptoms during night</td>
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<tr>
<td>Hematochezia (except from anal lesions, e.g. hemorrhoids, fissure)</td>
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<tr>
<td>Fever, dehydration</td>
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<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Symptom progression or onset of new symptoms</td>
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</tbody>
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<table>
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<tr>
<th>Physical examination</th>
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<tbody>
<tr>
<td>Abdominal mass</td>
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<tr>
<td>Signs of malabsorption, bowel obstruction, thyroid dysfunction</td>
</tr>
<tr>
<td>Extraintestinal manifestations (arthritis, skin lesions)</td>
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<table>
<thead>
<tr>
<th>Laboratory findings</th>
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<tr>
<td>Occult blood in stools</td>
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</table>
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Section 6

- Infectious colitis
- Medication side effects
- Secretory diarrhea
- Vipoma.

Laboratory testing or diagnostic imaging is not recommended for younger patients (< 50 years) with typical IBS symptoms and without "alarm features". Patients with IBS-D or IBS-M should have serologic testing for celiac disease. Patients greater than 50 years age should have more extensive testing, including a colonoscopy.

Upper GI endoscopy with possible biopsy is indicated in patients with persistent dyspepsia, weight loss, symptoms suggestive of malabsorption, or if celiac disease is a concern. Colonoscopy is indicated for patients with warning signs such as bleeding, anemia, chronic diarrhea, older age, history of colon polyps, cancer in the patient or first-degree relatives, or constitutional symptoms such as weight loss or anorexia.

TREATMENT

Patient education remains the cornerstone of successful treatment of IBS. Successful management relies on a strong patient-doctor relationship. Reassure the patient and emphasize the expected chronicity of symptoms with periodic exacerbations. Teach the patient to acknowledge stress factors and to use avoidance techniques.4

Diet

Around 60–70% of patients believe that certain foods aggravate their symptoms. The response rate of various exclusion diets varies from 12.5% to 67%. Data show some benefit of soluble fibers in relief of symptoms and some benefit for treatment of constipation. Insoluble fibers are not beneficial and may even worsen IBS. Lactose and fructose intolerance should be considered in IBS-D and excluded from the diet if required.

Pharmaceuticals

The selection of pharmacologic treatment remains symptom directed. Agents 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 (Table 3).

Antispasmodics

They provide relief of abdominal pain/discomfort but data on long-term efficacy does not exist. Commonly used antispasmodics are nonselective anticholinergics which, in addition to acting on gastrointestinal tract (GIT) act on other systems too, thus having side effects. A Cochrane systematic review found that several antispasmodics, including peppermint oil, pinaverium, trimebutine and cimetropium/dicyclomine, are significantly better that placebo at improving IBS symptoms.

Antidiarrheals

Loperamide has been studied extensively. It is µ-opioid receptor agonist that acts on myenteric plexus of the large intestine. It increases the stool transit time, colonic movement and suppresses the gastrocolic reflex. Trials have showed reduced stool frequency and improved stool consistency in patient with IBS-D.

Laxatives

No trials have evaluated their roles and more research are needed.

Antibiotics

Rifaximin, neomycin and clarithromycin have been evaluated for the treatment of IBS. The studies show statistically significant improvement in global IBS symptoms and bloating as compared to placebo. A large study on 1,260 patients with IBS without constipation showed that treatment with rifaximin (550 mg PO tid for 14 days) provided better symptom relief (e.g. bloating, abdominal pain, loose/wetery stools) compared with placebo. Similarly, a 2012 meta-analysis of 5 studies, incorporating 1,803 patients, determined that rifaximin is more effective that placebo for global symptom relief and bloating. Rifaximin is recommended for patients with IBS-D or IBS with predominant bloating symptoms as an off label use.

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**TABLE 3 | Drugs used in different subtypes of irritable bowel syndrome**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Drug target</th>
<th>Physiological effect</th>
<th>Drugs</th>
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<tbody>
<tr>
<td>IBS-M</td>
<td>Serotonergic and adrenergic receptors</td>
<td>↑ compliance, ↔ motility</td>
<td>Venlafaxine, fluoxetine</td>
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<tr>
<td></td>
<td>Intestinal flora</td>
<td>↔ motility, ↓ bloating, ↓ pain</td>
<td>Probiotics</td>
</tr>
<tr>
<td></td>
<td>Cholinergic receptor antagonists</td>
<td>↓ intestinal motility, ↓ pain</td>
<td>Cimetropium, pinaverium, hyoscine, otilonium, mebeverine</td>
</tr>
<tr>
<td>IBS-D</td>
<td>5-HT3 receptor antagonists</td>
<td>↓ intestinal motility, ↓ pain</td>
<td>Ondansetron, alosetron, cilansetron</td>
</tr>
<tr>
<td></td>
<td>Selective M3 receptor antagonists</td>
<td>↓ intestinal motility, ↓ pain</td>
<td>Zamifenacin, darifenacin</td>
</tr>
<tr>
<td></td>
<td>α2-agonist</td>
<td>↓ intestinal motility, ↓ pain sensation</td>
<td>Clonidine</td>
</tr>
<tr>
<td></td>
<td>µ-opioid receptor agonist</td>
<td>↓ intestinal motility, ↓ peripheral pain</td>
<td>Loperamide</td>
</tr>
<tr>
<td>IBS-C</td>
<td>Chloride channel modulator</td>
<td>↑ intestinal motility, ↑ water secretion</td>
<td>Lubiprostone</td>
</tr>
<tr>
<td></td>
<td>5-HT4 agonists</td>
<td>↑ intestinal motility, ↑ water secretion</td>
<td>Metoclopramide, domperidone, cinitapride</td>
</tr>
</tbody>
</table>

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**Probiotics**
Patients with IBS have found to have altered microflora but not proved to have any role in pathogenesis. A recent systematic review summarized the current data of probiotics in IBS. There was no difference in the probiotics used but combination of probiotics showed a statistically significant effect in terms of improvement in abdominal pain and flatulence.

**5-HT3 Receptor Antagonist**
Food and Drug Administration (FDA) approved the use of alosetron in female patients with severe, chronic IBS-D who failed conventional therapy. Constipation and ischemic colitis should be watched out for.

**5-HT4 Receptor Agonist**
Tegaserod is more effective than placebo at treating global IBS symptoms, abdominal discomforts, satisfaction with bowel habits and bloating. The most common side effect is dose-related diarrhea. This drug has now been withdrawn from many countries because of tenfold rise in heart attack and stroke.

**C2 Chloride Channel Activators**
Lubiprostone is the only selective C2 chloride channel activator. It is poorly absorbed and works topically in intestinal tract. Studies have shown it to improve global symptoms in IBS-C and abdominal pain/discomfort, stool consistency, straining and constipation severity. The most common side effects include nausea, diarrhea and headache.

**Antidepressants**
Both TCA and selective serotonin reuptake inhibitor (SSRI) have been extensively studied with numerous trials, but with inconclusive results. Theoretically, TCAs and SSRIs are may be more effective in IBS-D and IBS-C respectively.

**Psychological**
Cognitive behavior therapy, hypnotherapy, relaxation therapies and interpersonal psychotherapy have been tried but there is no data to support or refute its efficacy.

**Herbal Therapies and Acupuncture**
Further research is needed before these therapies can be recommended.

**PROGNOSIS**
Irritable bowel syndrome is a chronic relapsing disorder characterized by recurrent symptoms of variable severity. The life expectancy, however, remains similar to that of the general population. Clinicians should inform and reassure patients, because the knowledge may help allay undue fears. IBS does not increase the mortality or the risk of inflammatory bowel disease or cancer.

The principal associated physical morbidities of IBS include abdominal pain and lifestyle modifications related to altered bowel habits. Absenteeism from work resulting in lost wages is more frequent in patients with IBS.

**REFERENCES**