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Review Article

Overview of functional bowel disorders

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Abstract

The true incidence of functional physical disorders is higher in general practice including functional bowel disorders. It leads to a high socio-economic burden by way of delayed diagnosis. ROME III criteria are used to diagnose these disorders. Although there are specific clinical diagnostic features, definite diagnostic investigations are unavailable. Recent scientific studies link the mind and body as part of a system where their dysregulation can produce illness and disease where psycho-social factors do play a role in addition to genetic susceptibility and environmental factors. The brain-gut axis is now an area of intense research in studying these functional disorders and psychotherapy, behavioral modification and psycho-pharmacotherapy are becoming increasingly important to manage such disorders.

Key words

Functional bowel disorders, Brain-Gut axis, Psycho-somatic disease, IBS, irritable bowel syndrome.

Introduction

One of the most challenging tasks in clinical medicine is the diagnosis and management of functional disorders which account for 36-50% of all out patient consultations in hospital setting [1]. This implies that the actual incidence of functional physical disorders is higher in general practice [2]. The same is apparent in bowel diseases in gastroenterology, where functional disorders cause significant distress to the patients that translate into quite a high economic burden to the society by way of absenteeism, poor quality of life and medical expenses. With rise in population, these disorders will definitely pose a diagnostic dilemma to us in future because there is already a high prevalence of GI disorders in general population [3].

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Functional bowel disorder

A functional bowel disorder (FBD) is diagnosed by characteristic symptoms for at least 12 weeks during the preceding 6 months in the absence of

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a structural or biochemical explanation [2]. It must be understood that FBD is only a subgroup of functional gastrointestinal disorders (FGID) which have definite diagnostic criteria and these clinical criteria have been modified from time to time. Therefore, it is emphasized that there must be chronological criteria to be fulfilled before making a diagnosis of FGID. These criteria have been revised since the first consensus meeting held in 1989 at Rome and are known as ROME criteria, the latest being ROME III which is followed in this presentation. It maintains the principle of symptom-based diagnostic criteria like the DSM classification for mental disorders. The classification relies on the organs where the symptoms presumably are produced. They are in order from esophagus to anus. The recent classification of FGID in adults and children is shown in **Table - 1.**

For adults, the FGID include 6 major groups: Esophageal (category A), Gastro duodenal (category B), Bowel (category C), Functional abdominal pain syndrome (category D), Biliary (category E), and Anorectal (category F).

Each category site contains several disorders, each having relatively specific clinical features. So, the functional bowel disorders (category C) include: Irritable bowel syndrome (C1), Functional bloating (C2), Functional constipation (C3) and Functional diarrhea (C4), which anatomically are attributed to the small bowel, colon, and rectum. Thus, while symptoms (e.g., diarrhea, constipation, bloating, pain) may overlap across these disorders, irritable bowel syndrome (C1) is more specifically defined as pain associated with change in bowel habit, and this is distinct from functional diarrhea (C4), characterized by loose stools and no pain, or functional bloating (C2), where there is no change in bowel habit. Each condition also has different diagnostic and treatment approaches. In this article, focus will be placed only to this category i.e. functional bowel disorders out of which irritable bowel syndrome (IBS) is by far the commonest. However, treatment of these conditions is beyond the scope of this article.

The symptoms of the FGID are derived from combinations of their physiological determinants: a) increased motor reactivity, b) enhanced visceral hypersensitivity, c) altered mucosal immune and inflammatory function (which includes changes in bacterial flora), and d) altered central nervous system (CNS)-enteric nervous system (ENS) regulation (influenced by psychosocial and socio cultural factors and exposures) [4, 5, 6]. For example, fecal incontinence (category F1) may primarily be a disorder of motor function, while functional abdominal pain syndrome (category D) is primarily understood as amplified central perception of normal visceral input (hypersensitivity to pain). IBS (category C1) is more complex, and results from a combination of dysmotility, visceral hypersensitivity, mucosal immune dysregulation, alterations of bacterial flora, and CNS-ENS dysregulation [7, 8]. The contribution of these factors may vary across different individuals or within the same individual over time. Thus, the clinical value of separating the functional gastro intestinal (GI) symptoms into discrete conditions is that they can be reliably diagnosed and better treated.

The Rome III classification system is based on the premise that for each disorder there are symptom clusters that “breed true” across clinical and population groups [9]. This presumption provides a framework for identification of patients for research that is modified as new scientific data emerges. The rationale for classifying the functional GI disorders into symptom-based subgroups are based on the site-specific differences between symptoms, i.e., the fact that symptoms result from multiple influences, from epidemiologic

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data showing similar frequencies of these disorders across cultures, and finally, out of the need for diagnostic standards in order to conduct clinical care and research.

The basic paradigm of the modern medicine has traditionally relied on the concepts promoted by Descartes of biological reductionism and dualism, which in medicine, seeks to find a single biological etiology for every clinical condition [10]. In the last decades, we have moved away from this reductionistic model of disease to a more holistic paradigm of the biopsychosocial model of disease. Here, illness (the person's experience of ill health), and disease (objective histopathological findings) are viewed as equally important in understanding the clinical expression of a medical condition, and this refuted the traditional reductionistic model of disease. The reductionistic disease-based biomedical model harmonized with Descartes' separation of mind and body at the time when society was accepting the concept of separation of church and state. What resulted was permission to dissect the human body (which was previously forbidden), so disease was defined by what was seen (i.e., pathology based on abnormal morphology). This approach has led to centuries of valuable research producing appropriated treatments for many diseases. However, the concept of the mind (i.e., the central nervous system, CNS) as being amenable to scientific study or as playing a role in illness and disease was marginalized: The mind was considered the seat of the soul, and was not to be tampered with [11].

More recent scientific studies link the mind and body as part of a system where their dysregulation can produce illness and disease. By embracing this integrated understanding, the biopsychosocial model allows for symptoms to be both physiologically multi determined and modifiable by socio-cultural and psychosocial influences [12, 13].

The application of this model of Engel to the Functional Gastrointestinal Disorders (FGID) helps to explain how changes in early life, genetic factors and environmental factors, may affect the psychosocial development (susceptibility to life stress, psychological state, coping skills, abnormal illness behavior, social support) and/or the development of gut dysfunction (i.e., abnormal motility, visceral hypersensitivity, inflammation, or altered bacterial flora), all of which lead to the clinical expression of the disorder. Furthermore, these brain-gut variables mutually interact to influence their expression. Therefore the FGID are the clinical product of the interaction of psychosocial factors and altered gut physiology via the brain-gut axis [14]. For example, an individual with a bacterial gastroenteritis or other bowel disorder who has no concurrent psychosocial difficulties and good coping skills may not develop the clinical syndrome or, if it does develop, may not feel the need to seek medical care. Another individual with coexistent psychosocial co-morbidities, high life stress, abuse history, or maladaptive coping, may develop a FGID and visit more frequently the physician and have a worse clinical outcome. The number of studies and publications on the FGID has increased along with the progress of newer investigative methods leading to wider acceptance of these conditions by the physicians than before. These studies have served to legitimize these conditions in a positive way, not just by exclusion of other disorders. The assessment of motility has improved. The wider use of the barostat, as the main technique for assessing visceral hypersensitivity has provided evidence for the role of visceral sensitivity in understanding these conditions. Finally, another novel area of development has been the progress in brain imaging like positron emission

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tomography (PET), and functional magnetic resonance imaging (fMRI) [8]. These modalities offer a window into the central modulation of GI function and its linkages to emotional and cognitive areas which were not possible even a decade back [15]. Thus the nature of FGID as disorders of brain-gut interactions is now eminently amenable to scientific study. The psychological instruments permitting the categorization and quantification of emotions, stress, and cognitions have also been better standardized, and these measures help us determine the role of psychosocial factors on symptom generation, and its effect on quality of life and health outcomes. These developments emphasize the role of brain-gut dysregulation in FGID [14].

Finally, the molecular investigation of brain and gut peptides, mucosal immunology, inflammation, and alterations in the bacterial flora of the gut provide the translational basis for GI symptom generation. All physicians now recognize the FGID as true clinical entities. These disorders are now a prominent part of undergraduate and postgraduate medical curricula, clinical training programs, and international symposia. The number of papers in the FGID in peer-reviewed journals has increased dramatically. But now there are future challenges to be faced like a need for an improved understanding of the relationships between mind and gut, and the translation of basic neurotransmitter function into clinical symptoms and their impact on the patient's health status and quality of life [15]. There is also a need to educate clinicians and the general public on this rapidly growing knowledge and, in the process, continue to legitimize these disorders to society.

The approach to FBD (or any other FGID) aims primarily at excluding a structural/ anatomical/ histopathological or biochemical anomaly. It is important to know that only half of all patients will consult their general physicians and of these about 20% will need referral to a higher centre. While approaching a suspected case of FBD, the history is very important, as we have already mentioned that the diagnostic criteria of FGID are symptom specific. They have no disease markers [15]. We only investigate the symptoms of such patients. However, we must always look out for certain "ALARM SYMPTOMS" in all cases so that more dangerous, truly structural and treatable (infectious/metabolic) conditions are not missed. Therefore, FBD are diagnosed by a process of exclusion.

Irritable bowel syndrome

Irritable bowel syndrome (IBS) has a prevalence of 10-20% in western population and is the most common FGID [15]. Ethnic differences have been reported in a few studies. Cultural factors like diet and socio-economic status may play a part. IBS is responsible for 40-60% of referrals in gastroenterology outdoor patient department most commonly involving age group of 30-50 years [3]. It is a multi factorial disorder - basically a dysregulation of gut-brain axis with GI motor and sensory dysfunction, enteric and CNS irregularities, neuro immune dysfunction and a post-infectious inflammation in some cases. Genetics and psycho-social factors may play a role. Large numbers of IBS patients have a low visceral pain threshold. Disorder of gut motility is not universally present. True food allergy in IBS is very uncommon. But many patients tell their doctors that particular food items exacerbate their symptom(s). The exact etiology of IBS is unknown. The hall-mark symptoms are a) lower abdominal pain/discomfort b) altered bowel function, and c) bloating. These symptoms are found in variable combinations in different patients [16]. But, without pain, a diagnosis of IBS is never made. The symptoms of abdominal pain, diarrhea or constipation or

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both, mucus discharge in stool and changes in the form/appearance of stools may be precipitated by a bout of gastroenteritis. The abdominal pain is often relieved by defecation. Non GI symptoms common in IBS are lethargy, poor sleep, fibromyalgia, backache, frequent urination and dyspareunia.

It is usually a chronic recurrent, often life-long disease, common in women (M: F = 2: 1) and no diagnostic test is available for a definitive diagnosis. Similarly, physical examination is normal except for mild abdominal or rectal tenderness. Hence, we should try to take a thorough history to identify the criteria that define IBS first, and then try and establish the stool pattern - diarrhea is predominant (IBS-D) or constipation (IBS-C), or both (IBS-A) [3]. This is done by asking the patient about stool consistency. This is important for treatment purpose. Large volume stools, bloody stools, greasy stools and nocturnal diarrhea do not occur in IBS. But mucus may be present in 50% cases. Recently, reports have indicated overlapping of other FGID like gastro esophageal reflux disease (GERD) and epigastric pain syndrome (functional dyspepsia) with IBS [16]. A diagnosis of IBS is done in general practice observing the patient over time in most cases. Dietary and drug history, family history, social history should be taken.

After this we must look out for the ALARM SYMPTOMS: Weight loss, Rectal bleed, Anemia, Family history of colorectal malignancy/ Inflammatory bowel disease, Fever, Nocturnal symptoms, Persistent diarrhea, Severe constipation, High ESR/CRP and Age > 40 years. These symptoms hold true for all FGID so that simple initial evaluations of all cases are done to detect serious diseases. Colonoscopy should be done in all cases who are >50 years of age, persistent diarrhea or severe constipation that do not respond to treatment. Stool routine examination and occult blood, blood sugar, complete blood count (CBC), C-reactive protein (CRP) and thyroid profile should be done in all cases.

Depending upon the predominant symptom, the differential diagnosis include Malabsorption (post gastrectomy, celiac sprue, pancreatic insufficiency), Lactose intolerance, Bacterial overgrowth, Alcoholism, IBD, HIV, Endometriosis, Psychiatric disorders (panic states/depression) and rarely GI endocrine tumors.

Because of the complex nature of IBS, treatment is never successful with any single modality and includes a combination of diet/ lifestyle modifications, pharmacological, psychosocial and complementary medicine strategies. Patient education and reassurance is important. It must be stressed that survival in IBS is not less compared to normal people.

In patients of suspected IBS who do not respond, it is difficult to recommend how far one has to proceed with further investigations [17]. This constitutes the smallest number of IBS cases (~5%). Patience is required from both the sufferer and the healer and a realistic goal should be established after spending time discussing with each other. Often, a trial-and-error method of treatment is required. Intensity of symptoms and other co-morbid conditions should be taken into account and treatment or further investigation is individualized accordingly. However, a study has shown that approximately <10% of previously diagnosed IBS patients developed an organic gastro-intestinal disease. Similarly, in another study celiac disease was diagnosed in 4% of cases who fulfilled the criteria for IBS previously but did not respond to treatment [18]. Therefore, in a minority of patients, in spite of a multidisciplinary treatment approach if there is no response after 6 weeks,

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and if any alarm symptoms appear or the IBS symptoms progress, or are atypical with a short history, and age >45 years, then further evaluation may be ordered depending upon the predominant symptom [19]. These include: a) IBS-C: Colonic transit study, Anorectal motility/ sensory/ balloon expulsion test, Defecography, Pelvic MRI. b) IBS-D: Lactose/ bacterial overgrowth tests, Stool for giardia/ fat/ osmolality, Celiac antibodies (tTG IgA), Small bowel/ large bowel biopsy. c) PP abdomen, small bowel follows through studies, CT/MR.

IBS is a benign disease but the prognosis depends upon length of history and ongoing life stress (both indicating a lesser chance of improvement). At 7 years of follow up 55% will still have symptoms, 21% will improve and only 13% will improve completely [17].

Functional Constipation

Functional Constipation diagnosed by at least 2 of the following [20].

a) Straining during 25% or more of defecations.
b) Lumpy/ hard stools during 25% or more of defecations.
c) Sense of incomplete evacuation or anorectal obstruction during 25% or more of defecations.
d) Manual evacuation of 25% or more of evacuations.
e) Less than 3 bowel movements per week. Loose stools rarely occur in them without laxative use.

It is always necessary to exclude IBS as well as other causes like colonic or rectal malignancies/ inflammatory conditions, neurological diseases (parkinsonism, spinal injuries, multiple sclerosis, scleroderma), metabolic and endocrinal diseases (hypokalemia, hypercalcemia, hypocalcemia, uremia, hypothyroidism, diabetes mellitus), medications (opiods, calcium channel blockers, antacids, anti-cholinergics, Iron, anticonvulsants, antidepressants, diuretics or antispasmodics) and physical or mental retardation. Rarer causes to exclude are anorexia nervosa, anorectal disorders and small gut pseudo-obstruction. A digital rectal examination should be always performed. Alarm symptoms are: Bloody stools, Weight loss, Evidence of Systemic illness and Risk factors for Colo-rectal carcinomas. Chronic constipation as a whole is a very common condition with approximately 27% prevalence. However, only half of them will meet the ROME III criteria.

Functional diarrhea (FD)

Functional diarrhea (FD) is also called non-specific chronic diarrhea (NSCD) and is diagnosed by a daily passage of painless, recurrent passage of 3 or more, large, unformed stools during a period of at least 4 weeks. It is more common in young children and toddlers (6 – 36 months of age) but interestingly the children thrive well and this is the strongest pointer to the diagnosis [14]. There is no dehydration. FD is also seen in adults especially after a bout of acute gastro-enteritis. In many adults, FD may occur due to small intestinal bacterial over-growth. Alarm signs are failure to thrive (in spite of adequate caloric intake), abdominal pain, blood in stool and emesis. Exact cause is unknown but sorbitol, starch or fructose malabsorption may play a part by altering gut motility. It is usually self limiting and does not require treatment except for reassurance, but the above mentioned food items may be avoided. However, celiac disease, infection and other inflammatory conditions need to be ruled out. Giardiasis can mimic FD but causes pain abdomen, not present in FD. In any case, infectious diarrhea is to be ruled out.

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Functional Bloating

Functional Bloating is the persistent feeling of abdominal fullness with discomfort and is quite common especially in elderly females. [15] Treatable conditions that need to be excluded are Lactose intolerance, carbonated drinks (fructose intolerance), bulking agents, bacterial overgrowth and constipation. In functional bloating there is no altered bowel or stool formation. Obstructive causes need to be ruled out by history and physical examination. Rarely imaging studies are needed.

Apart from these FBD there are several conditions which do not or partially fulfill the criteria laid down by ROME III meet, and they are yet to be specified properly [9]. As mentioned earlier, FGID may overlap in the same patient. Treatment of these disorders is dependent upon the presenting/predominant symptoms and is highly individualized.

Conclusion

In conclusion, FGID and especially FBD like IBS are very common. The etiology is unknown. The incidence is high in general practice. They cause significant distress to the patients and lead to poor quality of life in the majority. It is recommended that well-set criteria are followed while diagnosing these conditions. This procedure, along with awareness of alarm symptom/signs will guide the physicians toward an optimal and cost-effective management of these patients which at present is not very satisfactory. Multiple therapeutic strategies including lifestyle changes and psychiatric help is often needed to manage these patients. Better ways to identify which patients will respond to specific treatments are required to be investigated in future.

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Table – 1: Classification of Functional Bowel Diseases.

FUNCTIONAL GASTROINTESTINAL DISORDERS	
A.	**Functional Esophageal Disorders**
A1	Functional heartburn
A2	Functional chest pain of presumed esophageal origin
A3	Functional dysphagia
A4	Globus
B.	**Functional Gastro-duodenal disorders**
B1	Functional dyspepsia
	B1a Postprandial distress syndrome(PDS)
	B1b Epigastric pain syndrome (EPS)
B2	Belching disorders
	B2a Aerophagia
	B2b Unspecified excessive belching
B3	Nausea and vomiting disorders
	B3a Chronic idiopathic nausea (CIN)
	B3b Functional vomiting
	B3c Cyclic vomiting syndrome (CVS)
B4	Rumination syndrome in adults
C.	**Functional Bowel Disorders**
C1	Irritable bowel syndrome
C2	Functional bloating
C3	Functional constipation
C4	Functional diarrhea
C5	Unspecified functional bowel disorders
D.	**Functional Abdominal Pain Syndrome**
E.	**Functional Gallbladder and Sphincter of Oddi Dysfunction**
E1	Functional gallbladder disorder
E2	Functional biliary SO disorder
E3	Functional pancreatic SO disorder
F.	**Functional Anorectal Disorders**
F1	Functional fecal incompetence
F2	Functional anorectal pain F2a : Chronic proctalgia F2a1 : levator ani syndrome F2a2 : Unspecified functional anorectal pain F2b : Proctalgia fugax
F3	Functional defecation disorders F3a: Dyssenergic defecation F3b: Inadequate defecatory propulsion
G.	**Functional Disorders : Infants and Toddlers**
G1	Infant regurgitation

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G2	Infant rumination syndrome
G3	Cyclic vomiting syndrome
G4	Infant colic
G5	Functional diarrhea
G6	Infant dyschezia
G7	Functional constipation
H. Functional Disorders : Children and Adolescents	
H1	Vomiting and aerophagia
	H1a : Adolescent rumination syndrome
	H1b : Cyclic vomiting syndrome
	H1c : Aerophagia
H2 Abdominal pain related FGID	
	H2a: Functional dyspepsia
	H2b: Irritable Bowel Syndrome H2c: Abdominal migraine
	H2d : Childhood functional abdominal pain
	H2d1: Childhood functional abdominal pain syndrome
H3 Constipation and incontinence	
	H3a: Functional constipation
	H3b: Non-retentive fecal incontinence